Diagnostic and Interventional Radiology in Liver & Kidney Transplantation

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BAŞKENT UNIVERSITY
1993

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ISBN 978-605-06251-0-3

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Telephone: +90 (312) 212 73 93 Fax: +90 (312) 215 08 35

Printed by Elma Teknik Basım Matbacılık Tic. Ltd. Şti.
İvedik OSB Matbaacılar Sitesi 1516 / 1 Sokak No: 35
Yenimahalle 06378, Ankara-Türkiye (+90.312) 229 92 65

Their pain is our pain,
Their lives are our lives,
Their future is our future,
Those who has passed away and
Those who carry on with us

TO ALL CHRONIC ORGAN FAILURE PATIENTS...

Preface

Since the mid-19th century, organ transplantation has been accepted as a valid and advanced treatment method applied in many chronic organ diseases. Organ transplantation achieved a significant breakthrough in medicine, and thus made the impossible possible.

Transplant medicine remains one of the most challenging and complex areas of modern medicine. Although important medical breakthroughs such as immunosuppressive drugs have allowed for more organ transplants and a longer survival rate, transplant professionals still face serious problems, especially with regard to achieving correct diagnosis and treating postoperative complications.

Advances in imaging techniques, including in computed tomography, magnetic resonance imaging, and ultrasonography, and the use of interventional radiology have allowed transplant professionals to provide more accurate results both for diagnosis and for treatment of complications that occur after liver and kidney transplant. Moreover, with the use of interventional radiology, transplant professionals can now reach deep structures of the body, enabling correct diagnoses and treatment without performing surgery.

With this book, we aim to provide guidance to our colleagues regarding the importance of diagnostic and interventional radiology in order to be able to save more patient lives.

Finally, we would like to thank to our colleagues who have contributed to this work, our English editor Rasa Hamilton, our assistants Ayşegül Gürman and Didem Heperler and our graphic designer Ayşegül Ustaoğlu.

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Foreword

On behalf of Başkent University, I would like to express my gratitude and appreciation to our colleagues for introducing such a significant and valuable work to the medical community. This book is the result of hard work and dedication by our colleagues and, at the same time, forms the basis of the success of Başkent University for the last 26 years.

Our founder, Professor Mehmet Haberal, has been heralded as a pioneer in the fields of general surgery, transplantation, and burn treatment in Turkey and the world since 1975 and is renowned internationally in the medical community. His efforts to enact the law on organ transplantation resulted in a true milestone in the development of organ transplantation in Turkey.

His team performed the first successful living-related kidney transplant in Turkey on November 3, 1975, the first deceased-donor kidney transplant in Turkey on October 10, 1978, and the first successful local deceased-donor kidney transplant in Turkey on July 27, 1979, right after the Law No. 2238 on harvesting, storage, grafting, and transplant of organs and tissues was passed in the Parliament on June 3, 1979. His team performed the first successful deceased-donor liver transplant in Turkey, in the Middle East and in Northern Africa on December 8, 1988. This was followed on March 15, 1990 with the first pediatric segmental living-related liver transplant in Turkey, the region, and in Europe and immediately succeeded by the first adult segmental living-related liver transplant (left lobe) in the world on April 24, 1990. On May 16, 1992, Prof. Haberal and his team performed a combined liver-kidney transplant from a living-related donor, which was the first operation of its kind anywhere in the world.

On a final note, I truly believe that this book will provide an insight to our colleagues in the field of transplantation and radiology on the importance of diagnostic and interventional radiology and will save the lives of many patients around the world with chronic liver and kidney diseases.

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Contents

PART I

1 COVID-19 SUMMARY
MEHMET HABERAL

3 HISTORICAL SUMMARY OF LIVER AND KIDNEY TRANSPLANTATION IN TURKEY AND IN THE WORLD
MEHMET HABERAL

25 DIAGNOSIS OF BRAIN DEATH AND CENTRAL NERVOUS SYSTEM COMPLICATIONS AFTER LIVER AND RENAL TRANSPLANT
A. MUHTEŞEM AĞILDERE

PART II

42 COMPUTED TOMOGRAPHY AND MAGNETIC RESONANCE IMAGING OF LIVER TRANSPLANT COMPLICATIONS
MEHMET COŞKUN

60 DOPPLER ULTRASONOGRAPHIC FINDINGS OF VASCULAR COMPLICATIONS AFTER LIVER TRANSPLANTATION
NİHAL USLU

68 COMPLICATIONS OF LIVER TRANSPLANT: VASCULAR COMPLICATIONS
GÖKHAN MORAY

84 ROLE OF INTERVENTIONAL RADIOLOGY IN HEPATIC ARTERY COMPLICATIONS ASSOCIATED WITH LIVER TRANSPLANT
FATİH BOYVAT

99 PORTAL VEIN INTERVENTIONS IN LIVER TRANSPLANTATION
ALİ HARMAN

116 HEPATIC VEIN AND INFERIOR VENA CAVA INTERVENTIONS OF LIVER TRANSPLANT
ALİ FIRAT

Contents

129 BILIARY COMPLICATIONS FOLLOWING LIVER TRANSPLANTATION
EBRU H. AYVAZOĞLU SOY, A. SERDAR KARACA, FEZA YARBUĞ KARAKAYALI

133 INTERVENTIONAL RADIOLOGY IN THE MANAGEMENT OF BILIARY COMPLICATIONS AFTER LIVER TRANSPLANT
ÖZGÜR ÖZEN

151 OTHER COMPLICATIONS AFTER LIVER TRANSPLANT
EBRU H. AYVAZOĞLU SOY, MAHİR KIRNAP

159 LIVER BIOPSY IN LIVER TRANSPLANT RECIPIENTS
BEHLÜL İGÜS

166 FLUID COLLECTIONS, HEMATOMA, AND ABSCESS INTERVENTIONS AFTER LIVER TRANSPLANT
BEHLÜL İGÜS

175 COMPLICATIONS OF LIVING-DONOR HEPATECTOMY
SEDAT YILDIRIM

PART III

191 ULTRASOUND IMAGING OF RENAL TRANSPLANT COMPLICATIONS
FERİDE KURAL RAHATLI

203 COMPUTED TOMOGRAPHY IMAGING: COMPLICATIONS OF RENAL TRANSPLANTATION
KEMAL MURAT HABERAL

211 VASCULAR COMPLICATIONS AFTER KIDNEY TRANSPLANTATION
AYDINCAN AKDUR, EMRE KARAKAYA

222 ENDOVASCULAR TREATMENT OF VASCULAR COMPLICATIONS OF RENAL TRANSPLANTATION
ERKAN YILDIRIM

Contents

235 **POSTTRANSPLANT UROLOGIC COMPLICATIONS**
AYDINCAN AKDUR, EMRE KARAKAYA

242 **INTERVENTIONAL RADIOLOGY IN THE MANAGEMENT OF UROLOGIC COMPLICATIONS AFTER RENAL TRANSPLANT**
E. UMUT ÖZYER

255 **RENAL BIOPSY**
ÇAĞRI KESİM, ÇAĞATAY ANDİÇ

264 **PERIGRAFT FLUID COLLECTIONS, ABSCESS, HEMATOMA MANAGEMENT**
ÇAĞRI KESİM

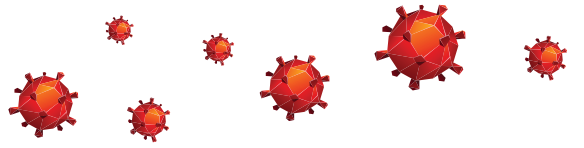
274 **OTHER COMPLICATIONS AFTER KIDNEY TRANSPLANT**
MURAT KUŞ, KENAN ÇALIŞKAN

281 **LIVING KIDNEY DONOR COMPLICATIONS**
ERDAL KARAGÜLLE, EMİN TÜRK, ERKAN YILDIRIM

Diagnostic and Interventional Radiology in Liver & Kidney Transplantation

PART I

COVID-19 SUMMARY



Dear Colleagues,

The outbreak of the coronavirus disease (COVID-19) continues to be the focus for all of us in the medical community worldwide. COVID-19 is an infectious disease caused by a newly discovered coronavirus. Most people infected with COVID-19 will experience mild to moderate respiratory illness and will recover without requiring special treatment. However, older people and those with underlying medical problems, like cardiovascular disease, diabetes, chronic respiratory disease, and cancer, are more likely to develop serious illness.

More importantly, the coronavirus pandemic may present a significant threat for transplant patients, donors, and transplant programs around the world.

Unfortunately, as of 04.05.2020, the number of confirmed cases is 126045 with 3397 deaths and 63151 recoveries. **Out of 558 kidney and liver transplant patients (461 kidney and 52 liver recipients), 1 kidney transplant patient is diagnosed with COVID-19 so far. The patient has been treated without any severe complications and is fully recovered.**

During these difficult times, valuable up-to-date information is needed on prevention and treatment methods, strategies, and available resources, as well as different protocols applied by different countries. Although there are no specific vaccines or treatments yet available for COVID-19, many ongoing clinical trials are presently evaluating potential treatments.

Interestingly, the rate of COVID-19 has been really low among our dialysis patients. We have 21 dialysis centers all over the country, with 2420 hemodialysis patients. Only 8 patients have been diagnosed with COVID-19, who have been fully recovered and discharged.

In a randomized study of 602 of the 2420 dialysis patients at Başkent University who were analyzed hepatitis A antibody with the ELISA Architect Plus i 1000SR, 584 patients (97%) were shown to be positive and 65% had Bacillus Calmette-Guérin (BCG) vaccine scar. At Başkent University Health Centers, we will continue to carry out this study as it reveals very important findings.

Among our transplant community, societies like TTS (The Transplantation Society), MESOT (Middle East Society for Organ Transplantation), TOND (The Turkish Transplantation Society), and TDTD (Turkic World Transplantation Society) have already formed COVID-19 committees and prepared guidelines to provide their members with the most accurate data. These guidelines also include information on how to manage and handle the anticipated onslaught of coronavirus cases together with care of other patients with chronic diseases and with the usual surgical activities in their hospitals and countries. It is of utmost importance for our members to contact these committees through the headquarter offices of the above-mentioned societies to reach updated information and to direct queries if need be.

We are all navigating through uncertainty and I hope that we will soon leave behind these challenging times.

Mehmet Haberal, MD, FACS (Hon), FICS (Hon), FASA (Hon), FIMSA (Hon), Hon FRCS (Glasg)

President, The Transplantation Society

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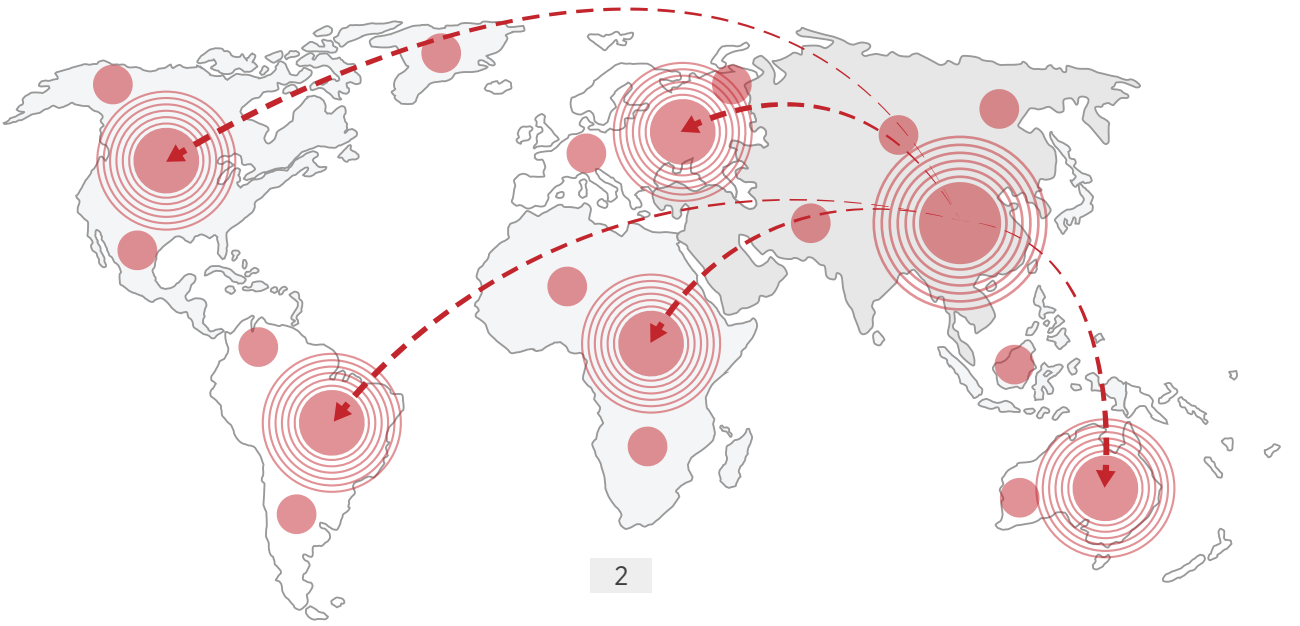


Historical Summary of Liver and Kidney Transplantation in Turkey and in the World

Mehmet Haberal

It is impossible to examine the development of transplant methods completely in a single article. However, I think it will be useful to review the history of organ transplantation, which is defined as an important development of medicine in the 21st century. The first chapter of such a study approaches the method of transplantation from different aspects in the world and Turkey.

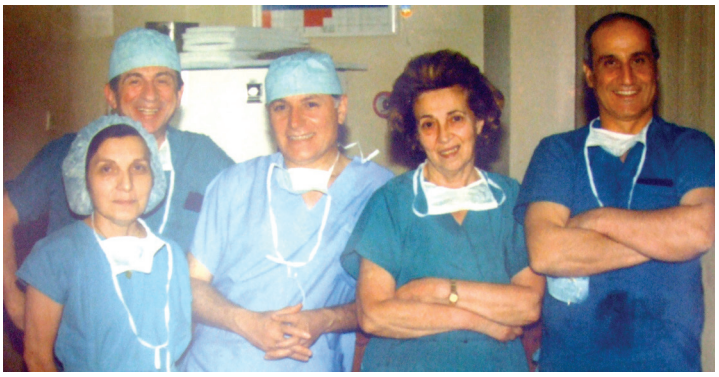
The organ transplant method, which is one of the most complicated and problematic fields of modern surgery, has maintained its actuality since the prehistoric ages and has become one of the focal points of scientists. Within the literature of modern medicine, it is noted that the first kidney transplant operation was performed by the Hungarian surgeon Dr. Ullman in Wien in 1902 on animals.[1] In the same year, the young French surgeon Alexis Carrell published an article with the title "Suture of Blood Vessels and Transplantation of Organs" in Lyon, and he was entitled to receive a Nobel Prize in 1912 with this article.[2]

At the beginning of this century, studies were conducted on the immunological nature of tissues and organ transplant. Sir Peter Medawar contributed to create a suitable ground for transplantation with his skin graft study he conducted in 1943 and then with his study he conducted in 1953 related to the immunological tolerance gain.[3]

The modern era for kidney transplant on humans started with the kidney transplant from a deceased donor conducted in 1933 in Russia by Voronoy[4] whose results were published in a not well-known journal in 1936. A series of kidney transplant operations was conducted by Hume, Merrill, Miller and Thorn[5] in Boston in 1950, 1953, and 1955. Thus, a new process was initiated for clinical research in this field. With those studies, basic immunologic comprehension was started to be considered together with the clinical productivity of the organ transplant method, and then the first successful kidney transplant operation was conducted through relatives (maternal twins) by Murray and associates in Boston and by Hamburger and associates in Paris in 1954 for the first time.[6,7] In 1958 and 1959, another kidney transplant operation was conducted again in Boston and Paris through relatives (but not maternal twins) by not using the whole body irradiation as immunosuppressant.[7,8] The longest living patient after this operation was reported as 22 months by Dr. Hamburger and associates.[9]

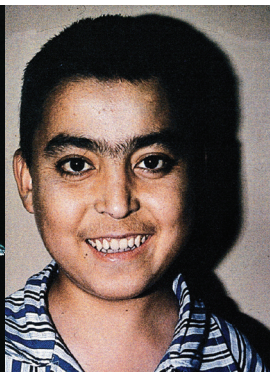
The difficulties compared with whole-body irradiation as an immunosuppressive modality were extremely great. This issue required more practical immunosuppressive methods. In 1958 and 1959, Schwartz and Damshek published their study indicating immunological tolerance inhibition with drug-induced through "antimetabolite 6-mercaptopurine" and antibody production.[10] The possibility to direct the immune response through drugs for kidney transplantation was identified by 2 independent surgical teams. In 1960, Professor Roy Calne[11] who was working in London and Boston and Dr. Zukowski[12] from Richmond reported extended survival as a result of a kidney transplant operation conducted on a

Figure 1. The First Successful Living Related Kidney Transplantation, Hacettepe University Hospitals, Ankara, Turkey, November 3, 1975



Surgical Team
Left to Right: Prof. Gülnaz Arslan, Prof. Nevzat Bilgin, Prof. Mehmet Haberal, Prof. Mualla Karamehmetoğlu, Prof. Nebil Büyükpamukçu

Mürvet Çalışkan (Mother)



Bahtiyar Çalışkan (Son)
12 years old

dog through 6-mercaptopurine. Dr. Hitching from Burroughs Welcome developed a derivative for 6-mercaptopurine that was less toxic and would be later called azathioprine (Imuran). Dr. Hitching and Dr. Elion were awarded with a Nobel Prize thanks to their contributions including changing this drug.[13]

Thanks to this immunosuppressive method, a new era began for organ transplant and Hume reported the results of 31 non-twin human renal homotransplants in 1964.[14]

In 1965, Starzl published[15] his experiences on kidney transplantation, including leukocyte antigen adaptation; in the same year, Reemtsma reported the long life of a patient after xenograft (chimpanzee kidney) to a human recipient.[16] The collaboration developed through a basic laboratory research, and clinical surgery made way for new clinical fields called "surgical biology" or "immunologist surgery".[17] In 1967, while Starzl reported the results of the successful liver transplantation on children,[18] Christian Bernard performed the first cardiac transplantation on humans.[19]

With these surgical developments, immune-biological studies became more urgent, and the concept of "brain death" was started to be discussed with the issue of organ donation.[20,21] The study of Belzer on "continuous pulsatile perfusion machine" accelerated organ preservation in 1972.[22,23] Following those studies, there were successive kidney transplant operations from several countries.[8,24]

Twenty-one years after the first successful living related kidney transplant in the world, **the first kidney transplant through relatives was conducted on November 3, 1975 for a 12-year-old male patient from his mother in Turkey by our team** (Figure 1).[25] **At that time, no legislation was in existence regarding transplantation;** therefore, any transplantation that was performed was simply conducted with the written consent of the donor and the recipient. Also, the only option for transplant candidates on waiting lists in Turkey was to receive a graft from a first-degree living-related donor. Again, there were plenty of patients but not enough organs.[26]

Our next goal was to perform deceased-donor kidney transplantation at our center and in Turkey. I realized that it was very important for us to show the public that kidneys from a deceased-donor would give patients with chronic kidney disease a new life. As there was no organ transplantation law in Turkey at the time, I had to apply to Eurotransplant International Foundation in Leiden, Netherlands. **Finally on October 10, 1978, we received an organ supplied by Eurotransplant International Foundation within a vacuumed**

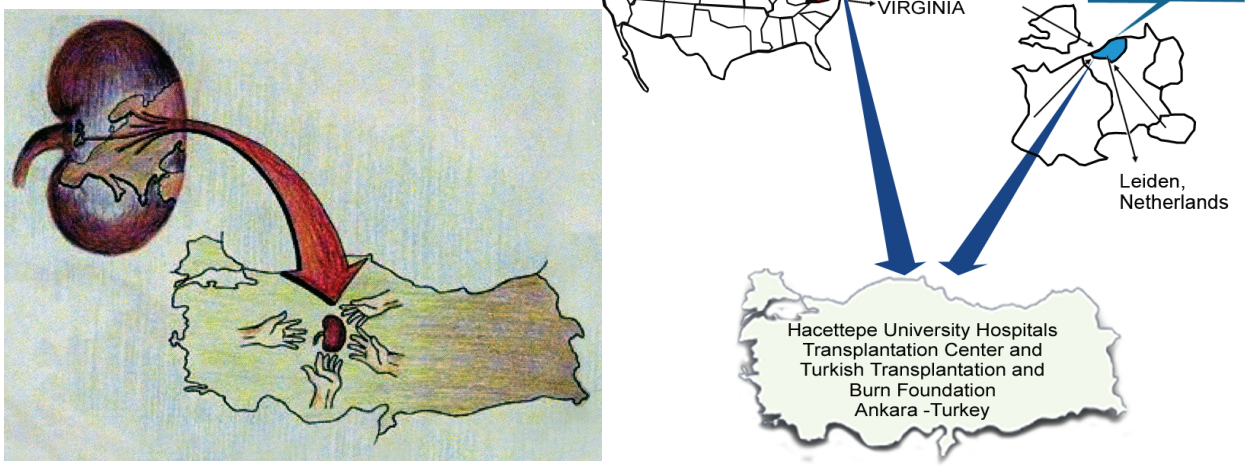
Figure 2A. The First Successful Deceased-Donor Kidney Transplantation, Hacettepe University Hospitals, Ankara, Turkey, October 10, 1978

Erol Emeksizoğlu (Recipient)
41 years old

Vacuum bottle

Container

Figure 2B. Donation by Eurotransplant International Foundation and SEOPF



bottle and container (Figure 2A). Back then, no one was using deceased kidneys older than 12 hours cold ischemic time. The ones we received had a cold ischemia time of over 24 hours. After making necessary tests, we found that it was a healthy kidney and the cross match was negative. We performed a successful operation, and the kidney transplant functioned very well. This was the first successful deceased-donor kidney transplant in Turkey.[27]

In fact, this was a major achievement; in addition to Eurotransplant Foundation, I contacted the Southern Eastern Organ Procurement Foundation (SEOPF) in the Unites States and started to receive kidneys from them also (Figure 2B).

Figure 2C. Some Examples of Deceased-Donor Kidney Transplantations with Prolonged Cold Ischemia Time

November 3-6, 1999

Left to Right:
Ayşe Tuncer (Patient)*
30 years old
Lived for 25 years after the transplantation
Prof. Mehmet Haberal
Prof. Thomas E. Starzl

We proved that kidneys could be transplanted successfully with an increased cold ischemia time of more than 100 hours (Figures 2C and D). At that time, I had presented a paper on this subject during the first ESOT Congress in Zurich, in 1983, which was followed by other internationally published articles.[28,29]

I started to work with the government authorities, with the Board of Religious Affairs, charity organizations, such as the Lions and Rotarians, and various groups in mass media trying to raise public awareness on deceased-donor transplantation and organ donation and the related challenges that face health professionals. I began to make guest appearances on television and radio programs together with my transplant patients. We tried to create public awareness on transplantation, organ donation, and its necessity. Meanwhile, I decided to establish the Turkish Dialysis and Transplantation Society with our colleagues. These efforts allowed people to understood that transplantation was a life-saving procedure and that transplant recipients were continuing their lives as healthy human beings. Through our use of the media, we were able to persuade our Parliament, officials at the Board of Religious Affairs, the Ministry of Health, and those in other governmental institutions; following our efforts, a statement was published by the Board of Religious Affairs emphasizing that **"Only the person to whom one donates one of his/her organs oneself is responsible for all his/her good and evil deeds"** (Figures 3A, 3B, 3C, 3D and Figures 4A, 4B, 4C, and 4D).

Figure 2D. The First ESOT Congress in Zurich, November 1983


T.ORGAN NAKLİ ve YANIK TEDAVİ V.KİTAPLIĞI GAZETENIN ADI Newsweek (Turkish Digest) 20. Ocak. 1984

Professor Mehmet Haberal, who discovered a way of preserving kidneys taken from the dead for a longer time reported his technique to the world during the first meeting of the European Transplantation Association which took place in Zurich between November 23 and 25, 1983.

A new technique of Prof. Haberal

A Turkish doctor has achieved "the impossible" in kidney transplantations. Now the whole world uses his technique which enables kidneys taken from the dead to be preserved for up to 95 hours.

Professor Mehmet Haberal proved that a donor's kidney which has been preserved for 48-95 hours under certain conditions functions well after transplantation. The 39-year-old doctor reported his technique to the World during the first meeting of the European Transplantation Association which took place in Zurich between November 23 and 25, 1983.

Prof. Haberal, who shared the Sedat Simavi Foundation 1983 Medical Sciences award, with Professor Özcan Kökmen, said that, kidneys taken from

Prof. Mehmet Haberal

Figure 3A. TV Programs Regarding Organ Donation

Prof. Dr. Mehmet Haberal with Prof. Dr. Ali Bardakoğlu, Chairman of the Board of Religious Affairs

Figure 3B. Statement of the Board of Religious Affairs

The Supreme Board of Religious Affairs stated in its Resolution dated March 6th, 1980/396, that organ transplantation is lawful. According to this resolution organ transplantation may only be performed under the following conditions:

1- Under necessity: that is, when a medical doctor, whose professional efficiency and integrity is respected, states that organ transplantation is the only way to save a patient's life or one of his vital organs.

2- When the medical doctor is of the prevailing opinion that organ transplantation is the only way to cure the disease.

3- When it is certain that the person whose organ or tissue to be removed is dead.

4- When the patient who will receive a transplanted organ gives this consent to the operation.

Only the person to whom one donates one of his/her organs oneself is responsible for all his/her good and evil deeds.

Figure 3C. Supporting Statement by the Chairman of the Board of Religious Affairs on Legislation Proposal

Appendix 1. English translation of the original document

T.C.
DİYANET İŞLERİ BAŞKANLIĞI
ANKARA

DİK.D/1-4/79

KONU : Organ nakli Hk. 171 25 Ocak/1979/197—

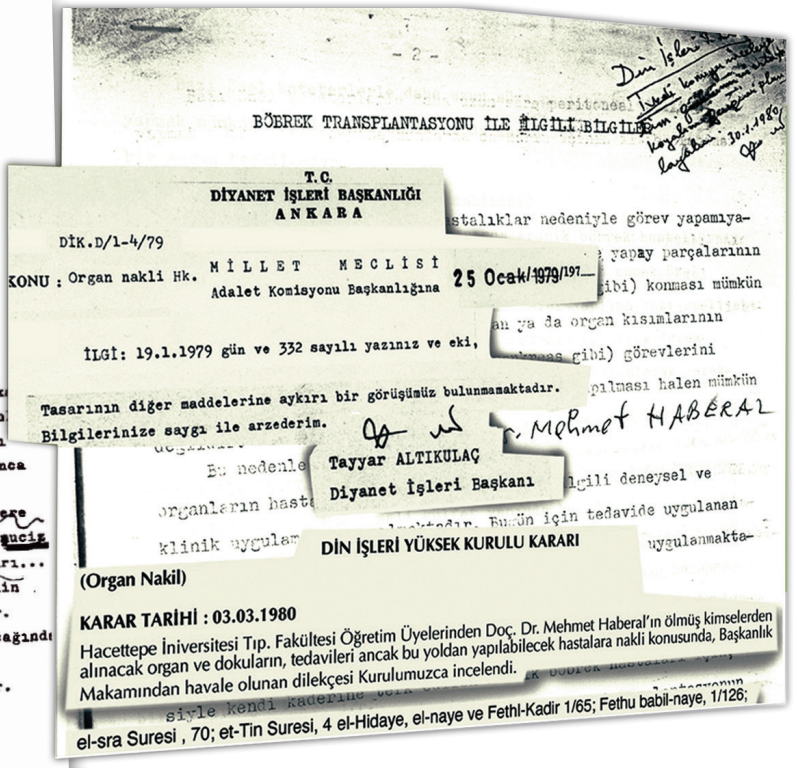
MİLLET MECLİSİ
Adalet Komisyonu Başkanlığına

İLGİ: 19.1.1979 gün ve 332 sayılı yazınız ve eki,

Organ nakli konusundaki ilgi yazı ve eki yasa teklifi incelendi:
Dini delillerin delâletlerinden de anlaşılacağı üzere, tedavi maksadıyle ve zarurete binaen diri veya ölmüş kimselerden, ya da diğer canlardan alınacak organların, muvafakat, vasiyet veya varislerin rızası sağlanmak suretiyle başka bir kimseye nakledilmesinde dinen bir sakınca bulunmadığı mütalaa olunmuştur.
Ancak, yasa teklifinin 3. Maddesinde geçen "yaşamı sona ermek üzere olan" ibaresinin metinden çıkarılması görüşüne varılmıştır. Tıbbın "şuuçiş dediği haller, olağan üstü irade sayesinde ölümden geri dönme olayları... gözönünde bulundurulduğu takdirde yaşamı sona ermek üzere olan kişinin herhangi bir organının alınmasındaki sakınca daha iyi anlaşılacaktır.
Burada bir anlamıyle ölüme sebebiyet gibi bir ihtimalin ortaya çıkacağında şüphe yoktur.
Tasarının diğer maddelerine aykırı bir görüşümüz bulunmamaktadır.
Bilgilerinize saygı ile arzederim.

Tayyar ALTIKULAÇ
Diyanet İşleri Başkanı

EK: 4 (Fotokopi)



- 2 -

BÖBREK TRANSPLANTASYONU İLE İLGİLİ BİLGİLER

T.C.
DİYANET İŞLERİ BAŞKANLIĞI
ANKARA

DİK.D/1-4/79

KONU : Organ nakli Hk. MİLLET MECLİSİ
Adalet Komisyonu Başkanlığına 25 Ocak/1979/197—

İLGİ: 19.1.1979 gün ve 332 sayılı yazınız ve eki,

Tasarının diğer maddelerine aykırı bir görüşümüz bulunmamaktadır.
Bilgilerinize saygı ile arzederim.

Tayyar ALTIKULAÇ
Diyanet İşleri Başkanı

DİN İŞLERİ YÜKSEK KURULU KARARI

(Organ Nakil)

KARAR TARİHİ : 03.03.1980

Hacettepe İniversitesi Tıp. Fakültesi Öğretim Üyelerinden Doç. Dr. Mehmet Haberal'ın ölmüş kimselerden alınacak organ ve dokuların, tedavileri ancak bu yoldan yapılabilecek hastalara nakli konusunda, Başkanlık Makamından havale olunan dilekçesi Kurulumuzca incelendi.

el-sra Suresi , 70; et-Tin Suresi, 4 el-Hidaye, el-naye ve Fethl-Kadir 1/65; Fethu babil-naye, 1/126;

Figure 3D. Application to the Board of Religious Affairsby Prof. Haberal regarding Harvesting, Storage, Grafting, and Transplantation of Organs and Tissues

Figure 4A. Legislative Proposal to the Presidency of Republican Senate and General Assembly on Harvesting, Storage, Grafting, and Transplantation of Organs and Tissues

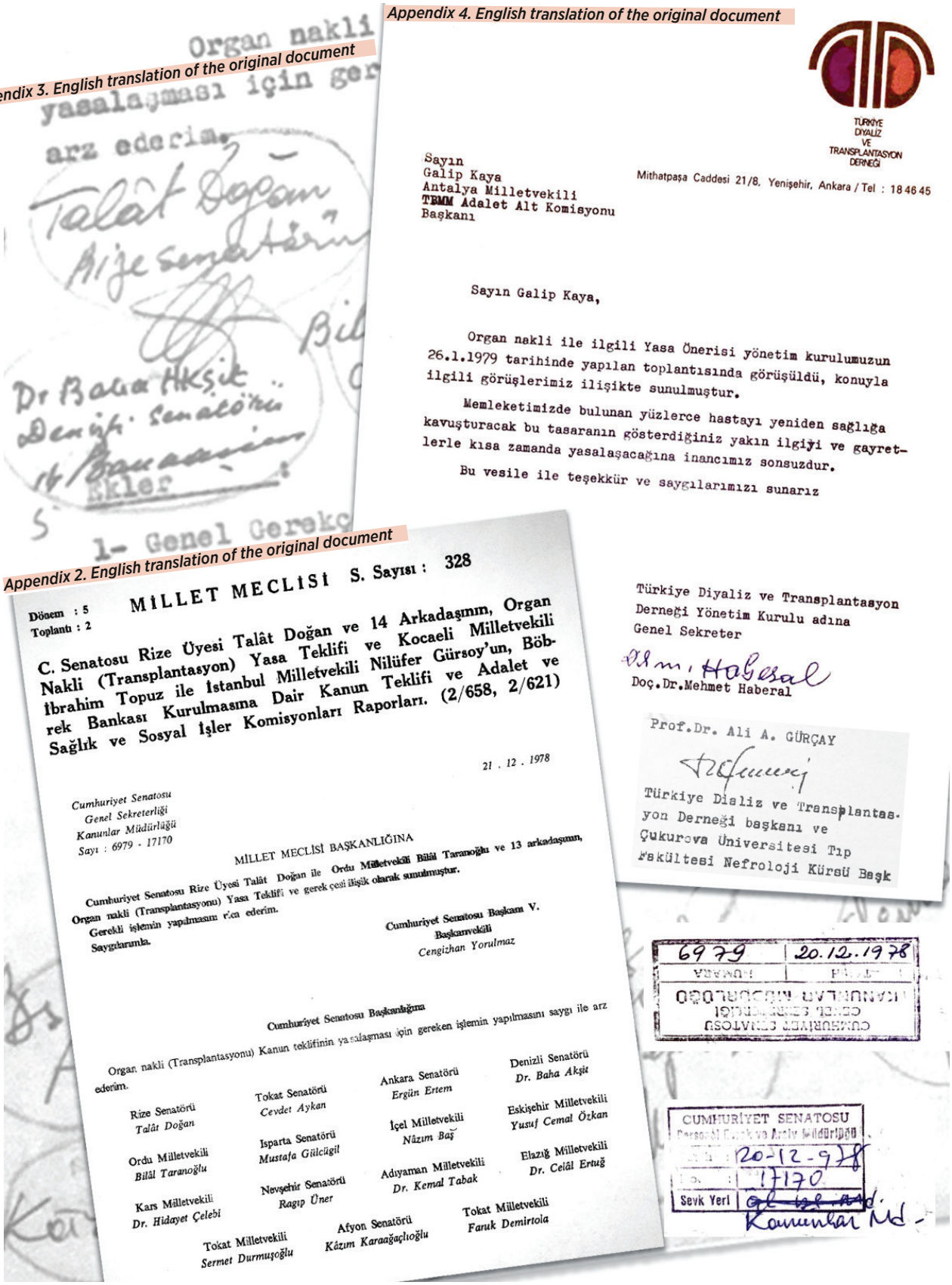
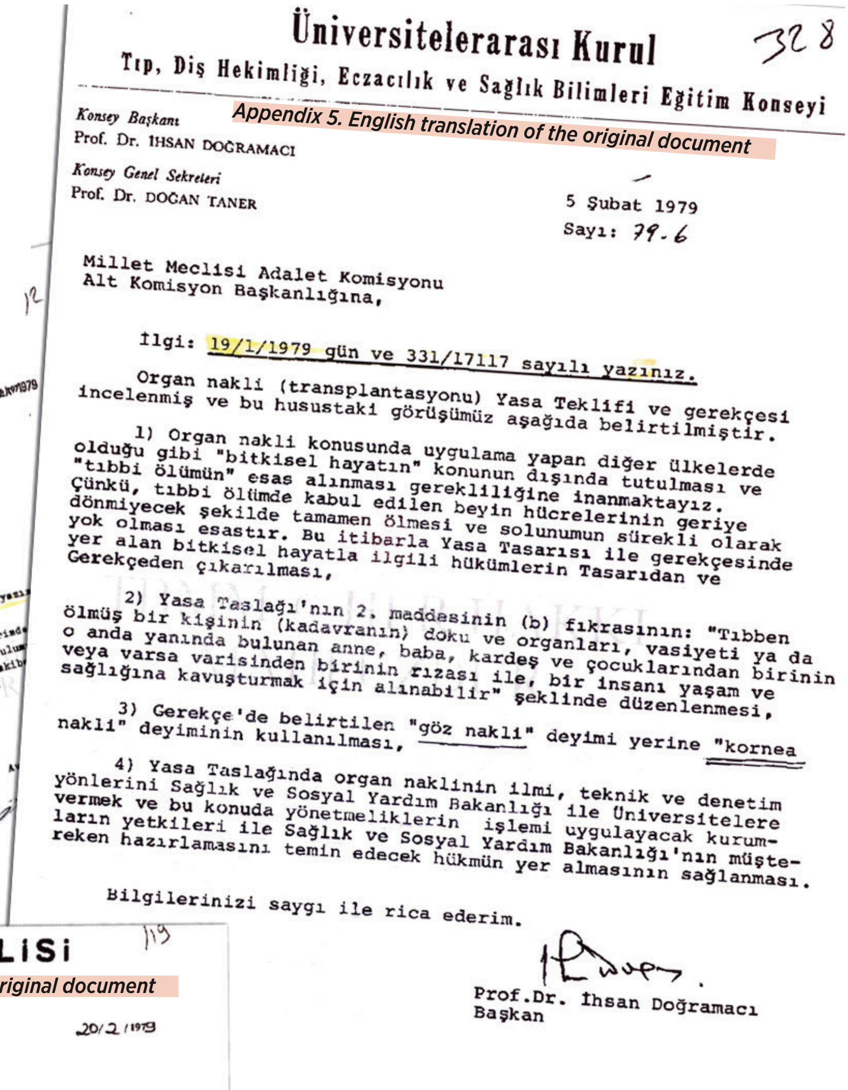


Figure 4B. Supporting Statement of the Interuniversity Board (Faculty of Medicine, Dentistry, Pharmacology and Health Sciences Eduction Council)



Üniversitelerarası Kurul 328

Tıp, Diş Hekimliği, Eczacılık ve Sağlık Bilimleri Eğitim Konseyi

Konsey Başkanı
Prof. Dr. İHSAN DOĞRAMACI

Appendix 5. English translation of the original document

Konsey Genel Sekreteri
Prof. Dr. DOĞAN TANER

5 Şubat 1979
Sayı: 79-6

Millet Meclisi Adalet Komisyonu
Alt Komisyon Başkanlığına,

İlgi: 19/1/1979 gün ve 331/17117 sayılı yazınız.

Organ nakli (transplantasyonu) Yasa Teklifi ve gerekçesi incelenmiş ve bu husustaki görüşümüz aşağıda belirtilmiştir.

1) Organ nakli konusunda uygulama yapan diğer ülkelerde olduğu gibi "bitkisel hayatın" konunun dışında tutulması ve "tıbbi ölümün" esas alınması gerekliliğine inanmaktayız. Çünkü, tıbbi ölümde kabul edilen beyin hücrelerinin geriye dönmiyecek şekilde tamamen ölmesi ve solunumun sürekli olarak yok olması esastır. Bu itibarla Yasa Tasarısı ile gerekçesinde yer alan bitkisel hayatla ilgili hükümlerin Tasarıdan ve Gerekçeden çıkarılması,

2) Yasa Taslağı'nın 2. maddesinin (b) fıkrasının: "Tıbben ölmüş bir kişinin (kadavranın) doku ve organları, vasiyeti ya da o anda yanında bulunan anne, baba, kardeş ve çocuklarından birinin veya varsa varisinden birinin rızası ile, bir insanı yaşam ve sağlığına kavuşturmak için alınabilir" şeklinde düzenlenmesi,

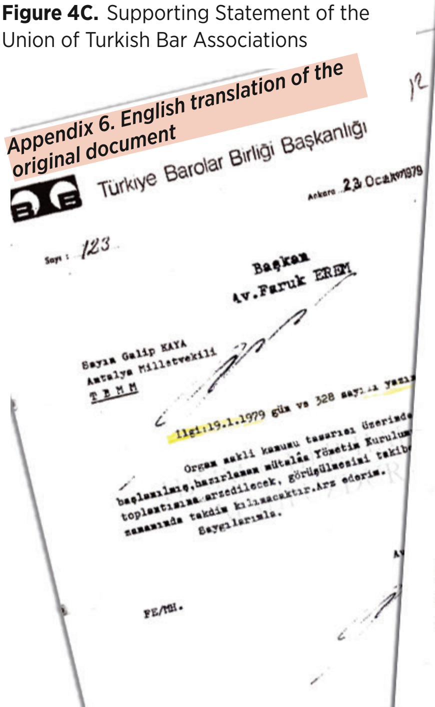
3) Gerekçe'de belirtilen "göz nakli" deyimi yerine "kornea nakli" deyiminin kullanılması,

4) Yasa Taslağında organ naklinin ilmi, teknik ve denetim yönlerini Sağlık ve Sosyal Yardım Bakanlığı ile Üniversitelere vermek ve bu konuda yönetmeliklerin işlemi uygulayacak kurumların yetkileri ile Sağlık ve Sosyal Yardım Bakanlığı'nın müştereken hazırlamasını temin edecek hükmün yer almasının sağlanması.

Bilgilerinizi saygı ile rica ederim.

Prof.Dr. İhsan Doğramacı
Başkan

Figure 4C. Supporting Statement of the Union of Turkish Bar Associations



Appendix 6. English translation of the original document

Türkiye Barolar Birliği Başkanlığı

Ankara 23 Ocak 1979

Sayı: 123

Başkan
Av.Faruk EREM

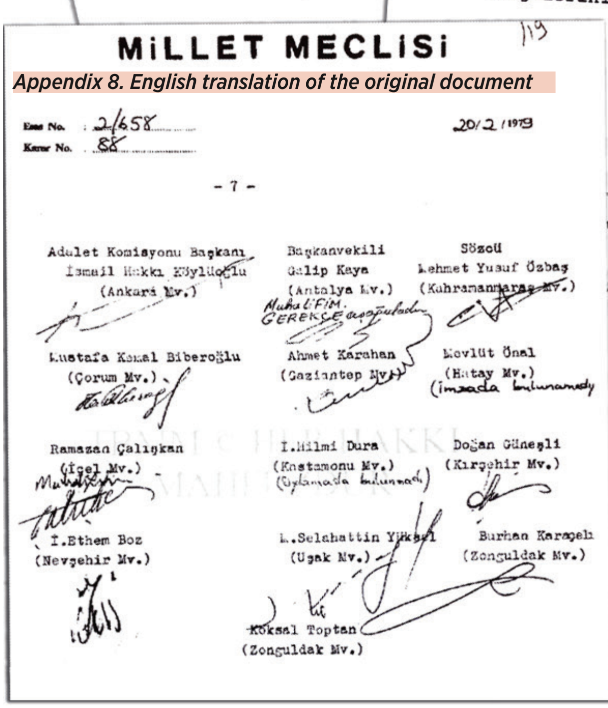
Sayın Galip KAYA
Antalya Milletvekili
T B M M

İlgi: 19.1.1979 gün ve 328 sayılı yazı

Organ nakli konusu tasarısı üzerinde başlanılmış, hazırlanan mütalâa Yönetim Kurulu toplantısına arzedilecek, görüşülmesini takiben sonucunda takdim kılınacaktır. Arz ederim.

Saygılarımla.

FE/TSI.



MİLLET MECLİSİ

Appendix 8. English translation of the original document

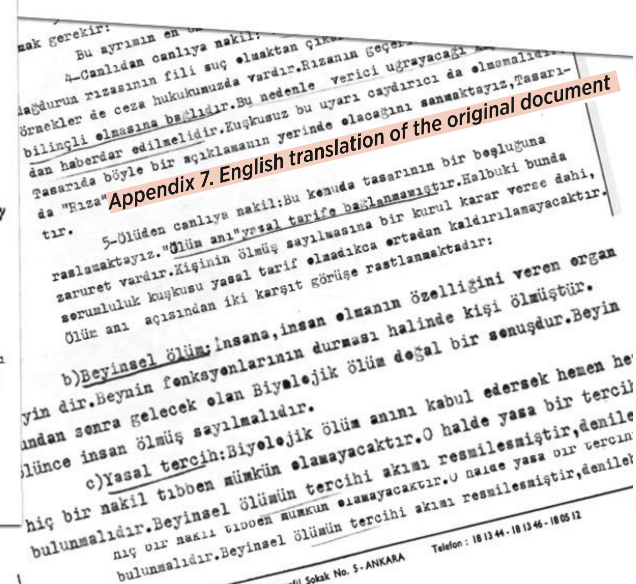
Esas No. 2/658
Karar No. 88

20/2/1979

- 7 -

Adalet Komisyonu Başkanı İsmail Hakkı Köylüoğlu (Ankara Mv.)	Başkanvekili Galip Kaya (Antalya Mv.)	Sözcü Mehmet Yusuf Özbaş (Kahramanmaraş Mv.)
Mustafa Kemal Biberoğlu (Çorum Mv.)	Ahmet Karahan (Gaziantep Mv.)	Mevlüt Önal (Hatay Mv.) (imzada bulunmadı)
Ramazan Çalışkan (İçel Mv.)	İ.Hilmi Dura (Kastamonu Mv.) (Oylamada bulunmadı)	Doğan Güneşli (Kırşehir Mv.)
İ.Ethem Boz (Nevşehir Mv.)	M.Selahattin Yüksel (Uşak Mv.)	Burhan Karagöl (Zonguldak Mv.)
	Köksal Toptan (Zonguldak Mv.)	

Figure 4D. Committee of the General Assembly for the Legislative Proposal on Harvesting, Storage, Grafting, and Transplantation of Organ and Tissues



Appendix 7. English translation of the original document

...mak gerekir. Bu ayrımın en ...
4-Canlıdan canlıya nakil: ... suç olmaktan çıkar ... Rızanın geçerli ...
...doğurun rızasının fili suç ... hukukumuzda vardır. Rızanın ... verici uğrayacağı ...
örnekler de ceza hukukumuzda ... Bu nedenle ... caydırıcı da olmamalı ... Tasarı-
bilinçli olmasına bağlıdır. Kuşkusuz bu uyarı caydırıcı olacağını sanmaktayız, Tasarı-
dan haberdar edilmelidir ... yerinde olacağını ...
Tasarıda böyle bir açıklamanın ... tasarının bir boşluğuna
da "Rıza" ... bağlanmamıştır. Halbuki bunda ...
tır. 5-Ölüden canlıya nakil: Bu konuda tasarının bir tarife bağlanmamıştır ... karar verse dahi,
raslamaktayız. "Ölüm anı" yasal tarife ... bir kurul ... kaldırılamayacaktır.
zaruret vardır. Kişinin ölmüş sayılmasına ... ortadan ...
sorumluluk kuşkusu yasal tarif olmadıkça ... rastlanmaktadır:
Ölüm anı açısından iki karşıt görüşe ...
b) Beyinsel ölüm; İnsana, insan olmanın özelliğini veren organ yin dir. Beynin fonksiyonlarının durması halinde kişi ölmüştür. Beyin...
...ndan sonra gelecek olan Biyolojik ölüm doğal bir sonuçdur.
...lünce insan ölmüş sayılmalıdır.
c) Yasal tercih: Biyolojik ölüm anını kabul edersek hemen hemen hiç bir nakil tıbben mümkün olamayacaktır. O halde yasa bir tercih bulunmalıdır. Beyinsel ölümün tercihi akımı resmileşmiştir, denile...

...Kızılay - Karanfil Sokak No. 5 - ANKARA
Telefon: 18 13 44 - 18 13 46 - 18 05 12

Finally, on June 3, 1979, the Law No. 2238 on harvesting, storage, grafting, and transplantation of organs and tissues was passed in the Parliament; this law was deemed progressive enough to be used as a model by many other countries. After the Law No. 2238 was passed, our team performed the first domestic deceased-donor kidney transplantation in the Transplantation Unit on July 27, 1979, through a kidney from a citizen who died in a motorcycle accident at Hacettepe University Hospitals (Figure 5A and 5B).[30,31]

Regardless of the fact that blood type ABO was a precondition for a successful kidney transplant for many years, recent studies have shown that kidney transplant operations through kidneys from donors with blood type A2 to patients with the blood type O produced positive results, and it is possible to conduct a kidney transplant operation for the cases where there is blood ABO incompatibility between the patients and donors through splenectomy and plasmapheresis application before the transplant operation.[34,35]

Seeking ABO blood compatibility before kidney transplant limits the organ sources for patients with kidney diseases.

It is not a rare case where the patient has a relative with ABO blood incompatibility despite the HLA compatibility. Therefore, we developed the "donor-specific skin graft" model for patients with ABO blood incompatibility.[36] With this model, which we apply as a preliminary examination for patients with ABO blood incompatibility, it is possible to conduct transplant operations for patients with several organ diseases.

Liver transplant methods have been developed through experimental operations conducted in dogs. The first article on liver transplant in dogs

Figure 5A and 5B. First Successful Local Deceased-Donor Kidney Transplantation at the Hacettepe University Hospitals, Ankara, Turkey Following the Transplantation Legislation Law No. 2238

A. Transplantation Legislation Law No. 2238[32,33]

On the Harvesting, Storage, Grafting and Transplantation of Organs and Tissues (June 3, 1979)

ARTICLE 3- The buying and selling of organs and tissues for a monetary sum or other gain is forbidden.

ARTICLE 4- Except for the distribution of information having scientific, statistical, and new characteristics, all advertisement in connection with the harvesting and donation of organs and tissues is forbidden.

ARTICLE 5- Harvesting organs and tissues from persons under the age of 18 or who are not of sound mind is forbidden.

ARTICLE 6- In order to be able to harvest organs and tissues from any person over the age of 18 who is of sound mind, a protocol, which beforehand the donor has approved of in writing and subscribed to verbally before at least two witnesses, should be approved by a physician.

ARTICLE 11- In connection with enforcement of this law, the case of medical death is established unanimously by a committee of 4 physicians consisting of 1 cardiologist, 1 neurologist, 1 neurosurgeon, and 1 anesthesiologist by applying the rules, methods and practices which the level of science has reached in the country.

ARTICLE 12- The physician who will perform the transplant surgery cannot be among the group which pronounced the donor as dead (Article 11).

ARTICLE 15- Those harvesting, storing, grafting and transplanting organs and tissues in a manner not conforming to this law, and those intermediating in such actions as the buying and selling of organs and tissues and those brokering same, in the case that it does not require any heavier punishment, shall be sentenced to punishment of two (2) to four (4) years, and of 50,000 to 100,000 Turkish Lira.

B. First Successful Local Deceased-Donor Kidney Transplantation, July 27, 1979


Türkiye'de ilk kez bir Türk'ten alınan sağlam böbrek, bir başka gencin hayatını kurtardı. Şimdiye kadar birkaç kez Almanya'dan böbrek getirilip, böbrek hastası Türkler'e takılmıştı. Yasa çıkıncaya kadar, ölüden canlıya organ nakli yasaktı.

Oğlunun böbreği ile bir gence hayat verdi

●Trafik kazasında ölen oğlunun böbreğinin hasta bir gence takılmasına izin veren baba mutlu

●Ölüden canlıya organ nakline izin veren yasa ilk defa uygulandı.

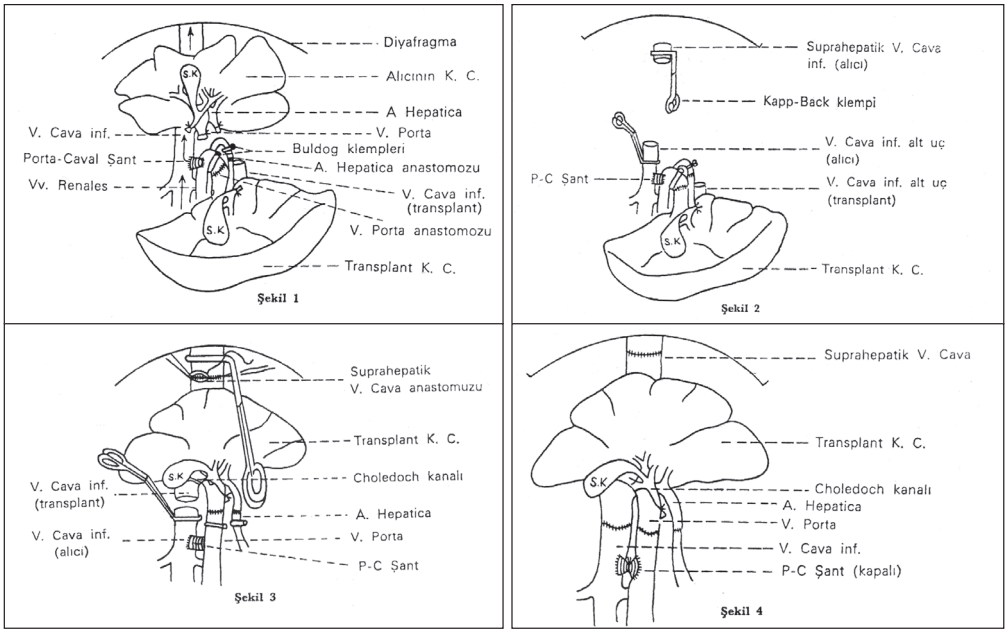
Musa Ambarcı
22 Years old

was published in 1955 by C. S. Welch.[37] The first liver transplant operation was conducted on a human in 1963 by Dr. Thomas E. Starzl; however, the patient died shortly after the operation.[38]The first successful liver transplant operation was conducted by Dr. Starzl in 1967, but the patient was kept in the center for treatment of liver failure.[39] According to Starzl, Dr. R. Calne (Cambridge) and Dr. Pichmayr (Hannover) conducted liver transplant operations in their countries.[40,41] Until the 1980s, approximately 200 liver transplant operations had occurred around the world as developments in immunosuppressive treatments and use of cyclosporine A had started; these were put into use in several centers in America, Europe, Australia, and South Africa.[42,43]

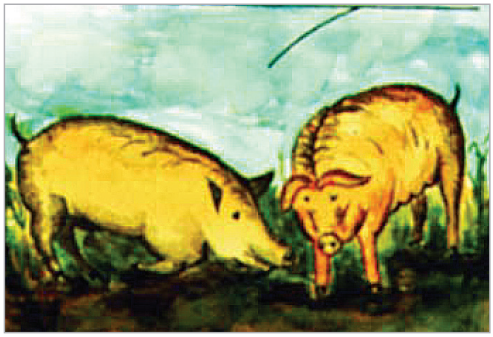
In 1970, a transplant research program was established at Hacettepe University Hospitals in the Department of General Surgery, and I was a third year resident during that time. We began performing experimental liver transplantations on pigs using porta to right atrium bypass with Dr. Burhanettin Savan, but this method was unsuccessful and I decided to continue the program using dogs (Figure 6A) and performed liver transplantation without bypass and it was successful (Figure 6B).[44]

Figure 6. Orthotopic Experimental Liver Transplantation on Dogs in 1970s (Hacettepe University Hospitals)

A. Summary of the Surgical Technique[44]



B. Experiments on Animals



First trial on pigs (unsuccessful)

Final successful trial on dogs (Post-operative 24 Hours)

In the 1980s, I also successfully performed partial auxiliary heterotopic experimental liver transplantations on dogs (Figure 7A and 7B).

Figure 7A. Summary of the Surgical Technique[45]

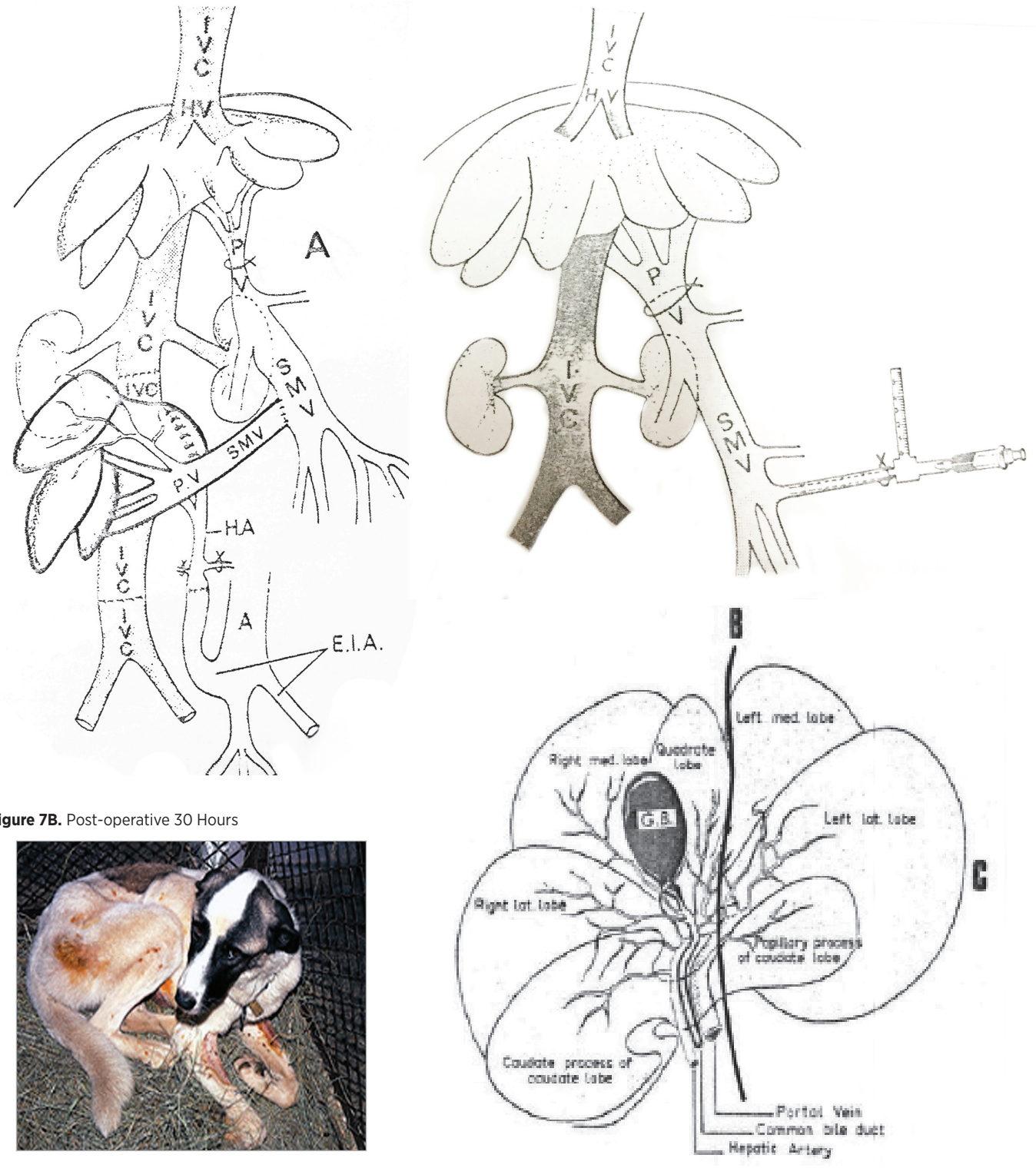


Figure 7B. Post-operative 30 Hours

In the meantime, even after the Law No. 2238 was passed and the number of facilities had increased, it was still apparent some years later that the organ supply from deceased donors was still not enough. Unfortunately, thousands of people in Turkey were dying in car accidents, and again, perfectly viable organs were being lost. Therefore, **in 1982, I applied again to the government, and the law on organ and tissue transplantation was amended (Law No. 2594) on January 21, 1982** (Figure 8A). This law stated that, after a car accident or a natural disaster, if the relatives of a deceased person could not be reached, then the organs could be harvested without having to obtain the consent of the relatives. In such cases, a post mortem examination is carried out and the report of the Examination Committee is recorded in the protocol for judicial examination. Today, organ transplants are still performed according to these laws (Law No. 2238 and Law No. 2594).

Following the new law, **the first successful deceased-donor liver transplantation in Turkey, in the Middle East, and in Northern Africa was performed by our team on December 8, 1988, at the Turkish Transplantation and Burn Treatment Foundation Hospital** (Figure 8B).[46,47] After this first liver transplant operation, our "Liver Transplantation Program from Deceased-Donor" started to be applied as a standard treatment method in our center and in Turkey.

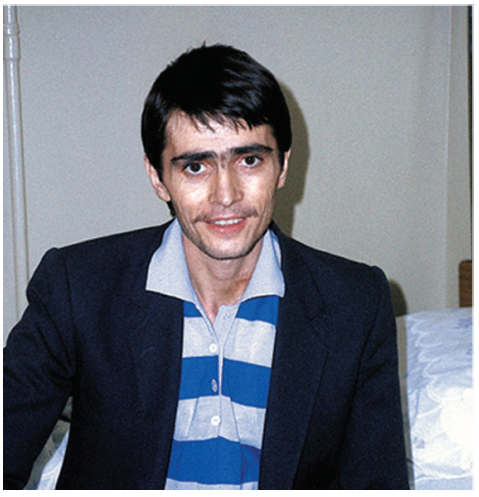
At that time, liver transplantations were performed only from deceased donors. However, it was not enough due to the high number of patients on the wait lists. Therefore, I started to think about partial left liver lobe living related donor transplantation in which the first attempts were made by Raia and associates,[48] Strong and associates[49] and Broelsch and associates.[50] After a while, **our team performed the first pediatric segmental living-related liver transplantation to a 1 year old on March 15, 1990 at the Turkish Transplantation and Burn Treatment Foundation Hospital, and this was the first in Turkey, the Middle East, and in Europe**[51,52] (Figure 9).

Figure 8A. Law No. 2594

TURKISH LAW No. 2594 ADDENDUM (January 21, 1982)

ARTICLE 4 - In the event of any accident or natural death, provided that the cause of death is not in any way related to the reason for organ harvesting and according to the conditions stated in Article 11, the suitable organs and tissues can be transplanted into persons whose lives depend upon this procedure without permission from the next of kin.

Figure 8B. The First Successful Deceased-Donor Liver Transplantation in Turkey, Middle East and Northern Africa, Turkish Transplantation and Burn Treatment Foundation Hospital, December 8, 1988



Fuat Koç, *27 years old*
Post-operative 3rd month

Figure 9. The First Pediatric Segmental Living-Related Liver Transplantation in Turkey, the Middle East, and Europe, Turkish Transplantation and Burn Treatment Foundation Hospital, March 15, 1990

Hüseyin Mert (Father)
Çağdaş Anıl Mert (Child) - (Recipient), *1 year old*
Gül İsmet Mert (Mother) - (Donor)

One month later, our team succeeded in performing the first adult segmental living-related liver transplantation (left lobe) in the world on April 24, 1990, at the same hospital (Figure 10).[53-55]

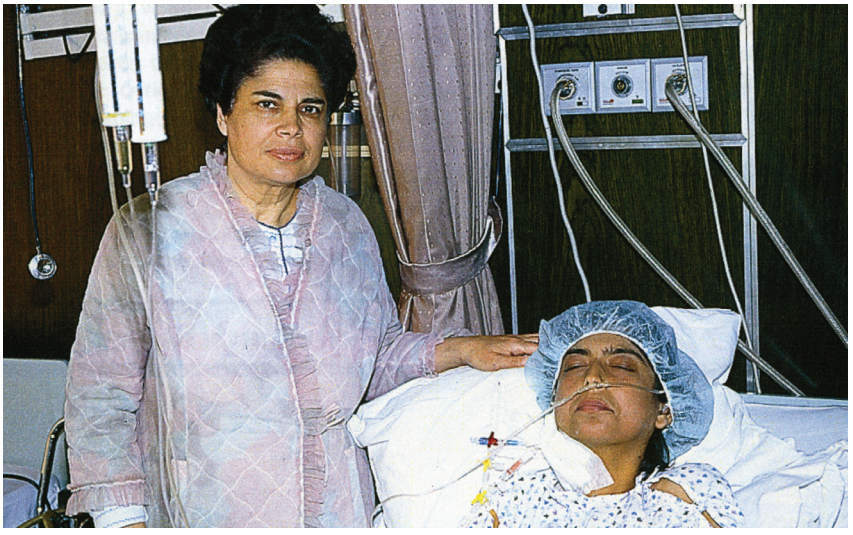
Figure 10. The First Adult Segmental Living-Related Liver Transplantation (Left Lobe) in the World, Turkish Transplantation and Burn Treatment Foundation Hospital, April 24, 1990

Hasan Işık (Father) - (Donor)

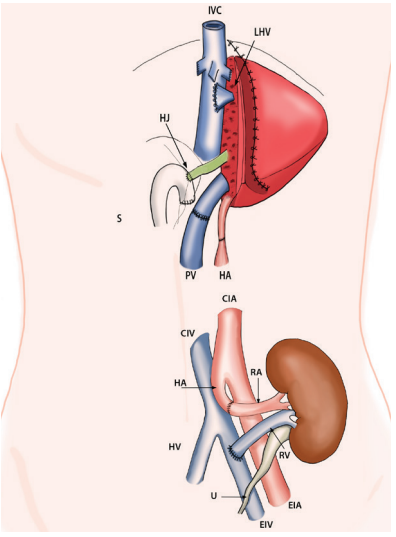
Erdemir Işık (Son) - (Recipient)
22 years old

On May 16, 1992, our team performed the first combined liver-kidney transplantation from a living-related donor, which was the first operation of its kind anywhere in the world[56] (Figure 11).

Figure 11. The First Living Related Combined Liver-Kidney Transplantation in the World, Turkish Transplantation and Burn Treatment Foundation Hospital, May 16, 1992



Nevin Teke (Mother)(Donor)
Ayşenur Teke (Daughter) (Recipient), *24 years old*



Summary of the surgical technique

Multiple organ transplantations are still applied as an alternative method even though they are rare. As a matter of fact, its practicability was shown by our team when we conducted a transplant operation with a segmental liver and a kidney at the same time.[56] **Additionally, heterotopic partial living-related and deceased-donor transplantations were performed by our team as well** (Figure 12).[57-64]

Figure 12. Heterotopic Deceased-Donor Partial Liver Transplantations, Başkent University Hospitals

Nihal Güngör (1998) – Still alive
17 years old

Sırma Erceyiş (2007) – Still alive
27 years old

Table 1. Başkent University Team Transplantation Activities

Başkent University Team Transplantation Activities in Turkey from October 1975 to April 2020			
Organ/Tissue Donor	**Living Donor**	**Deceased Donor**	**Total**
Kidney	2390	714	3104
Liver	449	210	659
Heart	0	142	142
Heart Valve	0	2	2
Pancreas	0	2	2
Cornea	0	347	347
Bone Marrow	1038	0	1038

Table 2. Transplantation Activities in Turkey

Transplantation Activities in Turkey from November 1975 to April 2020			
Organ/ Tissue Donor	**Living Donor**	**Deceased Donor**	**Total**
Kidney	32 830	8917	41 747
Liver	11 188	4549	15 737
Heart	0	1126	1126
Heart Valve	0	343	343
Pancreas	0	197	197
Cornea	-	27 418	27 418
Bone Marrow	12 934	-	12 934

The level of social awareness raised in recent years has made organ transplant research studies more current and popular both in Turkey and in the world. Tables 1 and 2 and 3 show transplant activities including kidney, liver, heart, heart valve, pancreas, cornea, and bone marrow transplant operations, which have been conducted successfully both in Turkey and in Başkent University hospitals from

Table 3. Transplant Centers in Turkey

Transplant Type	No. of Centers
Kidney	77
Liver	46
Heart	16
Lung	4

1975 to January 2020. Our goal is to develop new and alternative solutions for transplant problems, especially ones related to deceased-donor transplant, which remains an important global problem. Deceased-donor transplant provides many patients with chronic organ disease an opportunity to live.

Despite ongoing research since the 1970s on Tissue and Organ Transplantation operations, continued studies and interinstitutional coordination will provide good results in the near future and will allow patients with chronic organ disease to have hope.

CONCLUSIONS

Organ shortages remain the greatest challenge facing the field of organ transplantation today. Millions of people die and are buried with healthy organs, which could save the lives of many patients who continue to wait on transplant lists. This is the responsibility of the international transplant community to ensure that the growing demand for organs is met within ethical and legal boundaries and to create a system of meeting the organ demand entirely with deceased organ donation.

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Appendix 1. English translation of the original document

REPUBLIC OF TURKEY
DIRECTORATE OF RELIGIOUS AFFAIRS
ANKARA

DIK.D/1-4/79

SUBJECT : Re: Organ Transplantation 25 January ~~1979~~/197…
171

To the Office of the Justice Commission
of THE NATIONAL ASSEMBLY

REF.: Your letter dated 19.1.1979 and no. 332 and the enclosure thereof.

The ref. letter and the legislative proposal annexed therein with regard to organ transplantation were reviewed:

As is also indicated by religious evidence, it has been considered that it poses no risk in aspects of religion to transplant organs removed from people, either deceased or alive, or from other living things, to another person for the purposes of treatment or for other compelling reasons, on the condition that his/her prior will or the consent or approval of his/her heirs is obtained.

However, it has been concluded that the statement "the person who is about to pass away", written in Article #3 of the legislative proposal, should be excluded from the text. The risk in removing any organ from a person who is about to pass away will be better comprehended, considering the phenomena deemed as "miracle" by the science of medicine, and the incidences of 'rising from the dead' thanks to supernatural willpower. It goes without saying that such practice could lead to a chance of "causing death."

We hold no opinion contrary to the other articles of the legislative proposal in question.
Kindly submitted for your information.

[signature]
Tayyar ALTIKULAC
Head of Religious Affairs

ANNEX : 4 (photocopies)

Appendix 2. English translation of the original document

Term : 5
Session : 2

NATIONAL ASSEMBLY

Page Nr.: 328

The Legislative Proposal on Organ Transplantation by Talat Dogan, a Member of the Republican Senate of Rize and 14 colleagues of his; the Legislative Proposal on Establishing a Kidney Bank by Ibrahim Topuz, a Member of Parliament for Kocaeli, and Nilufer Gursoy, a Member of Parliament for Istanbul; and the Reports of the Commissions of Justice and Health & Social Affairs (2/658, 2/621).

Directorate for Laws,
General Secretariat of
The Republican Senate 21.12.1978

Issue: 6979-17170

TO THE OFFICE OF THE NATIONAL ASSEMBLY

The Legislative Proposal on Organ Transplantation by Talat Dogan, a Member of the Republican Senate of Rize, and Bilal Taranoglu, a Member of Republican Senate of Ordu and 13 colleagues of his, as well as the legislative intention thereof are enclosed herein.

Kindly request you to take the necessary action.

Yours respectfully,

Cengizhan Yorulmaz
Deputy Speaker of the Republican Senate

To the Office of the Republican Senate

Kindly request you to take the necessary action to enact the Legislative Proposal on Organ Transplantation.

Talat Dogan
Senator of Rize

Cevdet Aykan
Senator of Tokat

Ergun Ertem
Senator of Ankara

Dr. Baha Aksit
Senator of Denizli

Bilal Taranoglu
Member of Parliament for Ordu

Mustafa Gulcugil
Senator of Isparta

Nazim Bas
Member of Parliament for Icel

Yusuf Cemal Ozkan
Member of Parliament for Eskisehir

Dr. Hidayet Celebi
Member of Parliament for Kars

Ragip Uner
Senator of Nevsehir

Dr. Kemal Tabak
Member of Parliament for Adiyaman

Dr. Celal Ertug
Member of Parliament for Elazig

Sermet Durmusoglu
Member of Parliament for Tokat

Kazim Karaagaclioglu
Senator of Afyon

Faruk Demirtola
Member of Parliament for Tokat

Appendix 3. English translation of the original document

1

To the Office of the Republican Senate

I hereby kindly request immediate action to enact the Legislative Proposal on Organ Transplantation.

Talat Dogan
Senator of Rize
[signature]

Bilal Taranoglu
Member of Parliament
for Ordu
[signature]

Cevdet Aykan
Tokat
[signature]

Ergun Ertem
Ankara
[signature]

1 **2** **3** **4**

Dr. Baha Aksit
Senator of Denizli
[signature]

Mustafa Gulcugil
Isparta
[signature]

Nazim Bas
(Icel)
[signature]

5 **6** **7**

Ragip Uner
[signature]

Yusuf Cemal Ozkan
Member of Parliament for Eskisehir
[signature]

Dr. Hidayet Celebi
Member of Parliament for Kars

8 **9** **10**

Dr. Kemal Tabak
Member of Parliament
for Adiyaman
[signature]

Dr. Celal Ertug
Member of Parliament for Elazig
[signature]

Sermet Durmusoglu
Tokat
[signature]

11 **12** **13**

Kazim Karaagaclioglu
Senator of Afyon
[signature]

Faruk Demirtola
Member of Parliament for Tokat
[signature]

14 **15**

Annexes:

1- Legislative Intention in General
2- Legislative Proposal

Appendix 4. English translation of the original document

6
[logo]
SOCIETY OF DIALYSIS AND
TRANSPLANTATION, TURKEY

Hon. Galip Kaya
Member of Parliament for Antalya
Chairman of the Justice Sub-Committee
Grand National Assembly of Turkey

Mithatpasa Caddesi 21/8, Yenisehir, Ankara / Phone: 18 46 45

Hon. Galip Kaya,

The Legislative Proposal on Organ Transplantation was discussed at the meeting of our administrative council, held on 26.1.1979, and our opinions regarding the matter are attached herein.

We deeply believe that the proposed law, which will allow a great number of patients in our country to recover their health, will pass into law sooner rather than later, thanks to the close attention and efforts you devote.

We would like to take this opportunity to extend our thanks and appreciation to you in this respect.

[signature]
Assoc. Prof. Dr. Mehmet Haberal
Secretary General
For and on behalf of the Administrative Council
of the Society of
Dialysis and Transplantation

Prof. Dr. Ali A. GURCAY
[signature]
President of the Society of Dialysis and
Transplantation Turkey and
The Head of Nephrology, Faculty of Medicine
Cukurova University

Appendix 5. English translation of the original document

328

Interuniversity Board

Educational Council of Medicine, Dentistry, Pharmaceutics and Health Sciences

President of Council
Prof. Dr. IHSAN DOGRAMACI

General Secretary of Council
Prof. Dr. DOGAN TANER

5 February 1979
No: 79.6

To the Office of Sub-committee of
the Justice Commission of the National Assembly,

Ref.: Your letter dated 19/1/1979 and no. 331/17117

The Legislative Proposal on Organ Transplantation and legislative intention thereof were reviewed, and our opinions related to this matter are submitted as follows:

1) We are of the opinion that we should concentrate more on the term of "clinical death", rather than on the "vegetative state", as is the case in other countries carrying out practices in the field of organ transplantation. This is because the state of clinical death requires the death of brain cells completely and irreversibly and the cessation of breathing (respiratory arrest) permanently. Therefore, it is required that the provisions concerning the vegetative state as stated in the Legislative Proposal and the Legislative Intention be removed from the Proposal and Intentions;

2) It is required that the clause (b) of the article #2 in the draft Legislative Proposal be amended as follows: "The tissues and organs of a clinically dead person (corpse) can be taken upon his/her own prior will or the consent of either of his/her parents, siblings or children who attend on him at that time or of any of his/her heirs, in order to restore and recover the health of someone else..";

3) It is required to replace the term "Eye Transplantation" mentioned in the Legislative Intention, with "Corneal Transplantation";

4) It is required that the draft Legislative Proposal include a provision that will ensure that the scientific, technical, and supervisory aspects of organ transplantation are conferred to the Ministry of Health and Social Welfare and the universities, and that the regulations on this subject are prepared jointly by the authorities that will perform the operations and the Ministry of Health and Social Security.

Kindly submitted for your information.

[signature]
Prof. Dr. Ihsan Dogramaci

Appendix 6. English translation of the original document

President

12

[logo]
Union of Turkish Bar Associations

Issue: 123 Ankara, 23 January 1979

Hon. Galip KAYA
Member of Parliament for Antalya
Grand National Assembly of Turkey

Ref. : Your letter dated 19.1.1979 and no. 328

Preliminary reviews have been commenced on the drafted legislative proposal with regard to organ transplantation, and the remarks prepared will be presented at the meeting of our Administrative Body, which will be held on January 27th, and the remarks of the Union, once prepared following the discussions, will be submitted to you in due time. Kindly submitted for your information.

Yours respectfully,

Atty. Faruk EREM
[signature]
President

FE/MH.

Appendix 7. English translation of the original document

398

[logo]
Union of Turkish Bar Associations

Issue: Ankara, 29/1/1979

...

5- Transplantation from a deceased person to a living person: We identified a gap concerning this matter, in the proposal. The "time of death" lacks a formal definition. However, it is imperative to have a definition for it. Even if it is a board that decides a person is deceased, the suspicion of responsibility will not be eliminated unless a legal definition is in place. There are two opposing views in terms of the time of death:

a) Biological death: Biological death occurs in the event that the major life functions performed by circulatory and respiratory systems stop (no longer functioning). In such cases, the death will have occurred with the last breath and last heartbeat of the person.

b) Brain (cerebral) death: The brain is the organ that gives us the characteristics of being a human. The person will be considered deceased when his/her brain functions stop. The biological death to follow is a natural result of it. When the brain is dead, the person should be considered dead, too.

c) Legal preference: If we were to take the time of biological death, almost none of the transplant operations will be medically feasible. Therefore, the law has to specify a preference. It is fair to say that the trend in the preference for brain death has become official.

Appendix 8. English translation of the original document

Telegram: BAROBIRLIK Kizilay-Karanfil Sokak No: 5-ANKARA Phone: 18 13 44 - 18 13 46 – 16 05 12

119

NATIONAL ASSEMBLY

Commission of ...

File No : 2/658 20/2/1979
Decision No : 88

-7-

Ismail Hakki Koyluoglu
(Member of Parliament for Ankara)
Director of Justice Commission
[signature]

Galip Kaya
(Member of Parliament for Antalya)
Deputy Speaker
Dissented.
See below for JUSTIFICATION.
[signature]

Mehmet Yusuf Ozbas
(Member of Parliament for Kahramanmaras)
Spokesperson
[signature]

Mustafa Kemal Biberoglu
(Member of Parliament for Corum)
[signature]

Ahmet Karahan
(Member of Parliament for Gaziantep)
[signature]

Mevlut Onal
(Member of Parliament for Hatay)
(Not available for signature)

Ramazan Caliskan
(Member of Parliament for Icel)
Dissented.
[signature]

I. Hilmi Dura
(Member of Parliament for Kastamonu)
(Not available during voting)

Dogan Gunesli
(Member of Parliament for Kirsehir)
[signature]

I. Ethem Boz
(Member of Parliament for Nevsehir)
[signature]

L. Selahattin Yuksel
(Member of Parliament for Usak)
[signature]

Burhan Karcaeli
(Member of Parliament for Zonguldak)
[signature]

Koksal Toptan
(Member of Parliament for Zonguldak)
[signature]

[initials]

Diagnosis of Brain Death and Central Nervous System Complications After Liver and Renal Transplant

A. Muhteşem Ağıldere

DIAGNOSIS OF PATIENTS WITH BRAIN DEATH

Patients with brain death are a potential source of solid organs for deceased-donor transplant. Brain death is the irreversible loss of neurologic function of the brain, including the brain stem, by definition. The underlying pathophysiology involves development of extensive cerebral edema, increased intracranial pressure, and the eventual cessation of cerebral blood flow. Although brain death is a clinical diagnosis, confirmatory tests, including neuroradiological imaging techniques, have been widely used. Absence of cerebral blood can be demonstrated through imaging modalities such as digital substraction angiography of cerebral vessels, transcranial Doppler ultrasonography, cerebral scintigraphy, computed tomography (CT), CT perfusion (CTP), CT angiography (CTA), magnetic resonance imaging (MRI), and MR angiography (MRA). The type of modality used depends on the patient's status, availability of modality, and expertise of the radiologist.[1,2]

Although brain death has a triggering event (mostly trauma or subarachnoid hemorrhage), intracellular and extracellular brain edema may develop that restores the imaging findings. Intracellular edema can develop secondary to hypoxia or osmolar regulation, whereas extracellular edema occurs secondary to disruption of the blood brain barrier and loss of autoregulation. The different imaging modalities each have advantages or disadvantages depending on the technical aspects and the required imaging findings (Table 1). Cerebral angiography, cerebral scintigraphy, and transcranial Doppler are validated techniques to diagnose brain death by the American Academy of Neurology. Transcranial Doppler and MRI are advantageous because of the absence of ionized radiation. Cerebral angiography is excellent for demonstrating intracranial blood flow. Imaging shows absence of blood flow as lack of opacification in CTA, absence of flow void in MRI, and absence of cerebral uptake in scintigraphy. For intracranial opacification in CTA, 4 and 7 points scales are used.

The use of CTP can show decreases in cerebral blood flow and cerebral blood volume. Anatomic details as uncal and cerebellar herniation, cerebral edema, and loss of gray-white matter differentiation are seen on CT (Figure 1). These findings can be more prominent on MRI. Diffusion-weighted images in brain MRI can demonstrate edema extending to the brainstem. Susceptibility-weighted images or gradient echo images may show transcerebral and transcortical veins and prominent medullary veins and hemorrhage in brain MRI. Transcranial Doppler requires a 2-MHz probe and operator expertise to demonstrate progressive loss of forward flow[1,2] (Table 1).

The choice of ancillary imaging modalities is variable, and diagnostic accuracy and reliability are unclear. MacDonald and colleagues[1] compared

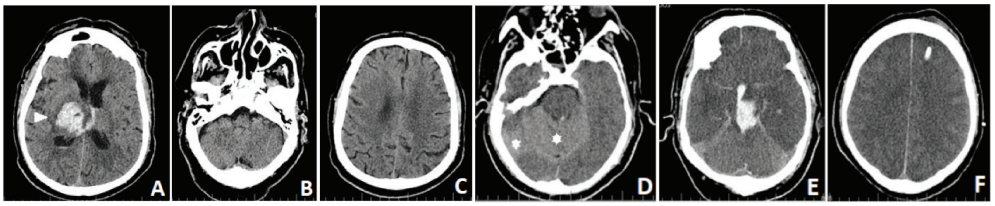

Figure 1. Brain Computed Tomography Images of Hypoxic-Ischemic Brain

Patient presented with mental status change. Upper raw, transverse images of right thalamic hematoma (arrowhead) **(A)** in cerebellum and cerebrum showed no edema **(B)** and **(C)**. One day later, there was increased density of cerebellum and tentorium (asterisks) **(D)** and **(E)** with newly developed cerebellar and cerebral edema, loss of white-gray matter differentiation, and effacement of basal and uncal cisterns **(D), (E),** and **(F)**. Computed tomography as an ancillary tool provides anatomic details at diagnosis of brain death.

Table 1. Differences in Imaging Modalities in Brain Death Determination

Modality	Advantages	Disadvantages
Cerebral angiography	▪ Excellent for demonstrating intracranial blood flow ▪ Validated by AAN-Considered "gold standard"	▪ Operator dependent ▪ Limited availability ▪ Contrast load ▪ Radiation dose ▪ Limited anatomic detail ▪ Possible damage to transplant organs with vessel occlusion
Cerebral scintigraphy	▪ Validated by AAN	▪ No anatomic detail ▪ Limited availability
Transcranial Doppler	▪ No radiation ▪ Validated by AAN	▪ Operator dependent ▪ Acoustic window may be limited
MRI	▪ No radiation ▪ Provides anatomic information	▪ Time consuming ▪ Expensive ▪ Not widely available ▪ Difficult to perform on ventilated patients ▪ Variable criteria for intracranial circulatory arrest
CT Noncontrast	▪ Widely available ▪ Rapid ▪ Provides anatomic information	▪ Radiation dose ▪ Contrast load with CTA/CTP ▪ Variable criteria for intracranial circulatory arrest

Abbreviations: AAN, American Academy of Neurology; CT, computed tomography; MRI, magnetic resonance imaging

Information is from Gastala and associates.[2]

different imaging tests, including CTP, CTA, radionuclide scans, cerebral angiogram, MRI, and nonenhanced CT in 74 patients who required diagnosis for cause of brain death. The most commonly used test was nonenhanced CT, but this test was found to be the least sensitive and specific for determination of brain death. Computed tomography perfusion was found to have the highest sensitivity, specificity, positive predictive value, and negative predictive value.[1]

DIAGNOSIS OF CENTRAL NERVOUS SYSTEM COMPLICATIONS AFTER LIVER AND RENAL TRANSPLANT

Central nervous system (CNS) complications may be seen after both liver and renal transplant. Postoperative CNS complications can develop secondary to surgery, metabolic disorders, or immunosuppression. However, many CNS manifestations of chronic liver and kidney parenchymal diseases may decrease or disappear after organ transplant.[3-6] For

proper patient treatment, CNS complications after transplant can be classified on the basis of methodological time period, etiology, and organ type.[6,7]

Central nervous system complications may develop secondary to the transplant procedure and to medication after transplant, as well as to parenchymal failure, depending on the patient's underlying pathophysiology. Chronic illness and comorbidities also contribute to CNS complications. In addition, similar CNS neuroradiological findings may be seen both before and after solid-organ transplant, with some regressing after transplant.[5,8-10]Neurologic symptoms posttransplant are variable and not specific to the disease and encompass a broad spectrum, including seizures, altered mental status, confusion, unconsciousness, headache, visual hallucinations, motor deficit, nausea, and vomiting. For the most part, diagnoses will involve use of CT and MRI,[3,6,11] mostly of the brain, although in some cases spine imaging may be required.[12-14] Computed tomography is easy to perform, particularly during the early posttransplant period, but it may not be sufficient in many cases and MRI is required.[11] Furthermore, some patients may need advanced MRI techniques, including diffusion, H^+-MRI spectroscopy (MRS), or CTP to diagnose CNS disease. Posterior reversible encephalopathy syndrome (PRES), CNS infections, brain infarction, intracranial hemorrhage, osmotic demyelination syndrome (ODS), posttransplant lymphoproliferative disorder (PTLD), and tumors are the most commonly seen posttransplant CNS complications.[3,6,7,13-15] Central nervous system complications are relatively common after liver but also can be seen after kidney transplant. Surgical procedures are highly complex, particularly with liver transplant.[3,6] The pathophysiology, presurgical neurologic status, comorbidities, time after surgery, and duration of complications are important for determination of patient prognosis. Authors have attempted to develop different evaluation methodologies based on the cause or timing and duration of these CNS complications and to classify CNS complications.[3,6,7,16] Bernhardt and associates[7] conducted neurologic evaluations of 136 patients who underwent orthotopic liver transplant. They classified CNS complications into 2 groups: metabolic and nonmetabolic. The metabolic group included patients with ODS, patients with PRES, and patients who had symptoms but negative imaging and cerebrospinal fluid results. The nonmetabolic group included patients with stroke, intracranial hemorrhage, and CNS infection. They concluded that patients in the metabolic group had prolonged hospital stays, and the nonmetabolic group had higher rates of mortality.[7] We evaluated brain MRI of 187 kidney and 29 liver transplant patients and classified patients into 3 groups for description purposes: CNS complications related to transplant, complications secondary to chronic parenchymal disease, and complications that were neither due to transplant nor chronic parenchymal disease.[3] The incidence of PRES is approximately 0.5% to 5% after solid-organ transplant.[17,18] Headache, seizure, visual disturbance, and altered mental function are the most common presenting symptoms. Both clinical and radiological studies are required for diagnosis. It is a reversible posterior leukoencephalopathy. Although primarily white matter is involved, gray matter can also be involved. Breakdown of cerebral autoregulation is the main cause. In its classical form, PRES is symmetrical, bilateral, in the parietooccipital and subcortical regions, and reversible and presents with vasogenic edema and with arterial hypertension (Figure 2).[17] However, this has many exceptions and different manifestations with diverse causes and can present after transplant. Hypertension is not a "rule," and shock,

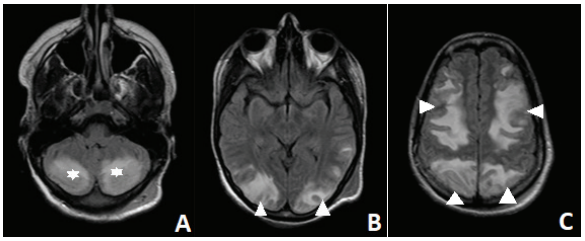

Figure 2. Posterior Reversible Encephalopathy Syndrome

Brain magnetic resonance images of FLAIR (fluid attenuated inversion recovery) sequence showing bilateral and symmetrical increased intensity at cerebellar (asterisks) **(A)** and posterior temporal and occipital **(B)**, and parietal and frontal lobes (arrowheads) **(C)**. Cases typically involve occipital and parietal regions.

sepsis, immunosuppression drugs (cyclosporine and tacrolimus), methotrexate, leukemia, lymphoma, infections, systemic lupus erythematosus, and hemolytic uremic syndrome may cause PRES. It may be in frontal or atypical locations/lobes in cerebrum, as well as in the cerebellum, brain stem, and cortical areas. It may not be reversible (10% of PRES patients) and may be seen as cytotoxic edema (15% of PRES patients).

On its own, the term "PRES" does not sufficiently define many cases of the disease. There are 3 theoretical concepts about the pathophysiology of PRES: (1) hypoperfusion theory, (2) hyperperfusion theory, and (3) endothelial damage theory. With the hypoperfusion theory, there is a sudden increase in arterial tension trigger autoregulation that causes vasoconstriction, with hypoperfusion resulting in cerebral ischemia and edema. With the hyperperfusion theory, there is a sudden increase of arterial tension that causes disruption of posterior autoregulation of the brain followed by a breakdown of the blood-brain barrier and capillary bed disruption, resulting in hyperperfusion and edema. These 2 theories have some limitations. Arterial blood tension for some patients is not high or not as high as would lead to disruption of autoregulation, and there is no correlation between the diffusiveness of the brain lesions and level of hypertension. These limitations resulted in the development of the endothelial theory. With the endothelial theory, there is activation of the endothelium after immune system stimulation that is followed by breakdown of the blood-brain barrier, resulting in vasogenic edema, which develops secondary to breakdown of cerebral autoregulation. It may be secondary to immunosuppression (through leukoencephalopathy induced by cyclosporine and tacrolimus) or hypertension. Hypertensive encephalopathy may involve the brain stem and cerebellum. Serum levels of immunosuppressive agents and blood pressure evaluation are important for differential diagnosis.[17,19] In children, there is an increased incidence of cerebellar involvement, perhaps showing that the posterior circulation in children with PRES is more vulnerable than in adults.[20]Manifestations of PRES can show some differences after liver (Figure 3) versus after renal transplant (Figure 4 and Table 2). After liver transplant, PRES usually presents during the first 3 months; however, after renal transplant, it may manifest at any time posttransplant, even after years. Blood pressure levels are generally high after renal transplant but may be normal after liver transplant. Brain edema is usually more after liver transplant (Figure 3) than after renal transplant. Coexistence of infection increases the risk of PRES in both liver and renal transplant. There is a greater chance of PRES recurrence after renal transplant.[21] In an evaluation of neuroradiological findings of CNS complications in 187 renal transplant recipients up to 8 years posttransplant and 29 liver transplant recipients up to 14 years posttransplant, PRES secondary to immunosuppressive toxicity was seen in 17.2% of liver and in 1.6% of renal transplant patients.[3] Accumulation of manganese in the basal ganglia, particularly in globus pallidus, may be seen in patients with chronic liver disease, and brain MRI

Table 2. Comparison of Posterior Reversible Encephalopathy Syndrome Features After Liver and Renal Transplant[21]

	Liver Transplant	Renal Transplant
Time after transplant	Short (usually 3 months)	Long (even after years)
Blood pressure	Normal	High
Brain edema	More	Less
Presence of coinfection	Increased PRES risk	Increased PRES risk
Risk of recurrence	Less	High

Abbreviations: PRES, posterior reversible encephalopathy syndrome

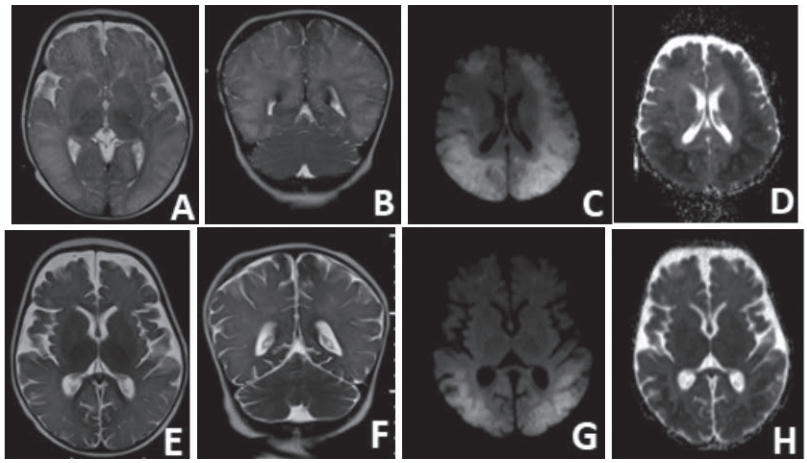

Figure 3. Posterior Reversible Encephalopathy Syndrome

Brain magnetic resonance images after liver transplant in 6-year-old patient with seizures. Upper raw transverse and coronal T2-weighted images **(A)** and **(B)** demonstrate diffuse edema, particularly in posterior temporal, parietal, and occipital lobes with diffusion restriction on diffusion images **(C)** and ADC map **(D)**, showing cytotoxic edema. Nine days later following a change in immunosuppressive regimen, edema decreased, as shown in lower raw transverse **(E)**, coronal TSE-T2-weighted images **(F)**, diffusion image **(G)**, and ADC map **(H)**. Usually cases show increased diffusion, but the presented case shows diffusion restriction. Edema is usually more prominent after liver transplant, as shown here.

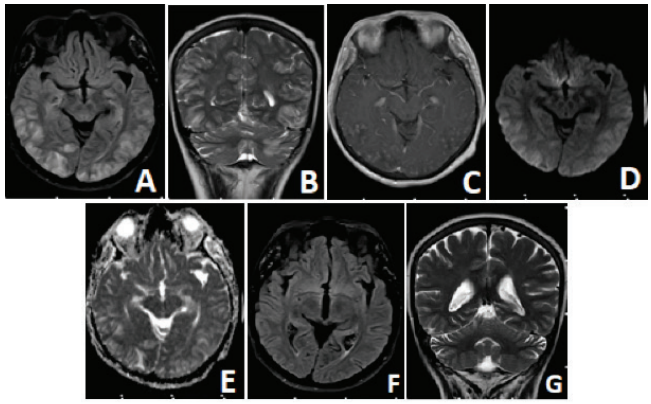

Figure 4. Posterior Reversible Encephalopathy Syndrome

Brain magnetic resonance images in 28-year-old patient with seizures after renal transplant. Upper raw images show that bilateral posterior temporal-occipital symmetrical intensity increased on T2-weighted images **(A)** (shows axial FLAIR and **(B)** shows coronal TSE-T2), images without any contrast enhancement **(C)**, and increased diffusion image **(D)**. Lower raw brain images are 1 month later, demonstrating disappearance of posterior temporal and occipital increased intensity (ADC map **(E)**, axial-FLAIR **(F)**, coronal TSE-T2). Typical of posterior reversible encephalopathy syndrome, increased diffusion is shown with less edema after renal transplant.

is helpful.[3,6,22] Manganese deposition secondary to portosystemic shunting may develop, and it may be present in the absence of hepatic encephalopathy.. Manganese accumulation can cause high signal intensity in T1-weighted images of brain MRI, typically in the globus pallidus[8,22] (Figure 5A). Increased levels of intensity are correlated with severity of liver damage and blood levels of manganese. Studies have shown quick regression of hepatic encephalopathy after liver transplant, whereas T1 signal intensity abnormalities need up to 1 year to resolve[3,8,22] (Figure 5B).

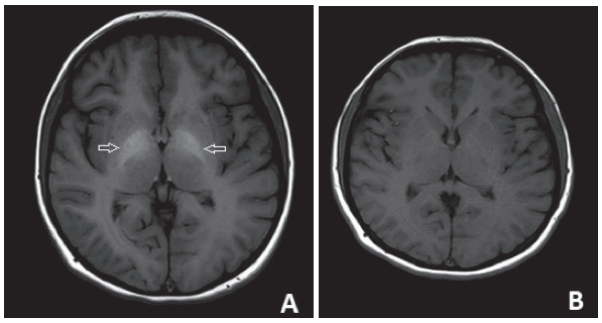

Figure 5. Basal Ganglia Increased Intensity in T1-Weight Magnetic Resonance Images

(A) Pretransplant T1-weighted images of patient with chronic liver disease demonstrates increased signal intensity (open arrows) bilaterally in basal ganglia. **(B)** Findings decreased after liver transplant. These changes were not correlated with hepatic encephalopathy but were correlated with blood manganese levels. If extended to substantia nigra, Parkinsonism-like clinical findings may occur.

In cases of acute liver failure, cerebral edema may develop, with advanced cases even presenting with cerebral herniation. Therefore, pretransplant neuroradiological evaluations of these patients are important. Increased ammonia may give way to neurologic disorders, resulting in neuroradiological findings. Hyperammonemic encephalopathy may develop after organ or graft failure. Imaging findings include symmetric involvement of cingulate gyrus and the insular cortex, with variable asymmetric cortical involvement.[23] Cerebral edema evaluation is an important marker of neurologic recovery after treatment. Depending on the amount of cerebral edema and patient status, brain CT or MRI can be useful for demonstration, with brain MRI being more useful. T2-weighted images may show increased intensity in the basal ganglia, periventricular white matter (Figure 6), and corticospinal tractus on brain MRI. T2-weighted images may not be sufficient, and other MRI techniques, including magnetization transfer, fast FLAIR (fluid attenuated inversion recovery), and diffusion-weighted images, may be required to demonstrate cerebral edema. Diffusion-weighted images may differentiate between 2 different types of cerebral edema: intracellular in acute forms and probably interstitial in chronic forms. In acute liver failure, mean diffusivity values are reduced, supporting increased cell volume secondary to massive intra-astrocytic increases of glutamine as the cause of cerebral edema.[3,6-8,22,24] Glial accumulation of glutamine leads to loss of other organic osmolytes, such as myoinositol, taurine, and choline. Those metabolite changes are reflected in H^+-MRS as increases in glutamine-glutamate peak and decreases in myoinositol and choline peaks[3,8,22,25] (Figure 6). One to 2 months after liver transplant, choline and glutamine-glutamate peaks are normalized; however, normalization of

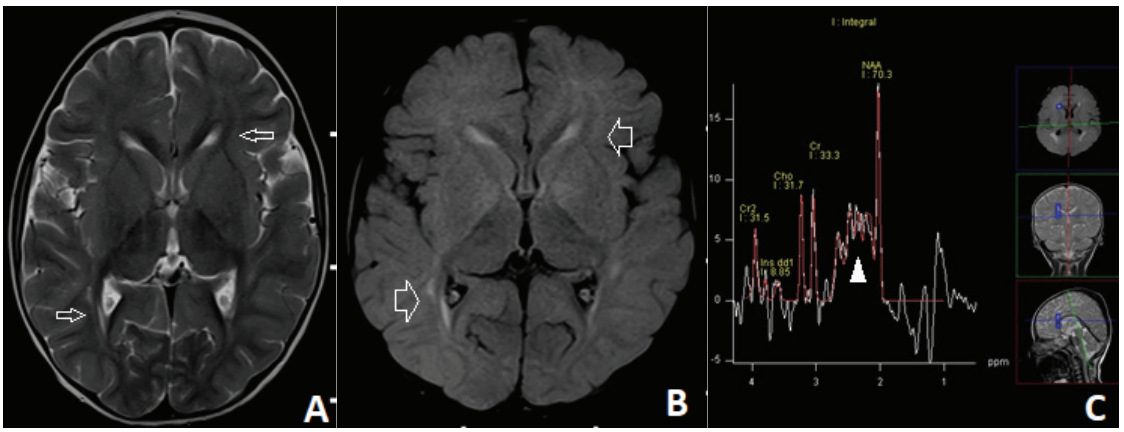

Figure 6. Hepatic Encephalopathy

T2-weighed **(A)** and FLAIR **(B)** images demonstrate bilateral symmetric increased intensity in periventricular white matter (open arrows in T2-weighted TSE image and open arrows in FLAIR image) and basal ganglia and edema. **(C)** Brain +H-magnetic resonance spectroscopy shows increased glutamine-glutamate complex (arrowhead), with decreased myoinositol and choline shown.

the myoinositol peak takes 3 to 7 months.[8,26] Brain H^+-MRS images of patients with cirrhotic hepatic encephalopathy may show decreased choline/creatine and myoinositol/creatine levels and increased levels of Glx/creatine of up to 25%. After liver transplant, usually T1 hyperintensity in basal ganglia and metabolic changes in H^+-MRS return to normal in the first year, with T1 intensity changes proceeding the MRS findings.[27,28] Comorbidities also contribute to brain MRI findings in these patients, and white matter lesions as increased T2-weighted intensity can be identified in patients with small vessel cerebral disease or as part of normal aging.[26] However, T2-weighted hyperintensities of periventricular white matter can decrease after resolution of hepatic encephalopathy or liver transplant.[29,30] In their study, Hattori and associates analyzed 11 children with fulminant hepatic failure after living related liver transplant with a mean follow-up of 28 months. The group concluded that children with grade IV hepatic encephalopathy with CT evidence of cerebral edema were at high risk of neurologic sequela.[31] Osmotic demyelination syndrome can be seen after liver or kidney transplant but more so after liver transplant and can present perioperatively and during the acute phase. It is also known as central pontine myelinolysis. Patients with ODS present with variable arousal impairment, including coma, pseudobulbar affect, and/or cranial nerve palsies. It occurs more often in orthotopic liver transplant recipients than in other solid-organ transplant recipients due to large volume losses and replacements with rapid correction of hyponatremia. Osmotic demyelination may be extra-pontine sides as basal ganglia, capsula interna, and periventricular white matter (Figure 7). Therefore, ODS is a more accurate term than central pontine myelinolysis. Osmotic demyelination syndrome is characterized by edema and demyelination in the pons and extrapontine areas[32-35] (Figure 7). Clinical and neuroradiological findings are similar regardless of the cause of ODS. In our retrospective evaluation of brain MRI in 17 patients on hemodialysis with neurologic symptoms, we detected pontin involvement in 65% of patients and extrapontine involvement in 71%. Four patients had the disequilibrium syndrome. Hyponatremia and low blood urea nitrogen-to-creatinine ratio are the major laboratory findings. Most lesions recovered, suggesting edema rather than demyelization in this group of patients.[32] Cerebrovascular accidents (CVA) are common and potentially life-threatening neurologic complications after renal and liver transplant.[6] Ischemic CVA secondary to perioperative hypotension, cardiac arrest, and emboli or intracranial hemorrhage due to coagulopathy, fungal infections, sinus thrombosis, and hypertension can be seen. Ischemic stroke is more common after renal transplant. Patients with end-stage renal disease (ESRD) on hemodialysis and patients with chronic liver disease also have a tendency for CVA because of atherosclerosis and comorbidities. Brain CT is diagnostic tool of choice in cases with suspicion of CVA and is useful to rule out

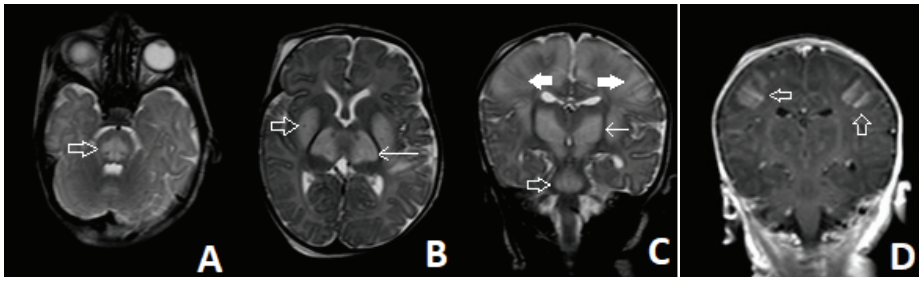

Figure 7. Brain Magnetic Resonance Images of Osmotic Demyelination Syndrome

Shown are transverse **(A)** and **(B)** and coronal **(C)** TSE-T2-weighted images demonsrating increased intensity in the central part of pons with preservation of periphery (open arrows in **A** and **C**), with additional bilaterally and symmetrically increased intensity of basal ganglia, (open arrow in **B**), thalamus (thin arrows in **B** and **C**), and frontoparietal cortical-subcorical cortex with contrast enhancement (open arrows in **D**) at the most cranial part of lesions. **(D)** Postcontrast T1-weighted coronal image.

intracranial hemorrhage (Figure 8). However, brain diffusion MRI can show acute ischemia much earlier than CT as restriction of diffusion (Figure 9). Brain MRI with gradient echo sequences and susceptibility-weighted imaging may demonstrate bleeding areas that are not shown with CT.[36] Periventricular white matter changes, cerebral atrophy, cognitive deficits, and high stroke prevalence are seen in patients with ESRD on hemodialysis secondary to low cerebral blood perfusion.[5,37] When we compared incidence of cerebral atrophy in 68 patients with ESRD on hemodialysis versus and 26 renal transplant patients, cortical and subcortical atrophy incidences were statistically higher than in a normal control group (n = 22). Subcortical atrophy group was higher in patients with ESRD on hemodialysis than in renal transplant patients. We concluded that the incidence of cerebral atrophy increases with the time period of hemodialysis and incidence of subcortical atrophy does not increase after renal transplant.[38] In their study of the incidence of periventricular white matter changes, Kurt and colleagues found that increases were related to length of hemodialysis, but they found no correlation between incidence of periventricular white matter changes and the period after renal transplant.[39]

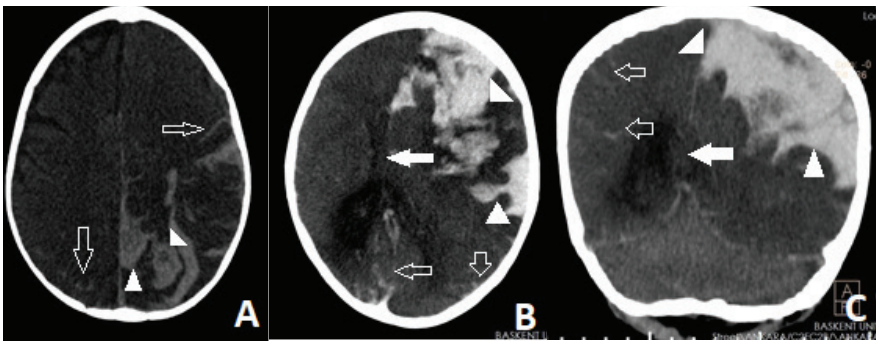

Figure 8. Brain Computed Tomography of Intracranial Hemorrhage

Transverse **(A)** and **(B)** and coronal images **(C)** show massive intracranial hemorrhage (white arrowheads) in the left frontal and parietal lob with edema and right-sided shift (thick white arrow) and serious mass effect, accompanying subarachnoid hemorrhage (open arrows).

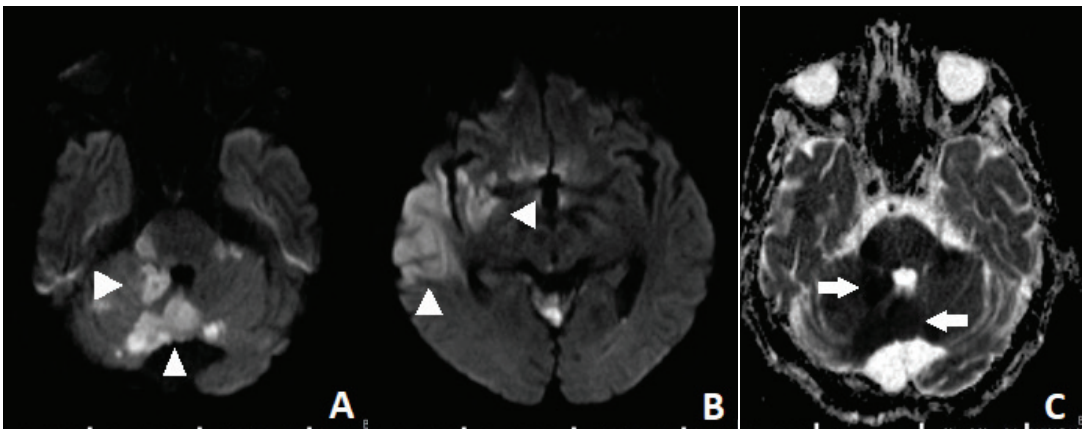

Figure 9. Acute Cerebral and Cerebellar Infarction

There are acute infarct areas (increased signal intensity on b:1000 diffusion images white arrowheads, **(A,B)**; decreased diffusion on ADC map, **(C)**, white arrows) in right cerebellar hemisphere, vermiş, pons, middle cerebellar peduncle, right temporal lobe, insular cortex, basal ganglia at the territory of superior cerebellar, basilarly and right middle cerebral artery. Multiple vascular territory suggests hypovolemia during long and complex surgery.

Central nervous system infections after organ transplant are not rare and are seen in 5% to 10% of patients and can occur secondary to immunosuppression of the host. Bacterial, fungal, viral, and parasitic infections may be seen. Bacterial CNS infections usually occur earlier than viral infections. Infections may be diffuse (meningitis, encephalomyelitis) or local as an abscess.[6,40,41] Meningitis usually occurs secondary to bacterial agents, such as *Nocardia* and *Listeria monocytogenes*. Leptomeningeal contrast enhancement is seen in patients with meningitis. Complications of CNS infections, including hydrocephalics and ventriculitis, are also shown by brain MRI. Various viruses may cause encephalitis, including cytomegalovirus, Epstein-Barr virus, herpes simples virus, human herpesvirus, and varicella zoster virus, and JC virus in immunosuppressed transplant patients.[6,40] In human herpesvirus-induced encephalitis, MRI shows hyperintense lesions on T2-weighted or FLAIR images of the medial temporal lobe involving the hippocampal formation and amygdala, classically with bilateral and symmetric involvement. This finding may be termed posttransplant acute limbic encephalitis.[42,43] Progressive multifocal leukoencephalopathy is a demyelinating disease of the CNS caused by JC virus reactivation in the presence of significant immunodeficiency. Magnetic resonance findings are typically localized to the subcortical white matter at the gray-white matter junction. However, enhancements are not usually seen and diffusion restriction may be shown.[6,44] Abscesses are usually nodular, corticomedullary located lesions and show ring enhancement and surrounding edema on brain CT or MRI (Figure 10). In patients with *Toxoplasma gondii* infections, MRI shows multiple mass lesions, mainly involving the basal ganglia. Lesions usually have regular ring enhancement, and some differences may be seen secondary to the immunosuppressive status of the patient. Tuberculosis usually locate at basal cisterns and may complicate with infarcts. *Aspergillus* species are the most common fungal agent responsible for brain abscesses. Solitary or multiple ring enhancing lesions are usually seen at the gray-white matter junction and are usually located in the frontoparietal region. Invasion of blood vessels may cause hemorrhagic lesions and infarcts[6,7,13-16,45] (Figure 11 and Figure 12).

Aspergillus spondylodiscitis is rare after transplant, but mortality is high; therefore, early diagnosis is important. About 1% to 15% of organ transplant recipients may present with aspergillus spondylodiscitis. Symptoms are usually silent, and radiologic findings are late, with findings mostly in the lumbar region. Discitis, vertebral involvement, and epidural abscesses may be seen. Differential diagnoses of the lesions can include tuberculosis and brucellosis osteomyelitis. In cases with vertebral involvement

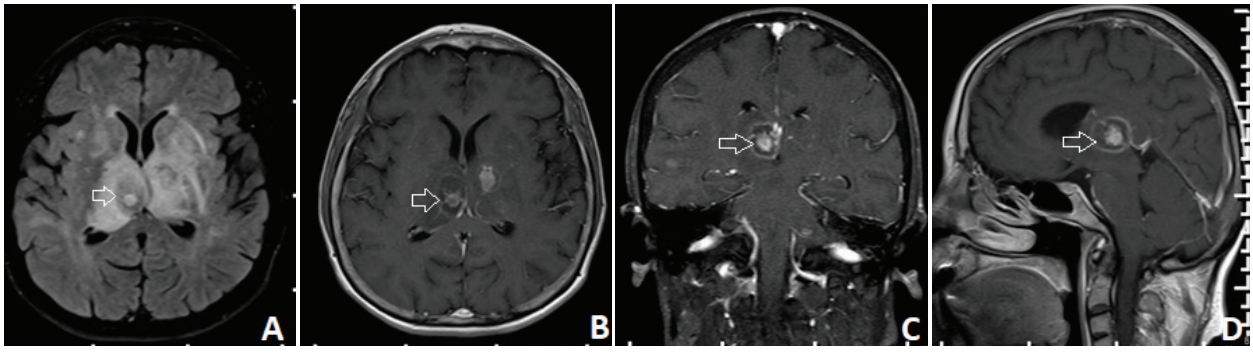

Figure 10. Brain Abscess

Brain magnetic resonance transverse FLAIR **(A)**, postcontrast transverse **(B)**, coronal **(C)**, and sagital **(D)**. Right thalamic ring is an enhancing lesion with central enhancement (open arrow in **B**, **C**, and **D**) and surrounding edema **(A)**. Additional left enhancing putaminal lesion accompanied periphal edema. Patient was 38-year-old renal transplant recipient with immunosuppression. Abscess usually locates at corticomedullary junction but is located in the deep gray matter in this particular case with suspicion for toxoplasmosis.

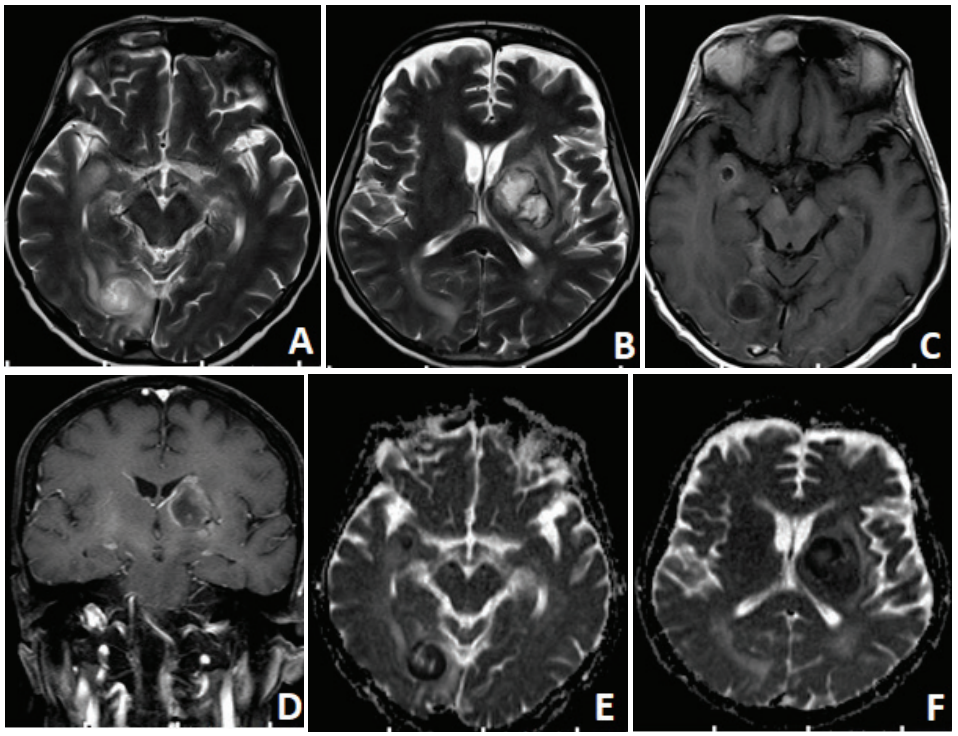

Figure 11. Aspergillus Abscess

Brain magnetic resonance images of 61-year-old patient. **(A)** and **(B)** Transverse TSE-T2-weighted. **(C)** Postcontrast transverse TSE-T1-weighted. **(D)** Coronal fat-supressed T1 weighted. Images show right occipital, right temporal, and left basal ganglia lesions enhancing after contrast injection. Transvers ADC maps **(E** and **(F)** demonstrate heavy diffusion restriction, implying presence of hemorrhage in right occipital, right temporal, and left basal ganglia.

of aspergillus spondylodiscitis, end-plate irregularities, serrated vertebral rims, and skipped lesions are seen without severe vertebral body destruction. Vertebral end plates may demonstrate subchondral T2 hypointense bands on T2-weighted images secondary to paramagnetism and ferromagnetic effects of fungus[12,13] (Figure 12). Rhinocerebral mucormycosis can involve paranasal sinuses and orbita and is usually hypointense on T1-weighted images; fungal elements tend to have low signals on T2. About 20% of patients may show increased signal. Unenhanced areas in the nasal cavity are defined as "black turbinate sign"[46,47] (Figure 13).

After solid-organ transplant, patients have 3 to 4 times more risk of CNS tumors. Pediatric transplant recipients are usually at higher risk. Occurrences are usually secondary to long-term immunosuppression, and a high incidence of infections involve oncogenic viruses. Cancer in transplant recipients may also originate from preexisting tumors in the donor organ. The most common CNS tumors are glioma and lymphoma after transplant[6,48-50] (Figures 14, 15, and 16). Posttransplant lymphoproliferative disorder may be seen up to 5% of patients. Heavy immunosuppression increases the risk of PTLD, with PTLD seen in 1% of renal transplant and in 3% of liver transplant recipients. Most cases of CNS PTDL are in kidney transplant recipients. Epstein-Barr virus and as a cofactor cytomegalovirus are risk factors. Brain MRI can show multiple nodular homogeneous enhancing lesions in periventricular white matter and basal ganglia[6,51-54] (Figure 17).

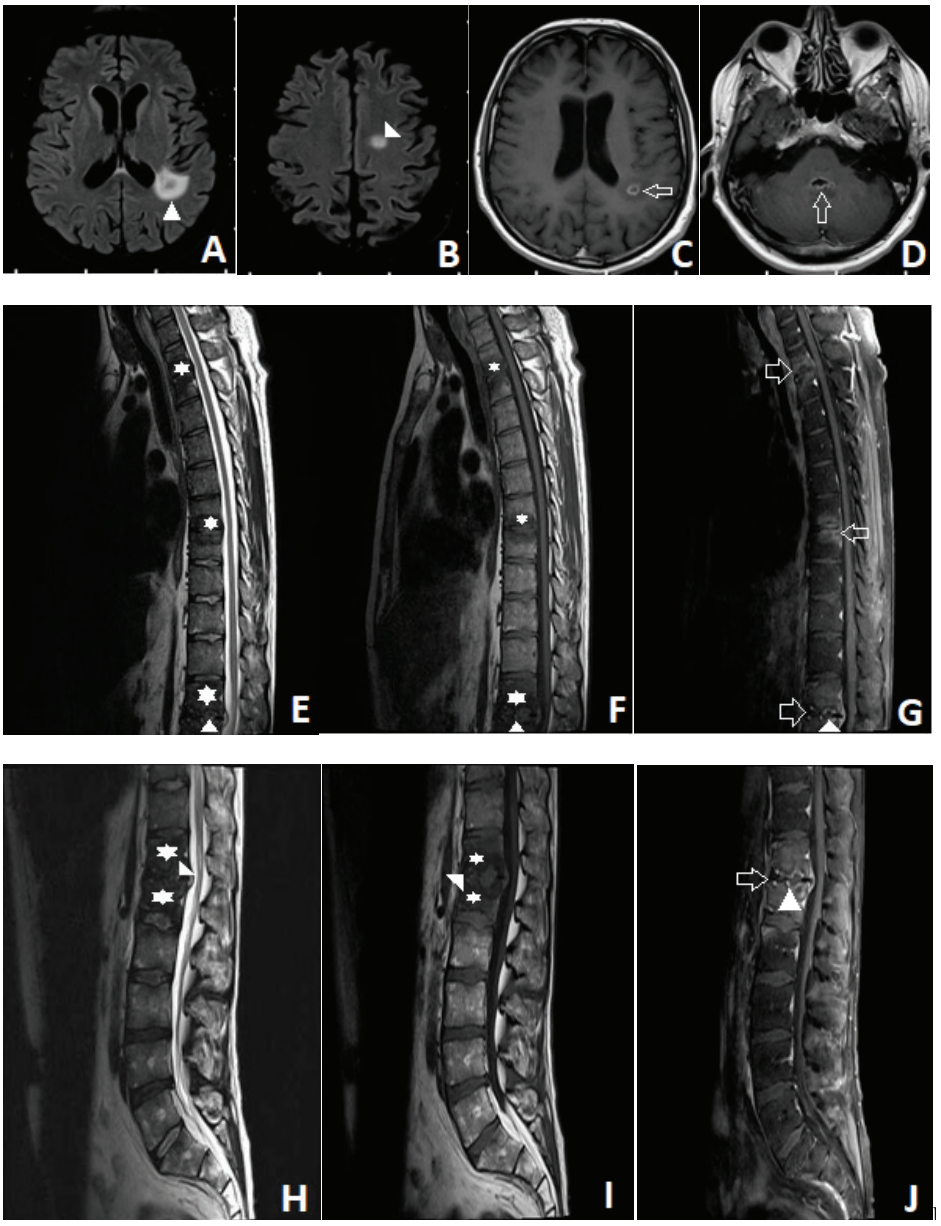

Figure 12. Aspergillus Abscess and Spondylodiscitis

Upper brain magnetic resonance images of 46-year-old male liver transplant recipients. Left sided 2 foci of abscess (white arrowheads), with one next to lateral ventricule, are shown in **(A)** and **(B)** (FLAIR images) and show ring enhancement (open arrow in **(C)**, postcontrast T1-weighted image). Contrast enhancement of fourth ventricule wall was consistent with ventriculitis (open arrow in **(D)**, postcontrast T1-weighted image), with slight hydrocephalus secondary to ventriculitis. Middle and lower raw thoracal and lumbar magnetic resonance images demonsrate Th2-3, Th7-8, and Th12-L1 vertebral body lesions with edema, inflammation (asterisks), contrast enhancement (open arrows) and serration of endplates (white arrowheads). Sagital thoracal **(E)** and lumbar **(H)** spine TSE-T2-weighted, sagital thoracal **(F)** and lumbar **(I)** spine TSE-T1-weighted, and sagital thoracal **(G)** and lumbar **(J)** spine postcontrast fat-supressed TSE-T1-weighted images.

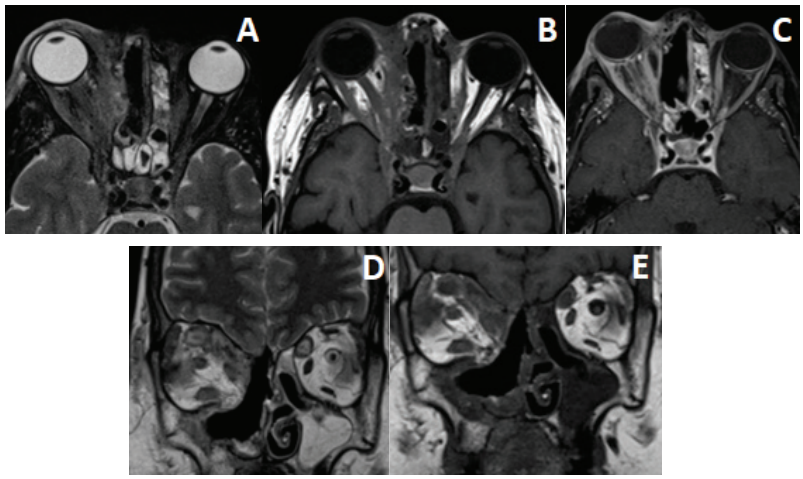

Figure 13. Rhinocerebral Mucormycosis

Orbita magnetic resonance images in 26-year-old renal transplant recipient shows mucosal thickening and fluid retantion of the ethmoid cellulary at the left side with surgical changes in the right. Soft tissue mass extends from ethmoidal wall to the right orbital fat tissue more prominent medially, dirtiness of fat and contrast enhancement. **(A)** Transverse TSE-T2-weighted. **(B)** TSE-T1-weighted. **(C)** Postcontrast FS-T1-weighted. **(D)** Precontrast coronal TSE-T2-weighted. **(E)** precontrast coronal TSE-T1-weighted.

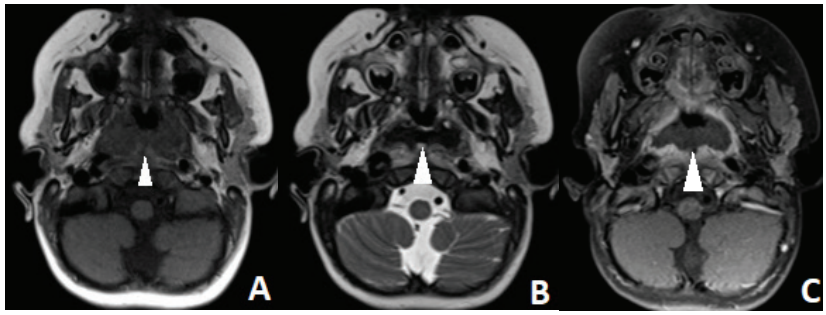

Figure 14. Nasopharyngeal Lymphoma

Magnetic resonance imaging of nasopharyngeal region shows results in 4 year-old patient after liver transplant.MRI of nasopharynx. **(A)** Transverse T1. **(B)** Transverse TSE-T2. **(C)** Postcontrast transverse fat-supressed T1-weighted images. Image in B show hypointense mass in nasopharynx (arrowhead), which is typical feature of lymphoma secondary to increased nucleus-to-cytoplasm ratio. Diagnosis was later proven as lymphoma by biopsy. Lesion demonstrates peripheral enhancement after contrast injection (arrowhead in **C**).

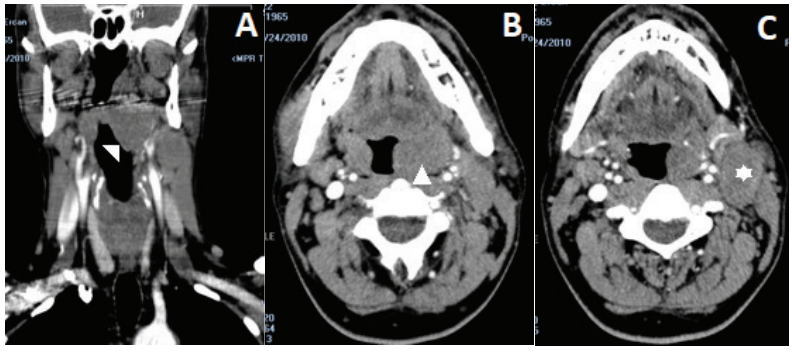

Figure 15. Computed Tomgraphy of Diffuse B-Cell Tonsillar Lymphoma

Images of neck region after contrast enhancement, showing coronal **(A)** and transverse **(B)** and **(C)** images, demonsrating left tonsillar asymmetrical mass (arrowheads), suggesting lymphoma in nasopharengeal wall **(A)** and **(B)** and left level 2 lympadenomegaly (asterisk) between submandibular gland, carotid space, and sternocleidomastoid muscle **(C)**. Biopsy resulted in diagnosis of diffuse B-cell tonsillar lymphoma.

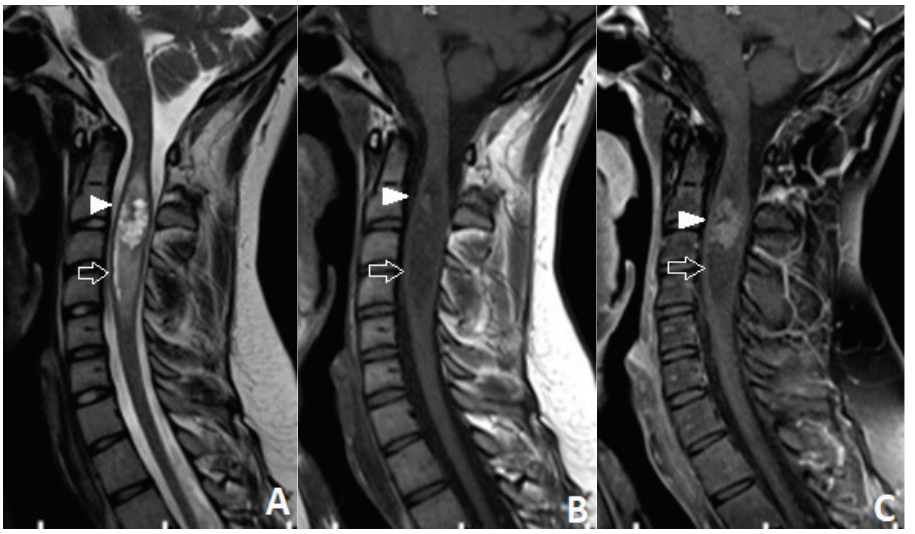

Figure 16. Magnetic Resonance Images of Cervical Spinal Cord Epandymoma

Cervical-sagittal TSE-T2 **(A)**, sagittal TSE-T1 **(B)**, and postcontrast sagittal fat-supressed T1 weighted images **(C)** demonstrate cervical cord expansile C2-4 mass lesion with solid component cranially (arrowhead) and cystic component caudally (open arrow). Patient was a 21-year-old renal transplant recipient who was surgically treated by surgical resection.

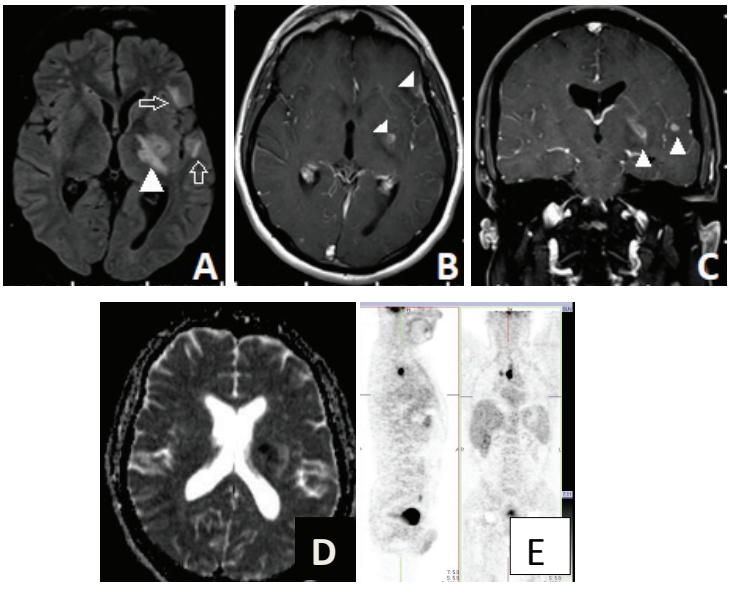

Figure 17. Posttransplant Lymphoproliferative Disease

Abbreviations: MR, magnetic resonance; PET-CT, positron emission tomography-computed tomography

Brain MR in patient after renal transplant with neurologic symptoms demonsrates lesions in left basal ganglia (arrowhead) and fronto-temporal subcortical area (open arrows) on FLAIR **(A)** and postcontrast transverse **(B)** and coronal **(C)** images with enhancement (arrowheads). **(D)** Diffusion restriction on ADC map in basal ganglia and subcortical lesion. **(E)** Whole body PET-CT shows mediastinal lymph nodes with 18F-FDG increased activity.

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Diagnostic and Interventional Radiology in Liver & Kidney Transplantation

PART II

Computed Tomography and Magnetic Resonance Imaging of Liver Transplant Complications

Mehmet Coşkun

Orthotopic liver transplantation (OLT) has become the treatment of choice for patients with end-stage acute or chronic hepatic disease. Over the past several decades, advances in surgical techniques, organ preservation, immunosuppressive therapy, and early detection methods for postoperative complications have increased survival rates after liver transplant. Early detection of postoperative complications is essential for graft and patient survival. Graft loss is a serious problem because of the complexity of the surgical procedures and the shortage of livers available for transplant. Clinical signs of complications are often nonspecific, and diagnoses are frequently based on imaging findings.

Ultrasonography (US) is the preferred postoperative screening method because it is cost-effective, accessible, noninvasive, and easily performed at the bedside. However, the method has inherent limitations that are well known; when US findings are inconclusive, imaging with other modalities is necessary. Cross-sectional imaging methods, such as computed tomography (CT) and magnetic resonance (MR) imaging, have greater overall sensitivity and specificity than US.[1]

COMPUTED TOMOGRAPHY

Computed tomography is a second-line imaging technique that is generally used to confirm or exclude clinical suspicious and/or US findings. The introduction to the clinical practice of multidetector CT (MDCT) has allowed for the acquisition of the whole volume of the abdomen, pelvis, and possibly also the thorax in a few seconds with a high spatial and temporal resolution, thus enabling the incorporation of both angiographic and parenchymal studies into a single acquisition. This ability is an advantage in obtaining a rapid diagnosis and has a better image quality in critical and less cooperative patients. Computed tomography has shown very high sensitivity (100%), specificity (89%), and diagnostic accuracy (93%) in the evaluation of vascular complications compared with digital angiography.[2-4]

Multidetector CT angiography (MDCTA) with maximum intensity projection (MIP) and volume-rendered images give a rapid, accurate depiction of hepatic arterial anatomy after OLT. Thus, this modality allows accurate detection of hepatic artery stenosis (HAS) or hepatic artery thrombosis (HAT). The excellent spatial resolution and fast scan times with a multislice scanner allow CT angiography to depict small vessels.[5]

In Boraschi and Donati's series of 27 patients prospectively evaluated after liver transplant, volume-rendered 3-dimensional (3D) MDCTA demonstrated a sensitivity of 100%, a specificity of 89%, and an accuracy of 93% for detection of hepatic artery complications.[3]

MAGNETIC RESONANCE IMAGING

Magnetic resonance imaging combined with MR cholangiography (MRC) and MR angiography (MRA) can be an effective diagnostic method in the postoperative work-up of a patient who has undergone liver transplant. These methods provide a more comprehensive evaluation of the transplanted liver. They can also reveal abnormalities of vascular structure and depict bile ducts, liver parenchyma, and extrahepatic tissues. An important advantage of MR imaging is the low toxicity of its contrast agents; hence, MRA can be used particularly in patients with renal insufficiency. The amount of radiation exposure associated with an imaging technique must be considered, particularly in young patients when selecting an imaging modality for a patient who has undergone liver transplant.[6]

A growing body of literature supports the accuracy of 3D MRA compared with that of conventional angiography. There has been good agreement between conventional angiography and gadolinium-enhanced 3D MRA for the depiction of arterial and venous abnormalities despite some limitations in small intrahepatic arteries. Magnetic resonance angiography shows a higher sensitivity and accuracy than conventional angiography for the detection of thrombosis or the assessment of vessel patency in any part of the portal venous system.[7] For HAS, Kim and associates found that the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of MRA were 100%, 74%, 29%, 100%, and 77%, respectively.[6]

Magnetic resonance, which is performed with high-field magnets (1.5 or 3.0 T), is the preferred noninvasive modality for investigating biliary complications. Moreover, the MRC technique is also required; it enables a detailed portrayal of the bile ducts, which appear as markedly hyperintense structures. Magnetic resonance cholangiography can depict the biliary system without direct contrast injection in contrast to direct cholangiography procedures. Alternatively, the biliary tree should be visualized by using MR hepatobiliary contrast agents.[8,9]

NORMAL COMPUTED TOMOGRAPHY AND MAGNETIC RESONANCE IMAGING FINDINGS AFTER LIVER TRANSPLANT

Transplantation implies the interruption of normal lymphatic drainage causing lymphedema. In the immediate postoperative period, lymphedema manifests small reactive lymph nodes in the porta hepatis and portocaval space and, more importantly, as periportal edema. Periportal edema is better appreciated on CT (Figure 1), and MR images presenting as a periportal collar of fluid attenuation or high-signal intensity on T2- or diffusion-weighted images should not be interpreted as a sign of acute rejection.[10,11]

Right-sided pleural effusion, ascites, or free fluid in the perihepatic region or intersegmental fissure can be seen. In addition, small fluid collections and/or hematomas can be found in the right subhepatic space, as well as along the parenchymal resection margin after split-liver-OLT and living-donor liver transplant (LDLT).[12]

With regard to bile ducts, mild anastomotic narrowing is a frequent cholangiographic and MRC finding that should be interpreted as normal unless

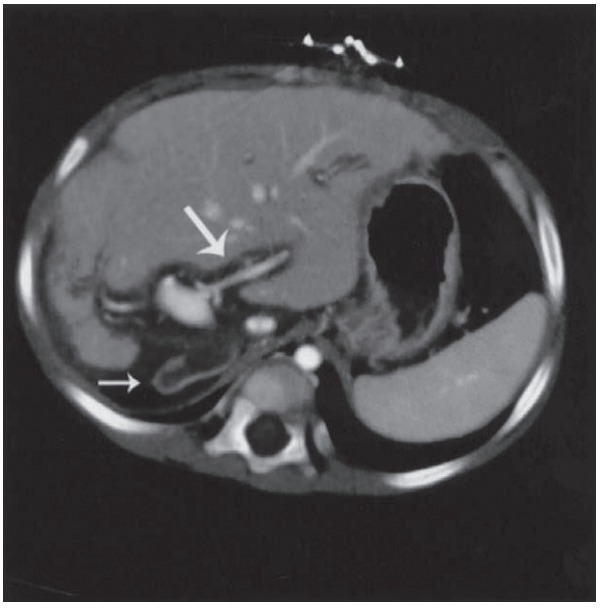

Figure 1. Periportal Edema Defined in Patient After Liver Transplant

biliary dilatation upstream and symptoms of biliary origin are present. In most cases, anastomotic narrowing is the effect of surrounding edema, resolving during the first week after OLT.[13]

VASCULAR COMPLICATIONS

Hepatic artery complications

Arterial complications are still a major source of morbidity and mortality after OLT. The hepatic artery plays a major physiological role because it provides the blood supply for both the liver parenchyma and the biliary tree. The etiology underlying most hepatic artery complications involve the anastomosis, including (1) HAT (the most frequent and pejorative), (2) HAS, (3) hepatic artery pseudoaneurysm, and (4) hepatic artery rupture.[1]

Kayahan Ulu and colleagues[5] detected hepatic artery complications with MDCTA in 38 liver transplant recipients. Of these, 15 had early complications and 23 had late complications. The overall sensitivity of MDCTA to detect hepatic artery complications was 100%, specificity was 87.5%, positive predictive value was 96.6%, and negative predictive value was 100%. The most common early complications were thrombosis (66.6%) and stenosis (26.6%). The most common late complications were stenosis (56.5%) and thrombosis.

Hepatic artery stenosis

Significant HAS is usually defined as a narrowing of the transverse diameter of > 50% on angiogram.[1] The incidence of HAS is about 2% to 11% in transplant recipients, and it occurs often at the anastomotic site (Figure 2). It usually results from clamp injury, intimal trauma caused by perfusion catheters at the time of surgery, or disrupted vasa vasorum, leading to ischemia of the arterial ends.[4] Many patients with HAS are asymptomatic, most commonly presenting with only abnormal liver function tests. Most asymptomatic patients are detected during routine Doppler US (DUS) screening.[1]

Doppler US is a well-established noninvasive method for the assessment of hepatic artery patency, and its efficiency in the early diagnosis of HAS has been reported in several studies. In early HAS diagnosis, DUS has shown a sensitivity of 100%, a specificity of 99.5%, a positive predictive value of 95%,a negative predictive value of 100%, and an overall accuracy of 99.5%.[14]

On CT, HAS is detectable as a filling defect within the hepatic artery during the arterial phase.[4] The use of MDCTA plus standard angiography can confirm the diagnosis, which is the criterion standard for

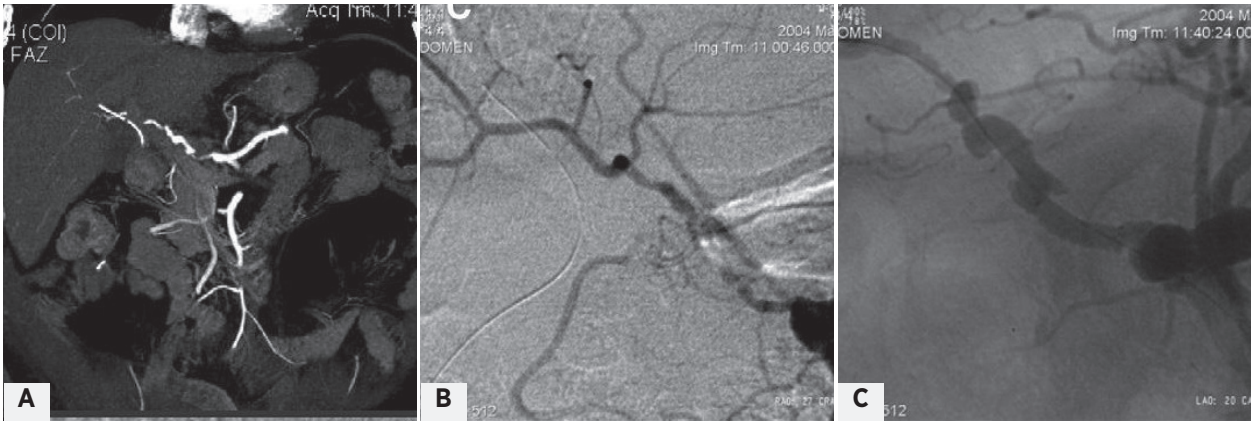

Figure 2. Hepatic Artery Imaging

(A) Coronal maximum intensity projection images show severe stenosis in the proximal portion of the hepatic artery in a 49-year-old deceased-donor recipient. **(B)** Conventional angiography confirmed severe stenosis at the anastomosis, as demonstrated on multidetector computed tomography angiography. **(C)** Conventional angiography after balloon angioplasty and stent placement, demonstrating almost normal patency of the hepatic artery at this site.

HAS diagnosis.[1] Volume rendering technique in CT angiography is a more accurate, better, and more useful noninvasive technique for detecting vascular complications in liver transplant recipients than MIP and shaded surface display techniques.[15]Bong Soo Kim and colleagues indicated that MRA tends to overestimate HAS.[6]

In a study of 33 liver transplant recipients, Ishigami and associates found that contrast-enhanced MR imaging had a sensitivity of 67% and specificity of 90% in predicting HAS greater than 50% or HAT, although it led to an overestimation of the severity of arterial stenosis in 15% of cases and to its underestimation in 25% of cases.[16] Digital subtraction angiography is the criterion standard for the diagnosis of vascular complications and allows a concomitant intervention procedure.[5]

Hepatic artery thrombosis

Hepatic artery thrombosis represents more than 50% of all arterial complications. It is the most frequent and severe vascular complication after OLT and is more frequent after pediatric liver transplant. Hepatic artery thrombosis is associated with a high incidence of liver transplant failure (more than 50%) and carries a mortality of more than 50% in the absence of revascularization or retransplant.[1]

The incidence of early HAT is approximately 5%, and it is a major cause of graft loss (53.1%) and mortality (33.3%) in the early postoperative period. Late HAT is associated with chronic rejection and sepsis. Hepatic artery thrombosis has a devastating effect on the biliary epithelium, inducing ischemia and necrosis. Symptoms, signs, and abnormal laboratory values are initially absent in early HAT; therefore, routine DUS screening is important.[17]

Doppler US is a proven noninvasive technique and is the criterion standard investigation to assess hepatic artery patency. It detects the absence of hepatic artery flow, even in its intrahepatic branches. The DUS diagnosis comprises the lack of hepatic artery signal (Se = 92%) or an increased resistive index.[18]

In the case of a suspicious or inclusive DUS, MDCTA or MRA investigations are required to confirm HAT. Thrombus appears as a filling defect within the hepatic artery or hepatic artery amputation (Figure 3), associated with intrahepatic infarction areas, bilomas, or abscesses and signs of biliary obstruction in the case of biliary strictures.[12]

Computed tomography angiography using MDCT provides for a good depiction of small vessels, such as

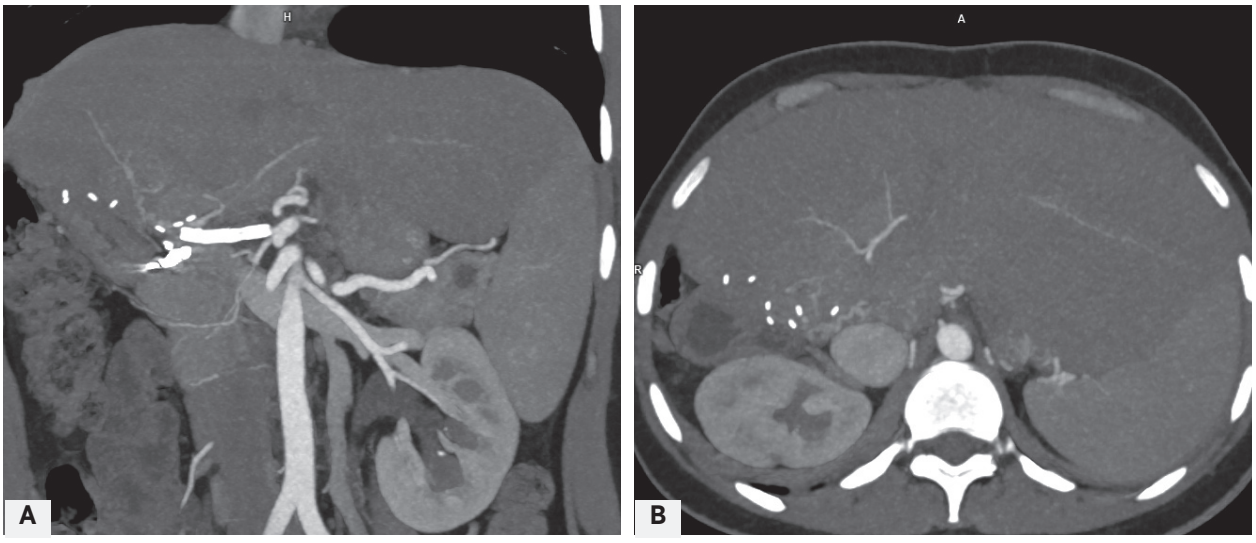

Figure 3. (A, B) Coronal and Axial Maximum Intensity Projection Computed Tomography Images Showing Occlusion of Hepatic Artery at Anastomotic Site, With Many Small-Caliber Collaterals Filling the Intraparenchymal Hepatic Artery Branches

the hepatic artery and its thrombosis. Acute HAT can appear as high-density narrowing on unenhanced scans.[4] Computed tomography angiography is the best technique to further evaluate difficult cases due to its high accuracy, short examination time, and facility to be performed with poor patient condition. Magnetic resonance imaging can have a diagnostic accuracy similar to US, whereas CT angiography is equivalent or even better.[19] Vogl and colleagues compared digital subtraction angiography and CT in the detection of HAT in 24 liver transplant recipients and found CT to have 89% sensitivity and 100% specificity.[20] Legmann and associates found a sensitivity of 100% for CTA with maximum intensity projection in the detection of HAT.[21]

Gadolinium-enhanced MR imaging is another accurate and noninvasive method for evaluating the hepatic vessels. Good agreement has been shown between findings with angiography and those with gadolinium-enhanced MR imaging for the detection of arterial abnormalities. Magnetic resonance imaging allows evaluation of the liver parenchyma and the hepatic vessels.[1]

In a study of 110 liver transplant recipients, contrast-enhanced CT was found to have a sensitivity of 100% and specificity of 87.5% for detecting arterial complications. The sensitivity of contrast-enhanced MR imaging for this purpose was found to be 86%. In addition, contrast-enhanced CT or contrast-enhanced MR imaging can be used to assess graft perfusion. Nonenhancement of the transplant is consistent with complete graft necrosis, whereas segmental necrosis may manifest regional areas of nonenhancement.[3,5]Digital subtraction angiography is usually reserved for interventional procedures when indicated by clinical conditions and cross-sectional imaging findings.[12]

Hepatic artery pseudoaneurysm

Hepatic artery pseudoaneurysm is defined as a dilated hepatic artery that occurs after iatrogenic injury in most cases, causing blood to leak and pool outside the artery wall into the surrounding tissue with a persistent communication between the hepatic artery and the resultant adjacent cavity. This is a very unusual event, with a reported incidence of 0.27% to 3%. In fact, most hepatic artery pseudoaneurysm occurrences are during the early postoperative period at around 1 month after OLT, with 69% of occurrences shown to present within 20 days and 81% within 35 days after OLT.[1] Lesion confirmation is obtained by MDCTA (Figure 4) or MRA, which depicts contrast distribution within the lesion similar to that of arterial vessels.[3,5-12]

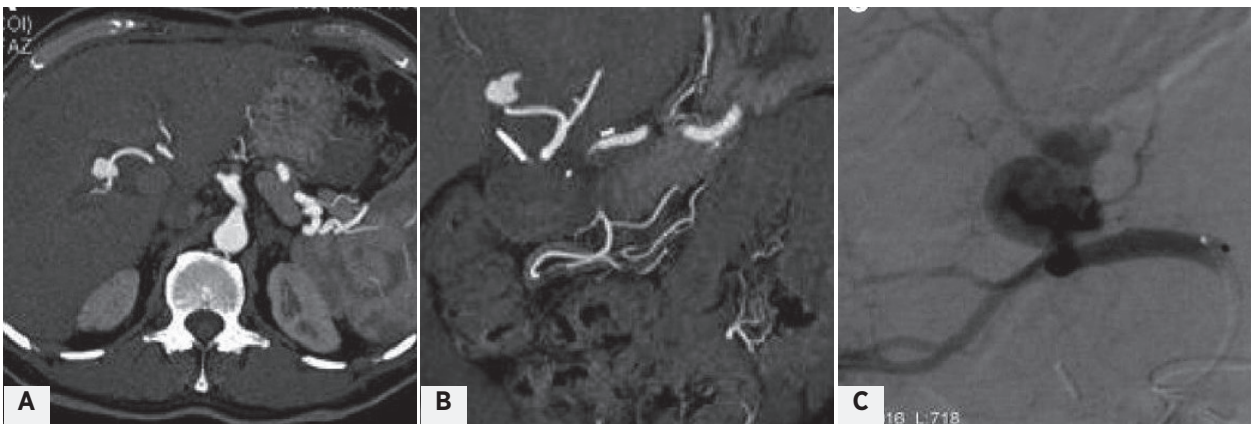

Figure 4. Pseudoaneurysm

(A) and **(B)** Axial and coronal maximum intensity projection images showing pseudoaneurysm in the distal portion of the hepatic artery in a 57-year-old male deceased-donor liver transplant recipient. **(C)** Conventional angiography confirmed the multidetector computed tomography angiography findings.

Intrahepatic arterioportal fistula can also occur secondary to liver biopsy. Arterioportal fistula may be seen at up to 50% of posttransplant biopsies performed in the first week, decreasing to 10% of biopsies performed in subsequent weeks. Computed tomography findings include early arterial phase enhancement of peripheral portal veins and of the corresponding wedge-shaped region of liver parenchyma that is supplied.[22,23]

Hepatic artery rupture

Hepatic artery rupture is defined as a severe hemorrhage from the trunk or from a main branch of the hepatic artery (Figure 5). It is a serious complication that results in the disruption of the arterial blood supply of the transplant. This is an exceptional but a dramatic complication after OLT that has a high incidence of liver transplant loss and high mortality rate. The incidence of hepatic artery rupture has been reported to be 0.64%, with clinical presentation always a sudden hemorrhage.[1]

HEPATIC VEIN AND INFERIOR VENA CAVA COMPLICATIONS

There are several anastomotic options for the inferior vena cava (IVC) in OLT. Anastomosis of the donor and recipient IVCs can be performed with end-to-end or the "piggyback" technique. With LDLT, the donor hepatic vein is anastomosed to the recipient's IVC. It is helpful to know the type of anastomosis because stenosis may occur at the anastomotic site. Complications include IVC stenosis and thrombosis, as well as hepatic vein stenosis and thrombosis, which altogether occur in only 1% to 2% of transplant procedures.[24]

Hepatic venous stenosis is specific to LDLT, with an incidence of 2% to 4%.[25] Technical factors, such as a size discrepancy between donor and recipient vessels or suprahepatic caval kinking from organ rotation, may cause acute IVC stenosis. Delayed caval stenosis may be secondary to fibrosis, a chronic thrombus, or neointimal hyperplasia. Chronic caval stenoses are more common after retransplant and in children.[1] Clinical presentation

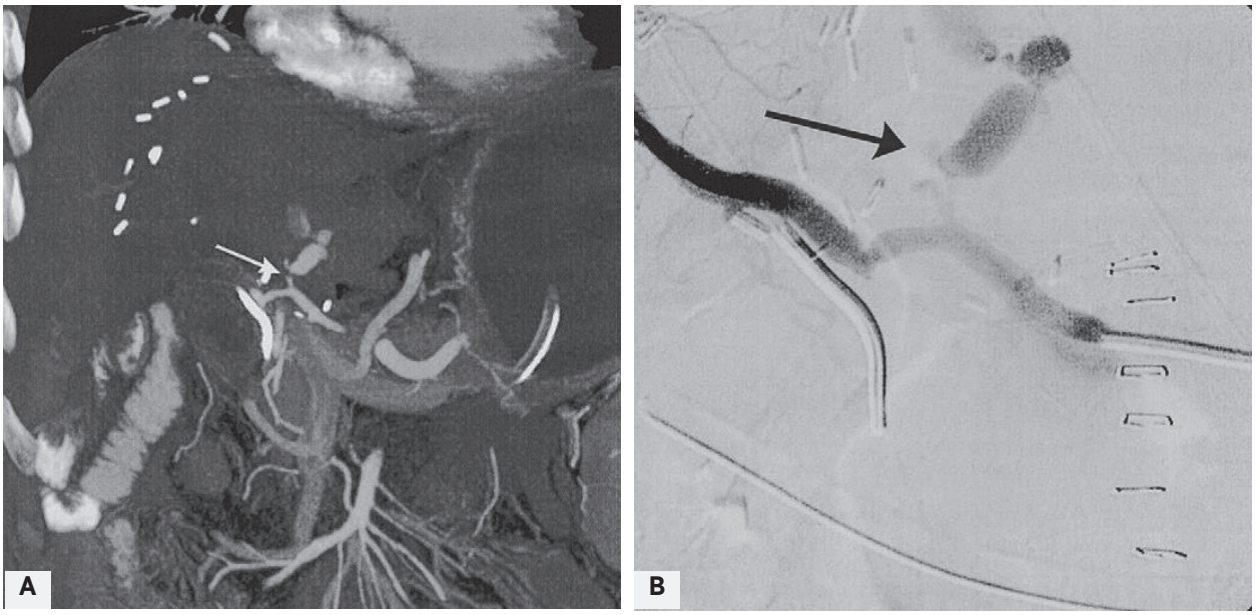

Figure 5. Hepatic Artery Rupture

(A) Coronal maximum intensity projection image from 49-year-old male liver transplant recipient demonstrating extravasation of contrast media superiorly from the transplant hepatic artery (arrow). **(B)** Selective arteriogram of the hepatic artery shows active bleeding at the same localization (arrow).

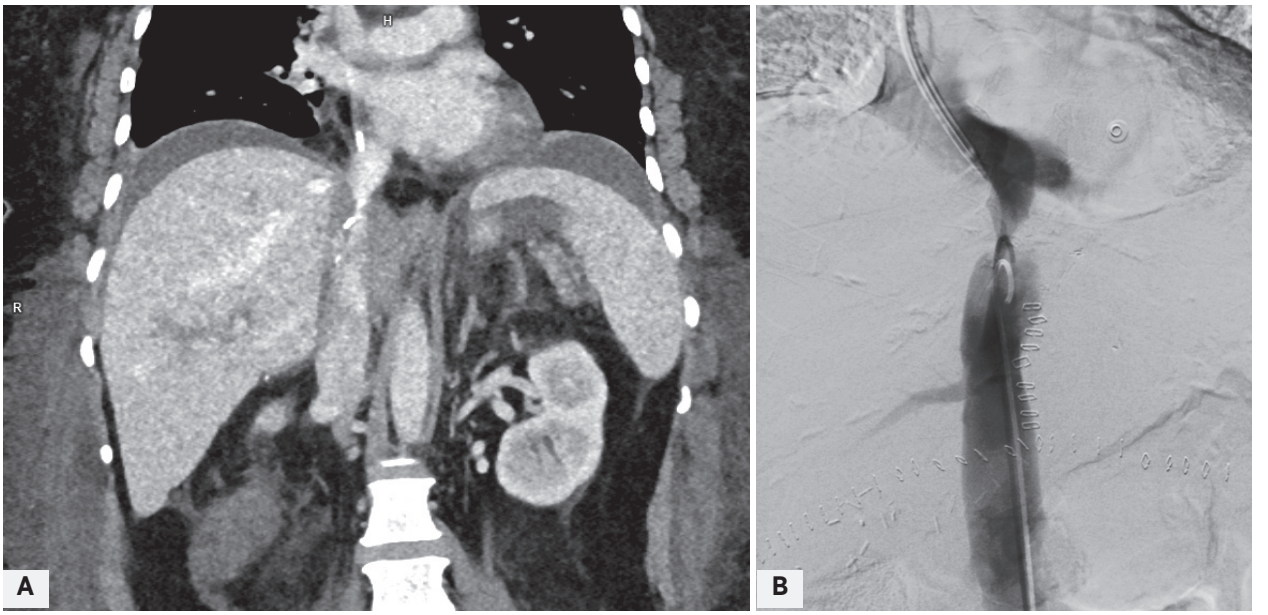

Figure 6. (A, B) Coronal MPR Computed Tomography Image and Venacavography Showing Prominent Narrowing at the Anastomotic Site of Deceased-Donor Liver Transplant Recipient

ranges from lower limb edema, hepatomegaly, ascites, pleural effusions, Budd-Chiari syndrome, and liver and renal failure to hypotension leading to allograft loss and multiorgan failure.[24]

Cross-sectional modalities, such as CT and MR imaging, are commonly used to confirm suspicions aroused by DUS findings or to exclude a clinical hypothesis when US results are normal or inconclusive.[1] The use of MDCT and MR imaging with sagittal and coronal reformation can provide a panoramic representation of IVC and hepatic veins, and these techniques are essential in defining the site and the extent of stenosis (Figures 6, 7, 8, and 9) and thrombosis. These results are used together with secondary findings, including hepatic vein distention, hepatomegaly, ascites, and signs of Budd-Chiari syndrome (liver mosaic pattern perfusion) and portal hypertension.[12]

PORTAL VEIN COMPLICATIONS

The incidence of portal vein complications after liver transplant is relatively uncommon, occurring in 1% to 3% of patients. These complications are associated with high morbidity and graft loss.

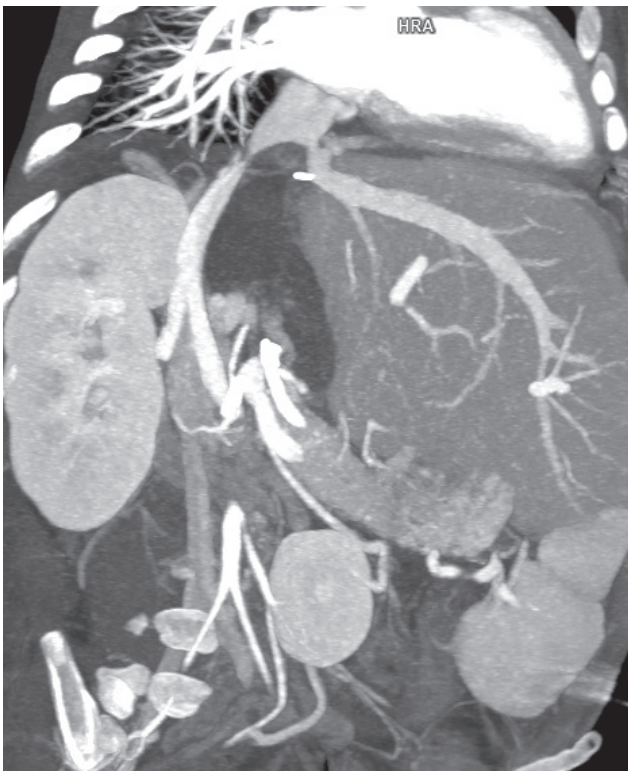

Figure 7. Multidetector Computed Tomography Coronal Plane Maximum Intensity Projection Image Showing Marked Narrowing at Hepatic Vein Anastomotic Site in Left-Lobe Lateral Segment Liver Transplant Recipient

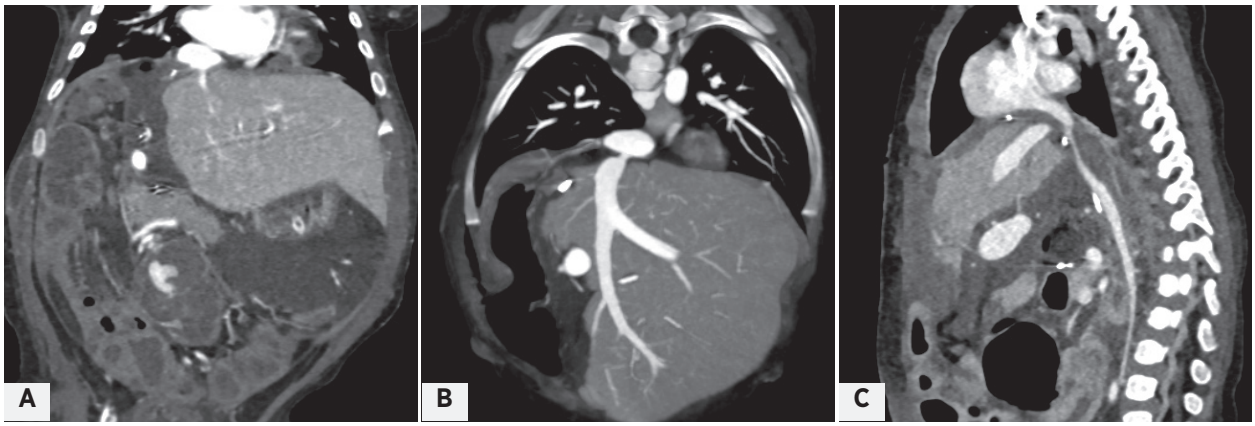

Figure 8. Inferior Vena Cava and Hepatic Vein Stenosis

(A) Contrast agent extravasation suggested high flow rate arterial bleeding from the jejunum after multidetector computed tomography procedure in left-lobe lateral segment liver transplant recipient after decrease in hemoglobin levels. **(B)** and **(C)** Patient also had significant stenosis in the hepatic vein anastomosis line and inferior vena cava.

Another important fact to mention is that portal vein complications are more common with split-liver and LDLT and in pediatric transplant procedures.[25] Clinically, the patient presents signs of portal hypertension, hepatic failure, massive ascites, or edema. Portal vein stenosis (PVS) is more common in pediatric liver transplants and is diagnosed when the PVS at the anastomotic site is > 125 cm/s or the anastomotic-to-preanastomotic velocity ratio is 3:1.[25]

Portal vein stenosis

In practice, most patients with PVS are asymptomatic, and the diagnosis of stenosis is an incidental finding detected on routine screening US.[25] Portal vein stenosis usually occurs at the anastomosis, and long-segment stenosis of the portal vein may also be seen. Portal vein stenosis has a reported incidence of 1% after liver transplant. Focal narrowing of the portal vein, usually at the anastomosis, may occur if there is a significant size discrepancy between the donor's and recipient's portal veins. This focal narrowing is not indicative of stenosis.[1]

Doppler US is sensitive to PVS, but it is not specific. The PVS criteria for diagnosis include portal caliber size and velocities at the anastomotic site and the pre-anastomotic and post-anastomotic gradients.[24]

Both CT angiography and MRA provide excellent depiction of filling defects and focal narrowing of the portal vein (Figures 9, 10, 11).[1] Contrast-enhanced MRA can provide excellent visualization of portal vein thrombosis and stenosis and can facilitate the distinction of thrombosis from slow flow.[25] Kim Bong Soo and colleagues reported that when narrowing (> 50%) of the portal vein was regarded as the diagnostic criterion for PVS, 100% sensitivity and 84% specificity were achieved. Magnetic resonance angiography clearly depicts the anastomotic narrowing of the portal vein. In addition, MRA may be performed to evaluate the extent and degree of the portosystemic collateral vessels resulting from portal hypertension. Results from Kim Bong Soo and colleagues showed high sensitivity and specificity in the detection of more than 50% of the PVS.[6]

Portal vein thrombosis

Portal vein thrombosis occurs in about 1% to 2% of cases.[1] and is usually seen within 1 month after liver transplant (with PVS being a late complication, that is, 6 months after liver transplant).[25] The clinical presentation depends on the time that the thrombosis occurs. When it occurs early, severe acute liver insufficiency or graft failure predominates.[24]

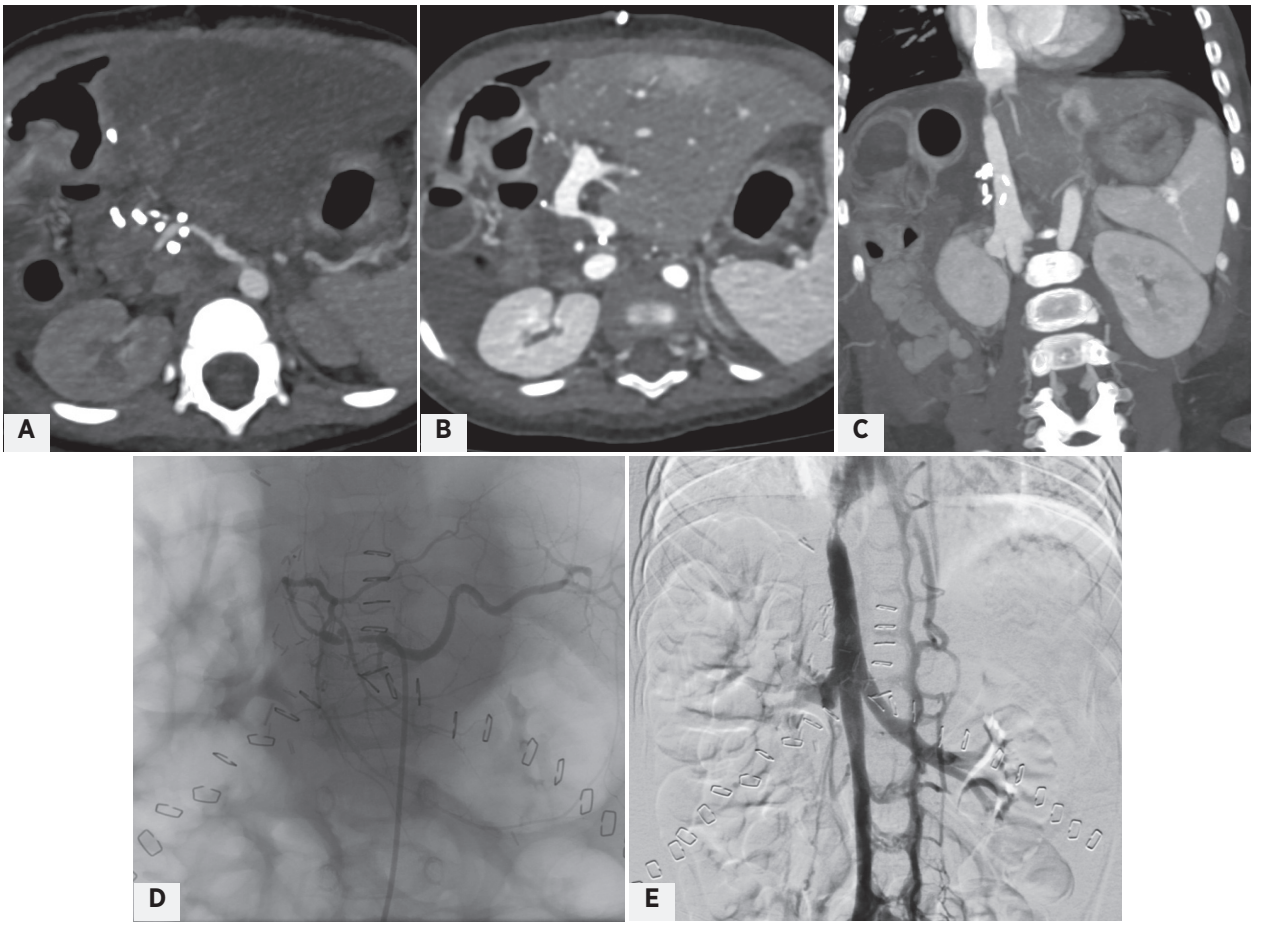

Figure 9. Hepatic Artery and Portal Vein Stenosis

(A-C) Routine postoperative ultrasonography control in patient with suspicious findings in terms of stenosis of the hepatic artery and portal vein. Marked narrowing was observed in the portal vein anastomosis and hepatic artery anastomosis. Computed tomography also showed marked stenosis in the inferior vena cava. **(D)** and **(E)** Stenosis in the hepatic artery and inferior vena cava was also confirmed by conventional angiography.

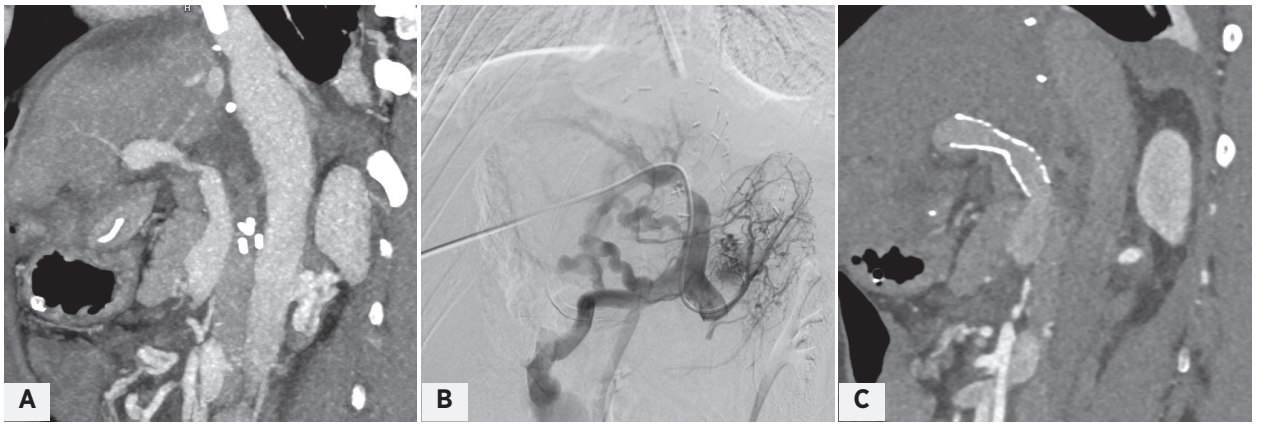

Figure 10. Portal Vein Stenosis

(A) Multidetector computed tomography in patient with increased velocity in the anastomosis line in the portal vein on ultrasonography, showing prominent narrowing at the anastomosis. **(B)** and **(C)** Stenosis was confirmed in angiography, and a metallic stent was applied to the narrow segment following balloon dilatation in the same session.

Doppler US should be the first imaging tool used and is easily employed to evaluate vascular patency. Doppler US allows, in most cases, for an immediate noninvasive diagnosis and provides a rapid evaluation of vascular flow patency.[24] When thrombosis occurs, an echogenic filling defect may be seen in the portal vein. Portal vein thrombus is seen as a filling defect in CT images (Figure 11). Occasionally, portal cavernoma may form with chronic portal vein thrombosis, and CT angiography and MRA are confirmatory.[25]

BILIARY COMPLICATIONS

Biliary complications occur in an estimated 25% of liver transplant recipients, usually within the first 3 months after transplant. These complications are the second most common cause of graft dysfunction (rejection is the most common). Biliary complications include stenosis, fistula, obstruction, stone formation, biloma (Figures 12 and 13), dysfunction of the Oddi sphincter, and recurrent biliary disease.[1] In a large study of 1792 OLT recipients,[23] biliary stricture occurred in 5%

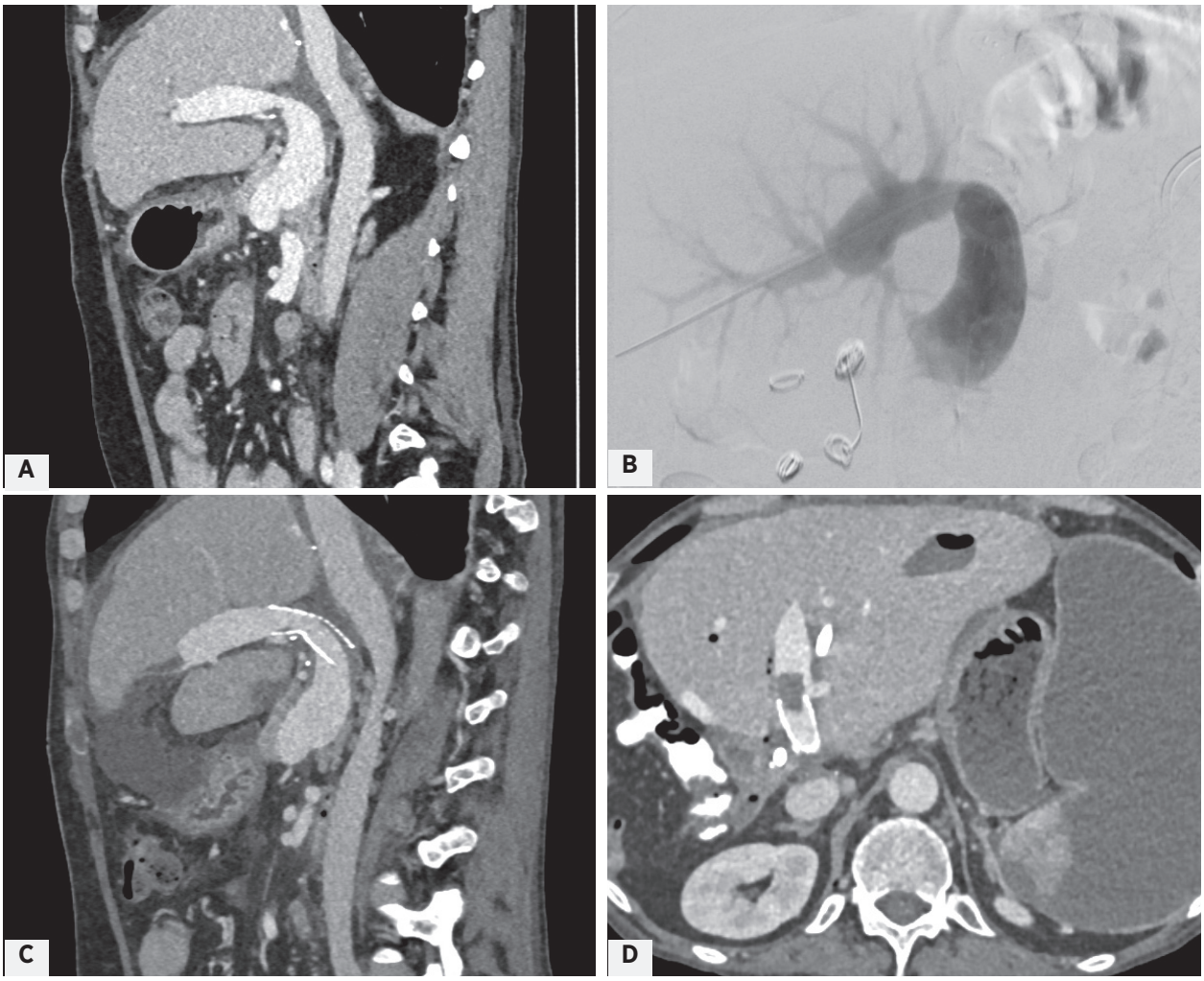

Figure 11. Portal Vein Thrombosis

(A-C) Metallic stent was placed in patient with anastomosis stenosis in the portal vein, which was detected on multidetector computed tomography confirmed by angiography. **(D)** After the procedure, partial thrombus developed in the portal vein, as detected by computed tomography.

of cases, bile leaks in 3%, ampullary dysfunction in 2%, and biliary obstruction in 1.6%.

Ultrasonography and T-tube cholangiography are the most often used imaging methods to evaluate the biliary tree in the first months after liver transplant. After the removal of biliary catheters, other imaging methods must be used; these may include MRC, endoscopic retrograde cholangiopancreatography (ERCP), and percutaneous transhepatic cholangiography.[1] Magnetic resonance cholangiography is the best noninvasive technique for the evaluation of the biliary tree. Although it does not provide a means of therapeutic intervention, it can

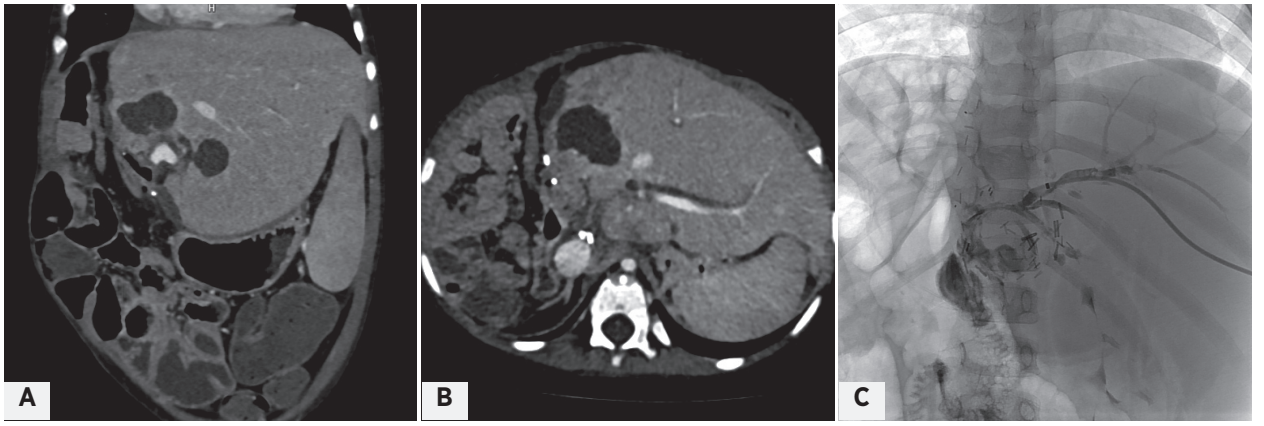

Figure 12. Biloma

(A) and **(B)** Along with mild dilatation in the intrahepatic biliary tract, axial and coronal multidetector computed tomography showed several biloma foci. **(C)** Leakage of contrast material from the dilated biliary tract into the biloma cavities was observed during percutaneous transhepatic cholangiography.

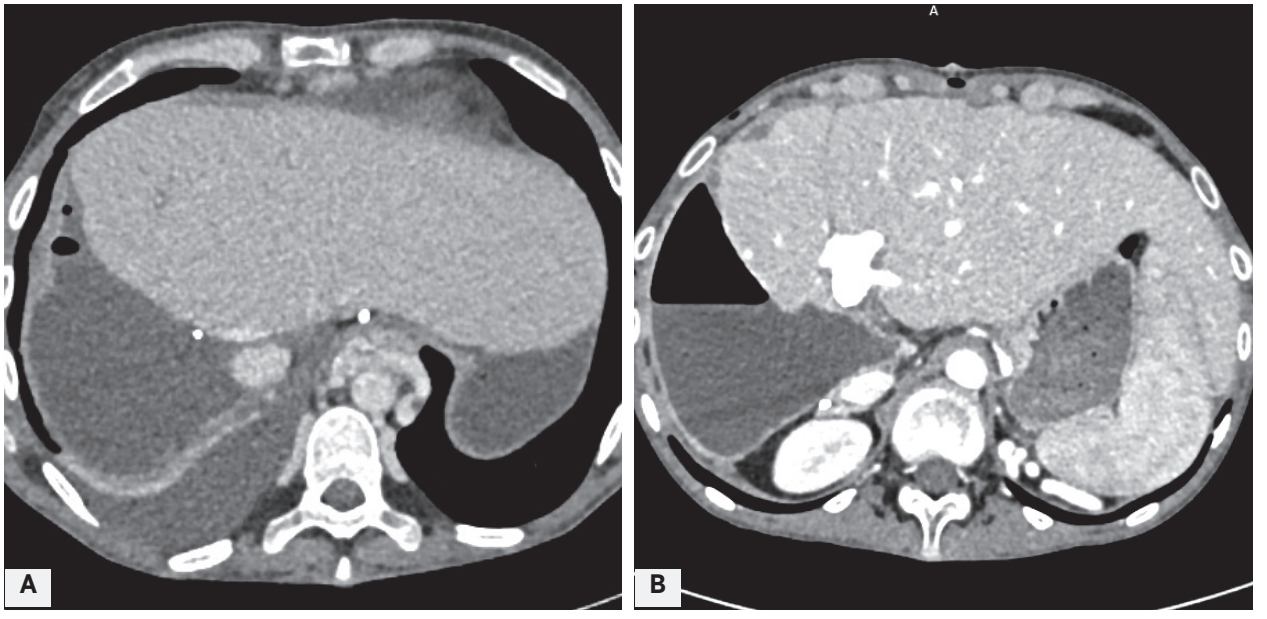

Figure 13. (A, B) Perihepatic Fluid Collection

Air in traced fluid collection in the right subdiaphragmatic region in multidetector computed tomography sections had increased over time. There was a prominent bile leak from the hepaticojejunostomy anastomosis line in the operation.

be used to plan percutaneous, endoscopic, and surgical treatments. Despite good sensitivity for the detection of strictures, MRC tends to lead to their overestimation.[1]

Biliary stricture

Strictures at the site of the biliary anastomosis and non-anastomotic sites are relatively frequent after liver transplant; these can occur in both duct-to-duct anastomosis and Roux-en-Y reconstruction. The reported incidence ranges from 0.6% to 17.6%. Most strictures occur within the first year after transplant, but they can be found many years after.[26] Rapid identification of stricture is important for ensuring the survival of both the organ and the patient after OLT.[4] Stricture at the anastomotic site is usually caused by fibrotic proliferation or, less commonly, by ischemia. Non-anastomotic strictures can occur because of HAT or without HAT.[25]

Ultrasonography is useful for detection of biliary dilatation, as an indirect sign of strictures.[26] Ultrasonography has a lower sensitivity (54%) for detecting biliary complications.[23] Hepatobiliary scintigraphy can be used; however, because of its rather low sensitivity, it has not gained routine use. Recently, well-conducted studies have indicated MR cholangiopancreatography (MRCP) as the noninvasive modality of choice for the diagnosis of biliary strictures.[26]

Magnetic resonance cholangiography is the best noninvasive tool to evaluate the number, site, and extent of strictures, during both the early and the late postoperative periods. Strictures appear as a tight, smoothly marginated focal zone of decreased signal intensity along bile ducts (Figures 14-18). Biliary dilatation upstream is common, although often delayed and less pronounced than expected, based on the degree of the stricture, possibly in relation to graft-related factors reducing bile ducts compliance.[12]

If there is a T tube in situ, T-tube cholangiography is preferable to MRCP because the distention of the bile ducts with contrast material permits better stricture analysis and functional assessment.[25]

In the study from Boraschi and colleagues,[27] the sensitivity, specificity, positive predictive value, and negative predictive value of the reviewers for the detection of all types of biliary complications in OLT recipients were 98%, 94%, 94%, and 98%, respectively. Direct cholangiography via an external drain, ERCP, and percutaneous transhepatic cholangiography (PTC) are the definitive investigations to diagnose strictures and are considered the criterion standard in most studies.[26]

Biliary leakage

Along with strictures, biliary leakage is the most encountered complication after transplant. The reported incidence rate ranges from 1.6% to 19%, with recent series reporting leakage in approximately 5% to 7% of transplants.[26]

Leakage after transplant can occur at different sites of the biliary system. Leakages from the site of anastomosis (Figure 13), the T-tube exit site, and the donor or recipient remnant cystic duct have been previously described. More diffuse leakage can occur from necrotic bile ducts (Figure 12) in the case of HAT. In cases of split-liver transplants or LDLT, bile can leak from the cut surface of the liver. Biliary leaks are suspected when there is a recent development of free fluid or intrahepatic/perihepatic fluid collection (biloma). Bile leaks usually occur within the first 3 postoperative months.[25]

Often, with biliary leakages, the first step will be a transabdominal US. Although the sensitivity and specificity of US has been questioned, some have claimed good results in excluding biliary complications. Hepatobiliary scintigraphy can be used as a next step. This test has reported sensitivity and specificity rates of 50% and 79% in detection of leaks.[26]

Although there is no formal criterion standard for diagnosis of biliary leaks, ERCP probably performs best. However, this approach is only possible in patients with a duct-duct anastomosis. In patients with Roux-en-Y hepaticojejunostomy, MRCP is the preferred technique.[26]

Imaging findings provided by cross-sectional modalities might be suggestive of biliary leakage in a proper clinical setting; they are frequently nonspecific, with a reported diagnostic accuracy ranging from 70% to 74%. Contrast-enhanced MRC with intravenous administration of hepatobiliary contrast agents can be extremely helpful in localizing the bile leak. Indeed, contrast-enhanced MRC, active biliary leakage can be demonstrated by visualizing contrast medium extravasation into the fluid collection, thus also allowing localization of the anatomic site of the bile leak. To confirm the presence of an active leak, invasive procedures, such as PTC or ERCP, should be finally performed to demonstrate contrast agent extravasation from the biliary system.[4]

Biliary sludge or stone

Sludge is a thick collection of mucus, calcium bilirubinate, and cholesterol. When left untreated, biliary casts can develop. Rates of incidences can range from 1.6% to 18%. Together, stones, sludge, and casts are also called bile duct filling defects. Sludge and casts tend to occur within the first year

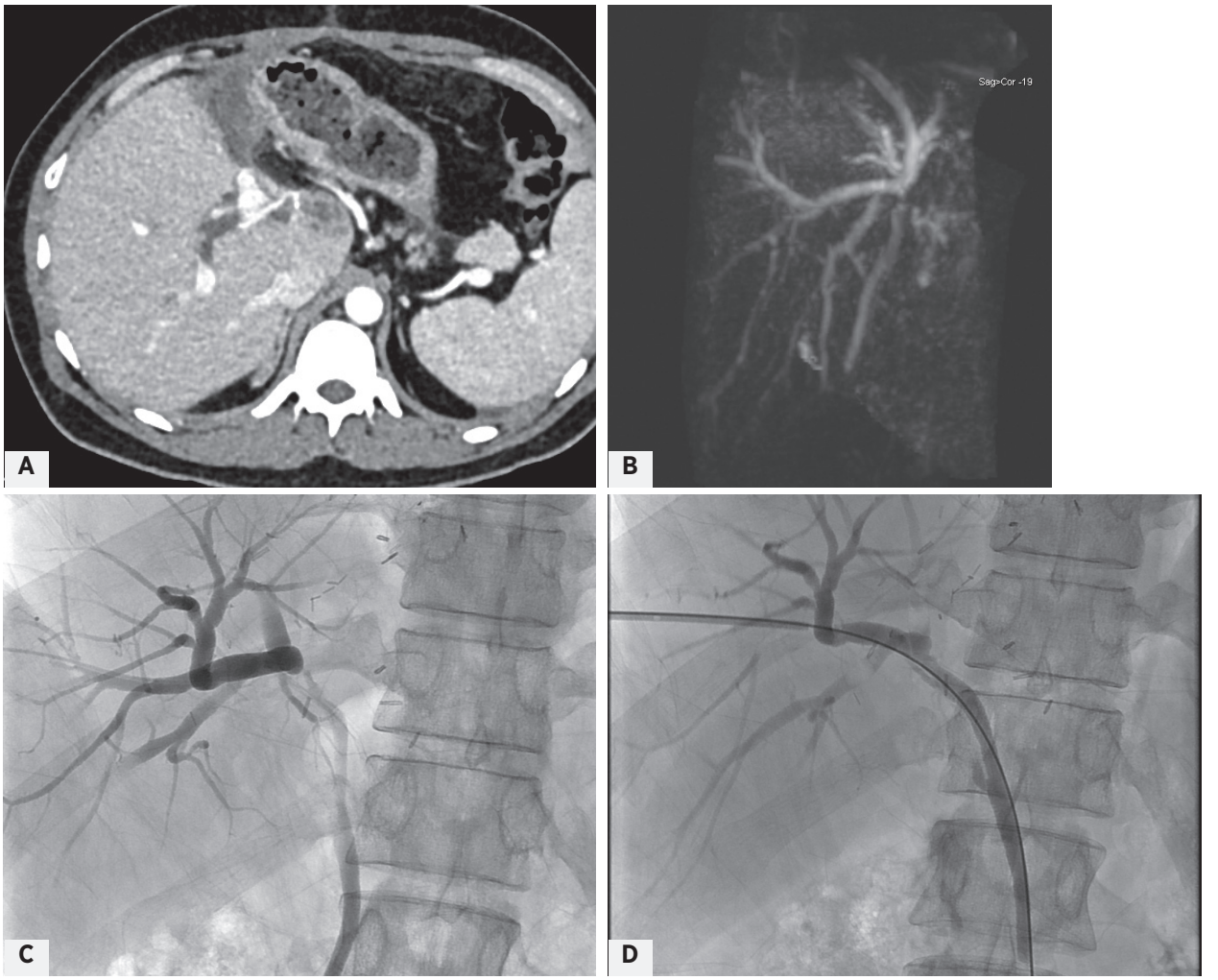

Figure 14. Biliary Stricture

(A) and **(B)** Severe dilatation of intrahepatic bile ducts was shown in computed tomography and magnetic resonance cholangiopancreatography of liver transplant patient. **(C)** Percutaneous transhepatic cholangiography image shows severe narrowing at anastomotic site. **(D)** After percutaneous balloon dilatation, lumen caliber almost turned to normal.

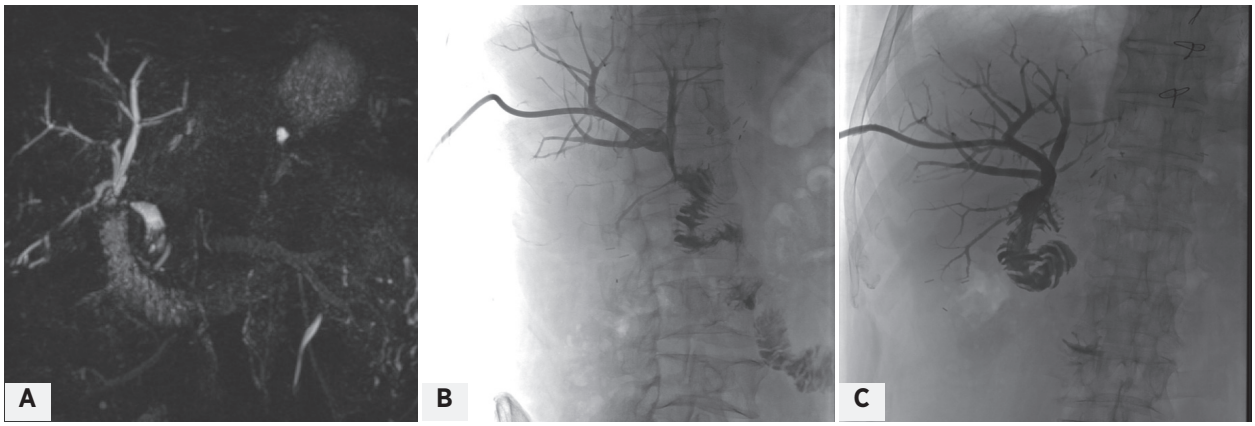

Figure 15. Biliary Stricture and Stone Formation

(A) Magnetic resonance cholangiopancreatography maximum intensity projection image shows severe narrowing at hepaticojejunostomy anastomosis of transplant patient. There were also filling defects, consistent with sludge or stone formation. **(B)** and **(C)** Percutaneous transhepatic cholangiography confirmed stenosis, with lumen caliber returning to normal after balloon dilatation.

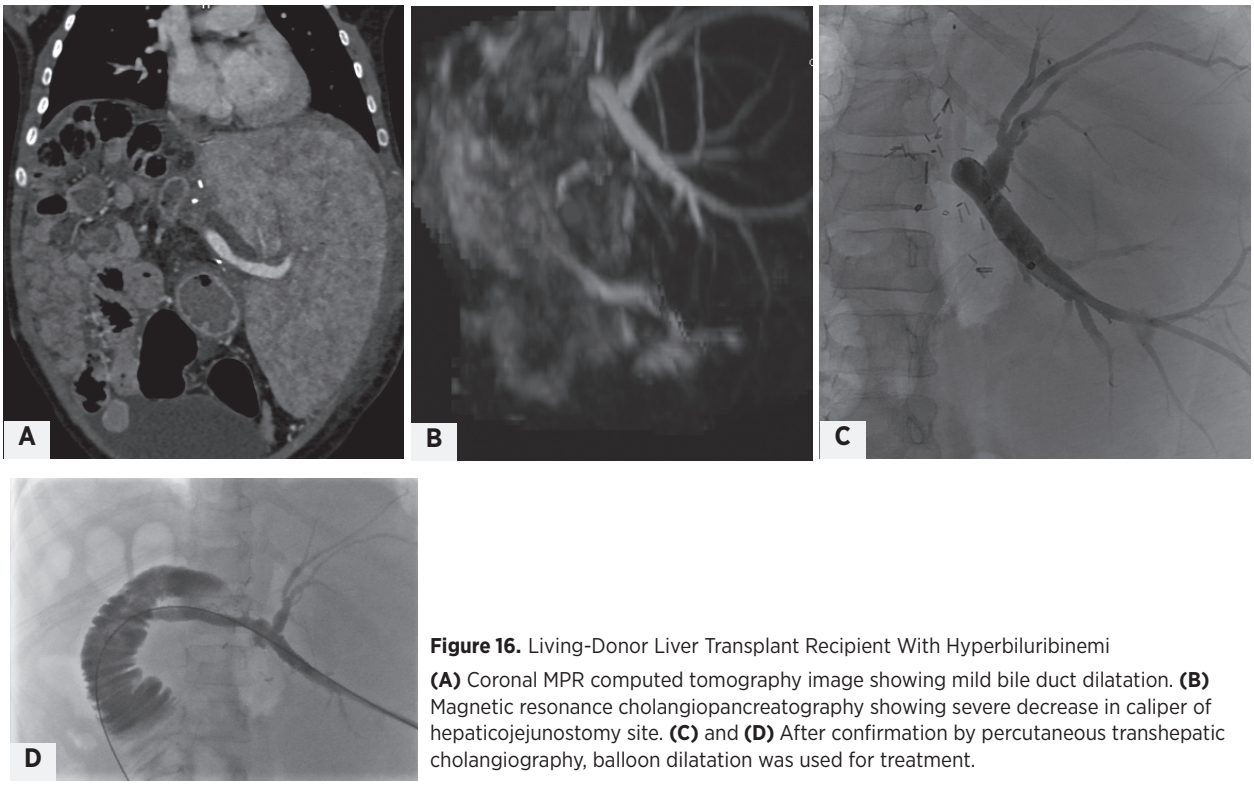

Figure 16. Living-Donor Liver Transplant Recipient With Hyperbiluribinemi

(A) Coronal MPR computed tomography image showing mild bile duct dilatation. **(B)** Magnetic resonance cholangiopancreatography showing severe decrease in caliper of hepaticojejunostomy site. **(C)** and **(D)** After confirmation by percutaneous transhepatic cholangiography, balloon dilatation was used for treatment.

after transplant, and stones usually occur later. Most consistently, biliary strictures (anastomotic or non-anastomotic) and ischemia are reported as the cause.[26]

Patients with stones, sludge, or casts present with abdominal pain, cholestatic liver tests, and frequently cholangitis. In a study from 1995 that compared different radiologic techniques,

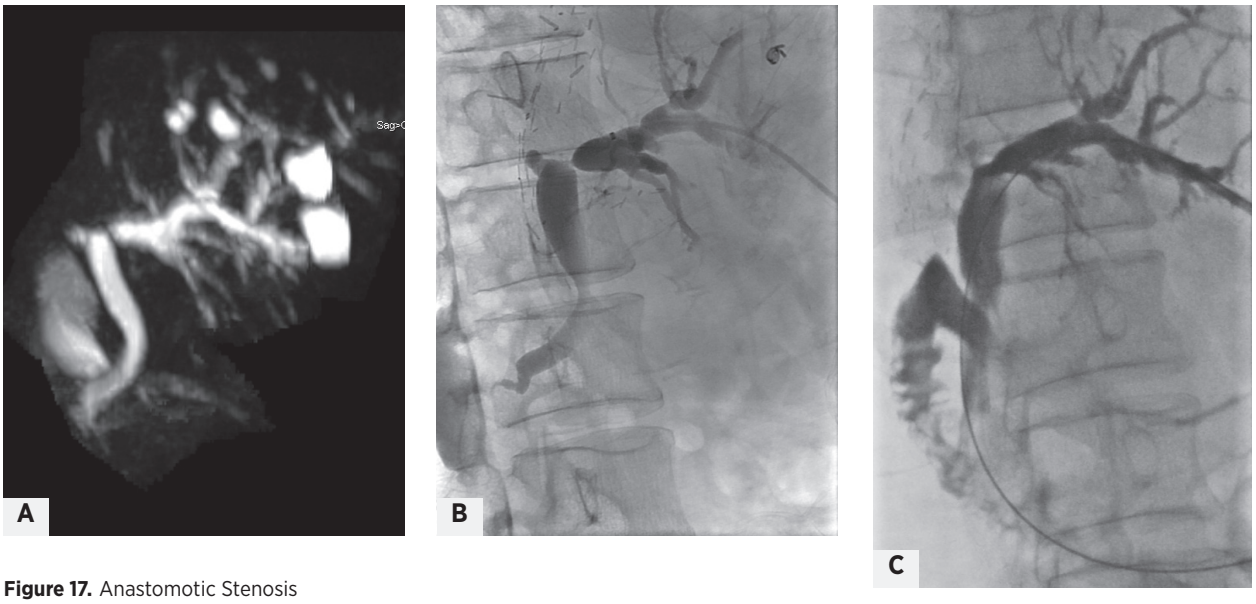

Figure 17. Anastomotic Stenosis

(A) Magnetic resonance cholangiopancreatography detected prominent stenosis in the choledochocholedochostomy anastomosis line in transplanted liver. **(B)** and **(C)** Percutaneous transhepatic cholangiography was used for confirmation, which was treated at the same time by balloon dilatation.

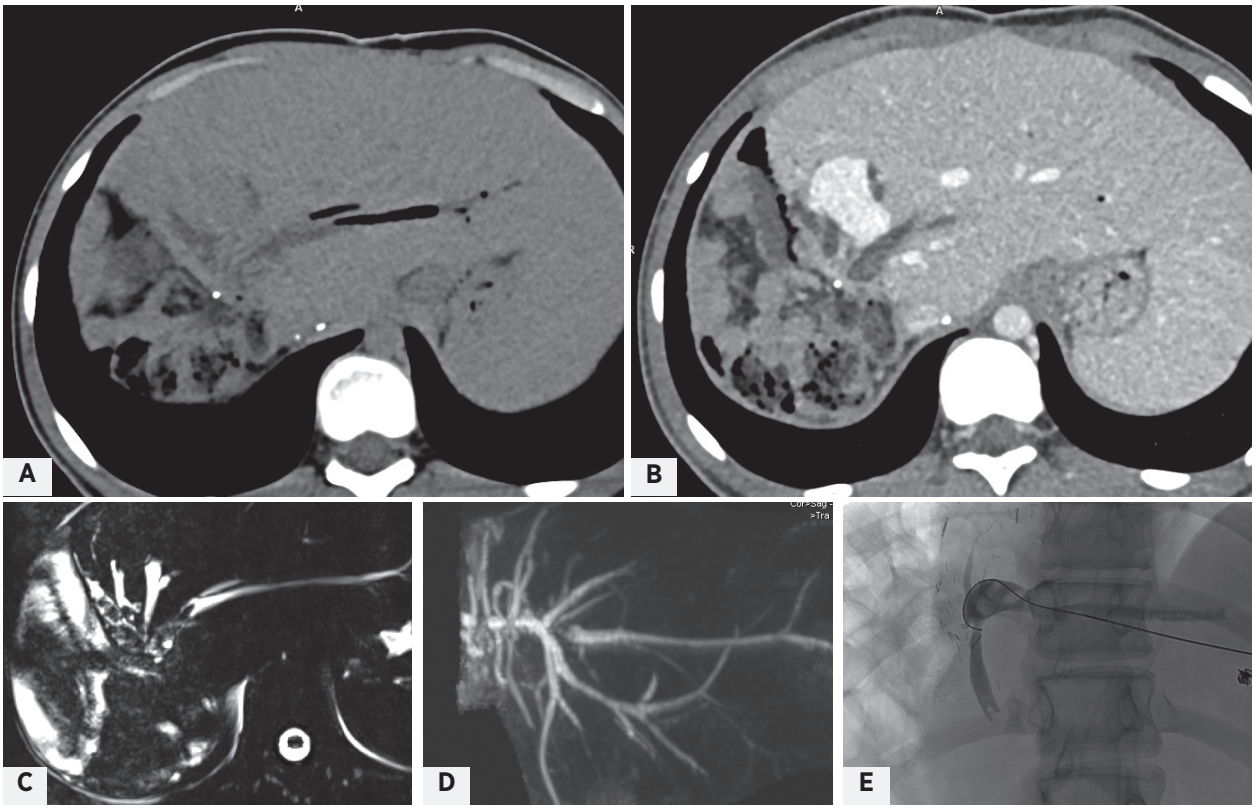

Figure 18. Images in Left-Lobe Liver Transplant Recipient With High Bilirubin Levels

(A) and **(B)** Precontrast and postcontrast multidetector computed tomography showed minimal hyperdense filling defects in central bile ducts. **(C)** and **(D)** Magnetic resonance cholangiopancreatography was used for confirmation, which indicated multiple filling defects compatible with sludge or stones in bile ducts proximal to a hepaticojejunostomy anastomosis. **(E)** Percutaneous transhepatic cholangiography also clearly showed these filling defects.

cholangiography (ERCP, PTC) was the only reliable imaging method for sludge; of note, US and CT scanning were of limited or no value. Although direct cholangiography remains the criterion standard, as in other complications, MRCP has often shown good results.[26]

The use of 3T MR imaging and MRCP have shown high diagnostic accuracy in detection of biliary stones, sludge, and casts in the intrahepatic and/or extrahepatic biliary tract. On MRCP, sludge and stones appear as endoluminal filling defects (Figure 18) surrounded by a thin rim of hyperintense bile, whereas biliary cast syndrome is typically hyperintense on T1-weighted images. Furthermore, with administration of Gd-EOB-DTPA, even small biliary calculi can be effectively discriminated from pneumobilia.[28]

NONBILIARY COMPLICATIONS

Over long-term follow-up, nonvascular or nonbiliary complications, such as hepatocellular carcinoma (HCC) recurrence, liver abscesses, lymphoma, adrenal hemorrhage, bowel obstruction, and incisional hernia, can developed; all can be correctly assessed with the use of MDCT. Most nonvascular or nonbiliary complications develop in the late period.[29]

Rejection

Rejection remains a common complication after liver transplant despite improvements in immunosuppression therapy. It should be classified as acute or chronic. Clinical and laboratory findings are nonspecific and indistinguishable from those observed with other complications.[4]

The role of imaging is limited because findings are nonspecific; use of imaging is mainly to exclude complications with clinical signs and symptoms similar to those of rejection. On DUS, acute rejection should appear as nonhomogeneity of the liver parenchyma with hypoechogenicity of the periportal space due to edema. On CT, the edema space appears as low signal intensity on T1-weighted images and as high signal on T2. Chronic rejection is caused by immunologic disorders, which can lead to irreversible damage to the liver arteries, veins, and bile ducts, with liver parenchyma having low attenuation values in the periportal edema space. On MR imaging, the periportal edema space appears as low signal intensity on T1-weighted images and as high signal on T2.[4]

FLUID COLLECTIONS

Hematoma

Seromas and hematomas are commonly observed near areas of vascular anastomosis (the hepatic hilum, the IVC) and in biliary anastomosis and in perihepatic spaces. Such collections are usually found during the first days after transplant and disappear within a few weeks. However, in most cases, collections of bile, lymph, blood, and pus all have the same appearance of a simple fluid collection.[25] Most hematomas will resolve spontaneously within a few weeks; however, in some cases, a superimposed infection can require catheter drainage or aspiration.[4]

Sonographic appearance is nonspecific because the fluid content can be equally uniformly anechoic, loculated, or inhomogeneously echogenic due to fibrin septa or separation of blood components. Bilomas have similar location and appearance on US. In addition, MDCT can be useful in assessing the hematic content because acute hematoma is hyperattenuating compared with simple fluid collections, whereas older hematomas can show hematocrit level. The best characterization is provided by MR imaging, which shows typical signal intensity patterns for fluid or hemorrhagic content.[12]

Abscess

Abscesses can occur as a result of HAT or HAS and biliary necrosis.[12] Predisposing factors also include biliary stricture and immunosuppressive medications. The presence of a complex fluid collection with a possible air-fluid level can be seen on US.[4]

Features of abscess can be typical on MDCT and MR imaging. On imaging, abscesses show peripheral, thick, irregular rim enhancement and intra lesional

gas and diffusion restriction on diffused-weight MR imaging. The role of imaging is to identify the site and amount of the fluid collection in order to plan interventional procedures, if required.[25]

Ischemia and liver infarction

Hepatic infarction is rare in normal patients because the liver is a richly vascularized organ with blood from different circuits. However, in liver transplant recipients, hepatic infarction is much more common. It is usually associated with arterial occlusion (85% of cases) and rarely with portal vein occlusion. Ischemia and liver infarction can be the consequences of all 3 described alterations of the hepatic artery: thrombosis, stenosis, and pseudoaneurysm.[19]

These lesions are seen as wedge-shaped, low-attenuation peripheral lesions on MDCT (Figure 19). They may liquefy, become infected, and occasionally calcify.[30] Infarctions are commonly revealed on MR images as peripheral or central lesions with wedge-shaped or round appearances and with no contrast enhancement; however, occasionally, some infarctions appear as periportal irregular lesions.[25]

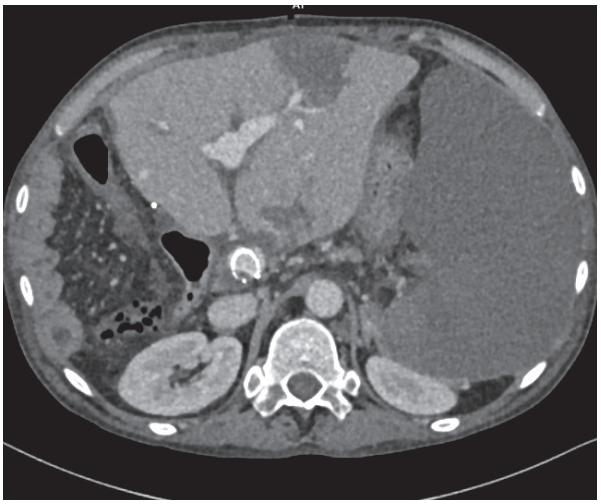

Figure 19. Focal Infarctions Shown inTransplanted Liver, With Spleen Totally Infarcted After Intraarterial Coil Embolization

Recurrence of hepatocellular carcinoma and de novo neoplasms

Orthotopic liver transplant is a curative option for HCC. However, the likelihood of HCC recurrence varies according to the selection criteria for OLT. Rates of recurrence at 4 years are 10% for patients with HCC within Milan criteria and up to 60% for patients with HCC outside Milan criteria.[12]

Posttransplant lymphoproliferative disorder is the most frequent de novo malignancy after liver transplant, accounting for approximately 20% of cases. Most of the commonly occurring neoplasms in patients who have undergone liver transplant are skin cancers other than melanoma, Kaposi sarcoma, and non-Hodgkin lymphoma.[4]

Based on location, rates of recurrence can range from 1% to 23% in the allograft only, 38.5% to 53% in extrahepatic sites, and 31% to 38.5% in both allograft and extrahepatic sites. These results are of interest both in making radiologists aware of studying specific locations where recurrence is more common and in suggesting that the most frequent way of HCC recurrence is intraabdominal seeding rather than hematogenous or lymphatic spread. Metastatic disease most frequently involves the lungs, lymph nodes, adrenal glands, and bone.[31]

The lesion usually is hypoechoic on US and hypoattenuating on CT and with T1 hypointensity and mildly T2 hypointensity on MR imaging. Contrast enhancement may be heterogeneous or occur at the periphery of the lesion. Liver involvement presents well-defined, hypovascular focal lesions or, less frequently, an infiltrative pattern showing similar US, MDCT, and MR imaging features than the extrahepatic masses. The preferred modality is MDCT due to ready availability and panoramicity. Computed tomography-positron emission tomography also has an important role, being used in evaluating the response to therapy, especially when there is a need to differentiate residual tumor from fibrosis or necrosis.[12]

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Doppler Ultrasonographic Findings of Vascular Complications After Liver Transplantation

Nihal Uslu

Liver transplantation is the only curative choice for end-stage liver disease. Over the past years, advances in surgical techniques and postoperative management of patients have markedly improved the outcomes of liver transplant. The common indications for liver transplant are cirrhosis secondary to alcohol, hepatitis, hepatocellular carcinoma, nonalcoholic steatohepatitis, cholestatic and metabolic diseases, and fulminant hepatic failure. Liver transplant procedures can be done in 2 ways: either from a living donor after performing a partial hepatectomy or from a deceased donor. Regardless of this choice of transplant method, the follow-up of the recipients is very important to promote a positive outcome.

Vascular complications after transplant are infrequent. Color Doppler ultrasonography (CDUS) is the most appropriate imaging test during and after transplant. This imaging method allows patency and vascular abnormalities to be seen. Because CDUS is an inexpensive, portable, and noninvasive test, it is used frequently. Here, we describe the normal appearances of vascular structures and vascular complications by grayscale ultrasonography and CDUS after liver transplant.

NORMAL POSTOPERATIVE DOPPLER FINDINGS

We perform the first grayscale ultrasonography and CDUS during the surgery, just after the vascular anastomoses are done, so that we can understand the vascular anatomy, which will guide us in the following days of patient recovery. During the first week after transplant, CDUS is done twice per day unless the recipient requires further investigation.[1]

For patients who receive deceased-donor liver transplant, the main, right, and left arteries should have similar findings when there is only 1 anastomosis. If there are more than 1 arterial anastomoses, then each anastomosis should be shown separately, indicating the velocities and resistive indexes (RI).

We have 3 important measurements to consider during assessment of the hepatic arterial flow. First, the normal hepatic arterial waveform has a rapid systolic upstroke. There are many studies that have shown significant variabilities in systolic acceleration time, but we agree that it should be less than 0.08 seconds. Second, the hepatic arterial RI is another value that should be used to assess the hepatic arterial waveform. This value is defined by the relationship between peak systolic velocity (PSV) and end-diastolic velocity (EDV), which is calculated with the following formula: (PSV - EDV)/PSV. The normal hepatic arterial RI ranges from 0.50 to 0.80. The third measurement is hepatic arterial PSV, which also has wide variability. Therefore, what is important here is that the PSV is stable after transplant (Figure 1).[1-6]

Hemodynamic changes can also occur after transplant, and arterial abnormalities seen just after the surgery may resolve soon after. The most common arterial abnormality is increased RI, which is most often due to the allograft edema, increased cold ischemia time, increased portal flow, or arterial spasm. The RI value becomes normal usually in 7 to 15 days after surgery.[1] On the other hand, a decrease in RI value usually shows an arterial problem; this may be due to the edema or spasm at the anastomoses site, and the radiologist should take care to discover the source of the problem. In addition to these abnormalities, vessel redundancy causing a vascular kink may lead to high PSV, so additional measurements are required after the correction of the kink. Keeping these transient hepatic arterial waveform changes in mind, clinicians should follow these changes carefully, and correlation of these findings with the patient's clinical findings is mandatory. Also, test results regarding patient liver function will be helpful in making a treatment decision. Persistent abnormalities should be evaluated by further radiological methods, such as computed tomography or magnetic resonance imaging.[1,2,6] *It is crucial to know that the first postoperative Doppler ultrasonography serves as the baseline, and, if follow-up imaging shows a worse finding, this indicates an arterial complication.* It is important to note that the patient must be followed by the same radiologist, if possible, so that the Doppler changes will be realized more easily.

The normal portal vein shows a monophasic hepatopedal flow pattern (Figure 2). The portal venous flow increases after the portal anastomoses, but it reaches normal values with the patient's adaptation to the hemodynamics. Postoperative fluid collections may cause a transient increase in portal flow due to the compression.[1]

Although the hepatic veins normally have a triphasic waveform (Figure 3), monophasic or biphasic waveforms may also be expected in the early postoperative period.[1,6]

VASCULAR COMPLICATIONS

Vascular complications after transplant are infrequent, with a reported incidence close to 7% for deceased-donor liver transplant and around 13% for living-donor liver transplant.[7]

HEPATIC ARTERIAL COMPLICATIONS

Hepatic arterial complications are related to graft loss and high mortality, and so patients must be monitored closely to maintain positive prognosis. Hepatic arterial complications include hepatic artery thrombosis (HAT), hepatic artery stenosis (HAS), hepatic

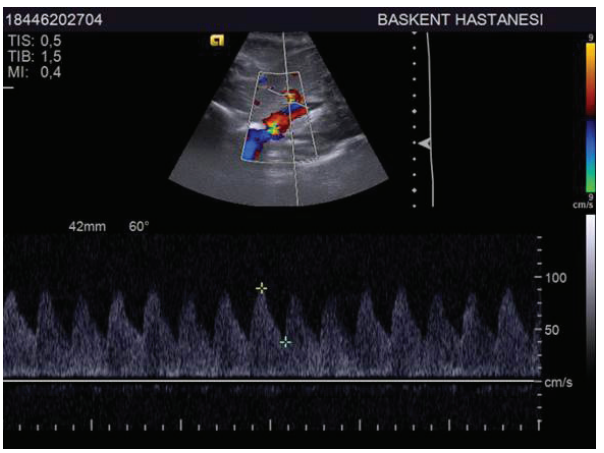


Figure 1. Normal Hepatic Arterial Flow Pattern Showing a Rapid Systolic Upstroke

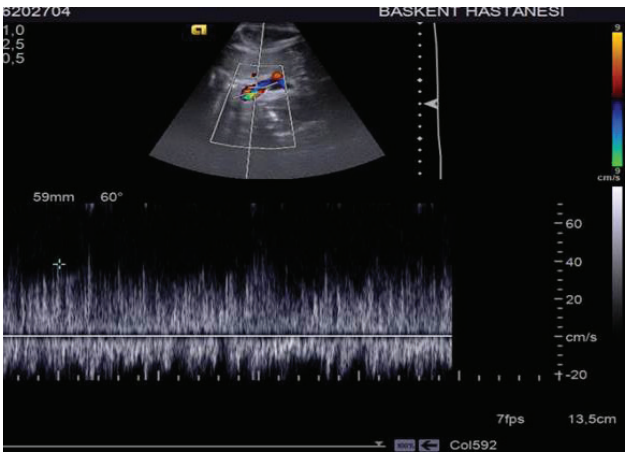
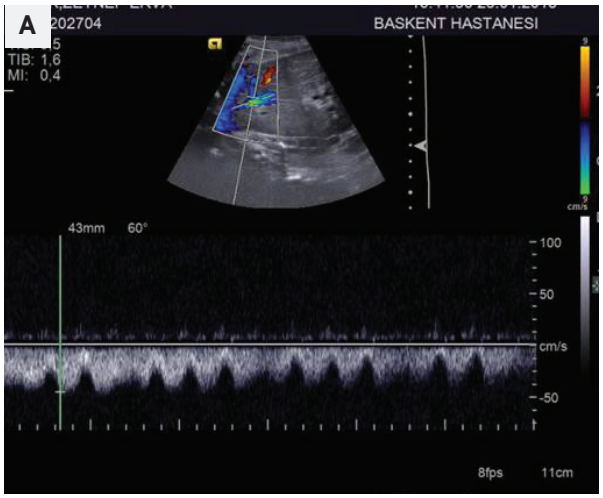


Figure 2. Normal Portal Venous Flow Pattern



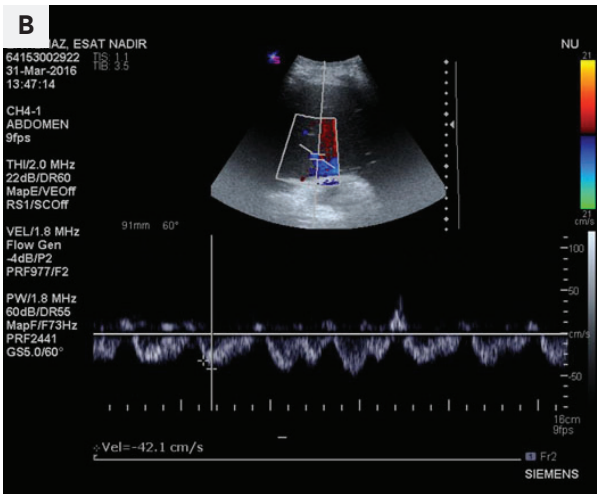


Figure 3. Normal Hepatic Venous Flow Patterns
Pattern can be monophasic, biphasic **(A)**, or triphasic **(B)**.

artery pseudoaneurysm, and splenic arterial steal syndrome (SASS). Because the only blood supply to the biliary tree is from hepatic arteries after liver transplant, arterial complications can cause biliary ischemia, leading to biliary strictures, necrosis, abscesses, and graft failure; therefore, its early diagnosis is crucial.[1,6-11]

Hepatic artery thrombosis

Hepatic artery thrombosis has high mortality rates and is the most serious complication, occurring in approximately 3% to 12% of adult recipients and 4.9% to 8.3% of pediatric recipients. When it is seen in the first weeks after transplant, it is called "early HAT"; however, if its onset is at least 1 month after transplant, it is called "late HAT." With early HAT, the clinical onset is noisy, whereas, in late HAT, the clinical course may be insidious. Clinical signs of HAT include fulminant liver failure, delayed bile leak, and intermittent sepsis of unknown cause. Major causes of early HAT include a small donor artery, prolonged ischemic time, ABO incompatibility, low-flow states, a faulty surgical technique, and acute rejection. On the other hand, chronic rejection causes late HAT, requiring retransplant in most of the cases unless surgical revascularization can be done.[1,4,10-16]

Pulsed, color, and power Doppler ultrasonography are sensitive and specific for diagnosis of hepatic artery

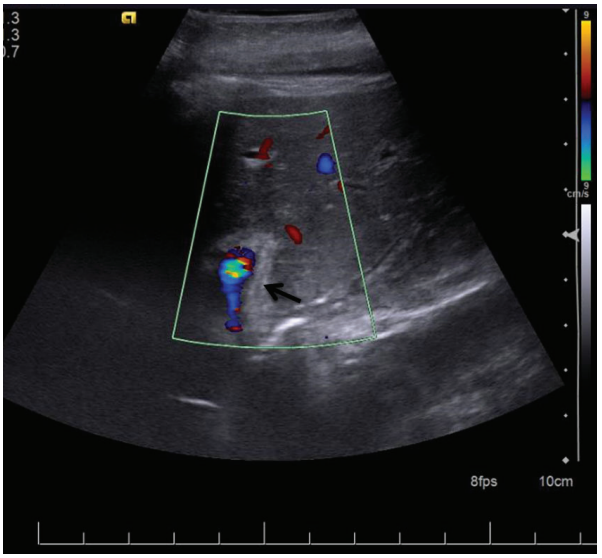


Figure 4. Hepatic Arterial Thrombosis After Liver Transplant
Hepatic artery located medial to the portal vein is seen hypoechoic (black arrow) in color Doppler imaging, showing there is no flow in it because of thrombosis.

complications, and its diagnostic rate is established to be 92%.[17] Figure 4 shows an absence of flow in the hepatic artery. If the proximal site of the thrombosis is sampled, then the RI value will be 1. Computed tomography or digital subtraction angiography is usually performed to support the diagnosis. Digital subtraction angiography may also be performed to maintain revascularization in the early stage. Arterial collaterals may occur after HAT in the late

phase. These collaterals specifically have the tardus parvus waveform.[1,4,10,17]

Hepatic artery stenosis

Hepatic artery stenosis occurs less commonly than HAT. The incidence of HAS is known to be 3% to 11% for adult and 6% to 7% for pediatric liver transplant recipients.[1,10,18] The most frequently affected location is the anastomosis. It may be clinically asymptomatic unless infarction or ischemic hepatitis is present. With HAS, parvus tardus waveforms are seen in spectral Doppler ultrasonography, distal to the stenosis. The RI value is less than 0.5, and systolic acceleration time is longer than 0.08 seconds (Figure 5). The stenotic segment displays a high flow rate, and PSV will be greater than 200 cm/s. Because of this high flow rate and turbulence in the artery, an aliasing artefact will occur. In the first days after transplant, RI values can be greater than 0.8 in approximately 50% of patients; thus, in this group, stenosis may not be diagnosed properly and computed tomography or digital subtraction angiography may be applied. Hepatic artery stenosis requires early treatment with percutaneous angioplasty or surgical revision.[1,6,7,10,19,20]

Hepatic artery pseudoaneurysm

Hepatic artery pseudoaneurysm is a rare complication occurring in approximately 2.5% of liver transplant cases. It may occur at any of the branches of the hepatic artery, as well as at the anastomosis site, and may be due to infection or may be iatrogenic, secondary to a biopsy or angioplasty. All cystic lesions should be evaluated by Doppler ultrasonography to exclude a pseudoaneurysm. If hepatic artery pseudoaneurysm is present, a disorganized turbulent flow will be seen, typically because of a swirl formed by the inlet and blood outlet, which is similar in appearance to the yin-yang symbol. This complication is treated with coil embolization, stent placement, or surgical repair.[1]

Splenic artery steal syndrome

Splenic artery steal syndrome was first mentioned by Langer and colleagues as a disorder occurring in patients who have undergone orthotopic liver transplant.[21] It has a reported incidence of 3% to 8% and is characterized by graft arterial hypoperfusion. The most common clinical finding is elevated liver function tests. A hypertrophied splenic artery caused by preexisting portal hypertension and splenomegaly may shift the

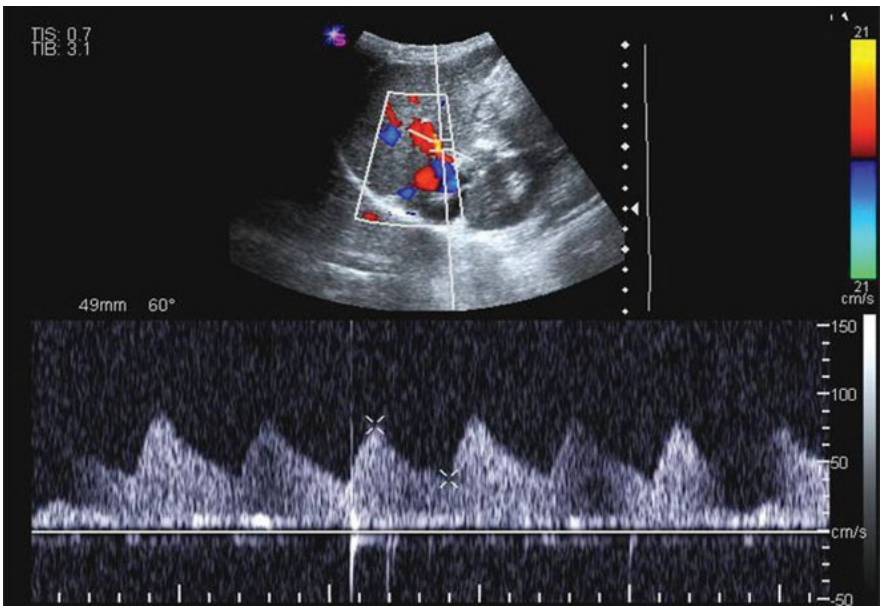


Figure 5. Hepatic Artery Stenosis
Resistive index (RI) value is at the lower limit, and systolic acceleration time (SAT) is greater than 0.08 s.

blood away from the liver toward the spleen after liver transplant. As a result, hepatic hypoperfusion occurs, and early detection and treatment of SASS are important for preventing the progression of hepatic failure and bile duct damage. *On Doppler ultrasonography, high resistance waveforms in the arteries are present, with arterial flow velocity decreasing over time. Of note, diastolic flow decreases, and, on CDUS, no color is sometimes seen in the artery during the diastolic phase* (Figure 6). Angiography is performed to confirm the diagnosis of SASS, and the condition is treated by splenic arterial embolization. Doppler ultrasonography has also been reported to be useful for follow-up of patients with SASS after splenic artery embolization. Doppler ultrasonography shows the progressive increase in the hepatic artery and the normalization of the arterial flow pattern.[1,6,10,22-24]

PORTAL VENOUS COMPLICATIONS

In the portal vein, a normal flow pattern is antegrade after transplant. The velocity changes in hours or days and tends to decrease. It may be high at the anastomosis site just after the surgery due to the edema at the anastomosis site. Portal vein complications mainly include portal vein thrombosis (PVT) and portal vein stenosis. These are not frequent, and the incidence is 2% in adults and 3% to 19% in children. Although the most common surgical technique is an end-to-end anastomosis, sometimes this is not possible; therefore, it is important to know the type of the anastomosis. Yerdel and colleagues[25] found the incidence of portal vein complications to be 12.5%, with occurrence more often seen in male patients, patients with history of severe portal hypertension and thrombosis preoperatively, and patients who received treatment for portal hypertension, such as sclerotherapy, transjugular intrahepatic portosystemic shunt, portocaval shunt, splenectomy, and splenic embolization.[21] *Because the hepatic blood supply is maintained from the portal vein in 70% to 80% of cases, complications in this vessel can lead to liver dysfunction.*[1,6,10,18,26]

Portal vein thrombosis

Portal vein thrombosis is the most common portal venous complication after transplant. With PVT, the thrombus is seen either anechoic or echogenic on grayscale ultrasonography. During this time, due to buffer response, hepatic arterial flow increases. The duration of the thrombosis affects the clinical manifestations of PVT. In the early stages, liver function impairment, portal hypertension, variceal bleeding, intestinal edema, or massive ascites can be seen. On Doppler ultrasonographic imaging, there is no flow in the vein. Power Doppler imaging should also be done so that the slow flow is not mistaken for thrombosis. If thrombosis is seen in

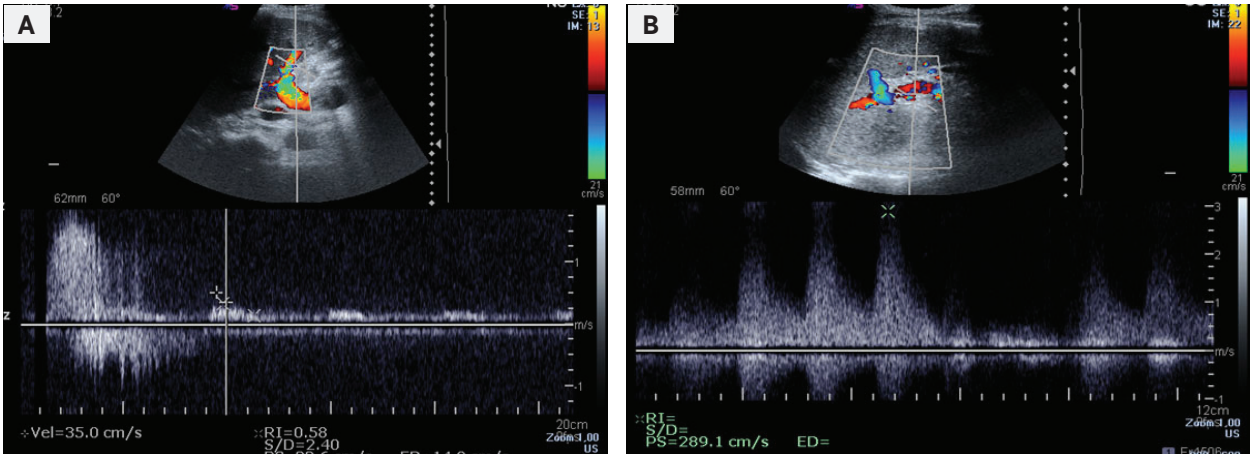


Figure 6. Splenic Arterial Steal Syndrome
(A) Decreased hepatic arterial flow. **(B)** Increased splenic arterial flow.

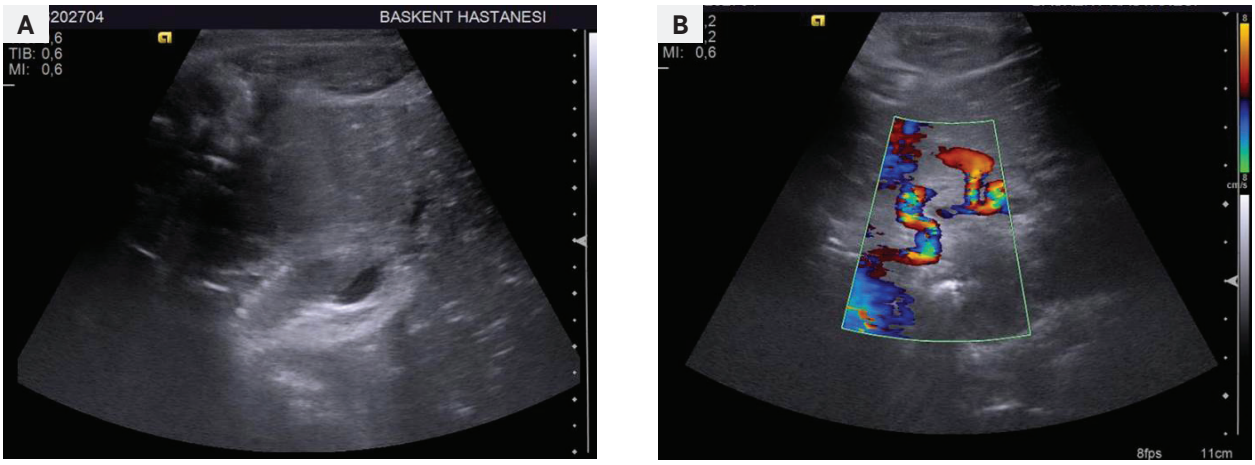


Figure 7. Portal Vein Thrombosis
(A) Grayscale image shows the thrombosis. **(B)** Increased arterial flow due to buffer response.

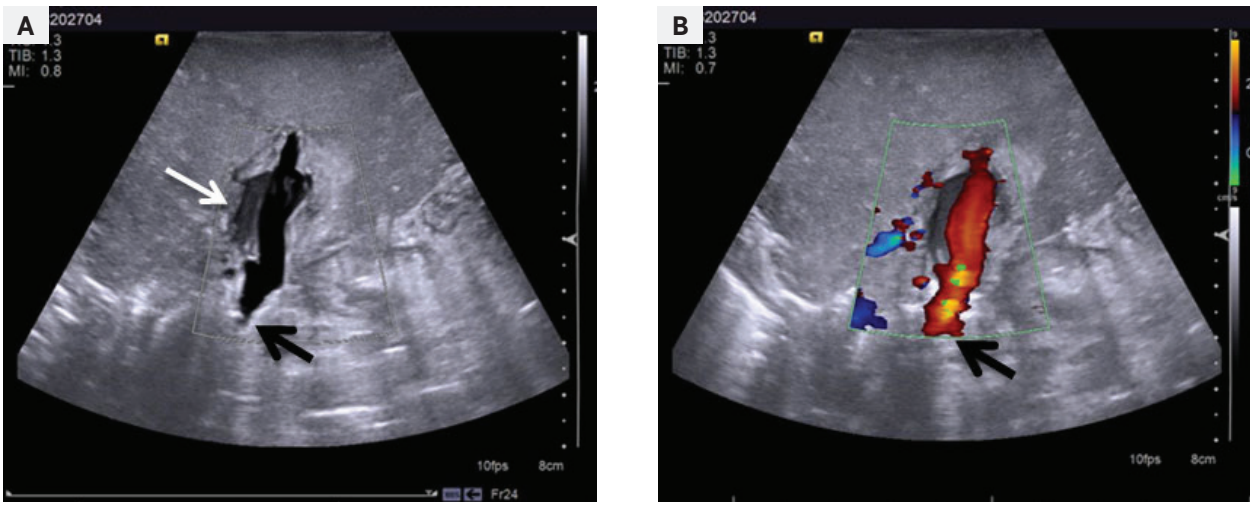


Figure 8. Portal Vein Stenosis
(A) Black arrow shows the stenosis site, and white arrow shows partial thrombosis, which is more echoic than patent lumen. **(B)** Color Doppler image of the portal vein stenosis; black arrow indicates the stenosis site and aliasing due to the stenosis.

the first 72 hours after surgery, surgical revision of the anastomosis is required. If the occurrence is later, percutaneous thrombolysis, angioplasty, or stenting is required. If these techniques are not practical, then surgery can be done (Figure 7).[6,10]

Portal vein stenosis

Portal vein stenosis is another complication occurring at the anastomosis after transplant and has been reported in 1% of adult patients and 5% of pediatric patients (Figure 8). Clinically significant portal vein stenosis is rare. It is usually known to occur in pediatric and living-donor recipients due to the small graft vein size. Portal vein stenosis that presents within 6 months is likely due to technical reasons. On Doppler ultrasonography, there is typically an increase in portal blood flow, which is observed to be a 3- to 4-fold increase in velocity at the stenotic segment compared with the prestenotic segment. Doppler measurements require using a

correct angle. Peak anastomotic velocity greater than 100 cm/s is 90% specific for the diagnosis, and greater than 125 cm/s is 95% specific for the diagnosis. Also, focal narrowing of the portal vein can be demonstrated on grayscale ultrasonography. This complication is treated with catheter-guided angioplasty and, if necessary, stenting.[1,6,7,10,18,27]

HEPATIC VENOUS AND INFERIOR VENA CAVA COMPLICATIONS

These are the least common vascular complications, occurring in less than 1% of adult patients and 1% to 4% of pediatric patients. Thrombosis and stenosis are 2 rare complications of the inferior vena cava and hepatic veins after liver transplant. These tend to occur at the anastomosis; therefore, knowing the surgical anatomy is important.[6-10,28]

The branches of the hepatic vein may be occluded by surgical material. This may cause a wedge-shaped area of parenchymal edema. If there is a thrombosis, it may be seen as an echogenic or anechoic material in the lumen, with Doppler ultrasonography showing no flow. Power Doppler ultrasonography should also be performed to show whether there is slow flow in the vessel.[7,10]

Inferior vena cava stenosis may be secondary to anastomotic narrowing and/or extrinsic compression due to graft edema or adjacent collections. This may cause passive hepatic congestion and imaging findings similar to those shown for Budd-Chiari syndrome. Focal narrowing of the inferior vena cava may also be present (Figure 9).[6,7,10]

The diagnostic criteria for hepatic vein stenosis are controversial. Normal hepatic veins have a triphasic waveform due to the transmission of cardiac pulsations of the heart. Hepatic vein stenosis prevents transmission of cardiac pulsations resulting in loss of triphasicity. However, loss of triphasic configuration is a very nonspecific finding and is often seen in normal postoperative patients. *Therefore, the presence of hepatic triphasicity can be used to exclude hepatic vein stenosis, although loss of triphasicity does not imply the presence of a hepatic venous complication.* Hepatic vein stenosis should be considered when a significant stenosis is revealed by grayscale ultrasonography or when a high-speed blood flow disorder appears at the stenosis. The ratio of stenotic top velocity to prestenotic blood flow velocity is greater than 3 to 4:1. Clinically significant hepatic venous outflow stenosis can be treated with venous angioplasty.[1,6,7,10]

SUMMARY

Modern follow-up protocols involve Doppler ultrasonography as a first-line modality for liver transplant recipients. Besides being a noninvasive, inexpensive modality, it is also easily performed at the patients' bedside in the intensive care unit, providing qualitative and quantitative morphologic and functional information. Both conventional grayscale ultrasonography and CDUS are the modalities of choice for evaluating vascular complications in liver transplant recipients. For prompt diagnosis, one should know the normal postoperative Doppler findings. In addition, early detection of vascular complications is crucial for graft and patient survival.

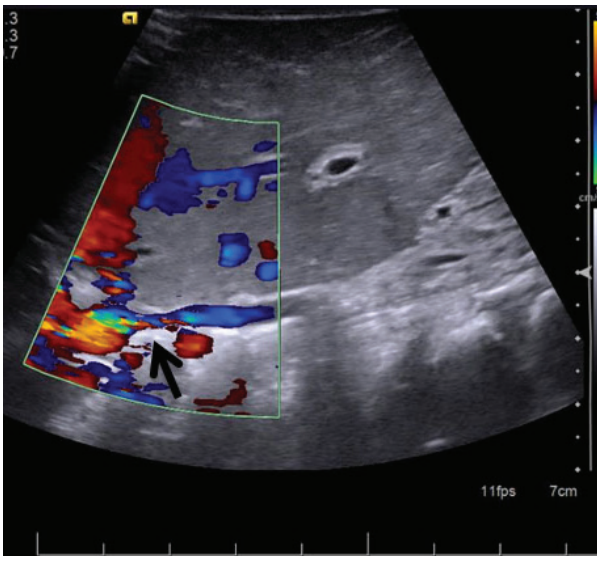


Figure 9. Inferior Vena Cava Stenosis
Black arrow shows the stenosis site and aliasing after the stenosis.

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Complications of Liver Transplant: Vascular Complications

Gökhan Moray

The blood supply of the liver is unique because of its duality, which is maintained by the portal vein and hepatic arteries.[1] The total hepatic blood flow is 100 to 130 mL/min per 100 g of liver or 30 mL/min per kilogram of body weight. One-fifth to one-third of hepatic blood flow is supplied by the hepatic artery, and the remainder is supplied by the portal vein. The high-pressure, well-oxygenated arterial blood mixes with the low-pressure, less-oxygenated, nutrient-rich flow, including hepatotropic factors, portal venous blood within the hepatic sinusoids. Hepatocytes are nourished equally by the portal vein and hepatic artery, whereas the intrahepatic biliary tract is mainly nourished by hepatic artery blood flow, so arterial complications will lead to biliary ischemia manifesting as nonanastomotic biliary strictures and bile leaks or bilomas.

The splanchnic venous blood reaching the hepatic sinusoids is not controlled by the liver. When the portal blood flow changes, the hepatic arterial flow changes in the opposite direction, thus trying to maintain the total hepatic blood flow constant, which resembles a buffering mechanism. Healthy hepatic blood circulation inherently needs an adequate hepatic outflow. When the outflow is blocked, it is impossible to maintain sufficient hepatic function.

Therefore, vascular reconstruction is critical for a successful liver transplant. Vascular complications are the most serious and devastating of problems that can occur after liver transplant, carrying high morbidity and mortality rates among recipients.

It has been reported that the incidence of vascular complications after liver transplant ranges from 2% to 25%.[2] These rates differ according to transplant type (such as with a deceased-donor whole liver transplant or partial living-donor/deceased-donor liver transplant) and recipient age (adult, child, or infant).[3] Adult deceased whole liver transplant carries the lowest incidence rate of vascular complications, whereas infant living-donor liver transplant carries the highest risk.[3]

Early diagnosis and appropriate treatment of vascular complications are extremely important. In this chapter, vascular complications will be evaluated under the arterial, portal vein, and hepatic vein (HV) subcategories.

ARTERIAL COMPLICATIONS

Arterial complications after liver transplant are classified as (1) hepatic artery thrombosis (HAT), (2) hepatic artery stenosis (HAS), (3) hepatic artery pseudoaneurysm (HAP), and (4) arterioportal fistula (APF).

Hepatic artery thrombosis

Hepatic artery thrombosis is the most common and severe vascular complication that occurs after liver transplant.[4,5] Mortality following HAT reportedly reaches 54.5%.[6,7] Although advances in surgical techniques have reduced the incidence of HAT, it still accounts for more than 50% of arterial complications.[8] The overall incidence of HAT after liver transplant ranges from 8% to 26% in pediatric patients.[4,5,9-20]

The hepatic artery has a relatively fragile intima and small diameter. Important predisposing factors for arterial complications are small vascular diameter and length of hepatic artery in both graft and recipient sites, pediatric recipient (with increased incidence among children of lower weight/size),[21-24] variant arterial anatomy, retransplant, celiac stenosis or compression by the median arcuate ligament, and cytomegalovirus mismatch (seropositive liver donor in seronegative recipient). Morbid obesity with deep peritoneal cavities is another technical challenge for vascular anastomosis in some patients.[6,7,11,15,25,26]

Other risk factors associated with HAT are excessive dissection of the hepatic arterial wall, traumatic manipulation of the intima, prolonged and forceful clamping of the hepatic artery, long graft artery, kinking, hematoma of the artery wall, continuous suture technique, imperfect anastomosis technique, complex back-table arterial reconstruction of the allograft, arterial conduits, aorto-hepatic grafting, prolonged operative time, long cold ischemia time, elevated hematocrit, high-resistance microvascular arterial outflow caused by rejection or severe ischemia-reperfusion injury, and low-volume transplant centers.[6-11,15,25-32]

Some authors have mentioned improved results with microscopic-assisted vascular techniques; however, microscopic-assisted vascular reconstructions are usually time consuming and cumbersome in patients who are particularly sick and coagulopathic.[17,33-37]

Hepatocellular carcinoma is another risk factor for HAT, creating a malignancy-associated generalized hypercoagulable state. Also, it is reported that the use of transarterial chemoembolization for treatment of hepatocellular carcinoma can cause hepatic artery injury, resulting in increased periarterial inflammation, friability, and a predisposition to HAT.[38] Hepatic artery thrombosis occurs nearly 5 times more frequently among pediatric patients with hepatic malignancies than among those without hepatic malignancies. The relationship between hepatic malignancy and HAT is probably due to a combination of coagulation derangements associated with both liver disease and systemic malignancy.[39,40]

Marginal livers (extended-criteria grafts and livers donated after cardiac death) are less tolerant to the additional ischemic insult of HAT. This situation is an additional risk factor for bad outcomes after HAT.

Some authors have focused on hematologic causes for HAT. Hematologic workup must be done routinely to identify patients at increased risk for thrombotic complications. Cytomegalovirus exposure may contribute to a procoagulant state by means of endothelial cell activation.[41]

Hepatic artery thrombosis can be classified as early or late, according to its occurrence time. Early HAT can occur intraoperatively or in the early postoperative period (hours to days, up to 1 mo) but usually occurs within the first 2 weeks after transplant.[42,43] Because the liver graft has no collateral blood supply from the retroperitoneum and diaphragm during this early postoperative period, the arterial supply of the graft is of great importance.

Early HAT is usually caused by technical problems or difficulties.[9,10,26] If immediate revascularization of the hepatic artery or retransplant of the liver is not performed, an irreversible ischemic damage of hepatocytes and bile duct epithelial cells resulting in recipient death can ensue.[43]

Late HAT is usually due to a hypercoagulable state, such as overtransfusion of platelets and/or fresh-frozen plasma, severe rejection episodes, or mass and inflammatory reaction of the bile leakage. In late HAT patients, collateral arterial circulation has usually developed, and this situation can be tolerated with portal flow.[44]

Early diagnosis and appropriate management of vascular complications can result in longer survival. Close surveillance of all vascular anastomoses using Doppler ultrasonographic (USG) imaging facilitates early detection and treatment of these complications before irreversible graft failure.[19,45]

Many transplant centers perform Doppler USG evaluation twice per day for the first postoperative week. With this strategy, HAT is usually diagnosed before the detection of elevated liver enzymes. If not, patients with early HAT usually present with acute hepatic failure, a sudden significant elevation of liver enzymes, unexplained sepsis, or liver infarction.

Contrast-enhanced USG imaging is another noninvasive diagnostic tool. This technique uses microbubble contrast to reduce the false-positive rate by detecting flow not captured on standard Doppler USG imaging.[46] Contrast-enhanced USG also has a high positive predictive value for HAT, if portal vein enhancement is observed prior to arterial tree enhancement.[6,47]

If HAT suspicion occurs upon USG imaging evaluation, the diagnosis must be reevaluated with computed tomography (CT) hepatic angiography. Conventional arteriography is the gold standard for HAT diagnosis, but it is not ideal for screening because of its high cost, invasive nature, associated risks, and potential complications. Multidetector CT angiography with maximum intensity projection and with volume-rendered images gives a rapid and accurate depiction of hepatic arterial anatomy after liver transplant. Thus, this modality allows accurate detection of hepatic artery stenosis or thrombosis. The excellent spatial resolution and fast scan times with a multislice scanner allow CT angiography to depict small vessels. Maximum intensity projection and volume-rendered images improve the diagnostic accuracy of CT imaging, and CT angiography is a noninvasive and cost-effective technique compared with conventional arteriography. Multidetector CT angiography is also a useful tool for detecting pseudoaneurysm and arteriovenous fistula malformations of the hepatic arteries.[48] It is a noninvasive modality that is used to select patients who must be treated with angiographic intervention or surgery.

If HAT suspicion or diagnosis still exists after CT angiography, then conventional arteriography is usually accepted as the subsequent procedure.[49-54] This is because conventional arteriography not only removes HAT doubts but can also solve the problem. Catheterization of the hepatic artery with a microcatheter or giving some vasodilators or thrombolytic agents directly through the native hepatic artery can solve many of the early HAT cases that are diagnosed with surveillance USG. However, if the diagnosis was made after recognition of elevated liver enzymes, it is generally difficult to solve the problem with interventional radiology.

After a patient is diagnosed with HAT, there are 3 choices for clinicians: revascularization, retransplant, or observation.[55] Treatment options are closely related to the time of the diagnosis, experience of the transplant center with interventional radiology, and collaboration of the surgical team with the radiology department. If the surgical team stands by the possibility of radiological complications, amazingly successful results can be achieved with early interventional methods, such as percutaneous thrombolysis and percutaneous angioplasty.[56] The success rate of surgical revascularization is greater than radiological interventions for HAT, but an attempt to use radiological methods can prevent the patient from having to experience another surgical trauma, if successful. There are many surgical techniques for primary and recurrent reconstruction of the hepatic artery. One of these is shown in Figure 1.[57] All techniques mention the importance of a wider anastomosis with an uninjured vascular endothelium. If all of these efforts are ineffective, then retransplant from a living or deceased donor is the only remaining option. In some rare situations, a desperate conservative approach (eg, waiting for a liver graft) can result in a miracle, and the patient can survive for several months or years with favorable liver function.

Late HAT is less common, and the presentation is often indolent. The thrombosis will be discovered during routine USG evaluations of the hepatic vasculature, a rejection episode, or a septic attack.[54] It may even be asymptomatic in half of patients affected due to the formation of collateral

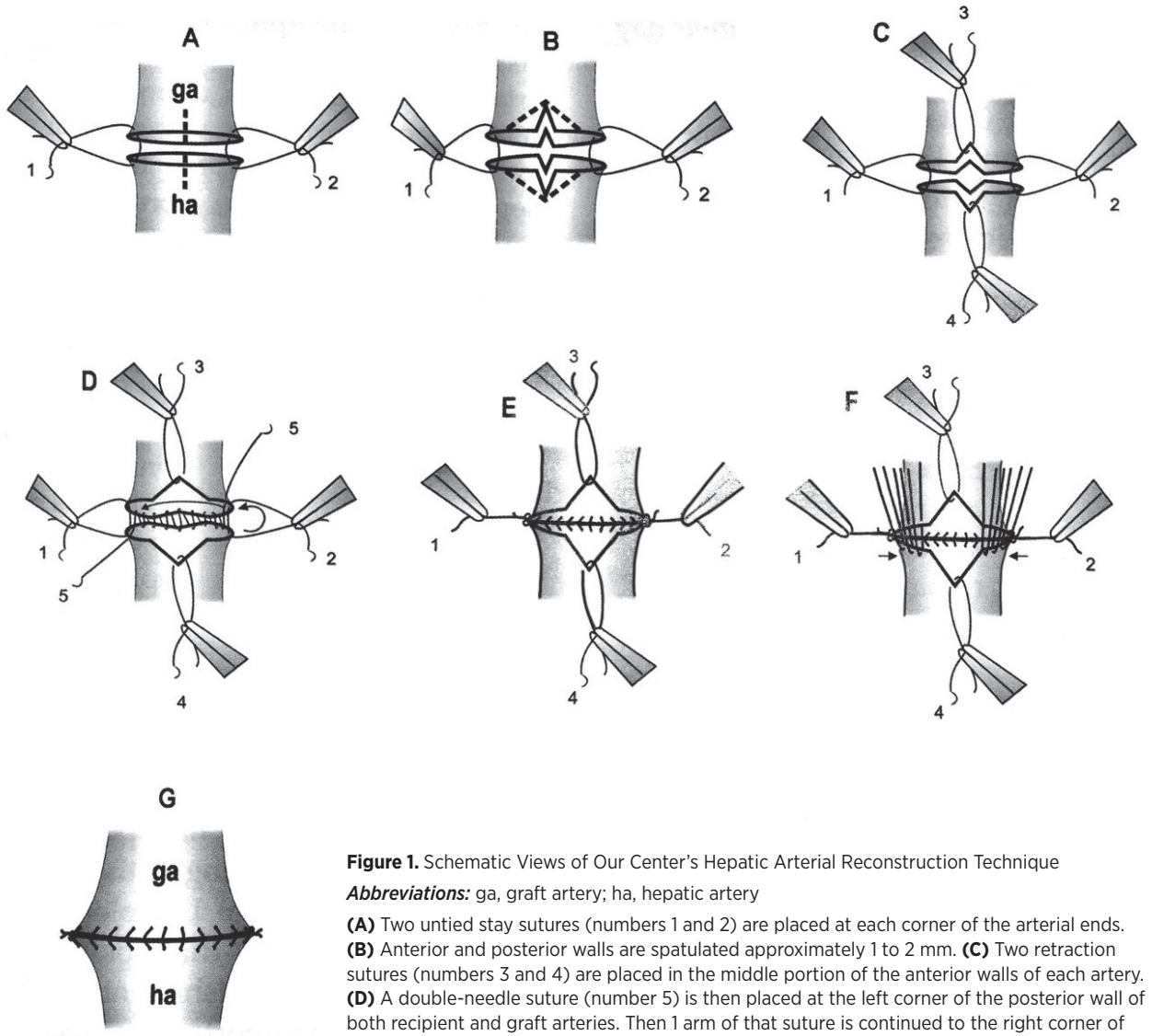

Figure 1. Schematic Views of Our Center's Hepatic Arterial Reconstruction Technique

Abbreviations: ga, graft artery; ha, hepatic artery

(A) Two untied stay sutures (numbers 1 and 2) are placed at each corner of the arterial ends. **(B)** Anterior and posterior walls are spatulated approximately 1 to 2 mm. **(C)** Two retraction sutures (numbers 3 and 4) are placed in the middle portion of the anterior walls of each artery. **(D)** A double-needle suture (number 5) is then placed at the left corner of the posterior wall of both recipient and graft arteries. Then 1 arm of that suture is continued to the right corner of the anastomosis. **(E)** After the posterior wall is finished, both open-loop stitch ends are pulled to the left and right corners to lessen the excess, and the posterior walls of both arteries are approximated tightly. Next, both untied sutures on the left and right corners (numbers 1 and 2) are tied. **(F)** The anterior wall of the anastomosis is sutured with interrupted sutures. **(G)** Completed anastomosis.

circulation within the hepatic parenchyma.[58-60] These patients can be cared for conservatively and cautiously, as 25% to 30% will develop biliary strictures that cause graft failure and require retransplant. Patients who have symptomatic late HAT usually present with biliary symptoms, such as a bile leak, an abscess, a stricture, or recurrent cholangitis. Although these patients can be initially treated with biliary stents or with biliary or vascular reconstruction, in the end, all of them require retransplants. Also, it must be remembered that there is a short window of opportunity in which these patients can undergo retransplant because of biliary sepsis, which is common and contributes significantly to the 50% retransplant mortality rate.

During the early postoperative period, a tight balance is needed to prevent thrombosis without increasing the risk of bleeding complications. Postoperative bleeding events and subsequent intraabdominal hematoma formation may lead to compression of the hepatic graft, which in turn may lead to vascular thrombosis.[23] There is no global consensus regarding prophylactic anticoagulation and antiplatelet regimens in liver transplant,[29] and every center applies their own regimen.

Patients who have both hematologic and operative risk factors are at higher risk of HAT than others. For these patients, routine anticoagulation in the postoperative period should be mandatory. Also, patients with extra-anatomic conduits and complex back-table reconstruction and patients who had preoperative transarterial chemoembolization are strong candidates for peritransplant anticoagulation with heparin or an antiplatelet agent. Some authors assert that the use of aspirin and alprostadil after transplant is effective in minimizing the incidence of HAT.[61]

In conclusion, prevention is better than any kind of treatment. Reconstructions most closely restoring normal anatomy and gentle handling of tissues are of paramount importance in hepatic arterial anastomosis. Postoperative routine Doppler USG surveillance provides the best chance for early diagnosis. Routine and well-titrated anticoagulation usually help to decrease the HAT rate. Interventional radiology in experienced hands is an excellent tool for HAT salvation.

Hepatic artery stenosis

The true incidence of HAS is unknown because it can present asymptomatically, but it reportedly ranges from 5% to 11%.[2,6,62] Hepatic artery stenosis can occur during the early postoperative (even intraoperative) period but is usually diagnosed more than 3 months after transplant.[63,64] Probable risk factors are clamp injury, intimal trauma from perfusion catheters, disrupted vasa vasorum leading to ischemia of the arterial ends, and inappropriate anastomosis technique.

Hepatic artery stenosis can lead to biliary ischemia and hepatic dysfunction. Severe stenosis can reduce blood flow, which can lead to thrombosis. Focally elevated velocities of up to 2 to 3 m/s can be measured at the site of the stenosis. Turbulence is present in the artery distal to the HAT. If the area of stenosis is not directly visualized, secondary signs like a tardus-parvus waveform can be seen in the intrahepatic arteries. The acceleration time is usually more than 100 ms, and the resistive index is less than 0.5. Mild stenosis may not be observable via Doppler USG imaging.[65]

The most common clinical presentation among symptomatic patients is abnormal liver function test results. Biliary complications as a result of HAS are less frequent than with HAT, as vascular collaterals often provide adequate blood flow to the allograft.

Hepatic artery stenosis can be treated more easily than HAT. The goal of treatment is to prevent future biliary complications. Balloon angioplasty and intraluminal stents are safe and often effective. However, we must note that some studies have shown that graft and patient survival for patients treated or managed conservatively for HAS are nearly equivalent.[62] On the other hand, some others have claimed that, when HAS is left untreated, it has a 65% chance of developing into HAT within 6 months.[62]

Stenosis located at the surgical site occurs among nearly 70% of patients.[27,66] Anastomotic stenosis is usually accompanied by reactive edema early after liver transplant. Additionally, anastomotic stenosis may not be relieved, and the risk of arterial rupture may be increased after balloon angioplasty.[67] Moreover, the restenosis rate can reach 60% after balloon angioplasty.[68] Stent placement can be used as the preferred treatment for early HAT accompanied by stenosis. Note that evaluation of the hepatic artery waveform with USG in the region of the stent may be challenging because of the change in the flow dynamics caused by the stent placement. Assessments of the intrahepatic arterial waveforms and the poststent portion of the hepatic

artery are important in these patients, checking for a return to normal sharp upstroke, normal velocity, and normal resistive index.[69,70]

Celiac artery stenosis may be seen because of atherosclerotic changes or medial arcuate ligament syndrome. If it has been diagnosed previously, medial arcuate ligament syndrome can be corrected during surgery, but atherosclerotic changes may require an aorto-hepatic graft interposition or other innovative arterial switches (such as gastroepiploic artery interposition).[69,70]

Hepatic artery pseudoaneurysms

The incidence of HAP is low, at close to 1% (0.3%-1.3%) after liver transplant.[71] Hepatic artery pseudoaneurysms are most often present early after transplant, but it can also occur late.

A HAP can be located at the intrahepatic (due to iatrogenic causes including biopsy, biliary tract interventions, or abscess formation) or extrahepatic vascular bed. Intrahepatic HAP is not a life-threatening complication. It is usually iatrogenic and caused by percutaneous interventional procedures. If it is not enlarging and is asymptomatic, then it is better to keep it under observation; however, large and symptomatic ones need surgical or interventional treatment. Ligation of the related intrahepatic artery, segmental resection of the transplanted liver, or in very extreme cases, retransplant are surgical options. With endoluminal or percutaneous transhepatic interventional radiology techniques, the intrahepatic HAP can be embolized in a minimally invasive manner.[6,72]

Extrahepatic HAP can be a devastating complication with a high mortality rate due to massive bleeding; it often requires immediate revascularization and even retransplant.[43,73] Extrahepatic HAP is commonly associated with localized infections (almost always fungal infections) or technical anastomotic problems.[10,71,74] The source of infection is often systemic or associated with a subhepatic infectious collection, frequently related to a biliary leak or small bowel perforation.[71,74] Percutaneous drainage is usually sufficient to treat patients with limited and clinically insignificant biliary or intestinal leaks.[75] However, surgical correction is needed and usually sufficient for patients with percutaneous drainage.[76] The clinician must be aware of the probability of a HAP when there is an infected subhepatic biloma. Although some HAP can cause compression and obstruction of the biliary tree, most present as rupture and hypotension. Patients may bleed intraperitoneally or into the gastrointestinal tract (eg, hemobilia), which means that the first sign of HAP can be sudden and massive life-threatening bleeding.

Hepatic artery pseudoaneurysm diagnosis is infrequent with radiology. Therefore, in every biliary leakage patient and if there is any suspicion, USG and CT imaging must be evaluated from this viewpoint and arteriography must be performed to detect HAP.[18] Additionally, arteriography creates the possibility of immediate therapeutic intervention.[71]

Hepatic artery pseudoaneurysm treatment is a challenging problem. Options depend on the hemodynamic stability of the patient and the facilities that the treating center has. Surgical ligation of the bleeding pseudoaneurysm can inevitably be the sole option for some patients. However, ligation results in an extremely high morbidity and mortality rate, especially during the early stage after liver transplant; therefore, ligation must be followed by retransplant.[43,73] If it is possible, excision and immediate revascularization of HAP is the optimal surgical option.[73] At the time of revascularization, bile leakage may also be repaired.

The experience and facilities of the interventional radiology team have a great role in the case of percutaneous treatment of HAP. Embolization alone of the bleeding artery has rarely been reported, but it is a lifesaving method in desperate situations. However, if it is not followed by a retransplant, the prognosis is generally fatal.

The indication for treatment in a nonbleeding HAP is a progressive increase in the size of the aneurysm.

The definitive treatment for this is the placement of endovascular covered coronary stent grafts.[77,78] This technique, which may be performed immediately after the diagnostic angiography, has the unique advantage of completely excluding the pseudoaneurysm without injecting embolic agents into the aneurysm and concomitantly preserves arterial blood flow to the graft. It must be noted that stent graft implantation in a visceral artery is not always possible because of tortuous anatomy or the requirement for anticoagulation therapy, which is mandatory after an endovascular stent procedure. Additionally, we must remember that placement of a stent or a graft in an infected area can provoke late graft disintegration and consequently rupture of the aneurysm, too.[79]

In conclusion, careful hepatic artery reconstruction and successful control of biliary anastomotic leaks are key factors in the prevention of HAP after liver transplant. Despite the therapeutic measures described above, hepatic artery aneurysms are fatal in more than 50% of cases.

Arterioportal fistula

Arterioportal fistula (APF) refers to abnormal shunt or fistulous connection between the portal venous and hepatic arterial systems, resulting in the redistribution of arterial flow into a focal region of the portal venous flow. Arterioportal fistulas can be classified as intrahepatic or extrahepatic and also hemodynamically significant or hemodynamically insignificant. Hemodynamically significant APFs are defined as those exhibiting opacifications of the main portal vein of the transplanted hepatic graft or its first-order branch, with or without portal venous changes, by Doppler USG imaging. Only 0.2% of hemodynamically significant APFs are reported after liver transplants. The incidence of APF among living related-donor or deceased-donor liver transplant recipients is the same, and APF is found in 0% to 5.4% of abnormal liver transplant angiogram series.[72,80]

Arterioportal fistula could be congenital (hereditary hemorrhagic telangiectasia, Ehlers-Danlos syndrome, and biliary atresia), idiopathic, or secondary (to cirrhosis, hepatic neoplasm, hepatic trauma, hepatic parenchymal congestion, inflammatory or infective disease, obstruction of HV or portal vein). Arterioportal fistula could be iatrogenic following percutaneous liver biopsy, cholangiogram, biliary drain placement, chemoembolization, etc. Erosion of splanchnic artery aneurysms into the portal circulation is a relatively common cause of extrahepatic APF.[81]

Most APFs are asymptomatic and diagnosed incidentally.[82,83] Others may present symptoms of portal hypertension, sepsis, hemobilia, biliary obstruction, or pulmonary hypertension,[83-88] and hemobilia can be life-threatening.[84] Hemodynamically significant APF can direct arterial blood away from the allograft parenchyma with resulting ischemia, which may cause graft dysfunction, failure, and even parenchymal infarction and necrosis. Large APFs may present symptoms of portal hypertension, ascites formation, and, if neglected, may lead to patient death due to graft loss, gastrointestinal hemorrhage, or both.[83,86,88]

Most APFs resolve spontaneously and few progress.[83,84,89] The prevalence of postbiopsy arterial injuries decreases from 52% at 1 week after the biopsy to 10% at 3 weeks later.[90,91] Furthermore, APFs have been known to resolve as long as 5 years after they have been diagnosed.[83] There are no predictors of their prognosis,[72] and the reasons that most APFs resolve and few progress are unknown.

Doppler USG is the main screening tool for APFs, with turbidity and aliasing seen at the site of the APF. Reduced arterial resistive index of the feeding hepatic artery should raise the suspicion of APF.[92] Reversal of flow in the receiving portal venous branch is always seen, and arterialization of portal vein flow may be seen in some cases.

Doppler USG can diagnose nearly half of APFs, and all APFs that are hemodynamically significant.[93] Computed tomography or magnetic resonance imaging findings include early and prolonged enhancement of the peripheral portal vein, before the main portal vein is enhanced,

or enhancement of the main portal vein, before the superior mesenteric and splenic veins are enhanced. Dilated intrahepatic vessels are seen during the arterial phase. Computed tomography and magnetic resonance imaging can also be used to diagnose the underlying cause of APF, including a tumor, inflammatory lesion, and thrombosis or compression of the portal or HVs.

Relatively compromised arterial flow and relatively poor compliance of transplanted livers (stiff graft) are a hindrance to the progression of a small APF to a hemodynamically significant one. Thus, some small APFs can regress spontaneously. Maybe this is the reason for a surprisingly low prevalence of APFs in liver transplant recipients, despite their having frequent biopsies and percutaneous biliary procedures as well as being under frequent imaging surveillance. An APF that causes portal hypertension tends to persist and may require treatment.[72]

Surgical ligation of the feeding artery of the fistula or simple resection treatment of the vascular anomaly is now generally replaced with endoluminal embolization of APFs.[83,84,88-90,94-96] The decision to embolize an APF should not be taken lightly because HAT is a known risk for allograft endangerment during this procedure.[72] Embolizing APF in liver transplant recipients is indicated only in symptomatic patients. However, partial or complete embolization of an asymptomatic but hemodynamically significant APF can be weighed against its potentially increased ischemic complication risk, which is associated with obliterating large intrahepatic arterial branches in the future.[72] Several embolization sessions may be needed to treat all hepatic artery branches communicating with portal branches from distal to proximal parts of the fistula as they are the existing intrahepatic collateral circulation pathways. Hepatic infarction is a potential complication. After the procedure, Doppler USG surveillance should be performed to evaluate the reversal of signs of hemodynamic significance. In some rare cases, retransplant is the last therapeutic option.

PORTAL VEIN COMPLICATIONS

Portal vein (PV) complications are less common than those of the hepatic artery (1%–2%) but are associated with a high incidence of graft loss.[97,98]

Portal vein complications are more frequent in pediatric liver transplant patients (3%-17%).[97-101] Some authors have reported grim patient and graft outcomes of PV complications.[101-103] However, many others have reported that PV complications did not significantly affect patient or graft survival.[21,104] Most PV complications occur within 60 months posttransplant.[101] The most frequent symptoms and signs of a PV complication are gastrointestinal bleeding, recurrent ascites, splenomegaly, and/or liver dysfunction.[98]

The risk factors for PV complications are patients with biliary atresia, young age, small body weight (< 6 kg), small PV size (< 5 mm), malrotation of the vessels, previous operation history (eg, portoenterostomy, portosystemic shunt), and emergent operation.[22,101,102,105-110] Large-for-size grafts may have an increased incidence of vascular complications because of vessel kinking, low portal flow, disproportion at vessel diameter, and increased intra-abdominal pressure.[69,70,105,111]

Preexisting PV thrombosis (PVT) is not a strict contraindication for liver transplant, but it may complicate the PV anastomosis.[112] The location and dimension of the preexisting PVTs are extremely important for a sufficient inflow.

The portal system is a low-pressure system; therefore, it is believed that PV reconstructions that preserve the splenomesenteric confluence as a source of inflow together contribute sufficient blood flow in the hepatopetal direction to prevent postoperative thrombosis.[10,104]

Diameter disparity between the PV size of the recipient and graft is another difficulty for PV anastomoses. Different surgical techniques are used to solve this kind of problem, such as suturing the graft PV to the bifurcation of the recipient PV or confluence of the splenomesenteric axis;

venoplasty of the graft's PV to reduce or widen its diameter; and vein grafts from the deceased- or living-donor's inferior mesenteric vein (IMV), saphenous vein, or iliac vein.[22,97,109,113-115] If it is necessary to use a conduit for PV anastomosis, it is better to choose a fresh vein graft taken from the donor (living or deceased) or autologous one (like external iliac vein) instead of cryopreserved vein grafts. Also, ligation of obvious portosystemic shunts along the retroperitoneum helps to augment the portal flow during reperfusion.[10]

If the recipient has a portal vein size < 5 mm or receives a large-for-size graft (graft-to-recipient weight ratio > 4%), at least 60 months of observation for early detection of PV complications is recommended, using Doppler USG imaging, even if the patient shows normal hepatic function.[116]

Portal vein thrombosis

Although postoperative surveillance USG is a useful tool to identify suspected or established vascular thrombosis, the presence of portal collaterals in long-term PVT may be misleading.[112] Therefore, CT angiography, MR angiography, or conventional angiography is recommended for confirmation of clinical or USG suspicion of PV complications, especially PVT.[104]

Most PVT occurs early after a transplant, but 30% can occur later. Early PVT may be amenable to attempts at recanalization (anticoagulation) or operative thrombectomy or retransplant may be needed.[40,93,101,117,118] The role of percutaneous treatment for PVT is growing. Portal vein thrombolysis and percutaneous portal vein thrombectomy and stenting have reasonable results.[119,120]

For chronic PVT, both interventional angioplasty and surgical shunting procedures have been attempted successfully.[104,121-124] Nevertheless, progressive graft fibrosis may develop, thereby necessitating retransplant.[122] Indeed, PVT negatively affects long-term graft and patient survival more than HAT.[12] This is probably because retransplant is a less frequent option after PVT as patients with severe PVT lack appropriate venous inflow from mesenteric circulation.

Portal vein stenosis

Portal venous stenosis (PVS) is a relatively less frequent vascular complication compared with arterial complications after liver transplant. Portal venous stenosis usually occurs several months after the transplant, and more often in younger male living-donor liver recipients. The rate of PV complications that include PVS or PVT in adult patients who have undergone orthotopic liver transplant has been reported to be < 3%.[120,125] The rate of PVS is higher among children with reduced-size liver transplants and living-donor transplants, affecting 2% to 14%; if not treated promptly, this complication may result in graft loss.[99,110,119,122]

In symptomatic patients, the clinical signs of portal hypertension such as diarrhea, gastrointestinal hemorrhage, ascites (especially stenosis > 80%), and splenomegaly usually exist. Low platelet count has been observed in nearly all patients with late-onset PVS. Sometimes elevated liver function can be seen, but it is not a reliable indicator of PVS. Delayed diagnosis and treatment of PVS may not only lead to graft failure but also to hepatopulmonary syndrome or pulmonary hypertension, which make retransplant difficult or impossible.[122]

Most patients are asymptomatic, and usually it is detected during routine Doppler USG or CT imaging, which is the most sensitive diagnostic test for early diagnosis of PVS. Splenomegaly, ascites, stenosis, low portal vein velocity, and poststenotic dilatation are the findings that can be detected with these tools.

In the past, PVS was treated with surgical reconstructions, such as venous reconstruction or portocaval shunting; however, these can be complicated owing to severe adhesions, scar tissue surrounding the graft, and limitations in the length of the involved venous structures. The mortality rate has been high in the past. After the first successful percutaneous balloon dilatation in 1991, this procedure became an alternative to surgical

treatment in PVS.[126] Nowadays, most patients with PVS are treated using radiological intervention techniques. The initial technical success rate is 76% to 100%.[110,127-129] For recurrent stenoses, percutaneous intravascular stent placement is recommended by most authors.[119,126,129]

Venoplasty may be better than stents for pediatric PVS after liver transplant because children are expected to grow and the stent is fixed in size.[130] Most centers prefer radiological intervention techniques (balloon dilatation or stent placement) for the treatment of PVS, and we concur.

HEPATIC VEIN COMPLICATIONS

During the pioneering years of liver transplantation, classic conventional whole liver transplants prevented hepatic venous outflow obstruction (HVOO) because of large cava-cava anastomoses; however, the inferior vena cava (IVC)-preserving piggyback technique quickly became popular because it eliminated almost all need of venovenous bypass. Subsequently, outflow obstruction from the anastomotic stricture of HVs after living-donor liver transplant emerged as a serious complication, especially among pediatric patients.[131] Hepatic venous outflow obstruction is the Achilles' heel of the piggyback technique and may result from a smaller caliber anastomosis or rotation and positional flattening or kinking of the venous outflow tract.[132,133] Hepatic vein complications occur less frequently as surgical experience increases, with overall incidence around 1% to 4%.[99,118,134] Imperfect surgical technique contributes to approximately one-third of cases (particularly when this complication presents early); however, the recurrence of Budd-Chiari syndrome may also contribute to venous outflow thrombosis or stenosis.

The size of the anastomotic orifice, the orientation of the vessels, and the position of the graft are important determinants of hepatic outflow maintenance, and a perfect outflow is not guaranteed postoperatively because the graft position may change during the regeneration of the liver parenchyma and during the accommodation of the graft in the abdominal cavity.

For partial grafts, the use of a wide-orifice outflow reconstruction between the graft and native HV decreases the incidence of HVOO (1%–4%).[99,118,134] The wide caliber of the anastomosis is achieved by either triangulation or by combining the orifices of the native HV into a common cloaca.[22,131] The avoidance of venous conduits achieves a short stump, which avoids anastomosis twisting.[118] Also, fixing the graft liver to the diaphragm is a good measure to prevent the anastomosis from twisting. Any significant rotation of the graft liver can cause a twist on both the hepatic vein anastomosis and the IVC, resulting in HV or IVC stenosis. This situation is more frequent in patients who have received a whole graft from a deceased donor, with hepatic outflow reconstruction performed between the suprahepatic vena cava of the graft liver and the orifice of the native hepatic veins.[135]

Hepatic venous outflow obstruction can be classified as intraoperative, postoperative acute, and chronic. When the blood supply of the graft is recovered during the operation, the intraoperative HVOO should show signs of liver swelling, portal hypertension, and even hypotension resulting from insufficient venous return. If these signs are relieved by adjusting the position of the graft, intraoperative HVOO is diagnosed. Hepatic venous outflow obstructions that occur during the first postoperative month are considered early or acute. Ultrasonographic surveillance of the graft vasculature twice per day is a good tool with early postoperative HVOO diagnosis. In case of any suspicion, CT imaging must be used; if the CT evaluation is ineffective, then invasive techniques like hepatic venography, venacavography, and manometry must be performed. Hepatic venous outflow obstruction is confirmed if the venous outflow has a pressure gradient > 3 mm Hg and/or the anastomotic stricture is > 50%.[135] The occurrence of HV stenosis or HV thrombosis is heralded by worsening ascites and graft dysfunction.[118,134] The roles of the diagnostic

tools and their efficacy are the same as for other vascular complications.

Percutaneous angioplasty via the internal jugular vein has excellent results, with improvement of symptoms in over 80% of patients; however, most require multiple sessions in order to maintain patency.[21,48,118,134] Nevertheless, complications are rare, and percutaneous therapy has replaced open surgical therapy in most cases.

INFERIOR VENA CAVA COMPLICATIONS

Inferior vena cava complications are classified as stenosis and thrombosis. Opposite to HV, complications involving the IVC occur particularly in patients who receive end-to-end anastomosis rather than piggyback anastomosis.[136] There are multiple reasons for IVC thrombosis, but those that occur after liver transplant are almost always caused by a stenosis, due to twisting of IVC or compression of a mass (eg, hematoma). Narrowing the IVC during repair of caval injuries is difficult in adults. They are more common in retransplant and pediatric populations than in other populations. Delayed caval stenosis may also occur.

Inferior vena cava stenosis after liver transplant is a rare but serious complication. Inferior vena cava stenosis affects less than 3% of transplant recipients and occurs most commonly in the early period after surgery.[27,137-139] Factors related to this complication include a surgical technique at the caval anastomosis, a hematoma close to the IVC, a mismatch between the donor's and recipient's vasculature, or kinking. In the long-term, perianastomotic hypertrophy creates chronic IVC stenosis.

Patients with IVC stenosis or thrombosis may be asymptomatic but experience lower extremity edema, dyspnea, ascites, and other signs of portal hypertension, depending on the location. Budd-Chiari syndrome and variceal hemorrhage may result from stenosis of the suprahepatic IVC; a higher incidence of Budd-Chiari syndrome and hemorrhage have been reported in recipients of living-donor and split-liver transplants because of hepatic venous reconstructions.[137] Untreated stenosis can result in thrombosis and is a potentially fatal complication of liver transplant with graft failure, depending on its location.[138]

The use of endovascular repair is preferred to surgical repair, which is complicated and needs complete dissection of the graft and sometimes even a transdiaphragmatic approach.[139] Both venoplasty and stenting are commonly used for treatment. However, the role of venoplasty is limited because of its ineffectiveness in cases of stenosis created by tortuous grafts, the risk of later restenosis, and the potential for anastomotic rupture.[138] The fibrous nature of the surrounding tissue is another predisposing factor for recurrence. Stenting, on the other hand, can achieve immediate and long-term patency, even in the face of overlying ascites, hepatic enlargement, fibrosis, and adhesions, with angioplasty of the stent performed as needed. Stenting is a safe and effective way of treating torsion, compression, and stenosis of the IVC following liver transplant.[138]

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Role of Interventional Radiology in Hepatic Artery Complications Associated with Liver Transplant

Fatih Boyvat

Liver transplant (LT) is a lifesaving treatment for pediatric and adult patients with end-stage liver disease, acute liver failure, and hepatocellular carcinoma.[1] However, vascular problems, such as thrombosis and stenosis of the hepatic artery, are serious complications after LT. These complications are more frequent among recipients of living-donor liver transplant (LDLT), especially among pediatric patients. The reported incidence of post-LT vascular complications is 7% to 15%, but it can be higher, up to 30.8%, with more complex surgeries, such as in split-liver transplants and LDLT.[2,3] There is a striking difference between adult and pediatric populations in terms of rates of complications, types of complications, timing of complications, and survival outcomes after LT.

There are several anastomotic possibilities with regard to the hepatic artery. In orthotopic LT, the donor celiac axis is anastomosed to the recipient artery at either the bifurcation into the left and right hepatic arteries or the take-off of the gastroduodenal artery. In patients with a small or diseased hepatic artery, a donor iliac artery interposition graft may be anastomosed directly to the recipient's aorta. In LDLT, the liver allograft is partial, and the arterial reconstruction is technically highly demanding.[4] The risk of hepatic artery complications is high due to the small caliber of the vessels. Knowledge of the type of anastomosis is important for radiological imaging and intervention.

Morbidities associated with hepatic arterial complications are significant, and surgical reconstruction of the hepatic artery for post-operative arterial thrombosis is often graft-saving and lifesaving. More recently, advances in endovascular therapy have led to an increasing role of interventional radiology for the treatment of hepatic arterial complications after LT.[5]

Hepatic artery complications after LT include hepatic artery stenosis, thrombosis, spasms, kinks, aneurysms, bleeding, and arterial steal syndromes. For this reason, early diagnosis and treatment are essential. Rates of hepatic artery complications are reported to range from 1.7% to 16.3%, with higher rates in children than in adults and in LDLT than in orthotopic LT.[6] Pediatric patients are at greater risk for vascular complications after LT because of their smaller arterial size compared with adults.

To treat these complications, there are 2 therapeutic options: endovascular interventions or surgery. Both treatment methods have some advantages and disadvantages.

HEPATIC ARTERY STENOSIS

Most vascular complications develop < 3 months after LT, with the most common being hepatic artery stenosis (HAS). Hepatic artery stenosis is found mostly at the anastomosis between the donor's and the recipient's artery. In orthotopic LT,

HAS occurs in 4% to 11% of recipients, mostly at the site of arterial anastomosis.[7,8] This rate appears to be higher for LDLT or pediatric recipients because of size differences between the graft's and the recipient's vessels. The development of HAS is associated with allograft rejection, microvascular injury from cold preservation of the liver, disruption of the vasa vasorum, clamp injury, caliber size mismatch, prior transarterial chemoembolization, extrinsic compression, and technical issues.[1] The clinical presentation is usually graft dysfunction or biliary tract complications related to decreased hepatic blood flow.[9] Hepatic artery stenosis usually has a subclinical presentation and manifests as an insidious form of graft dysfunction. When untreated, HAS may progress to hepatic artery thrombosis (HAT).[10] Routine Doppler ultrasonography is one of the best tools for detecting silent HAS, with sensitivity of close to 85%.[11] Endovascular intervention methods include percutaneous transluminal angioplasty (PTA) or stent placement. Percutaneous transluminal angioplasty is the first-line treatment method for HAS. A critical HAS is defined as > 50% narrowing of the internal lumen of hepatic artery. Symptomatic HAS is defined as the presence of either biological abnormalities (cytolysis, cholestasis) or biliary complications.[10]

When left untreated, 65% of patients with HAS will present with progression to HAT within 6 months.[12] Both PTA and stent placement have high rates of technical success (80%-93%) (Figure 1). With these procedures, rates of complication range from 7% to 10%; complications include access site complications (hematoma, pseudoaneurysm, arteriovenous fistula, femoral or external iliac artery occlusion) and hepatic artery dissection or perforation.[13] In a recent meta-analysis of 26 studies that compared the efficacy of PTA versus stent placement for the treatment of HAS, there were no differences in procedural success, complications, return to normal liver function, arterial patency, survival, or requirement for reintervention or retransplant.[14] However, a recent study on the endovascular treatment of HAS using stents reported improvements in overall outcomes and long-term patency rates over PTA alone.[15] This study showed a high reintervention rate of 38% for the PTA group versus 22% for the stent group. High primary patency (90%), excellent primary assisted patency (100%), and low reintervention (10%) after primary stent placement of HAS after LT were also reported.[15] During endovascular procedures, intra-arterial vasodilators and heparinization are crucial. Also, a loading dose of aspirin and clopidogrel are important medications to keep the artery patent. After stent placement, a 1-year follow-up for maintenance is suggested. Indeed, intra-arterial medications during the procedure and postprocedural antiplatelet medications may be critical in improving patency and reducing reintervention rates of primary stenting.

TECHNIQUES FOR HEPATIC ARTERY STENOSIS

Percutaneous transluminal angioplasty or stenting in HAS is usually performed via femoral, brachial, or axillary access. The femoral approach is the preferred way, but it also depends on the orientation of the celiac axis. If there is an acute angulation of celiac trunk, then brachial or axillary access is preferred. A 6F short or long sheath is placed through the femoral artery. Diagnostic angiographies are performed. With regard to hepatic artery manipulation, vasospasms may occur; therefore, intra-arterial administration of vasodilators may be necessary. The stenosis is crossed with a 0.014- or 0.016-inch soft tip guidewire and a microcatheter coaxially. Stenosis can be dilated with low-profile coronary angioplasty balloons (2.0-5.0 mm diameter); if results are not satisfactory, a stent can be placed (Figure 2). Exchange of catheter and balloon must be performed carefully, as inadvertent movement of the tip of the guiding catheter or long sheath may itself cause hepatic artery dissection.

If results are not satisfactory after PTA, the preferred option is coronary balloon-expandable stents. These self-expandable low-profile stents can be used if there is a tortuosity of the hepatic artery or if there is a mismatch between the donor's and recipient's hepatic artery. Vessel tortuosity can

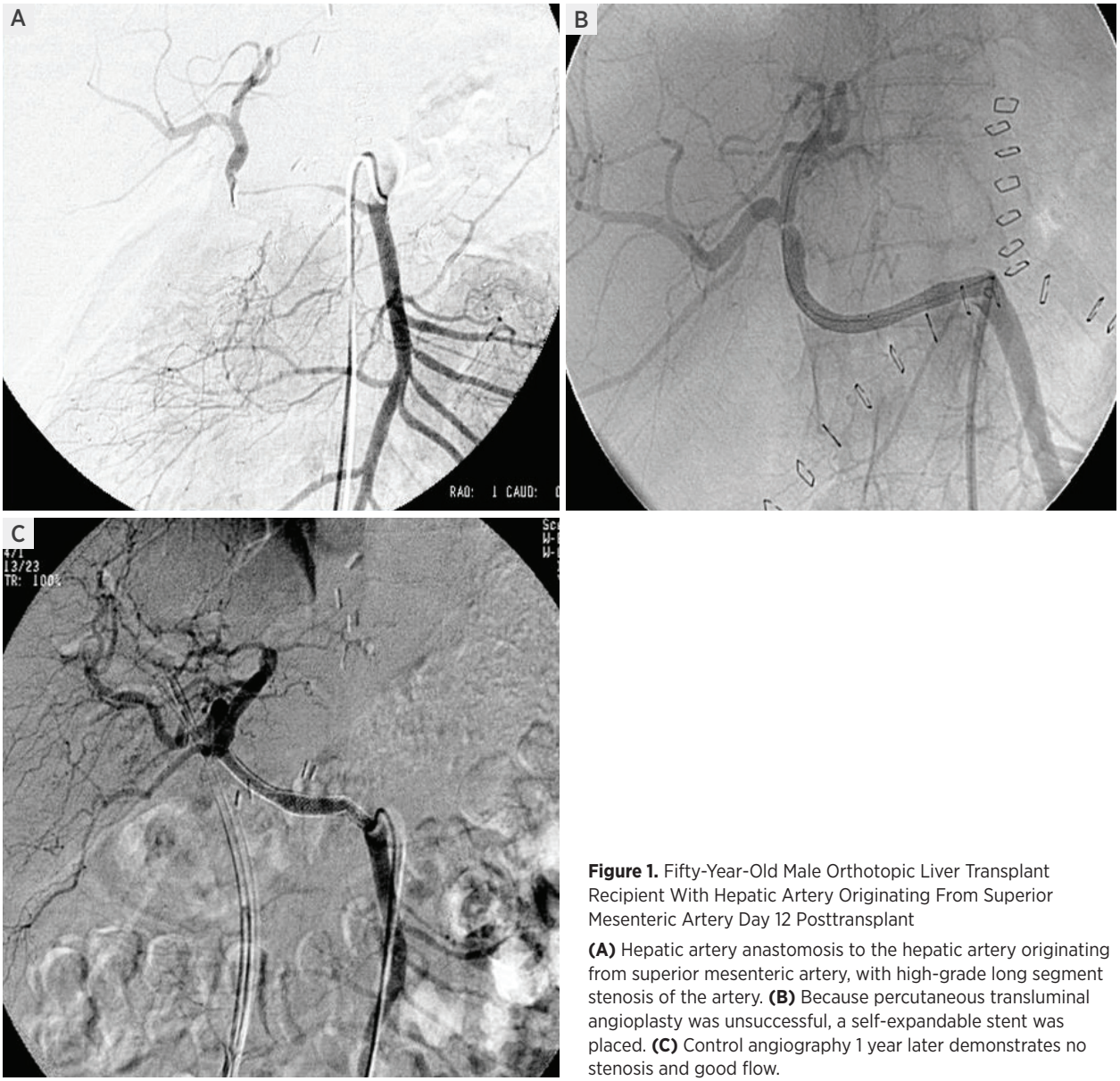


Figure 1. Fifty-Year-Old Male Orthotopic Liver Transplant Recipient With Hepatic Artery Originating From Superior Mesenteric Artery Day 12 Posttransplant

(A) Hepatic artery anastomosis to the hepatic artery originating from superior mesenteric artery, with high-grade long segment stenosis of the artery. **(B)** Because percutaneous transluminal angioplasty was unsuccessful, a self-expandable stent was placed. **(C)** Control angiography 1 year later demonstrates no stenosis and good flow.

be a risk factor for complications associated with endovascular HAS treatment. In patients with arterial kinks/tortuosity associated with HAS, PTA can result in greater complications in addition to tandem and distal stenosis.[16] In patients with kinks/tortuosity, technical success and complication rates are 14% and 29%, respectively, compared with 94% and 10% in patients with normal anatomy. Graft-covered coronary stents are lifesaving if the rupture occurs after PTA (Figure 3). After treatment, patients require dual antiplatelet therapy for 1 year.

With regard to endovascular interventions involving HAS after LT, timing remains an important question because there is a risk of hepatic arterial rupture. In previous reports, endovascular procedures for HAS were conducted within 1 week of LT and 21 days after LT.[10,16] However, if coronary covered stents are available, the endovascular procedure

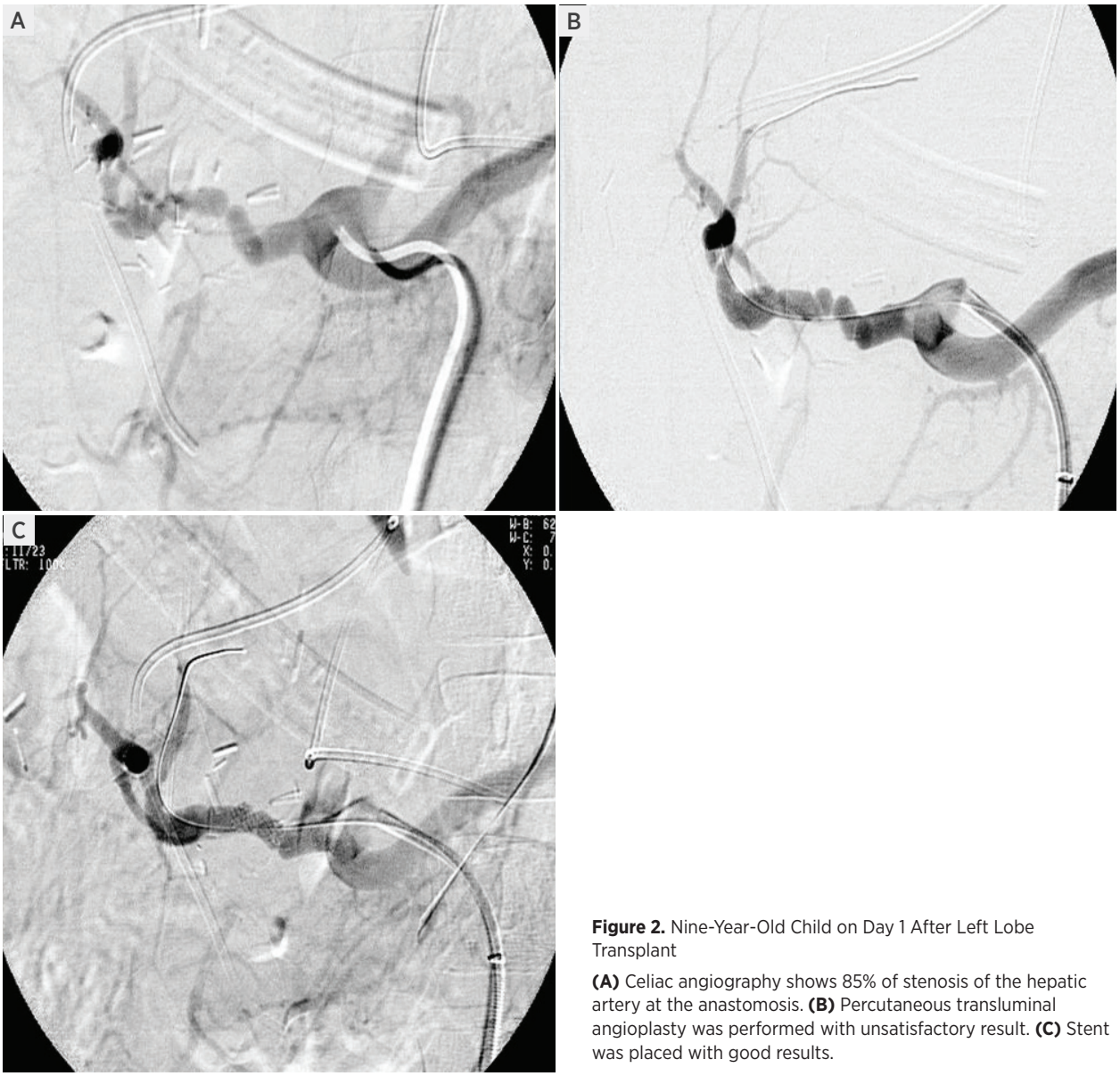


Figure 2. Nine-Year-Old Child on Day 1 After Left Lobe Transplant

(A) Celiac angiography shows 85% of stenosis of the hepatic artery at the anastomosis. **(B)** Percutaneous transluminal angioplasty was performed with unsatisfactory result. **(C)** Stent was placed with good results.

can be performed safely even on postoperative day 1.[5] If hepatic arterial rupture or bleeding occurs, a prolonged inflation of a balloon can be performed initially; if bleeding continues, then covered stents can be easily placed. If the vascular anatomy is not suitable for covered stents, a balloon must be inflated in the hepatic artery and the patient must undergo surgery for repair. Hepatic arterial rupture after PTA has been reported in 6% to 12% of patients.[17]

HEPATIC ARTERY THROMBOSIS

Hepatic artery thrombosis is a potentially devastating complication, having a high mortality rate of 27% to 58%, and is the most common cause of graft loss.[18] Posttransplant HAT is reported to occur in 4% to 11% of adult LT and 11% to 26% of pediatric LT recipients, although recent studies have shown rates as low as 4.8%.[19,20] For children, with an overall rate of HAT of almost twice the rate

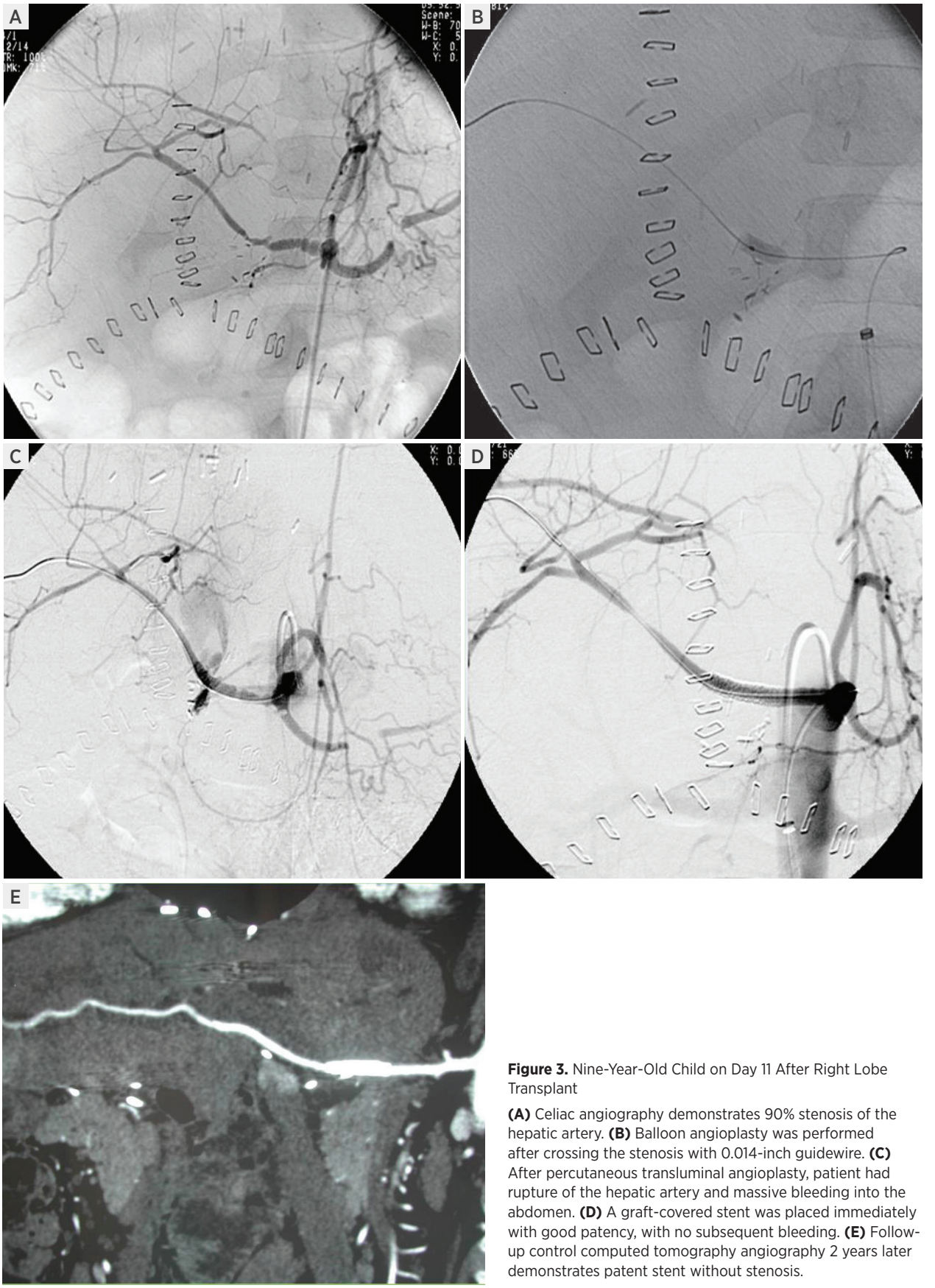


Figure 3. Nine-Year-Old Child on Day 11 After Right Lobe Transplant

(A) Celiac angiography demonstrates 90% stenosis of the hepatic artery. **(B)** Balloon angioplasty was performed after crossing the stenosis with 0.014-inch guidewire. **(C)** After percutaneous transluminal angioplasty, patient had rupture of the hepatic artery and massive bleeding into the abdomen. **(D)** A graft-covered stent was placed immediately with good patency, with no subsequent bleeding. **(E)** Follow-up control computed tomography angiography 2 years later demonstrates patent stent without stenosis.

in adults, HAT usually occurs within the first 2 weeks. In adults, only about one-third of incidences of HAT occur during the first month post-LT. Smaller children have even a higher incidence of HAT, where the lumen is smaller and where even a small degree of hypotension due to any cause can lead to HAT. A small-diameter hepatic artery and lower blood flow are well-described risk factors for HAT, with diameter of < 3 mm being a predominant risk factor. If the hepatic arterial flow is lower than 200 mL/min, risk of HAT increases 5 times. This is the main reason why the rate of HAT in children is almost twice that of adult patients.[8]

Causes of early HAT are related not only to surgical factors, such as redundancy of hepatic artery resulting in vessel kinking, stenotic anastomosis, and intimal dissection, but also to nonsurgical factors. Elderly donors, hypercoagulable state, and rejection episodes may cause this situation.[21] Postanastomotic stenosis is most likely from clamps used on the donor's hepatic artery, which may cause intimal damage resulting in stenosis or thrombosis.

Patients with HAT may present with nonspecific signs, such as fever, leukocytosis, increased liver function tests, pain, or fatigue. The most frequent clinical presentation (30%) of early HAT is acute fulminant hepatic failure.[22,23] Graft dysfunction is more commonly seen in early HAT (< 1 mo after LT), and biliary complications are more common in late HAT. Late HAT is usually due to ischemic or immunologic injuries, and up to 50% of patients may be asymptomatic with mild biochemical abnormalities. However, this can lead to recurrent cholangitis, liver abscess, and biliary leakage or stricture.[24,25]

In early HAT, there is a significant risk of death and graft loss, thus stressing the importance of early diagnosis. Duplex ultrasonography is the first diagnostic step to detect hepatic artery flow; if there is suspicion, computed tomography angiography may then be used. Revascularization, retransplant, or endovascular treatment can be used for patient treatment. Late HAT may have a better prognosis due to the formation of collaterals. Retransplant is necessary in at least one-half of patients with HAT; however, because of shortages in organs for retransplant, this treatment is often not possible. Therefore, surgical or endovascular revascularization is often attempted as a definitive treatment or as a bridge to retransplant.[13] In patients with early HAT, graft survival rate is high (up to 81%) with urgent revascularization. Surgical revascularization cannot relieve extensive thrombosis involving the intrahepatic arteries; in these cases, retransplant or catheter-directed thrombolysis must be considered. Traditionally, revascularization is through surgery. However, other endovascular interventions (catheter-directed thrombolysis, mechanical thrombectomy, PTA, and stent placement) have shown reasonable success rates.[26]

When endovascular interventions or revascularizations fail, a retransplant after HAT is necessary. After retransplant, survival rates in adult patients at 1, 5, and 10 years are 57.1%, 42.9%, 37.5%; for children, these rates are 80%, 80%, and 80%, that is, children have a better survival rate than adults. In adults, graft survival is 0% at 2 years for early and immediate thrombosis but 30.8% at 2 years and 11.4% at 11 years for late thrombosis. This is mainly due to the development of collateral circulation and the recanalization of the hepatic artery.[8]

Endovascular interventions are usually performed via the femoral artery, and selective catheterization of the celiac trunk or superior mesenteric artery (if the hepatic artery originates from) with a 4F catheter is necessary. Usually, an occluded stump of the hepatic artery is seen. A soft tip 0.014- or 0.016-inch guidewire with a microcatheter should be coaxially advanced into the thrombosed hepatic artery, with care taken not to create dissection of the thrombosed hepatic artery. Once the thrombosed hepatic artery is crossed, thrombolytic treatment is started with tissue plasminogen activator. A 1-mg or 2-mg infusion of tissue plasminogen activator is enough to make an effective thrombolysis for the fresh thrombus. Heparinization of the patient is necessary during thrombolytic treatment (Figure 4). A small thrombolytic dose at a high localized

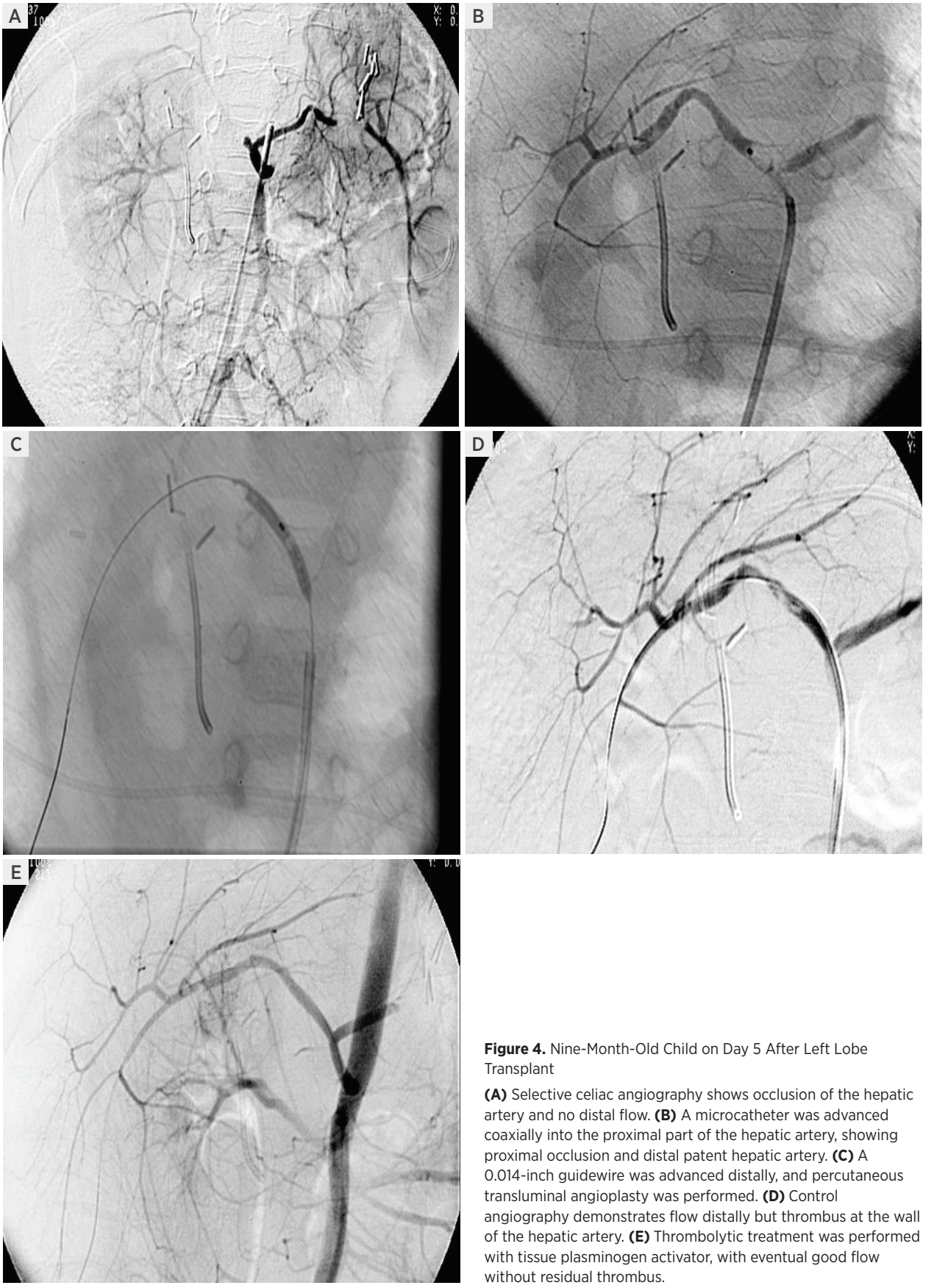


Figure 4. Nine-Month-Old Child on Day 5 After Left Lobe Transplant

(A) Selective celiac angiography shows occlusion of the hepatic artery and no distal flow. **(B)** A microcatheter was advanced coaxially into the proximal part of the hepatic artery, showing proximal occlusion and distal patent hepatic artery. **(C)** A 0.014-inch guidewire was advanced distally, and percutaneous transluminal angioplasty was performed. **(D)** Control angiography demonstrates flow distally but thrombus at the wall of the hepatic artery. **(E)** Thrombolytic treatment was performed with tissue plasminogen activator, with eventual good flow without residual thrombus.

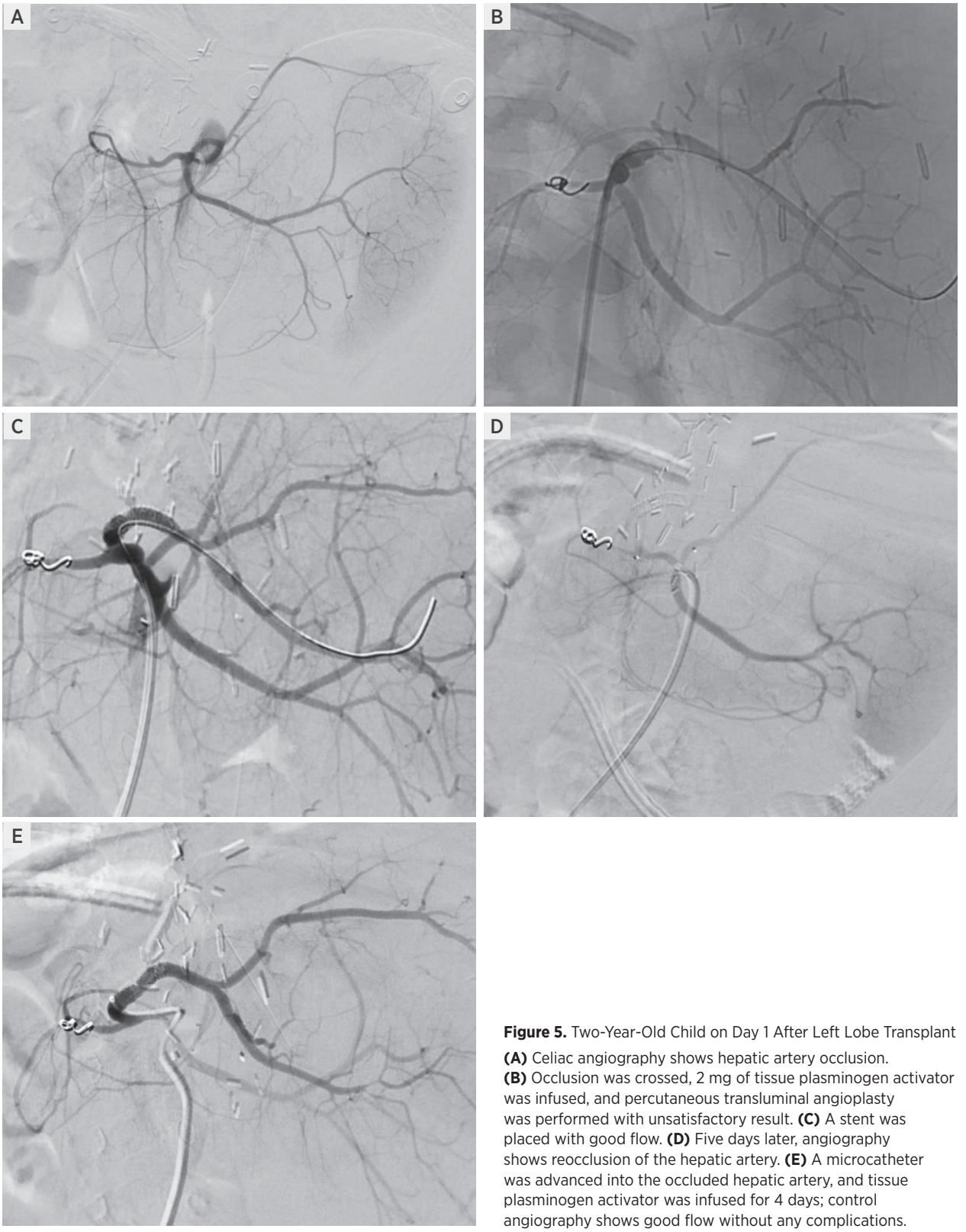


Figure 5. Two-Year-Old Child on Day 1 After Left Lobe Transplant
(A) Celiac angiography shows hepatic artery occlusion. **(B)** Occlusion was crossed, 2 mg of tissue plasminogen activator was infused, and percutaneous transluminal angioplasty was performed with unsatisfactory result. **(C)** A stent was placed with good flow. **(D)** Five days later, angiography shows reocclusion of the hepatic artery. **(E)** A microcatheter was advanced into the occluded hepatic artery, and tissue plasminogen activator was infused for 4 days; control angiography shows good flow without any complications.

concentration has little influence on systemic coagulation parameters. Despite its local effect, hemorrhage is the most common complication of intra-arterial thrombolysis. Therefore, patients must be followed closely, with regular checks of activated partial thromboplastin time, fibrinogen, prothrombin time, and platelet count. Thrombolysis can be continued for several days if control angiographies show a benefit of arterial flow. Restoration of flow using thrombolysis can uncover underlying anatomic problems, including kinking, stenosis, localized dissection, or intimal damage. Percutaneous transluminal angioplasty and/or stenting has been shown to have better patency and survival rates than thrombolysis alone (Figure 5). Graft-covered stents are lifesaving and effective to treat these patients if there is rupture or bleeding of the hepatic artery during these procedures.[27]

ARTERIAL STEAL SYNDROME

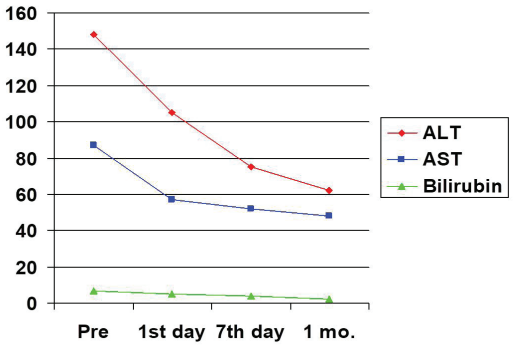
Arterial steal syndrome has been reported to occur after LT and may represent an underrecognized cause of graft ischemia.[28] Arterial steal syndrome is defined as decreased perfusion of one of the arterial branches because of diversion of blood flow into a different arterial branch originating from the same trunk. After LT, a shift of hepatic blood flow into the splenic artery (splenic steal syndrome) or gastroduodenal artery (gastroduodenal steal syndrome) can be observed. Impairment of graft perfusion is the common pathophysiologic mechanism of arterial complications, which occurs in 2% to 40% of patients after LT.[29] Liver transplant does not result in an immediate reduction of the total arterial blood flow in the spleen. After LT, diversion of most of the celiac blood flow is into the spleen, so that the liver gets diminished flow. In fact, the condition can be aggravated by such events as preservation injury, rejection, or hepatitis, which usually results in increased intrahepatic arterial resistance, with a further diversion of blood flow away from the hepatic artery into the splenic artery. When there is significant reduction in intrasplenic arterial resistance, associated or not, with some degree of increased hepatic arterial resistance, a steal phenomenon of the blood into the splenic artery may develop. This may cause hypoperfusion of the liver despite no hepatic artery stenosis or occlusion; furthermore, biliary damage and liver damage may also occur.

Clinical presentation of arterial steal syndrome

Patients with arterial steal syndrome present with elevated liver enzyme levels, cholestasis, ischemic biliary destruction, or acute graft failure. However, these symptoms also occur in patients with other vascular complications associated with insufficient arterial blood supply of the transplanted liver. Alanine and aspartate aminotransferase levels can be as high as 1520 and 1275 U/L, respectively, and gamma-glutamyltranspeptidase levels are also elevated. Patients can also present with mild elevations in alkaline phosphatase levels. Arterial steal syndrome may develop any time from the immediate posttransplant period to 5.5 years after LT. Figure 6 shows how the liver enzymes and the bilirubin levels respond after embolization of the splenic artery in patients with splenic artery steal syndrome.[30] Typical findings in patients with arterial steal syndrome include splenomegaly and marked enlargement of the splenic artery. However, an enlarged splenic artery, splenomegaly, and associated hypersplenism are also well-known conditions in patients with liver cirrhosis without steal syndrome.

Diagnostic imaging of arterial steal syndrome

Doppler ultrasonography is the first diagnostic test for vascular and biliary complications after LT. Evaluations of hepatic artery velocity, waveforms, and particularly vascular resistance are helpful for diagnosis. In patients with arterial steal syndrome, Doppler ultrasonography scans exhibit high resistance hepatic artery waveforms with low diastolic flow or reversal of diastolic flow. The resistive index in the hepatic artery of patients with arterial steal syndrome is usually greater than 0.8. Hepatic artery systolic velocities are unusually low (< 35 cm/s).[31] However, these findings are nonspecific and could be due to transient graft edema, rejection, or infection. Portal hyperfusion



	Pre	1st day	7th day	30th day
Mean ALT U/I	148.08	105.14	75.65	61.45
Mean AST U/I	86.48	55.82	52.12	48.64
Mean T.Bilirubin mg/dl	6.81	5.12	4.14	2.49

Figure 6. Liver Enzyme and Bilirubin Levels in Patients With Splenic Arterial Steal Syndrome After Embolization of Proximal Splenic Artery

can also be seen. Computed tomography may be helpful to demonstrate the vascular anatomy of the transplanted liver, but it does not give any information about the functional anatomy. Rather, information can be obtained about the sizes of the splenic and hepatic artery and the volume of the spleen. Angiography is the best technique to diagnose and at the same time treat the arterial steal syndrome. Key angiographic findings in patients with steal syndrome are slow hepatic artery flow relative to splenic artery flow in the absence of significant arterial anatomic defects. There is also delayed filling of intrahepatic arteries and poor peripheral parenchymal perfusion with early filling of the enlarged splenic artery (Figure 7). A more objective criterium is the simultaneous visualization of the hepatic artery and portal vein.[32]

Treatment of arterial steal syndrome

Endovascular treatment techniques are preferred over surgery because of fewer complications. Splenic artery embolization is the most common successful intervention for arterial steal syndrome. With distal embolization of the splenic artery, several complications can occur, including sepsis, need for splenectomy, graft failure, multiorgan failure, and death.[29] Proximal splenic artery embolization is the preferred technique; with this method, collateral flow to the spleen is possible. Coils, detachable balloons, or the Amplatzer vascular plug (AVP) may be used for embolization (Figure 8). If the splenic artery flow is too fast and the diameter is large, it is difficult to do proximal embolization with coils because coils tend to flow more distally; in these cases, AVP or a detachable balloon may be preferred. Together with coils or AVP, a Histoacryl-lipiodol mixture may be used.[30,33,34] After embolization, angiography should be performed to see the hepatic artery perfusion. An angiography can show a prompt increase in the hepatic arterial filling and the increased distal perfusion.

ARTERIOPORTAL FISTULA

Arterioportal fistulas (APFs) are rarely seen after LT. This complication occurs mainly as a result of biopsy or percutaneous interventions. Most APFs are asymptomatic and incidentally discovered. Doppler ultrasonography, computed tomography, and magnetic resonance imaging scans are usually enough for diagnosis; however, for definite diagnosis and for treatment if necessary, angiography can be performed. The APF may cause hemobilia, graft ischemia, or necrosis. If the APF is large enough, it may cause hyperdynamic portal hypertension. If it is small, treatment may be patient follow-up; however, for patients with

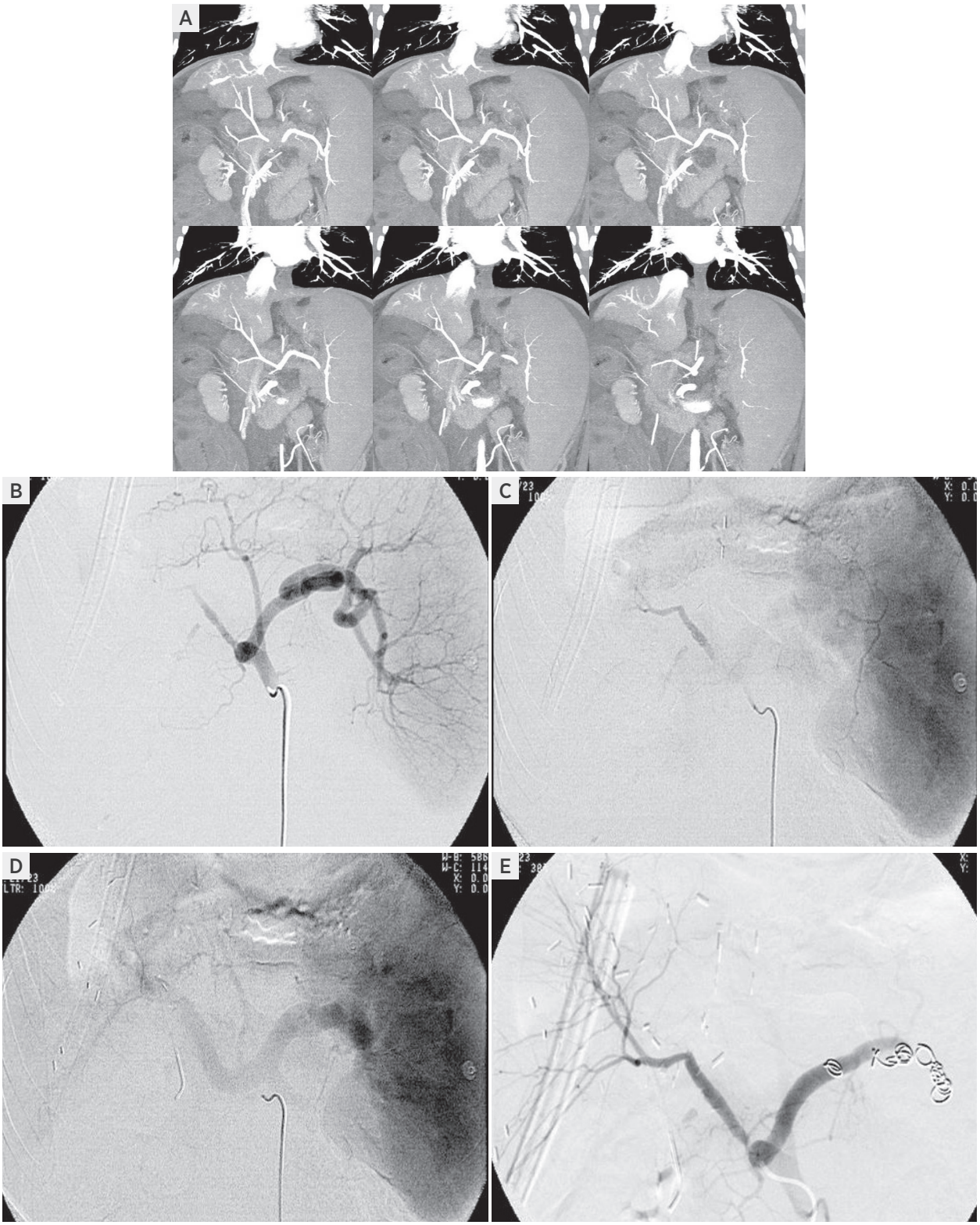


Figure 7. Liver Transplant Patient With Splenic Artery Steal Syndrome and Elevated Enzyme and Bilirubin Levels

(A) Coronal computed tomography angiography shows patent hepatic artery without stenosis. **(B-D)** Selective celiac angiography scans demonstrate slow filling of the hepatic artery, with decreased distal perfusion; distal hepatic artery and intrahepatic portal vein branches are also seen. **(E)** Proximal splenic artery embolization with coils was performed, with angiography showing increased flow of the hepatic artery and significantly increased distal perfusion.

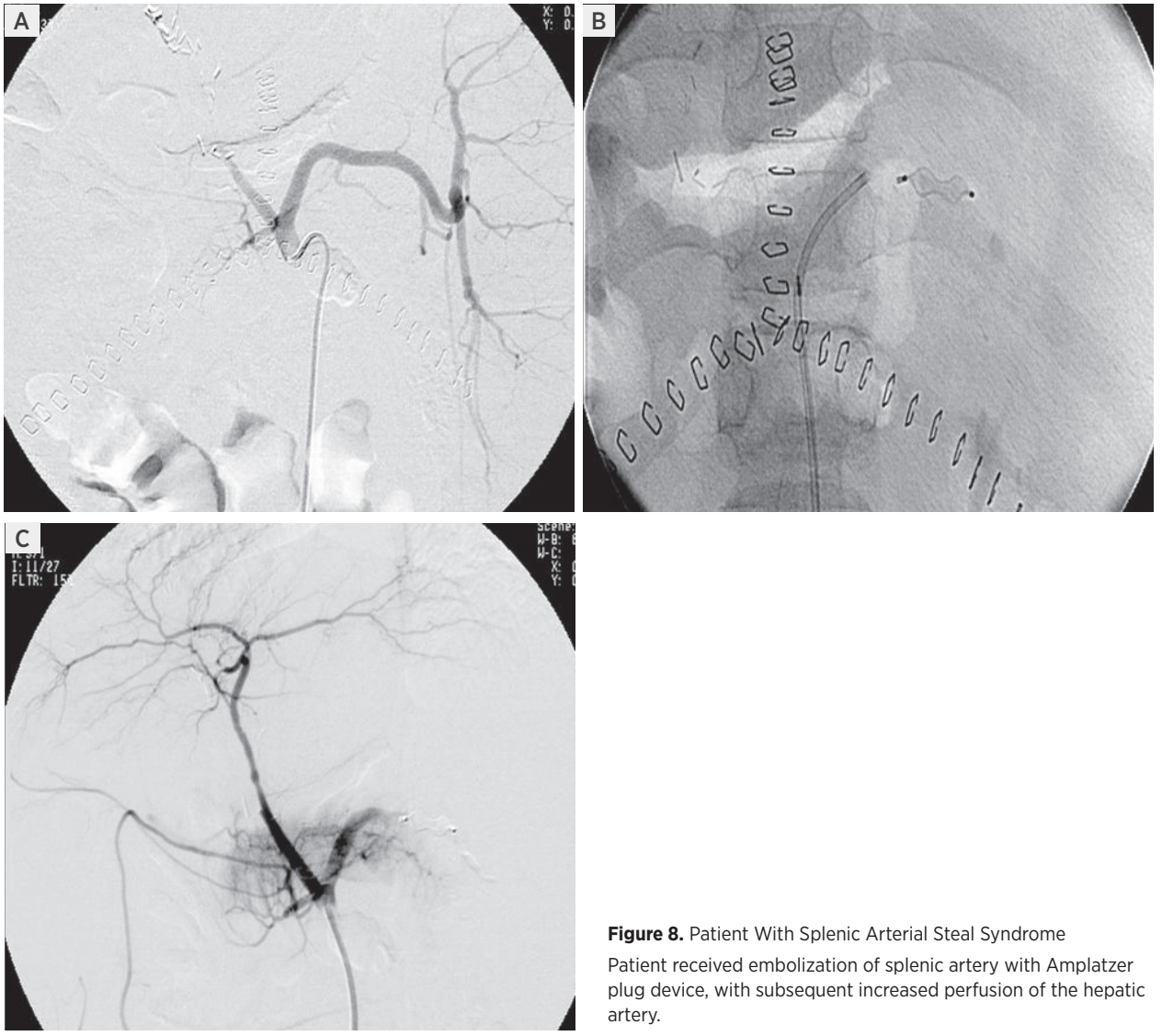


Figure 8. Patient With Splenic Arterial Steal Syndrome
Patient received embolization of splenic artery with Amplatzer plug device, with subsequent increased perfusion of the hepatic artery.

symptoms, the APF must be treated. Endovascular embolization is the treatment of choice. Coils or the AVP device and sometimes graft-covered stents are used to embolize the APF. Care must be taken especially for the distal APF embolization.

HEPATIC ARTERIAL ANEURYSMS AND BLEEDING

Pseudoaneurysms of the hepatic artery after LT are rare, with a reported incidence of 0.3% to 2%. If rupture and bleeding occur, it is an emergency condition. Usually, clinical symptoms are a sudden onset of massive bleeding and acute abdominal pain. A technical failure in the arterial anastomosis, the use of high-dose steroids, biliary complications (leakage, stenosis, or biliary infection), and bilioenteric anastomosis are closely related to the formation of pseudoaneurysms. Treatment may be either surgery or endovascular embolization or covered stent placement (Figure 9).[35] Recently, flow diverter stents have been available and may be used in difficult anatomy. Hepatic artery bleeding without aneurysm may occur during endovascular interventions or rarely from the side branches that ligated during surgery (Figure 10).

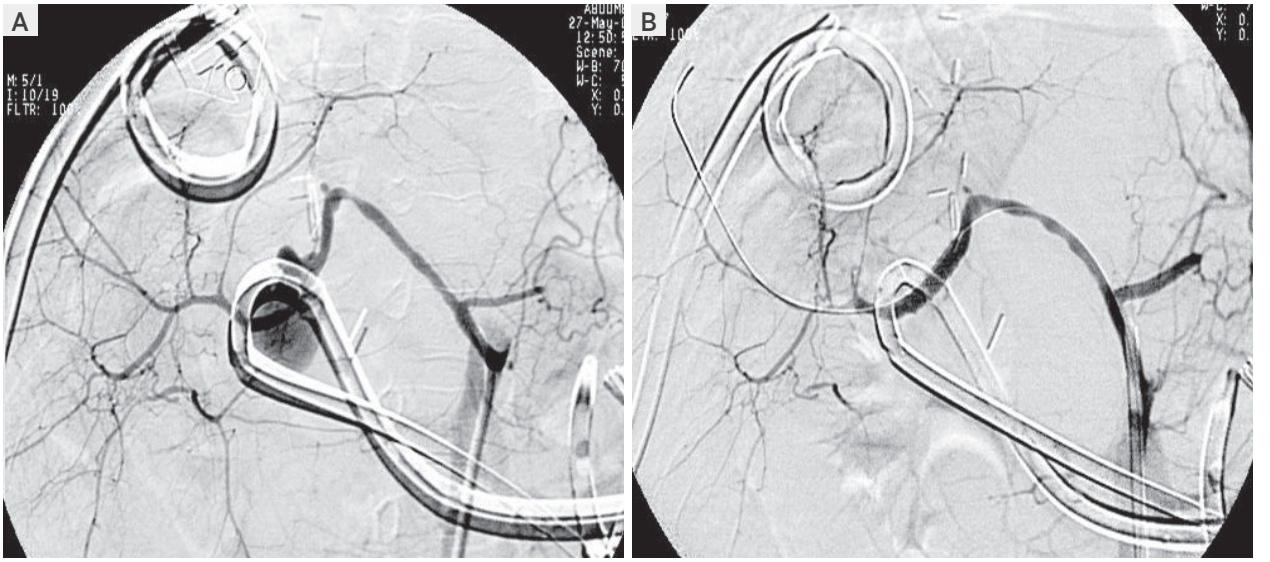


Figure 9. Pseudoaneurysm of the Hepatic Artery Due to Biliary Drainage

Pseudoaneurysm caused hemobilia in the liver transplant patient, requiring endovascular treatment with graft-covered stent.

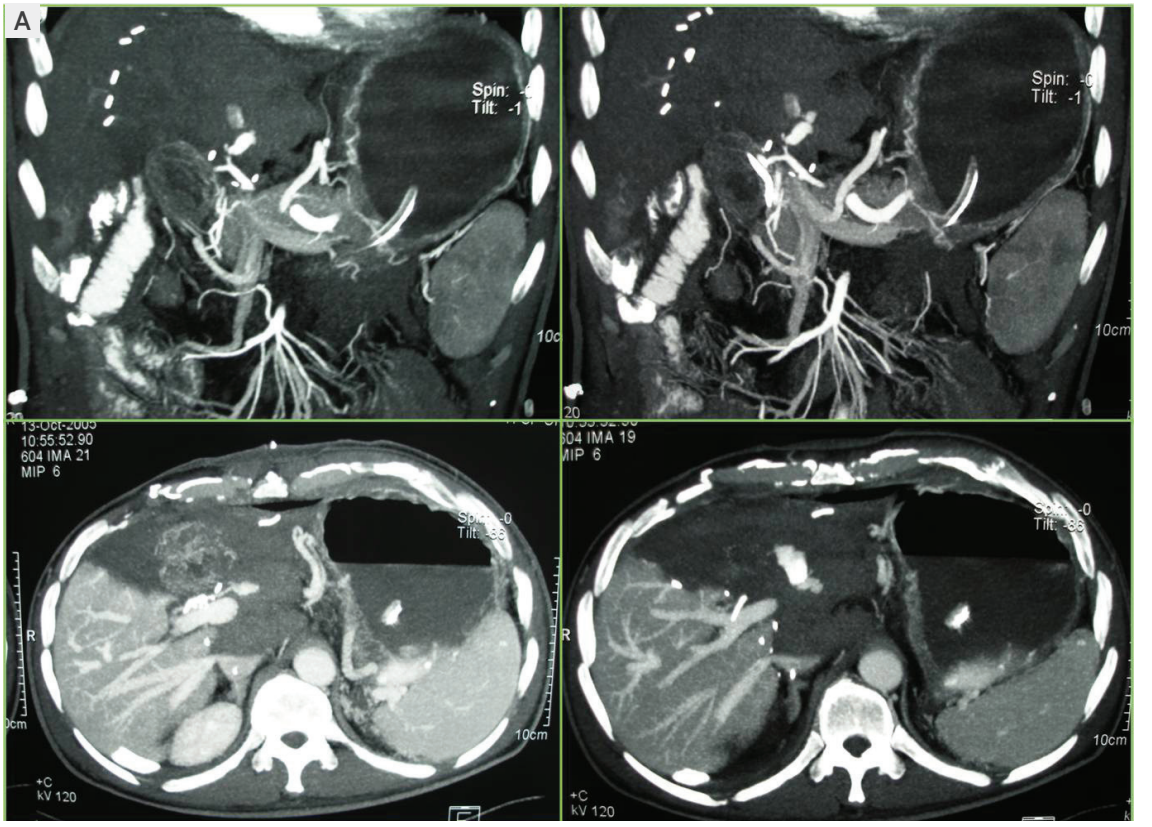


Figure 10. Fifty-Year-Old Patient on Day 2 After Right Lobe Transplant

(A) Coronal and axial computed tomography images show acute bleeding of the hepatic artery from the side branch.

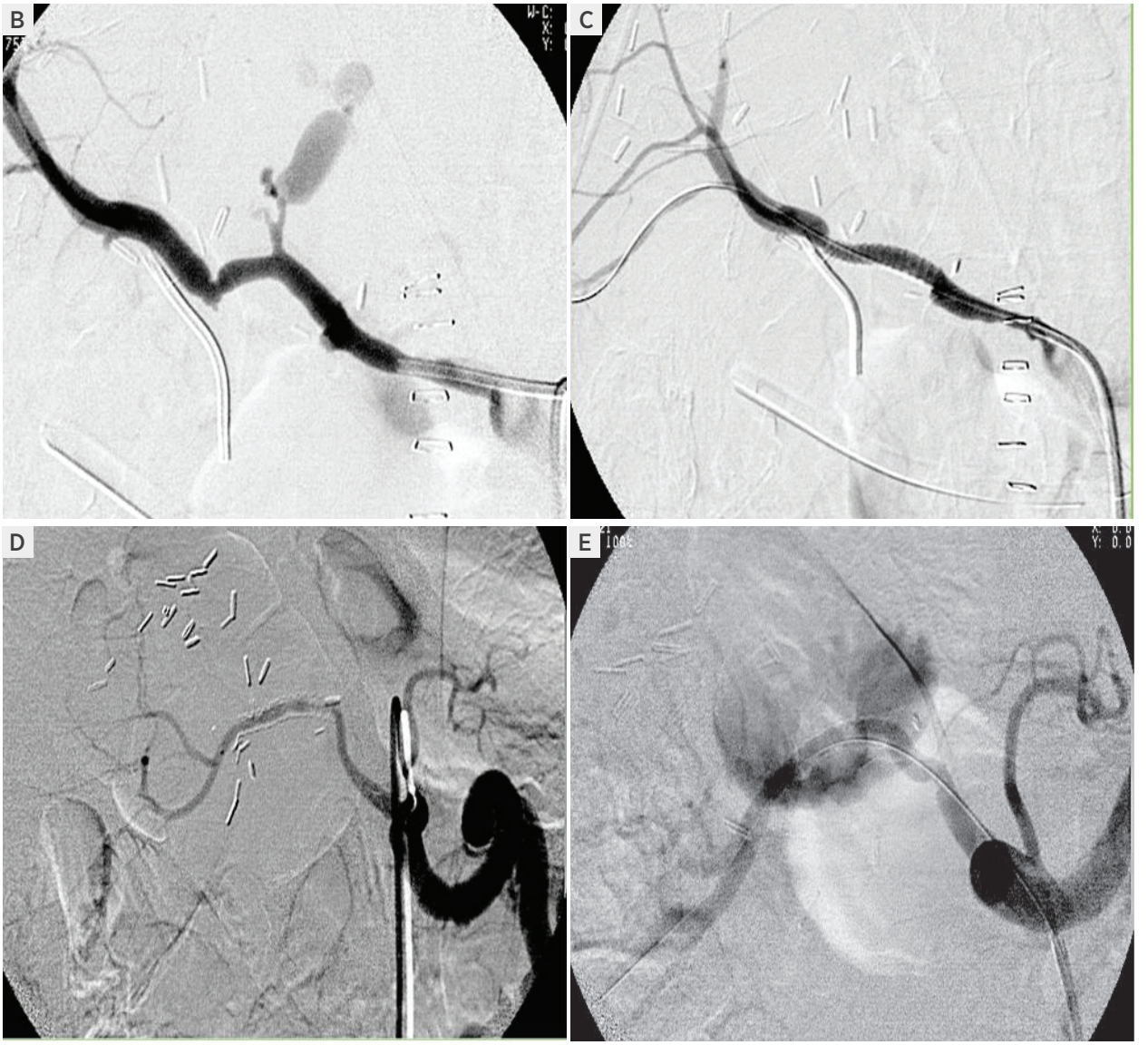


Figure 10. Fifty-Year-Old Patient on Day 2 After Right Lobe Transplant ***(Continued)***

(B) Selective hepatic angiography shows massive bleeding from the same branch. **(C)** Graft-covered stent was placed across the side branch of the hepatic artery, and there was no bleeding afterward. **(D)** Two years later, control angiography shows 50% stenosis of the stent. **(E)** Angiography after percutaneous transluminal angioplasty shows no residual stenosis and good flow.

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Portal Vein Interventions in Liver Transplantation

Ali Harman

INTRODUCTION

Liver transplantation (LT) has become the standard therapy for acute and chronic liver failure with different etiologies since the first successful procedure conducted by Starzl in 1967. With approximately 80 000 procedures in the past 25 years, there has been a significant improvement in survival rates (up to 96% and 71% at 1 and 10 years, respectively) after LT.[1,2] Prolonged survival after LT has been established by early diagnostic tools, developments in surgical techniques, better understanding of immunosuppression, and preservation therapies along with better care of postoperative complications. Despite these improvements, the overall postoperative complication rates remain high.[3] Some of the noteworthy complications are related to the inflow of the portal vein (PV) and the hepatic artery (HA) or the outflow of the hepatic vein (HV) and the inferior vena cava (IVC) along with biliary leaks or strictures, postoperative collections, abscesses, graft rejections, and posttransplant malignancy.

The diagnostic and therapeutic approach to postoperative complications after LT has shifted to interventional radiology (IR) due to its advances in the field, such as its minimally invasive nature and lower morbidity in contrast to comparable surgical procedures. In most cases, except for graft rejection, major surgery or even retransplant can be circumvented by IR.

The first year, in particular the first 3 months, is the most susceptible time for high mortality after LT, considering graft dysfunction, vascular and/or biliary complications, and infections.[4] The most severe complication (possibly resulting in early loss of allograft, long-term dysfunction, or even death) is early postoperative thrombosis in the arterial or portal inflow. The overall incidence of vascular complications in adults after LT appears to vary tremendously depending on the transplant center; however, it remains 7% in deceased-donor liver transplant (DDLT) and 13% in living-donor liver transplant (LDLT).[5-9] Children show a higher incidence (16%-18%) of vascular complications[5,10-13] mainly because of smaller vessels, size mismatches in LDLT, or cholangitis leading to hypoplasia/thrombosis in the recipient's PV in biliary atresia patients.[14]

The incidence of hepatic arterial complications (1% to 3%) appears to be more common than portal venous complications after DDLT.[15-18] On the other hand, the incidence of PV complications may go higher (9%-14%) in patients after LDLT or in patients who receive a reduced-size liver.[19-22]

Liver transplant recipients with PV stenosis (PVS), PV thrombosis (PVT), and recurrent liver cirrhosis accompanied by portal hypertension with or without gastric varices have better results from PV interventions. Some interventions worth mentioning are PV angioplasty with or without stent placement for PVS, PV thrombolysis with or without stent placement for PVT, transjugular intrahepatic portosystemic shunts (TIPS) or splenic arterial embolization for cirrhosis, and retrograde

transvenous obliteration for gastric varices. These entities and the minimally invasive management of complications are discussed in this chapter.

PORTAL VEIN STENOSIS

Incidence, clinical presentation, and imaging findings

Portal vein stenosis is an infrequent complication occurring in just 5% of LTs.[6,15,17] It is more likely to occur in cases where split grafts have been used (4% in adult split grafts and 7%-27% in pediatric split grafts). In adult whole-liver grafts, PVS occurs occasionally (< 1%-2%).[5,18,23-25] Consequently, most PVS cases occur in pediatric LT recipients.[23,24,26-32]

Portal vein stenosis is found mainly at the site of the anastomosis. Portal vein anastomosis is usually end-to-end and has a simple form in orthotopic LV. If there is a significant size difference between the donor and recipient, a tapered anastomosis may be required, which presents a stenosis risk. Usually, the PV of the recipient has a small diameter that causes an increased risk of PVS formation when split grafts (particularly pediatric left-lobe split grafts) are attempted. Surgical plication of the donor PV is required in these cases, which may lead to anastomotic stenoses.[29,33] Moreover, the shortness of the donor's PV segments makes the PV anastomosis challenging, although it seldomly requires interposition grafts or multiple/complex anastomotic reconstructions.[16,23] Prior splenectomy and the Mayo management protocol for cholangiocarcinoma are other known factors that could lead to PVS after transplant.[34]

Portal vein stenosis usually occurs more than 6 months after LT. Although delayed PVS is generally secondary to fibrosis or intimal hyperplasia, intraoperative or early PVS is considered to be related to technical reasons or postoperative anastomotic edema.[35]

Portal vein stenosis is asymptomatic in most patients. Postoperative stenosis is detected randomly in routine Doppler ultrasonography (DUS) scans and can be called pseudostenosis. It is necessary to differentiate between PVS and PV size mismatch by DUS. Having knowledge of preoperative anatomy and graft assessment is beneficial for differential diagnosis. The finding should be followed because of its susceptibility to the development of stenosis.[36] Because it is suspected primarily because of symptoms of portal hypertension (bleeding from gastroesophageal varices, ascites, and splenomegaly in the upper gastrointestinal tract) or lower limb edema with hepatic graft failure, PVS usually develops slowly after transplant.[18,25] The instability of abnormal liver function tests makes it unsafe for the diagnosis of PVS.[23]

It is difficult to assess significant PVS after transplant with computed tomography (CT) and magnetic resonance imaging (MRI). Although CT does not provide quantitative information about the degree of stenosis, it can confirm the morphologic degree of stenosis and other signs of portal hypertension. Because these are not common dynamic imaging methods, it is difficult to evaluate portal anastomosis when there is an angulation and/or a size mismatch between the diameter of the native and donor PVs.

Doppler ultrasonography is the most precise, noninvasive screening tool because it offers hemodynamic evaluation.[37] Doppler ultrasonography is sensitive to PVS, but its definition is controversial due to its lack of specificity and its lack of precise and objective criteria. If the anastomotic segment is reduced by 50% or more in diameter compared with the proximal normal vein, or if the absolute diameter is less than 2.5 mm, stenosis is diagnosed.[38] Significant stenoses can be accompanied by poststenotic dilatation and turbulent flow-related color aliasing. Turbulent flow, which should be evaluated in future controls for comparison, may also be a normal finding in the early postoperative period.[39] A 3- to 4-fold increase of peak velocity at the anastomosis, more than a 3-fold increase of portal velocity, and a peak velocity of > 125 cm/s are found to have 73% sensitivity and 95% to 100% specificity for significant PVS.[40]

Serious PVS and complete PV occlusion are often difficult to diagnose by ultrasonography. Contrast-enhanced ultrasonography (CEUS) can facilitate diagnosis by improving the display of the residual lumen of the stenotic PV via the dynamic representation of the microbubble contrast-agent filling state. This method has been shown to be less sensitive than ultrasonography with regard to heart-related artifacts, respiratory deficiencies, or patient compliance deficiencies.[41,42]

Transcatheter portography remains the gold standard technique because this method allows visualization of anastomosis and allows changes in portal pressure to be measured.[43] Nevertheless, the gradient showing a significant stenosis is uncertain, disputable, and does not have a reported standard.[23,35] Operators use mostly a > 4 to 5 mm Hg gradient as an indicator for a significant PVS.[35,44]

Management of portal vein stenosis

Treatment of PVS is a clinical decision. Asymptomatic patients without liver dysfunction need to be kept under biochemical surveillance and have DUS to check for the patency of the PV due to its possible conversion to PVT. The use of anticoagulant therapy is still controversial, and an international consensus has not been reached. In symptomatic patients, other causes such as outflow problems and parenchymal causes (rejection or hepatitis) need to be eliminated before contemplating treatment. Therapeutic intervention is required to prevent graft loss, retransplant, and mortality in patients with clinically and radiologically confirmed significant stenosis.

Traditionally, surgery was performed by primary repair of the anastomosis site or retransplant in the management of PVS. In 1990, Olcott and associates reported the first PVS balloon dilatation after transplant.[45] Since then, IR has been widely recognized as the first choice for post-LT PVS therapy because of its low periprocedural morbidity and being a less invasive technique.

Percutaneous transhepatic portal procedures are often performed under conscious sedation in adults. If conditions of patients are unstable, they cannot lie on their back for a long time, or if their airways are endangered, general anesthesia is admissible. In pediatric patients, all procedures are recommended under general anesthesia. Informed acceptance of all procedures should be received from parents/guardians or patients.

Portal vein access

Percutaneous PV interventions require minimally invasive access to the PV. These may include direct *transhepatic PV access, transsplenic access,* and *transjugular HV access* (TIPS access).[46]

Transhepatic PV access has a high success rate and is easy to implement. With the percutaneous transhepatic approach under ultrasonography or fluoroscopy, it is easy to reach most of the PVs, thereby providing a more favorable distance to the anastomosis.[37] The direct tract through the liver provides the best mechanical advantage for crossing severe stenoses.[27,43] In this type of access, there is a possibility of damaging the transplanted liver. In addition, if the recipient's intrahepatic PV branches collapse due to PVS or occlusion, the potential for failure in these accesses may increase. In the percutaneous treatment of anastomotic PVS, a right-sided transhepatic approach is often attempted. The peripheral segment II or III PV branch can be accessed with a subxiphoid approach in livers from living donors, especially in recipients who receive the left lateral segment. In the right intercostal approach, the risks of bleeding and pleural injury are higher than in the left portal approach.[37]

Transsplenic access under ultrasonographic guidance is less injurious to the liver and is recommended in pediatric patients because of the upper location of the graft in the left subphrenic region.[47] If the spleen is big enough and located in the normal position, the splenic vein is patent, and the target lesion does not reach to the confluence of the superior mesenteric vein and splenic vein, then this type of access can be applied to patients when the intrahepatic portal vein is collapsed due to severe PVS or PVT. The course of the splenic vein

and target lesion site also seem to be significant when determining a PV intervention through the transsplenic approach. The splenic vein may show an extremely curved course due to splenomegaly. This can prevent the negotiation of catheter or stent into the target lesion.

TIPS access can be preferred in cases of bleeding tendency or serious ascites. It can be difficult to puncture PV with this approach in total PV occlusions. The spatial relationship between the HV and PV after LT should be noted, especially in patients receiving left-lobe grafts. Because the TIPS portal access site is usually close to PVS, this approach takes longer and does not provide enough "study room" for portal anastomoses. Furthermore, transcatheter manipulations are more difficult because the TIPS approach is mostly incompatible with the long axis of the PV.[37]

Procedural technique

After regional anesthesia, the secondary or tertiary branch of the portal venous system is directly punctured with a 21-gauge EchoTip® needle or 22-gauge Chiba needle under real-time ultrasonographic guidance. After confirmation of the portal puncture via test dose injection of the contrast media, a 0.016- or 0.018-inch micro-guidewire is advanced into the main PV. This micro-guidewire is exchanged for a 0.035-inch angled hydrophilic guidewire using a size 4F micropuncture sheath or 6F coaxial dilatator system. A 5F to 8F vascular sheath is placed over the 0.035-inch guidewire. The stenosis is usually crossed with a directional 4F or 5F catheter. Where difficulty in crossing the lesion is experienced, either arterioportography or transsplenic puncture can be performed. Micro-guidewires and microcatheters can be used to cross severe stenotic lesions. To determine the length of the stenosis and surrounding collateral circulation, venograms are obtained after entering the superior mesenteric vein or spleen vein. Pressure gradients are measured across the stenosis. For the definitive diagnostic criteria of PVS, stenosis > 50% of the main portal vein diameter and > 5 mm Hg pressure gradient are determined. Before angioplasty, patients are heparinized with a single dose 75 U/kg of heparin. The wire is exchanged for a 0.035-inch stiff wire, and noncompliant high-pressure angioplasty balloons are used in a variety of sizes (5-14 mm) according to the patients' anatomy. The balloon diameter is based on the prestenotic PV diameter and is inflated to between nominal and rated burst pressure for 1 to 2 minutes. Repeat pressure measurements and venography are then performed to confirm success. For patients with a residual stenosis or significant pressure gradient following prolonged balloon inflation for 2 to 3 minutes, or for patients who have early restenosis within 3 to 6 months, stenting is preferred. Stents are placed eccentrically across the lesion, minimizing stent coverage of the recipient PV. If the deployed stent shows residual stenosis greater than 50% of its normal diameter, balloon angioplasty is performed. In pediatric patients, stents should be used with great care, as stents do not grow with the child. Self-expandable bare-metal stents are preferred in adults, whereas balloon-expandable stents that can be subsequently dilatated to a larger diameter (if required) are preferred in children.

The procedure in the transsplenic approach is similar to the transhepatic approach. Ultrasonographic guidance is an auxiliary factor to vascular puncture. Because the splenic vein is engorged and thin-walled, the needle and guidewire should be advanced gently.

Tract hemostasis

After PV interventions, bleeding from the transhepatic or transsplenic tract may be life-threatening. Good postprocedure hemostasis starts with meticulous nontraumatic PV or splenic vein access, preferably in the smallest branch that is accessible.

The traditional "closure" of the tract after portal interventions is usually done by Gelfoam pledgets or torpedoes and/or coils. The percutaneous access sheath is left in place, and an absorbable gelatin sponge is prepared in 2- to 3-mm-diameter rolls like torpedoes or pledgets. These Gelfoam particles can be slightly impregnated with contrast to make

them visible under fluoroscopy, and/or they can also be impregnated with reconstituted thrombin to promote thrombosis of blood bleeding back along the tract. Rolled Gelfoam torpedoes are introduced through the sheath one at a time and pushed with a blunted sheath dilatator as the sheath is withdrawn. Usually 2 to 5 torpedoes are deposited, depending on the length of the tract. Incomplete tract embolization or delayed bleeding may be observed due to the dissolution and the discontinuity of the gelatin sponge particles.[48,49]

It is preferable to use Gelfoam torpedoes with 0.035-inch coils of 4- to 8-mm diameter. Because the coils can be "opened" in the sheath and make it difficult to advance with the standard 0.035-inch or 0.038-inch guidewire, it is best to advance and deploy them through a 5F end-hole catheter. A small amount of contrast injected into the catheter is crucial to assess the tract. Given its proximity to the HA, bile ducts, and HVs, it is possible to cross these structures in transhepatic approach when access to the portal venous system is provided. Careful consideration should be given to avoid potential nontargeted embolization of the coils (eg, coils at risk of causing embolism in the lungs by accidental insertion into the HV branch). A multistep technique in the use of coils can lead to longer processing times, and it may be necessary to provide complete embolization with multiple coils. This prolonged procedure time is associated with an increased risk of accidental withdrawal of the introducer sheath and may result in incomplete embolization of the system. If the tract is too short, it may be difficult to pack the coils properly. Migration of the coils into the portal vein or peritoneal space may occur, especially if inappropriate coil size is used.[48,49]

Vascular plugs, another embolic agent, may require a longer processing time (minimum 5 min) for adequate thrombus formation and also have a risk of distal migration. The tract may be damaged if the plug size is too large, or the tract may remain open if the plug cannot reach its fully opened configuration. Additionally, plugs cost more than other embolic materials.[50]

N-butyl cyanoacrylate (N-BCA) is a long-lasting, fast-acting, and affordable liquid embolic material that is unlikely to cause rebleeding or to migrate. When N-BCA interacts with blood and similar ionic solutions, it rapidly solidifies by polymerizing.[51,52] The N-BCA/lipiodol mixtures can polymerize within 0.2 to 5.0 seconds, depending on the percentage of N-BCA in the mixture; the rate of polymerization is directly proportional to the concentration of the N-BCA component.[52,53] Some precautions should be taken when using N-BCA to prevent unintended, extensive embolization of the portal or HV in transhepatic access and the splenic vein in transsplenic access. To eliminate such negativities, the targeted vein should be accessed from the periphery if possible. Coil embolization may be required before N-BCA is injected. To make the procedure safer, N-BCA injection is applied to the parenchymal part of the tract after the sheath or catheter is withdrawn from the portal or splenic vein. Before injection, washing with 5% dextrose solution is preferred to prevent polymerization of N-BCA in the sheath or catheter. While the sheath or catheter is carefully withdrawn, injection of the N-BCA/lipiodol mixture is performed simultaneously under fluoroscopic guidance until the tract is completely embolized up to the skin. A 50% mixture of N-BCA and lipiodol (totaling 2 mL) is usually enough to embolize a short percutaneous tract occupied by a 4F to 7F, 11-cm-long sheath. Sheaths > 8F or longer than 11 cm have a larger dead space/capacity that is > 2 mL of the glue mixture.

DEFINITIONS AND FOLLOW-UP EVALUATIONS

In percutaneous angioplasty, < 20% to < 30% residual stenosis, < 3- to 5-mm Hg pressure gradients during stenosis, and ≥ 50% decreases in pressure gradient are accepted as technical success criteria[54-56] (Figure 1). The success of stent placement is defined as placing the stent in the intended location of the stenosis and improving the flow of the portal vein (Figures 2 and 3). Improvement of clinical symptoms of portal hypertension (ie, ascites, varicose bleeding, splenomegaly, hepatorenal

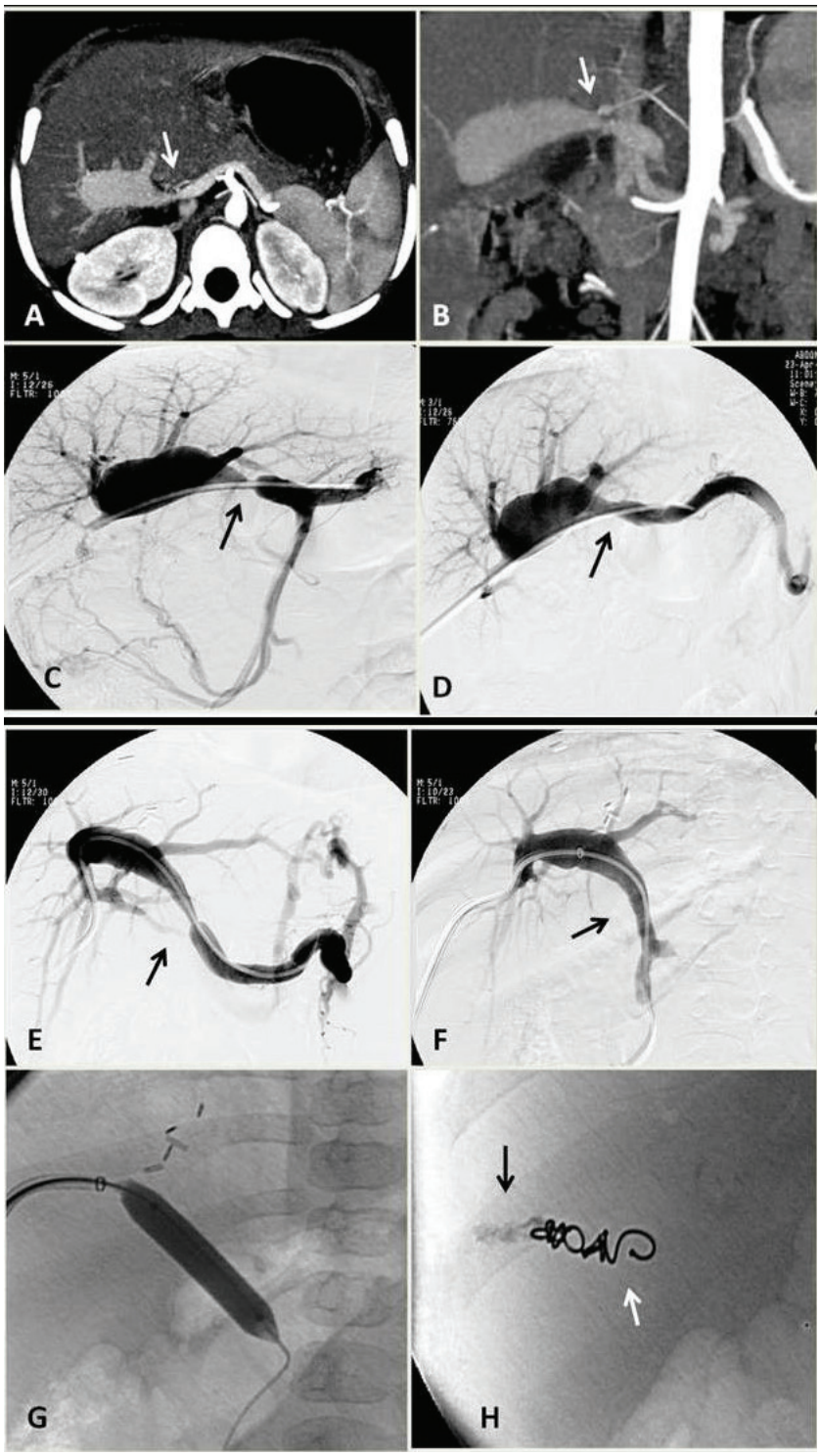

Figure 1. 3-Year-Old Left-Lobe Split Liver Transplant Recipient 11 Months Posttransplant

Axial **(A)** and coronal **(B)** maximum intensity projection CT images showing portal vein anastomotic stenosis (white arrows). **(C)** and **(D)** Pre-percutaneous transluminal angioplasty (PTA) and post-PTA, respectively, transhepatic portography images showing an anastomotic stenosis (black arrows). Pressure gradients across the stenosis were measured as 14 mm Hg and 2 mm Hg before and after PTA, respectively. **(E)** and **(F)** Same patient 3 months after first procedure (pre-PTA and post-PTA, respectively), with transhepatic portography images showing recurrence of stenosis (black arrows); pressure gradients across the stenosis were measured as 15 and 3 mm Hg before and after PTA, respectively. **(G)** Dilatation of the segment with 6 mm balloon catheter. **(H)** Transhepatic tract embolization performed with coils (white arrow) and N-butyl cyanoacrylate/lipiodol mixture (black arrow).

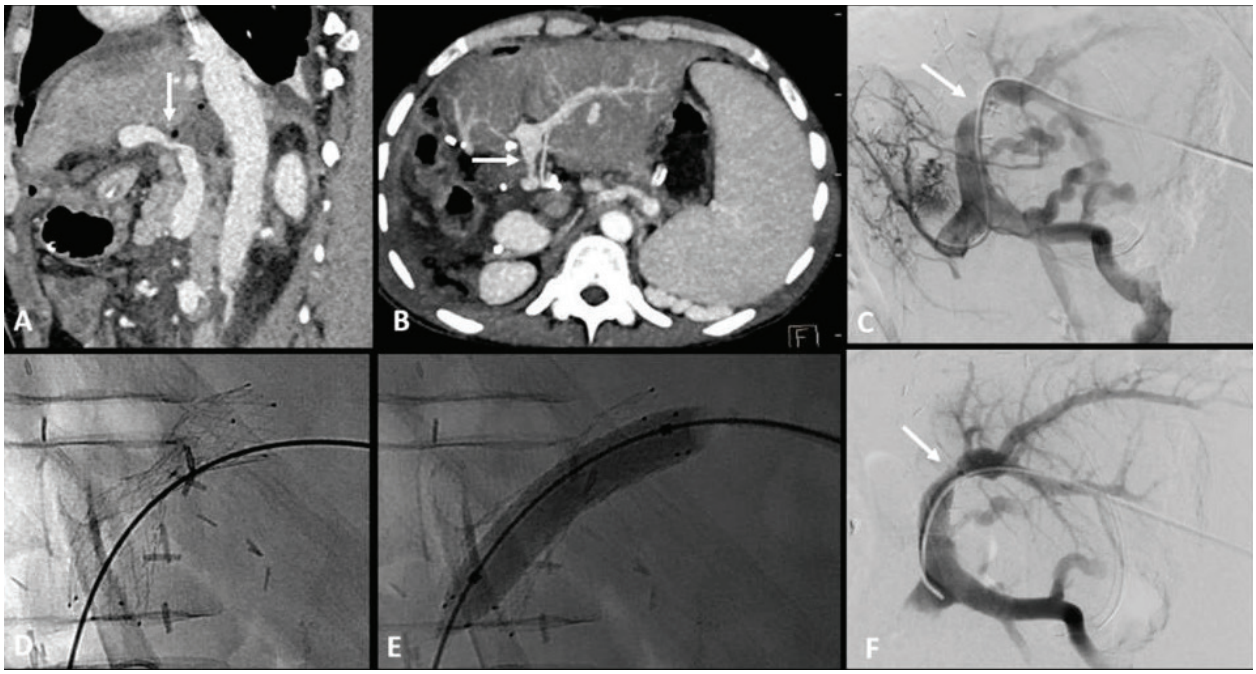

Figure 2. 27-Year-Old Male Patient 2 Days After Split Left-Lobe Liver Transplant

Sagittal **(A)** and axial **(B)** computed tomography reconstruction images showing portal vein anastomotic stenosis (white arrows). **(C)** Transhepatic splenoportography revealed stenosis (white arrow). **(D)** Primary stenting of the lesion with self-expandable bare stent. **(E)** Balloon dilatation of the stent. **(F)** Control portogram showing better filling of intrahepatic portal vein branches with decreasing gastric variceal blood flow.

syndrome, hepatopulmonary syndrome) and DUS findings indicate clinical success. Liver function tests, platelet count, and serum albumin levels are also taken into consideration. Patency is reported as primary and primary-assisted. Primary patency is defined as the interval between the first intervention and recurrent PVS necessitating reintervention. Primary-assisted patency is defined as patency after the initial angioplasty until repeated percutaneous intervention therapy is discontinued. Grading of complications is done according to the Society for Vascular Surgery reporting standards (ie, mild, moderate, and severe)[57] and Cardiovascular and Interventional Radiological Society of Europe (CIRSE) standards (grade 1-6).[58]

The use of anticoagulation before and after balloon angioplasty is variable. Although there is a theoretical justification for anticoagulation (keeping activated partial thromboplastin time approximately 1.5 times higher than normal or international normalized rate from 1.0 to 1.5), the literature has not specified how much is required for the procedure. Intravenous anticoagulation is recommended in the first days after stent placement to ensure that the international normalized rate is between 1.5 and 2.0. It is preferred to give oral antiplatelets for 6 months in patients without coagulopathy.

Follow-up DUS is preferred on the day after the procedure, with CT required to verify a possible abnormality. Doppler ultrasonography and liver CT are performed every 3 months during the first year after transplant and then every 6 months after the first year if there is no abnormality in the DUS or laboratory findings in the follow-up examination for patients with hepatocellular carcinoma. Patients without hepatocellular carcinoma should undergo DUS 6 months after LT and receive a liver CT at 1 year, followed by alternating DUS and liver CT every other year (Figure 4).

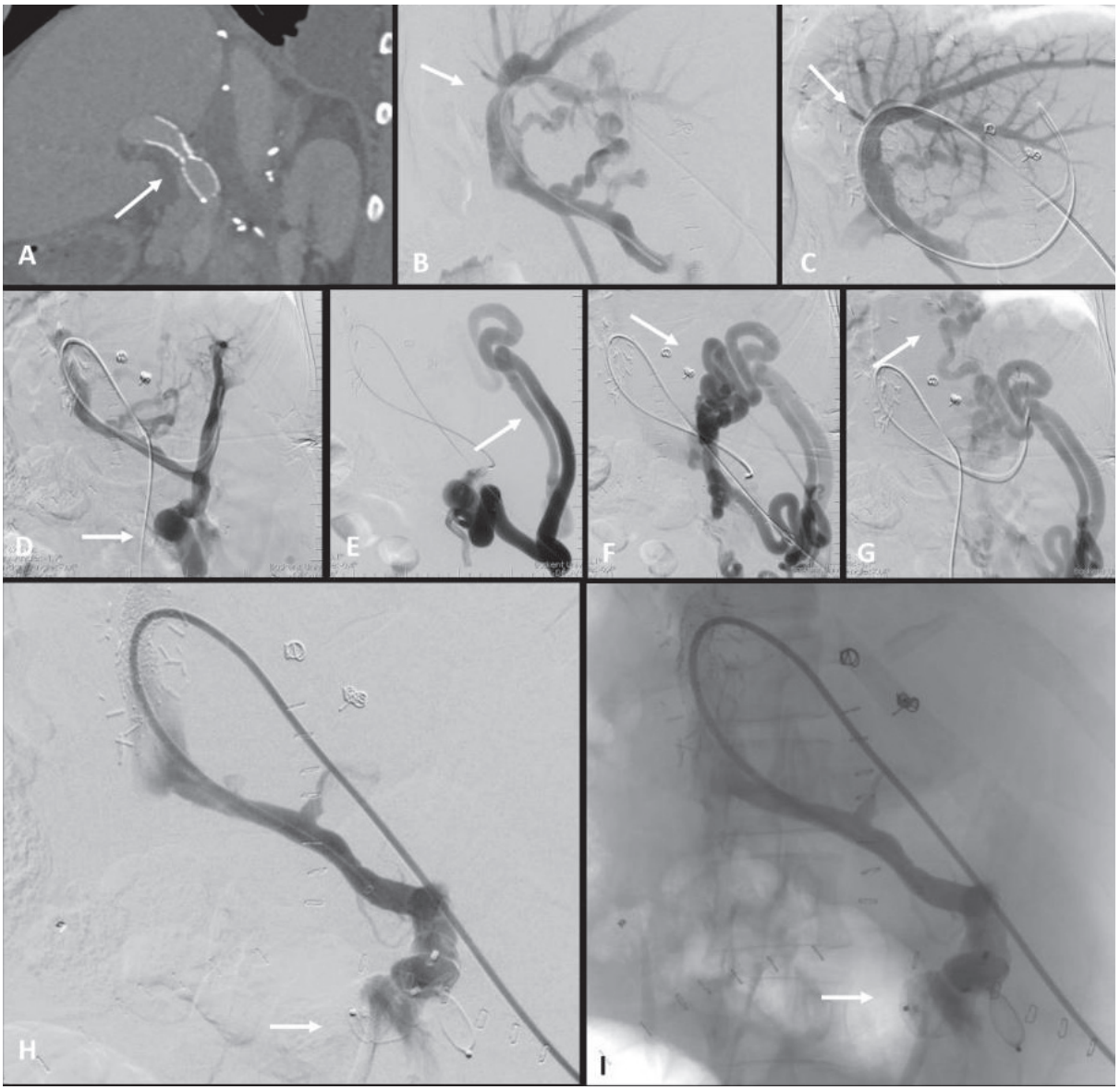

Figure 3. Computed Tomography 1 Month After First Intervention Because of Suspicious In-Stent Stenosis Findings in Doppler Ultrasonography and Presence of Portal Hypertension (same patient as in Figure 4)

Confirmed stenosis (white arrows) via computed tomography **(A)** and portography **(B)**. **(C)** Stenosis managed by placement of a balloon-expandable graft covered stent. **(D-G)** Opacification of multiple splenic and gastric varices (arrows). **(H)** and **(I)** Occlusion of major splenic varices using vascular plugs (white arrows).

A single balloon dilatation without stent placement has variable results, ranging from 36% to 71% long-term patency/success over 2 to 3 years in the long term.[24,27] After a successful angioplasty, stents are often considered for intraprocedural recoil and early restenosis (within 3-6 mo).[37] This is because stents may complicate future surgeries (retransplant) and, in the pediatric recipient population, focal relative narrowing at the stent edge may occur due to graft and recipient growth.[18,23] Most stents are self-expanding, and their patency has been determined to increase by 100% within 3 to 5 years.[27,59]

The largest comparable series published on pediatric transplant patients found that technical and clinical success ranged from 76% to 98%.[27,54,55]

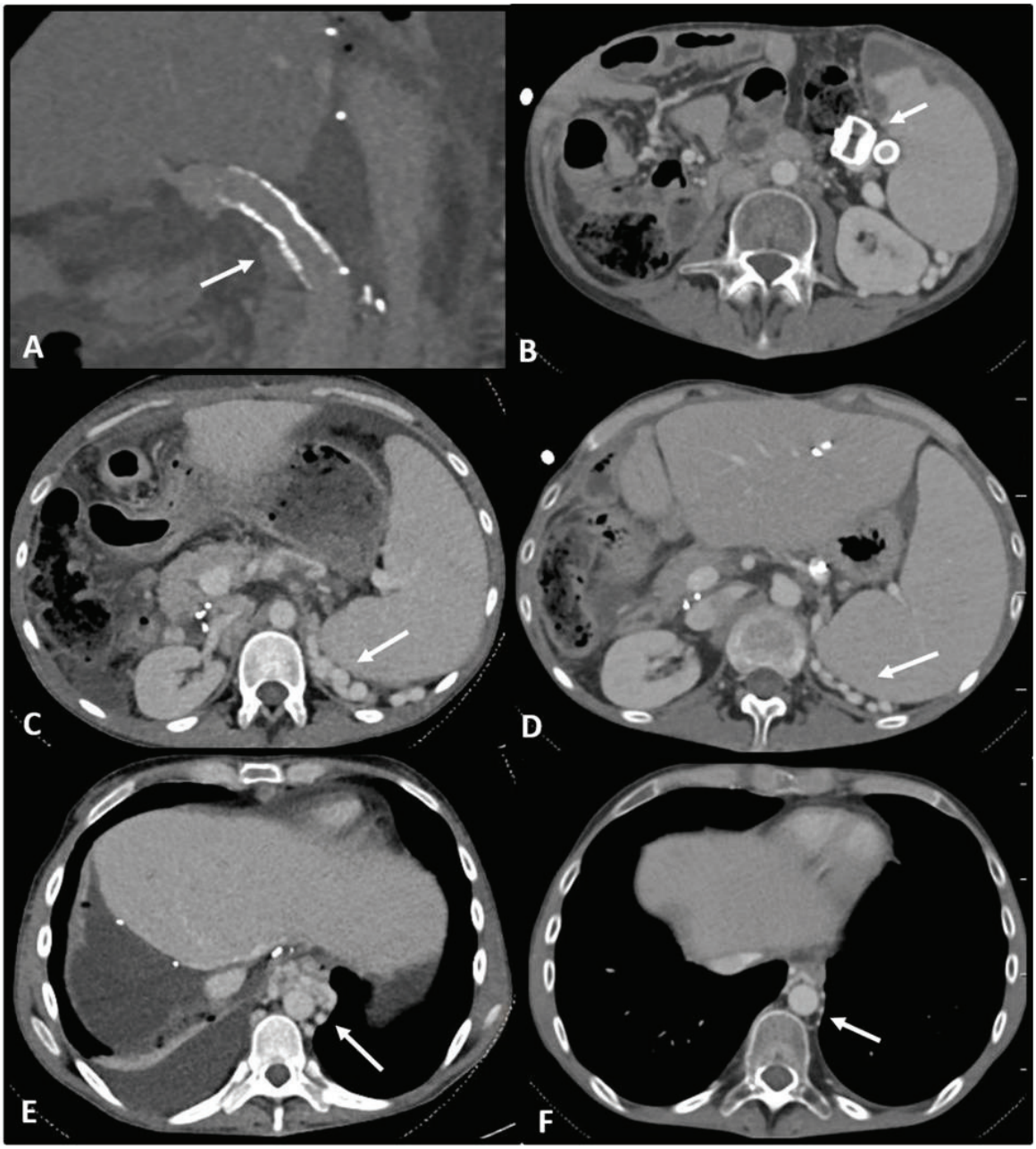

Figure 4. Same Patient as Figure 3 and 5

(A) and **(B)** Multidetector computed tomography control 3 months after second portal vein intervention showing a patent portal vein without anastomotic stenosis and vascular plugs in splenic varices (white arrows). **(C-F)** Regression of splenic and esophageal varices (white arrows) before **(C** and **E)** and after **(D** and **F)** vascular plugs.

The largest study reporting patencies with the longest follow-up period found 83%, 78%, 76%, and 70% primary patency rates and 100%, 100%, 100%, and 96% primary-assisted patency rates at 1, 3, 5, and 10 years, respectively.[54] Additionally, PVT, hemoperitoneum, and hemothorax are among complications arising from portal vein angioplasty or stent placement.[25,27,43,59]

In conclusion, PVS represents a rare venous complication after orthotopic LT especially in pediatric LT and LDLT. Doppler ultrasonographic

screening is an important diagnostic tool, especially for asymptomatic cases that can progress to PVT if not promptly treated. Percutaneous transhepatic radiological intervention with stent placement is the preferred method for addressing the complication, as it provides a high success and low recurrence and/or complication rate.

PORTAL VEIN THROMBOSIS

Incidence, clinical presentation, and imaging findings

Portal vein thrombosis is a severe complication that may occur during surgery or during the postoperative period. Early detection of thrombosis by DUS allows early intervention to avoid graft failure. The incidence of PVT ranges from 0.3% to 2.6% in orthotopic LT,[5,9,60,61] and the incidence of PVT in LDLT can reach 4% due to difficulties in PV reconstructions, especially with shorter vascular pedicles and limited vascular grafts. Portal vein thrombosis occurs more frequently (> 80%) in the early postoperative period (within 1 mo posttransplant).[5] Technical errors related to venous redundancy and kinking and/or stenosis of the anastomosis are the most common causes of PVT.[60] Some other reported risk factors are hypercoagulable conditions, portal venous stasis, former surgery of the portal or splanchnic venous system, a pretransplant portal thrombosis requiring thrombectomy during the operation, a small portal vein diameter (< 5 mm), previous splenectomy, hypoplastic portal vein, large portosystemic collaterals, and the use of venous conduits for portal vein reconstruction.[33,59] Small size PV, liver graft position, and the type of venous conduits, such as cryo-preserved veins, are considered specific risk factors in adult LDLT.[17,33,60,62-65] Portal vein thrombosis has been also reported as iatrogenic from intraprocedural angioplasty[27] or secondary to previously placed stents in PVS.[32]

If PVT occurs early, severe acute liver insufficiency or graft failure predominates; if it occurs later, the patient may present with manifestations of portal hypertension because of existing collateral portacaval circulation. The prognosis of early PVT, which leads to graft loss in up to 100% of cases, is poor.[5] Compared with that shown in LT recipients without portal vascular complications, PVT leads to a reduction in 5-year graft survival.[16]

To assess vascular patency, DUS should be the first imaging tool. Conventional ultrasonography provides an ideal specificity of 95% to 100% in the diagnosis of PVT,[41,66-68] but it is difficult to determine the duration and range of thrombosis. However, conventional ultrasonography has limits; that is, the portal vein may not be clearly visualized due to obesity, intestinal gas, and ascites. Colored DUS may be insensitive to deeply located, low-velocity portal blood flow, which can be perpendicular to the acoustic beam. The sensitivity of traditional DUS should be increased by using Power Doppler so that it does not detect slow flow in the portal vein as PVT. Although DUS protocols vary widely across transplant centers worldwide, daily ultrasonography examinations are usually recommended after transplant operations.

To assess the intensity of portal failure, CEUS may be helpful, allowing small thrombus to be shown in a peripheral portal branch.[69,70] Previous studies have shown that the diagnostic efficacy of CEUS is comparable to MRI, CT, or angiography.[70,71]

To better define the extension and intravascular filling defects for therapeutic purposes, CT or MRI angiography should be performed. Although medical treatment may help to resolve partial thrombosis, for complete thrombosis, various treatments ranging from thrombolysis to retransplant are required.

Management of portal vein thrombosis

Systemic anticoagulation, catheter-based throm-bolytic therapy, surgical revision, and retransplant are therapeutic options for PVT. Surgical thrombectomy, revision of anastomosis with various types of grafts, and arterialization of PV are among the surgical treatment options.[5] Different from the most common use of percutaneous transhepatic access in PVS, the portal venous approach for PVT

can vary from one operator or situation to another.[45,72-75]

In practice, there are 3 different therapeutic situations according to PVT presentation time and the extension of thrombosis: (1) early complete PVT within the first 72 hours after LT; (2) early PVT (complete or partial) between 72 hours and 30 days after LT; and (3) late PVT more than 30 days after LT.[72]

Early complete portal vein thrombosis within the first 72 hours after liver transplant

Surgical revision of the anastomosis is mandatory when symptoms of multiorgan failure are seen. Revision of anastomosis and systemic anticoagulation are qualified to resolve when there is a presence of thrombosis due to kinking or twisting. If a satisfactory portal transplant revascularization cannot be achieved, this procedure fails, and transplant becomes urgently needed.[72]

Early portal vein thrombosis (> 72 hours and < 30 days after liver transplant)

Nonsurgical treatment should be properly attempted, regardless of the PVT presentation (partial or complete). The most common procedure is percutaneous thrombolysis associated with or without stent placement(Figure 5).[45,76-78] Different endovascular methods have a variable success rate of between 68% and 100%, while mortality and morbidity rates range from 0% to 11%.[19]

Late portal vein thrombosis (> 30 days after liver transplant)

In cases of late PVT involving or not the superior mesenteric vein with normal liver function tests, observation can be the first option because of the appropriate venous inflow from the splenic circulation via de novo hepatoportal collaterals.[79] Percutaneous or transjugular transhepatic procedures should be preferred to treat symptoms when acute gastroesophageal bleeding or ascites occur in late PVT.

Procedural technique

Interventional procedure steps for PVT are associated with PVS treatment. Even in the early postoperative period, the percutaneous transhepatic approach is faster, less cumbersome, and safe (Figure 5). With the use of thrombolytic and fibrinolytic agents, the increase of bleeding risk is a disadvantage.[37] Streptokinase (SK) and urokinase (UK) have been shown to be effective for thrombolysis; however, both are characterized by limited thrombolytic potencies and major clinical disadvantages compared with recombinant tissue

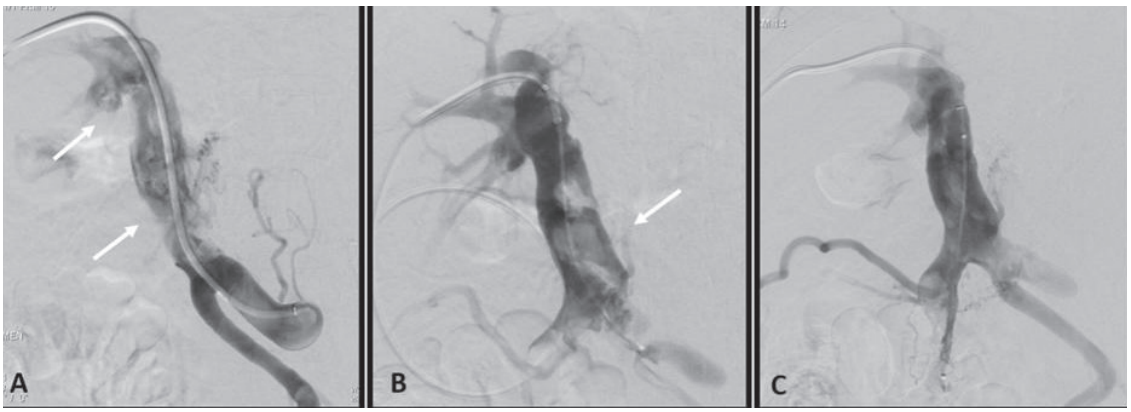

Figure 5. 42-Year-Old Female Liver Transplant Recipient With Acute Superior Mesenteric and Portal Vein Thrombosis
Management of thrombosis by selective thrombolytic infusion therapy combined with thromboaspiration and mechanical fragmentation. Transhepatic splenoportography images during the therapy showing changes of intraluminal thrombus material. **(A)** Before. **(B)** Control. **(C)** After.

plasminogen activator.[80] Unlike recombinant tissue plasminogen activator, both SK and UK do not have the fibrin-specific effect that causes systemic consumption of plasminogen and reduced thrombolytic activity, while SK has a high antigenicity. In addition, SK and UK may cause bleeding complications.[80] The transjugular/TIPS approach requires more resources and time because it requires general anesthesia, and when the outflow anastomosis has not matured, it may not be possible in the immediate postoperative period.[40] A percutaneous approach with larger (> 6F) access systems is unsafe as it carries a risk of hemorrhagic complications. The transjugular approach, if intrahepatic PVT exists, allows wide access to PV with low risk of intraperitoneal bleeding. There is no universal regimen for thrombectomy. Aspirating the clot with a guiding catheter and macerating it with balloon inflation-deflation or using snares for fragmentation are useful maneuvers in rapidly clearing the thrombus, which can be facilitated by using a thrombolytic agent (Figure 6). The underlying cause of thrombosis may need to be treated with angioplasty or stent placement. Stenting may decrease the dose of thrombolytic agents, reducing the procedure time and hemorrhagic risk[40] (Figure 7). Especially in the early postoperative period, the use of mechanical thrombectomy devices in PVT is controversial because they can damage the endothelium and cause the vessel to be sensitive to thrombosis or cause dissection.

The literature has reported good results in terms of morbidity and mortality in the case of rapid diagnosis and adequate management of PVT; otherwise, survival is very poor. As a result, although PVT rarely occurs in the early postoperative period, it creates a serious complication. Diagnosis of PVT should be made at the earliest with suspicious

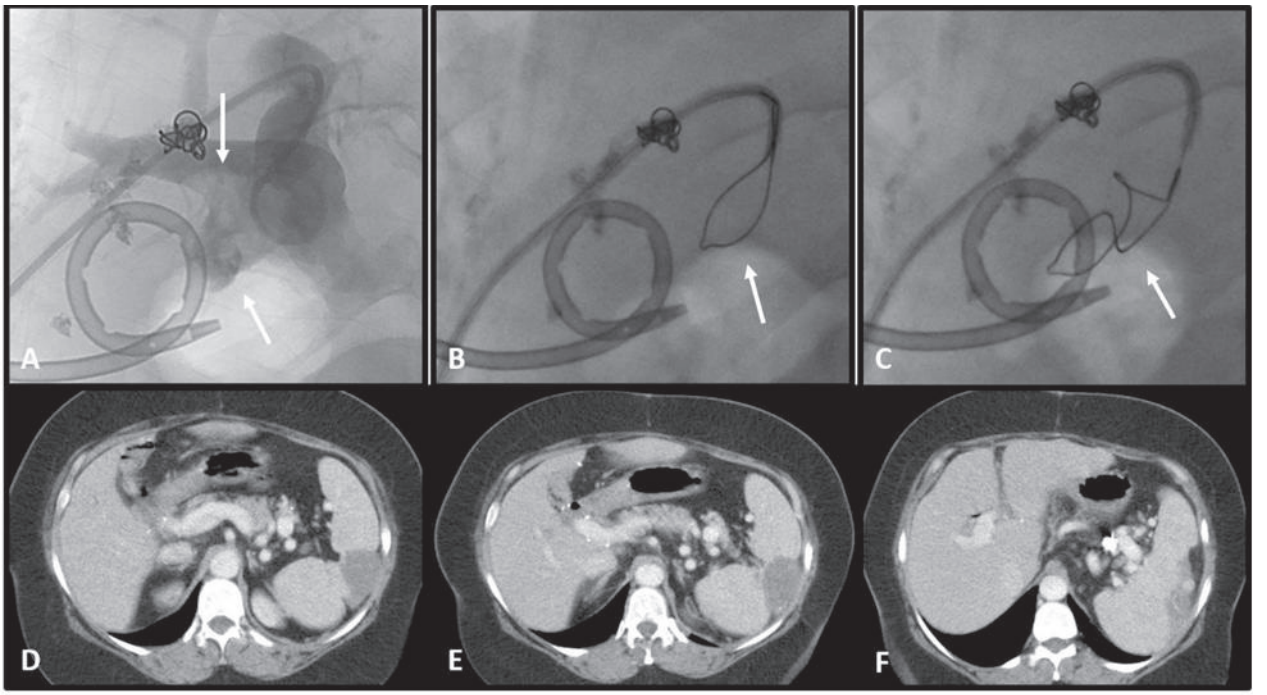

Figure 6. 48-Year-Old Female Patient 1 Month After Liver Transplant (same patient as in Figure 7)

(A) One month after first intervention, recurrence of thrombosis in main portal vein and right branch (white arrows). **(A-C)** Transhepatic thrombolytic therapy and thromboaspiration performed. **(B)** and **(C)** Mechanical fragmentation of thrombus done by using snare (white arrows). **(D-F)** Routine computed tomography control 7 years after the percutaneous management of acute portal venous thrombosis revealed patent portal venous system.

clinical or biological findings such as abnormal abdominal pain and/or high liver enzymes and unexpected platelet decline or DUS screening results. Although surgical thrombectomy remains valid in the early postoperative period, the percutaneous radiological intervention has good results and safety.

TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT AND EMBOLIZATION OF PORTOSYSTEMIC COLLATERALS

Liver transplant restores the stability of vascular resistance between splanchnic and systemic circulation, portosystemic collateral shrinkage, and recovery of splenomegaly.[81] Failures may be observed in partial liver grafts, resulting in decreased vascular bed and increased hepatic vascular resistance from the rapid regeneration of the graft, leading to continuation of the portosystemic collateral vessels.[82] The portosystemic collaterals are usually ligated during LT, which can remove blood from the PV, predisposing venous thrombosis and disrupting regeneration of the graft. Portosystemic collaterals may be a product of pretransplant portal hypertension instead of recurrence after transplant if the collaterals have not been resolved or ligated by surgeons (Figure 3). Recurrent hepatitis C infection, late graft failure (primary hepatic graft failure not explained by cirrhosis), and possibly poor grafts may be the cause of recurrent portal hypertension after LT.[83-85]

For recurrence of portal hypertension after LT, TIPS is the most common IR procedure. This method is performed in up to 2% of all transplant recipients, with TIPS in transplanted livers representing 5% to 6% of all TIPS procedures.[84] The main causes for TIPS administration are viral hepatitis recurrence (especially hepatitis C) and primary hepatic graft failure.[83-85] Nearly 80% to 90% of transplants undergoing TIPS are because of transudative complications (ascites and/or hepatic

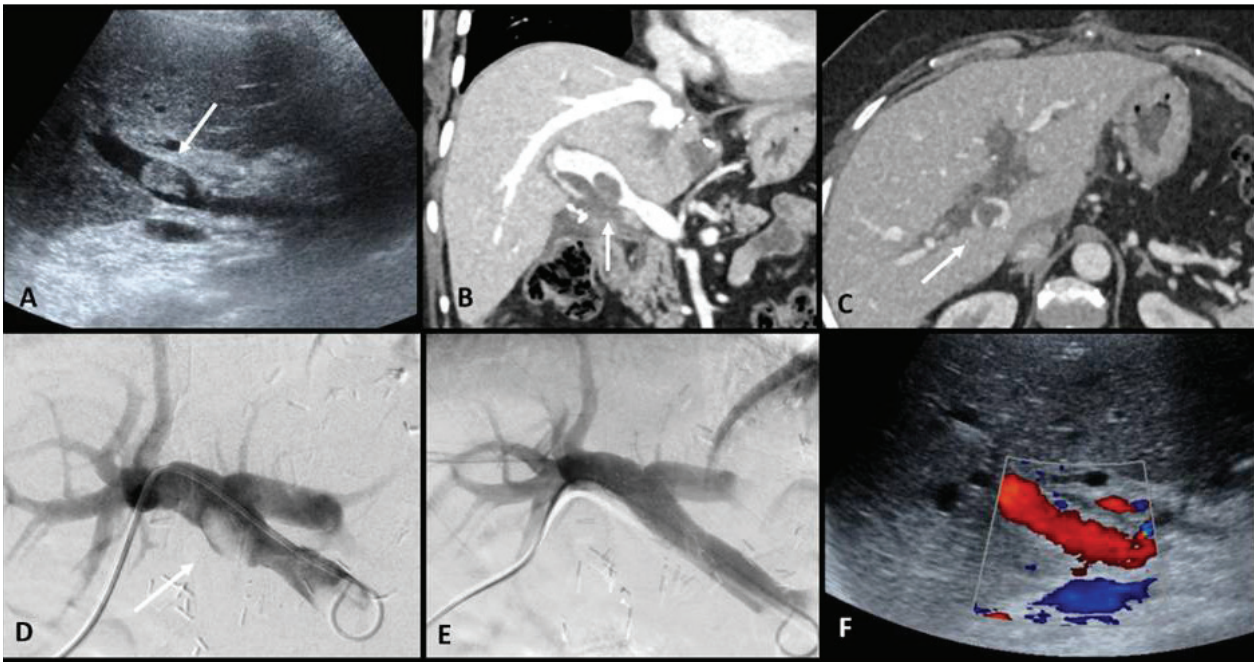

Figure 7. 48-Year-Old Female Patient 1 Month After Liver Transplant (same patient as in Figure 6)

(A) Grayscale ultrasonography. **(B)** and **(C)** CT coronal, axial reconstruction. **(D)** Conventional portogram showing thrombus in the main portal vein (white arrows). **(E)** and **(F)** Conventional portogram and Doppler ultrasonography, respectively, showing a patent portal vein after primary stenting.

hydrothorax) of portal hypertension.[83,84] The use of TIPS in transplanted whole grafts is considered as technically difficult as TIPS in native livers.[84]

The implantation technique of the HVs into the IVC is the main anatomic issue in performing a TIPS in orthotopic LT recipients. During a typical orthotopic LT procedure, the recipient IVC is replaced with an end-to-end caval anastomosis. In some patients, a piggyback technique is used, where the suprahepatic IVC of the donor is anastomosed to the recipient's HV. As an alternative, a lateral, large cavo-caval anastomosis between the anterior wall of the recipient IVC and the posterior wall of the donor IVC can be performed. These alternative surgical methods may cause difficulties in cannulating the right HV when performing a TIPS.

Transjugular intrahepatic portosystemic shunt in split grafts (especially left-lobe split grafts in children) are more challenging than in native livers[83,84,86] for several reasons: split grafts are small with less parenchymal distance to enter the portal vein, orientation is backward in left-sided grafts (interventionalists are generally used to right-lobe orientation), compensatory hypertrophy in undersized grafts (typically split grafts) can be nonuniform, and rotation of the graft may cause unconventional portohepatic venous orientations.[83,86] The clinical outcomes of TIPS in transplants appear to be worse than in native livers for 2 reasons: (1) responses to ascites treatment are worse than in native livers,[83,84] and (2) hepatic grafts are more sensitive to post-TIPS changes in portal hemodynamics. The MELD (Model for End-Stage Liver Disease) score threshold after TIPS appears to be lower in transplanted livers (MELD score of 15-17) than in native livers (MELD score of 17-19).[84,86,87] Transjugular intrahepatic portosystemic shunt has been shown to be applicable in orthotopic and split liver recipients. This group of patients may need a higher portosystemic gradient to maintain adequate hepatoportal perfusion pressure and to avoid liver failure.

Indications for the treatment of gastric varices/splenorenal shunts in LT recipients include gastric variceal bleeding, encephalopathy, portal venous steal from the hepatic graft (significant portal hepatofugal flow), and as an adjunct to other portal vein procedures for posttransplant portal vein complications (PVS or PVT).[40,88] Occluding large or hemodynamically significant portosystemic shunts and managing PVS at the same time provides optimized hepatopetal flow and reduced risk of PVT by maintaining patency of the portal vein (Figures 3 and 4). Balloon-occlusion catheters, vascular plugs, and coils are used for obliteration of large varices depending on the size and vascular anatomy, where they can be combined with other sclerosing/embolic agents, including ethanolamine oleate-iodinated contrast solution, N-BCA/lipiodol mixture, Gelfoam, and foam sodium tetradecyl sulfate (Sotradecol). The choice of sclerosant material is usually operator and institution dependent.

SUMMARY

Although portal complications after LT are rare, they may cause early loss of the allograft, long-term dysfunction, or even death in the early postoperative period. The diagnostic and therapeutic approach to pre- and postoperative portal complications after LT has shifted to IR due to its advances in the field, such as its minimally invasive nature, high technical success rate, and lower morbidity in contrast to comparable surgical procedures.

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Hepatic Vein and Inferior Vena Cava Interventions of Liver Transplant

Ali Fırat

Liver transplant (LT) is a life-saving treatment for recipients with end-stage liver disease and has become the treatment of choice for such recipients after the first successful LT by Starzl and associates in 1967.[1] Liver transplant has also been the curative treatment for acute decompensated hepatitis, hepatic malignancies, metabolic liver disease, and congenital hepatobiliary anomalies.[2] With the development of surgical techniques in LT, morbidity and mortality have decreased considerably.[3,4] Despite all these developments, such operations carry many life-threatening potential vascular complications.[5] Although hepatic artery problems are more common, hepatic venous outflow obstruction (HVOO) such as kinking, stenosis, or thrombosis of the inferior vena cava (IVC) or hepatic vein can also be encountered and can cause significant symptoms, impaired liver function, graft loss, and mortality if not treated in a timely manner.[5,6]

In conventional orthotopic liver transplant (OLT), the caval replacement technique has the advantage of a larger retrohepatic cava that prevents venous outflow or caval obstruction.[7] However, conventional LT has been replaced by "piggyback" (PB) anastomoses due to reduced venous return, splanchnic bed congestion, and reduced renal flow. In the PB transplant method, unlike conventional LT, the recipient's retrohepatic IVC is preserved. First performed by Calne and Williams, this technique maintains blood flow during the anhepatic phase, resulting in less hemodynamic instability, less fluid and blood product transport, and shorter operating times.[8] Hepatic venous outflow obstruction is more common in recipients who underwent PB LT rather than conventional OLT recipients with caval interposition.[9]

In living-donor liver transplant (LDLT), graft hepatic veins can be anastomosed to the recipient hepatic vein or directly to the IVC using different anastomosis techniques. Reconstruction of venous outlet drainage is more complex, especially in right lobe LDLT versus left lobe LDLT. In right lobe LDLT, adequate right hepatic vein, major short hepatic vein, and middle hepatic vein drainage of the liver graft is important for the maintenance of right lobe graft function. In these cases, due to the relative position of the hepatic veins, even liver-graft regeneration or slight movement of the graft may cause the vessels to buckle and slow the flow.[10,11] Especially because reduced grafts used in children often do not include the IVC, the use of these grafts involves specific anastomosis reconstructions that may cause postoperative vascular complications.[12,13] Caval replacement using vascular grafts in LDLT operations may be considered as an alternative; however, the graft has a risk of thrombus and infection. Furthermore, the long-term patency of the graft is unknown.[14]

Stenosis or thrombosis of the IVC is most commonly seen near the anastomoses. Anastomosis complications are mainly caused by technical factors, tight suture line, kinking, torsion, or thrombosis in the early postoperative period. Normal morphological changes and graft edema of the liver

can also cause such problems. In the late period (after 3 months), it occurs especially as a result of perivascular fibrosis, intimal hyperplasia, or extrinsic compression from the enlarged liver graft in the anastomosis region (Table 1).[15,16] Kinking is the condition in the anastomosis region where the inflow vessel does not connect vertically to the outlet vessel and connects at an angle. Kinking may occur as a result of the liver revolving around the IVC as a result of regeneration, or it may be caused by the mobilization of the liver as a result of evacuation of preexisting pleural effusion after the operation. Liver grafts usually show significant growth in the first 3 months after transplant. Therefore, the greatest effect of vein compression or bending due to liver regeneration or mobilization is seen especially in the first 3 months.[15,17]

Especially in the early posttransplant period, the patency of the hepatic venous outflow is very important for the survival of the graft.[6,18] Complications of the vena cava are a serious, often life-threatening, complication after LT.[19] Therefore, early detection and treatment of HVOO are important for good graft function and recipient survival.[6,20] Retransplant is required in almost one-third of recipients with failed surgical and endovascular interventions.[19,21] However, in some cases, thrombosis of one of the hepatic veins can be detected incidentally in postoperative controls without clinical symptoms.[22] Surgical treatments of HVOO using the graft's umbilical vein, a vascular graft, and veno-atrial anastomosis can be performed, but these surgical treatments are technically difficult and can cause life-threatening complications.[23-25] Advances in endovascular techniques and procedures in addition to surgical techniques have significantly reduced the morbidity and mortality of this life-saving procedure.[4,26,27]

INCIDENCE

The incidence of HVOO after LT is reported to be between 0.8% and 9.5%.[20,28-30] The incidence is higher in the pediatric population and in those who undergo LDLT versus those who receive a whole LT due to the complex reconstruction of the hepatic veins and small graft size.[12] Untreated hepatic venous outflow problems are associated with a high mortality rate of 17% to 24%.[28,31] In some studies, the reported incidence for HVOO is < 2% for caval replacement,[19,32] 3% to 4% for PB,[21,31] and 5% to 15% in pediatric recipients and recipients of partial grafts.[33]

CLINICAL FINDINGS

Patient with venous stenoses often present with nonspecific clinical signs such as ascites, splenomegaly, intestinal congestion, lower extremity edema, hepatomegaly, pleural effusion, and impaired liver function tests (Table 2).[6,26] The findings of IVC stenoses vary according to the localization of the stenosis: stenosis of the hepatic vein anastomosis is similar to hepatic vein stenosis, whereas stenosis under the hepatic vein anastomosis may present as lower limb edema or ascites.[4] Acute rejection, portal hypertension, small for size syndrome, tumor recurrence, or nodular regenerative hyperplasia should also be considered as other causes of ascites.[16] Signs and symptoms of hepatic vein stenosis may be similar to portal hypertension.[15]

Table 1. Anastomosis Complications

Early Postoperative Period	Late Postoperative Period (after 3 months)
Technical factors	Perivascular fibrosis
Tight suture line	Intimal hyperplasia
Kinking	Extrinsic compression
Torsion	
Normal morphological changes	
Graft edema	

Table 2. Clinical Signs of Hepatic Venous Outflow Obstruction

Ascites
Splenomegaly
Intestinal congestion
Lower extremity edema
Hepatomegaly
Pleural effusion
Impaired liver function tests

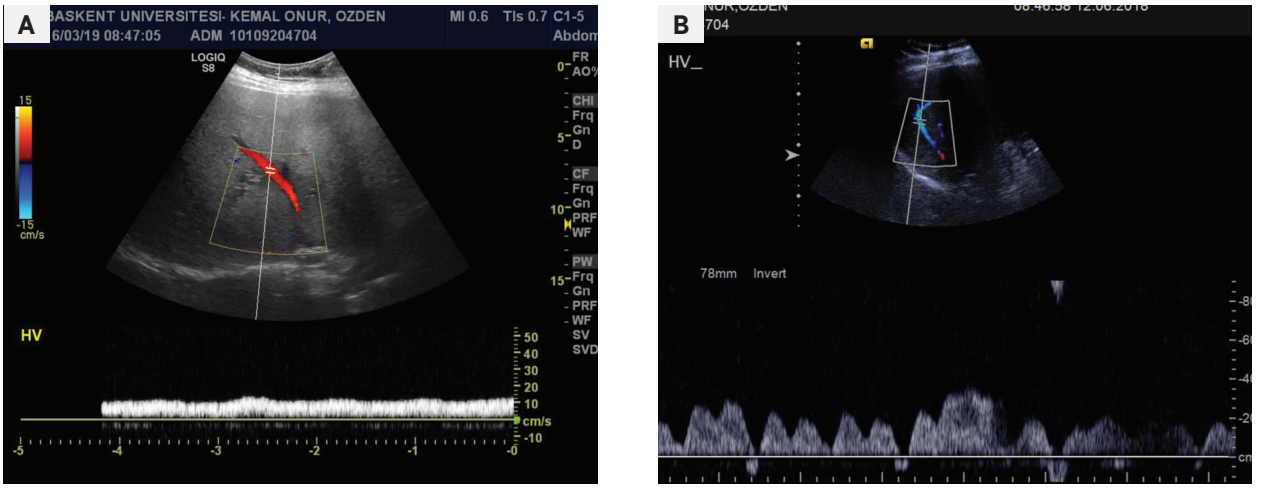


Figure1. Doppler Ultrasonography Images of Transplanted Liver

(A) Monophasic flow pattern in the hepatic vein before the procedure in a recipient with hepatic vein outflow problem in Doppler ultrasonography examination. **(B)** After the procedure, a hepatic vein flow pattern was biphasic-triphasic in the Doppler ultrasonography examination.

DİAGNOSIS

Ultrasonography, computed tomography, magnetic resonance imaging, and angiography modalities can be used to evaluate LT. However, ultrasonography combined with Doppler examination, which is an inexpensive and noninvasive method, continues to be the first-step screening test to evaluate transplant vasculature.[5,13] Ultrasonography also provides guidance in puncturing vascular structures during interventional procedures. Doppler ultrasonographic evaluation of hepatic vein outflow stenosis shows dilatation of hepatic veins, decreased mean velocity, and turbulence in anastomosis regions. In outflow occlusions, the right atrium waveform does not progress to the hepatic veins, which leads to dampened phase. Typical flow pattern in normal hepatic veins is triphasic, whereas biphasic flow is usually observed after transplant. In marked stenosis or occlusions, the wave pattern becomes monophasic (Figure 1). In computed tomography, the absence of hepatic vein opacification, heterogeneous opacification of the liver parenchyma, the development of collateral hepatic veins, or a stenotic aspect of anastomosis should suggest HVOO (Figure 2).[34-36]

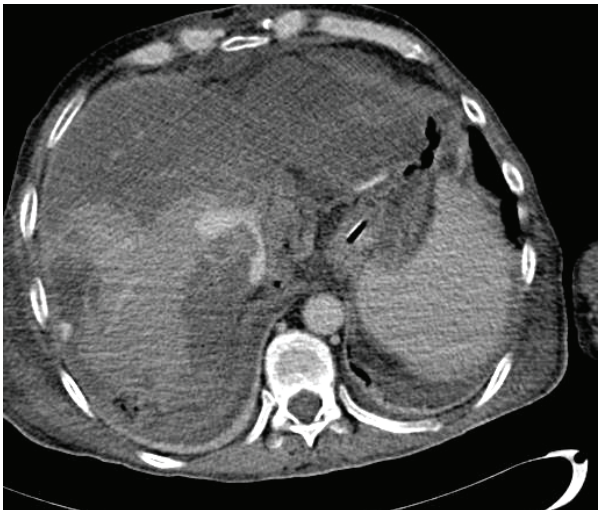


Figure 2. Axial Computed Tomography Image of Transplanted Liver

Heterogeneous opacification of the liver parenchyma on computed tomography imaging in a recipient with hepatic vein outflow obstruction.

Although ultrasonography and Doppler examination provide valuable information for diagnosis, venography and pressure measurement remain the gold standard. Venographic examinations should

be performed in recipients with suspected venous outflow problems. A venographic approach to the hepatic vein can be easily performed through the internal jugular or femoral veins. Direct transhepatic access to the hepatic vein may be required to assist catheterization if access via the internal jugular or femoral veins cannot be achieved in the event of high-grade stenosis or occlusion of hepatic vein.[4] The main diagnostic criteria for venography examination are as follows: narrowing of the vessel lumen by more than 50%,[37] stasis of the contrast agent, absence of contrast passage to the IVC or right atrium, opacification of the collateral vessels, and pressure gradient of more than 5 mm Hg between the hepatic vein and the right atrium (Table 3).[34,38] The formation of large intrahepatic collateral vessels between the hepatic vessels can be seen in HVOO; the size of the vessels is generally proportional to the degree of obstruction (Figure 3).[39]

Venography images are also used to determine the morphology, length, and diameter of the lesion and to select the appropriate balloon and stent. As a result of venography examinations, the degree of stenosis and occlusion are determined and invasive treatment is performed. For this purpose, angled guidewire is passed distally through the problematic segment with the help of an angled catheter.

ENDOVASCULAR PROCEDURE

An informed consent form should be obtained for each recipient prior to the procedure, which

Table 3. Main Diagnostic Criteria for Venography

Narrowing of the vessel lumen by more than 50%
Stasis of the contrast agent
Absence of contrast passage to the inferior vena cava or right atrium
Opacification of the collateral vessels
Pressure gradient of more than 5 mm Hg

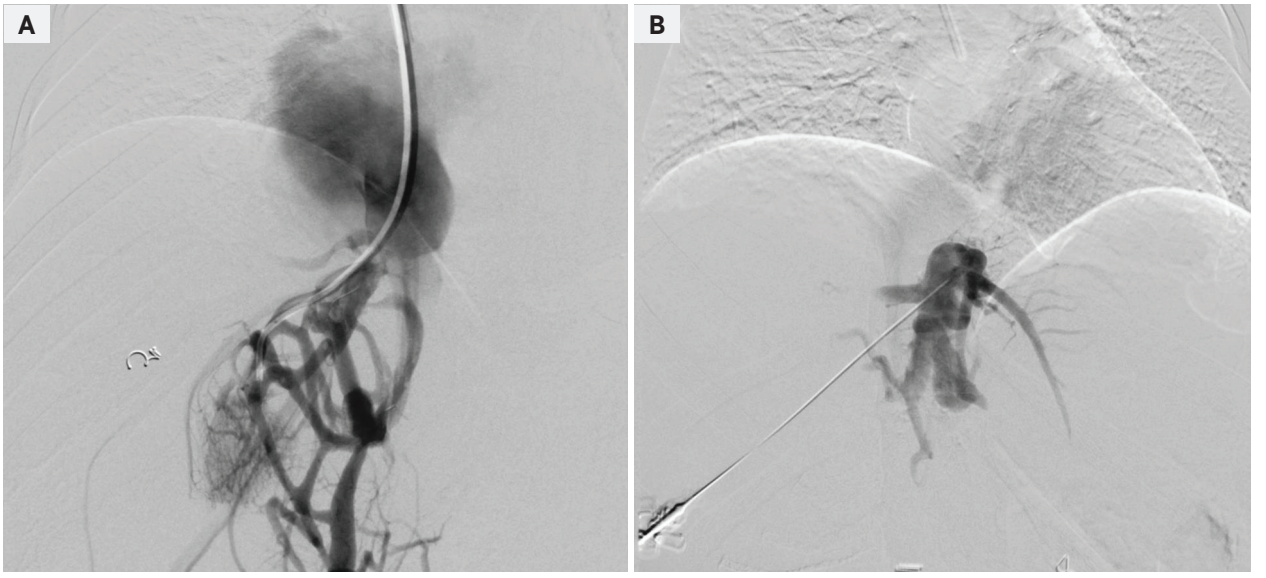


Figure 3. Transjugular and Transhepatic Venography of Transplanted Liver
Transjugular **(A)** and transhepatic hepatic **(B)** venography examinations show wide intrahepatic venous collateral veins.

includes information on the procedure and its possible risks and alternative treatments. Antibiotic treatment of recipients with fever or bacteremia would be appropriate prior to the procedure, especially if stent placement is considered. Prior to all procedures, administering blood products to recipients with prothrombin time greater than 17 seconds or platelet count less than 50 000/mm^3 is useful to prevent hemorrhagic complications.[40] Procedures are usually performed under conscious sedation or general anesthesia.

Treatment of hepatic vein outflow problems should be specific to the recipient. Endovascular treatment options in cases of hepatic venous obstruction are considered to be a useful treatment for vascular complications after LT. Treatment should be planned by evaluating the clinical findings, biochemical values, radiological examinations, stenosis morphology, and trans-stenotic pressure gradients.[41] The vascular anatomy of the liver is critical in the treatment of lesions involving venous drainage of LT. The femoral or jugular approach is used in recipients with caval interposition anastomosis, whereas the jugular approach provides more direct access to hepatic veins in recipients with PB anastomosis.[5] When the IVC is completely occluded and cannot be reached with the jugular access, occlusion can be passed using the femoral access. Especially in cases where jugular access is not supported and the guidewire is buckling, passing of occlusion through femoral access may be more successful.

In accordance with standard procedures with povidone-iodine or chlorhexidine, under local anesthesia and intravenous sedation, after puncturing the right jugular or right femoral vein using ultrasound guidance, the guidewire is advanced and the 5F vascular sheath is inserted. After insertion of the sheath, the vena cava patency is evaluated by inferior vena cavography by taking images in several different positions using a pigtail catheter. The appropriate angled catheter is then inserted into the hepatic veins from the IVC with the aid of an appropriate angled guidewire, and hepatic venography is performed. Replacing the short sheath with a long sheath after the venography will make the procedure easier and more manageable with regard to any complications that may occur. In cases of severe stenosis at the level of anastomosis, the contrast agent may not be transferred to the IVC as the catheter closes the stenotic segment. This may be mistaken for total occlusion. In these cases, the presence and degree of stenosis can be demonstrated by administration of a contrast medium near the anastomosis site using a long sheath.

If the hepatic vein origin is completely occluded or has a sharp angle with IVC and cannot be catheterized by the transjugular or transfemoral approach, then the transhepatic access option should be used. In the presence of significant amounts of ascites, drainage is required before percutaneous transhepatic intervention. After an ultrasonography-guided hepatic vein puncture with 20- to 22-gauge needles, hepatic venography is performed by injecting contrast material from the needle. If the problematic segment cannot be passed with the guidewire advanced through the needle, after a 4-5F sheath is placed on the guidewire, the guidewire is advanced into the IVC using 4-5F catheters from the stenotic or occluded segment. The snare advanced in the sheath previously placed by the transjugular or transfemoral route is placed near the stenotic segment in the IVC. The guidewire, which is advanced to the IVC by the transhepatic route, is caught by the snare and the procedure is continued by the transjugular or transfemoral route. To prevent postprocedural hemorrhagic complications, the transhepatic needle or the sheath access tract should be occluded with embolizing materials such as coil, histoacryl, or gelatin sponge slurry.

In HVOO, the presence of different collateral vessels in the transplanted liver may be observed to facilitate the return of blood to IVC in another way. Sometimes these collateral veins can be considered as an alternative way to access the proximal hepatic veins without the need for percutaneous hepatic venous access. In such cases, an alternative access pathway can be provided by entering one of

the hepatic vessels, and the guidewire is passed antegrade through the stenotic segment. Balloon dilation or stenting can then be performed after snaring the guidewire.[39,42]

Thrombolytic therapy can be used for treatment of thrombus formation detected in the anastomosis area, but care should be taken to avoid bleeding. To reduce the risk of bleeding, these thrombus formations can also be treated with mechanical thrombolytic devices.[15,35] Percutaneous catheter thrombosuction, which is a simple and effective method in the treatment of early venous thrombosis after LT, can be applied as an alternative treatment.[43]

Intravenous heparin during the procedure and 100 mg aspirin once a day after the procedure are important measures to prevent thrombotic events, since hypercoagulation conditions increase the risk of vascular complications after LT.[17]

BALLOON ANGIOPLASTY

After hepatic venography and access are performed, the next step is to treat stenosis or occlusion. Endovascular treatment options such as percutaneous balloon angioplasty and stent placement procedures are considered to be useful methods in the treatment of vascular complications after LT. Percutaneous balloon venoplasty is a less invasive method than surgical approaches to relieve venous outflow problems (Figure 4). The technical success rate in this process is close to 100%. However, re-venoplasty or metallic stenting

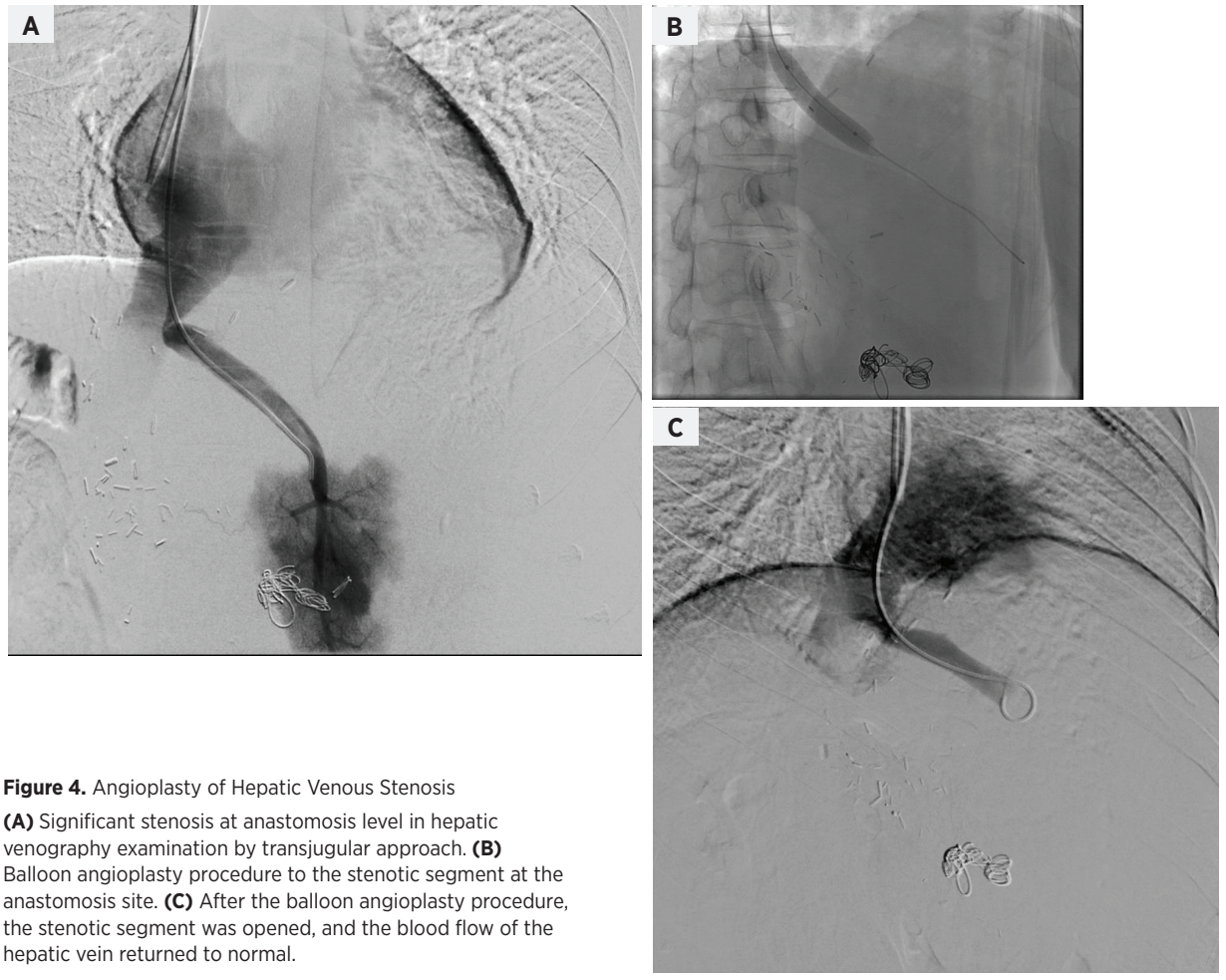


Figure 4. Angioplasty of Hepatic Venous Stenosis

(A) Significant stenosis at anastomosis level in hepatic venography examination by transjugular approach. **(B)** Balloon angioplasty procedure to the stenotic segment at the anastomosis site. **(C)** After the balloon angioplasty procedure, the stenotic segment was opened, and the blood flow of the hepatic vein returned to normal.

is required for recurrent stenosis in 55% to 81% of recipients undergoing venoplasty.[20,44,45] The treatment usually depends on the time and cause of the hepatic venous outflow problem. Although balloon angioplasty should be preferred in some studies for the treatment of lesions, it may not respond to angioplasty in the early postoperative period due to elastic recoil or resistant stenosis. In addition, rupture at the level of anastomosis during a balloon angioplasty procedure may cause dangerous results.[12] It is recommended to monitor the recipient for hypotension during balloon angioplasty. Therefore, primary stent placement may be required in most recipients. Surgical options such as thrombectomy, revision of anastomosis, cavacavastomy, and hepatopexy may be considered in the early postoperative period, but the options for late surgical treatment are limited.[16]

Some studies have shown that balloon dilatation alone in 76% to 79% of pediatric transplant recipients does not require more than 3 attempts for HVOO treatment.[12,37] In balloon angioplasty procedures, the balloon diameter inflated in the stenotic segment needs to be slightly oversized than the vessel diameter. Inflation of the balloon in the stenotic segment for about 1 to 2 minutes can help to stretch and tear the tissue that causes the stenosis and reduce immediate recoil.[15] The use of high-pressure balloons can be effective in cases of resistant stenosis that do not respond to plain balloons (Figure 5). Angioplasty with a cutting balloon can reduce the incidence of elastic recoil and recurrent stenosis, especially in recipients with no response to plain balloon angioplasty.[15,46]

STENT PLACEMENT

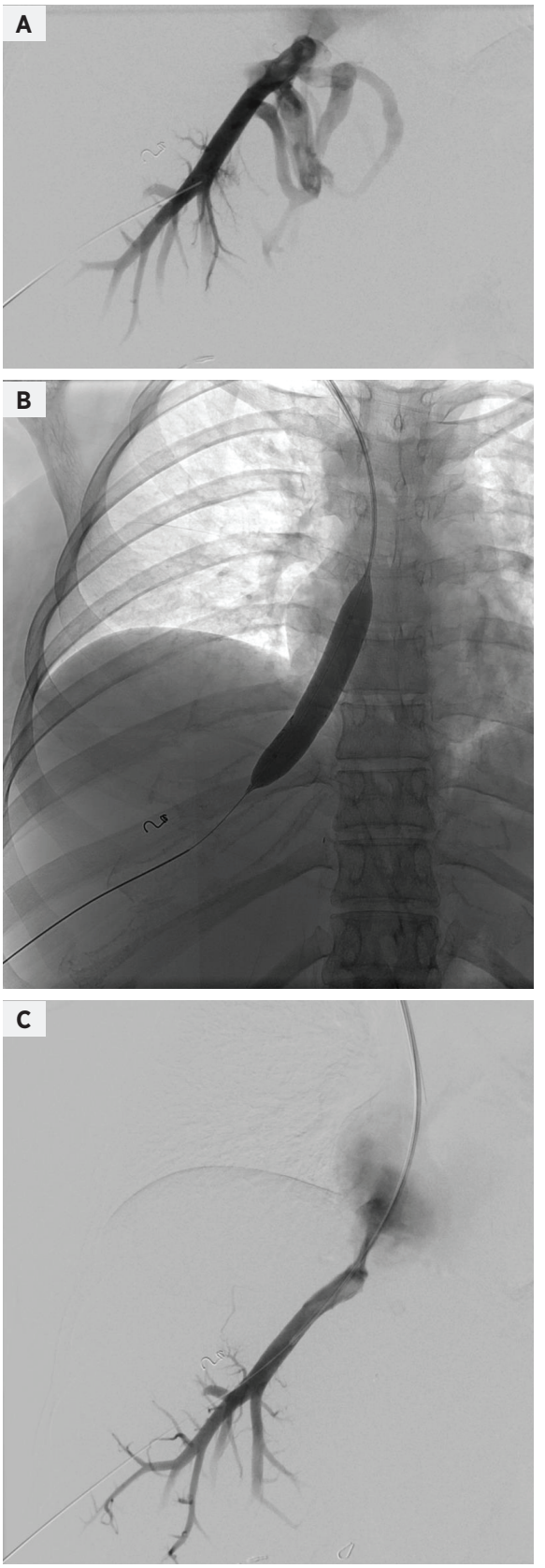
Stent placement may be the primary method for treatment of HVOO after LT because it provides clinically good success and long-term patency. Recent studies, especially in adult recipients, have reported that the primary stent placement is a safe and feasible method and has good long-term results.[20,35,40,47,48] Although life expectancy in children is high, the long-term patency of stents is still unknown.[12] Successful placement of the stents will prevent many dilatation procedures and prevent possible damage to the graft.[49]

Primary patency rates for stent placement were 80% to 93.8% at 1 year and 60% to 93.8% at 5 years.[20,45,50] In another study, primary patency rates after stent placement were 76% and 46% for 1 and 5 years, respectively, in recipients who underwent LDLT and detected HVOO within the first 60 days. Primary patency rates were calculated as 40% and 20% in recipients who were treated after the first 60 days.[17]

Some factors should not be ignored if stent placement is considered in pediatric recipients with HVOO. Of note, the long-term patency of the stent is not sufficiently known. The diameter of the hepatic vein may not match the size of the implanted stent when the recipient grows. The recipient's anticoagulant therapy and the presence of stent in the vein technically complicate retransplant in the future.[49] If stents are to be placed in pediatric recipients, stent placement with a larger diameter should be preferred, considering the future growth of the child. In cases where hepatic veins are small (< 8 mm), repeated angioplasty may be a better option than stent placement.[15]

In stents that extend to the IVC, it would be appropriate to place large-strat stents to avoid disrupting the hepatic vein flow.[5] If the stent is to be placed, balloon-expandable stents are preferred over self-expandable stents because the radial force is better. Depending on vessel size, preferred stent diameters are usually 8 to 12 mm in hepatic veins and 14 to 20 mm in IVC lesions (Figure 6).[15]

Stents can cause recurrent stenosis by inducing intimal hyperplasia, and a new stent may be needed if recurrent stenosis does not respond to balloon angioplasty. When retransplant is required, the location of the stent can cause difficulties in creating a new surgical anastomosis. In addition, complications such as migration during stent placement may occur.[37] To prevent stent migration, it is recommended that the IVC stents to be placed must have diameters approximately 20% larger than the vessel diameter.[51]



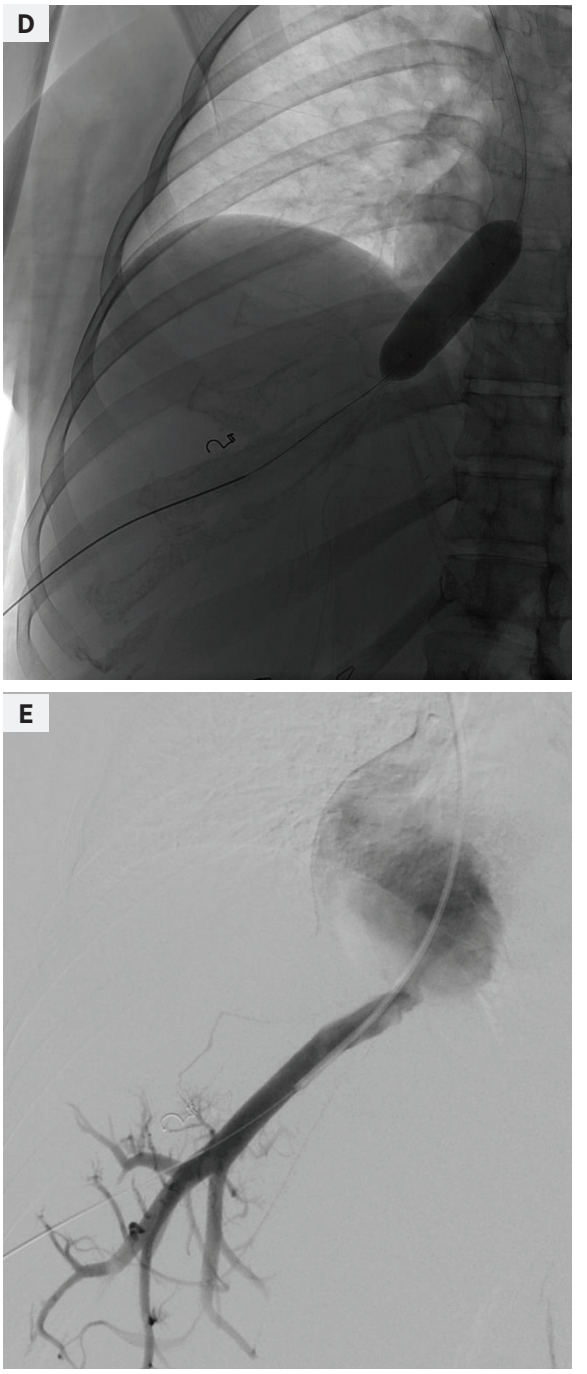


Figure 5. High-Pressure Balloon Dilatation of Hepatic Venous Stenosis

(A) Transhepatic venography showed significant stenosis and wide collateral intrahepatic veins at the level of anastomosis. **(B)** and **(C)** Control venography following angioplasty with a plain balloon showed anastomotic stenosis not responding sufficiently. **(D)** and **(E)** Adequate dilatation of the stenotic segment was achieved in control venography performed after angioplasty with larger diameter and high-pressure balloon.

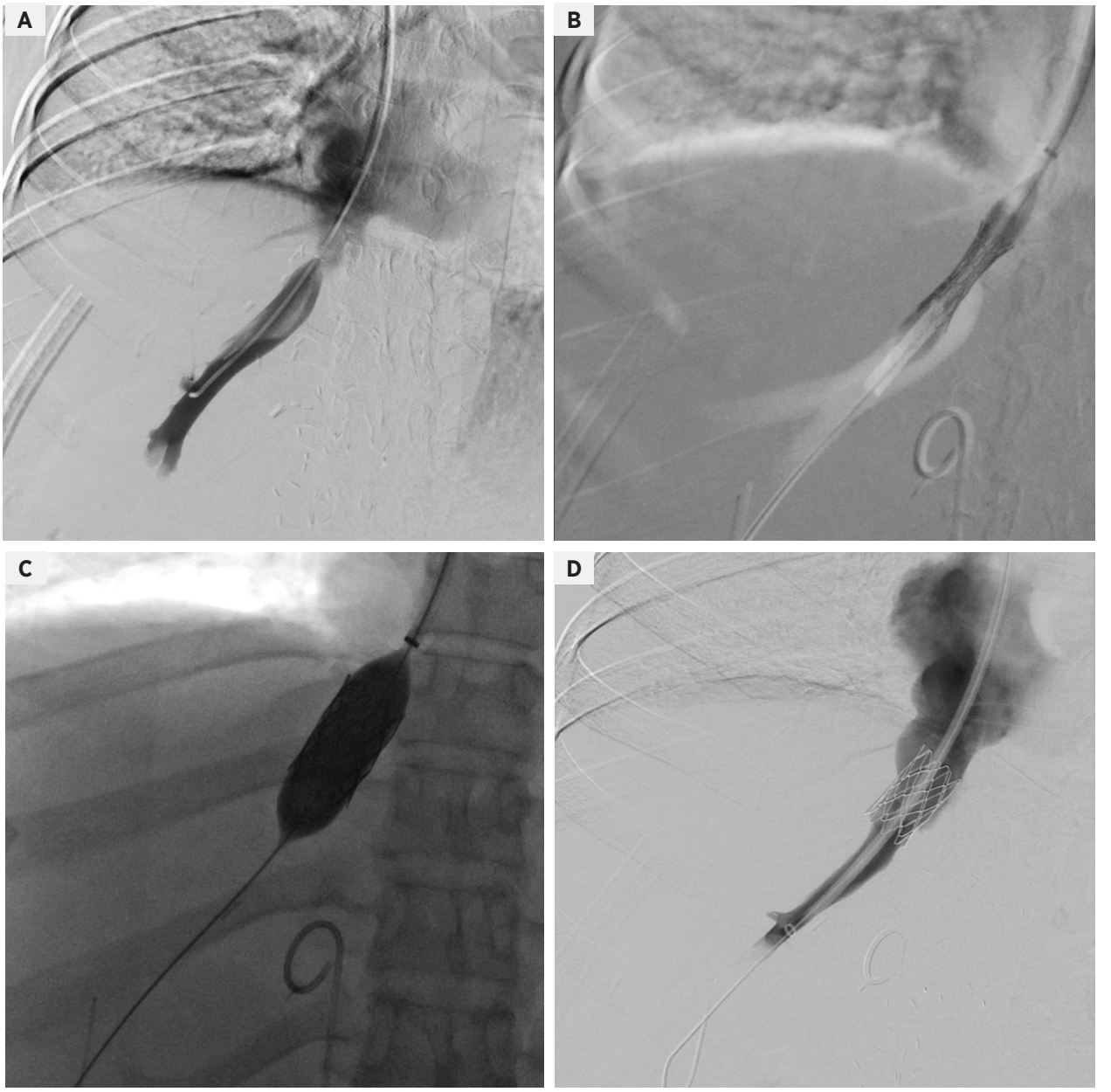


Figure 6. Stent Placement of Hepatic Venous Stenosis

(A) Significant stenosis at the level of hepatic vein anastomosis. **(B)** and **(C)** Placement of the large strut balloon-expandable stent within the stenotic segment. **(D)** Opening of stenotic segment and normalization of hepatic flow.

In addition, stents placed in the IVC may complicate subsequent interventions when the hepatic vein is jailed.[15] The stents to be used should not only be of sufficiently large diameters, but also the spaces between the stent struts should be large enough to minimize other vessel occlusions and facilitate subsequent interventions.[5] Because balloon-expandable stents have higher radial stiffness than self-expandable stents, these are more resistant to external pressure and more effective in the treatment of fibrotic vascular stenosis. On the other hand, self-expanding stents have better radial

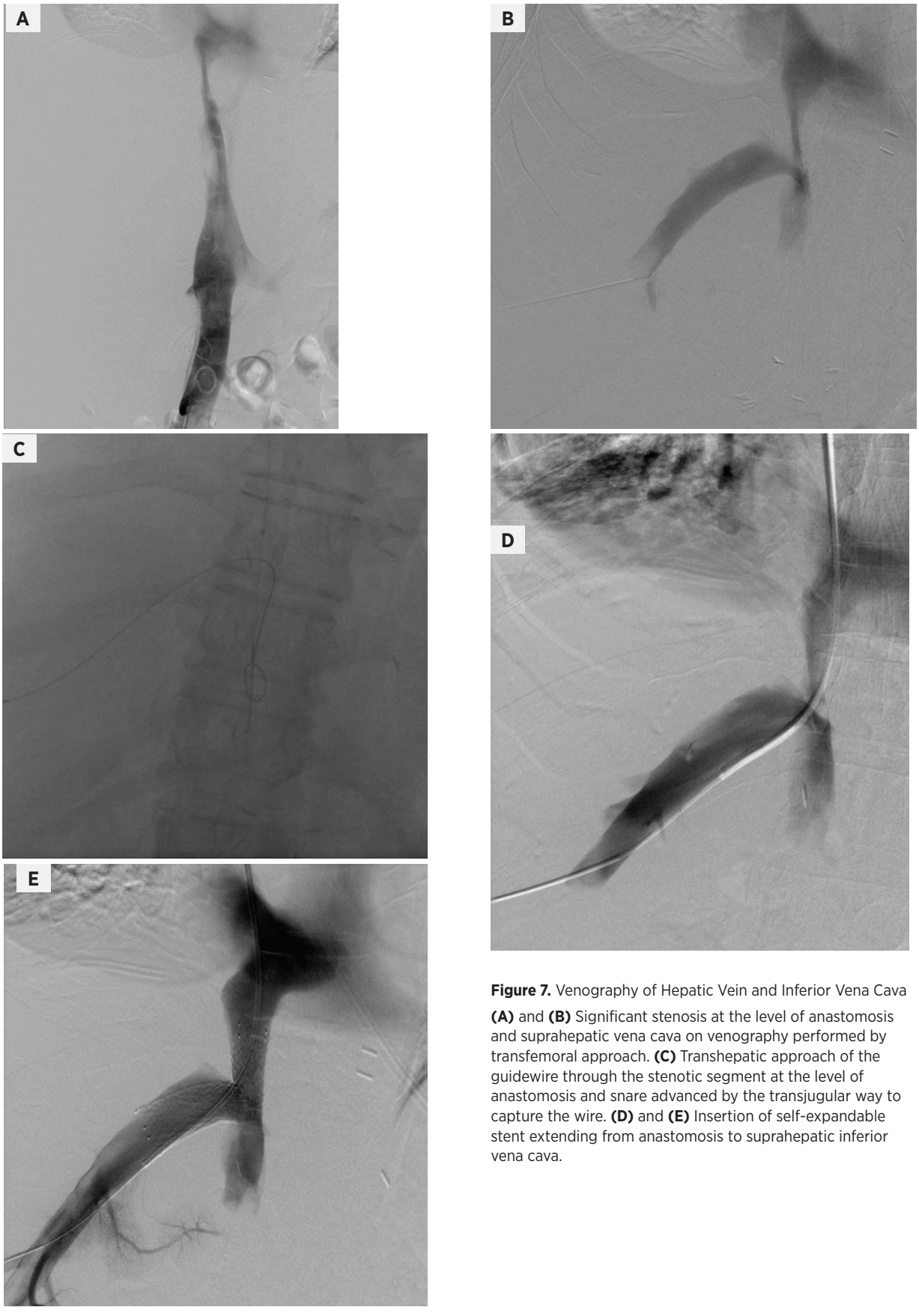


Figure 7. Venography of Hepatic Vein and Inferior Vena Cava

(A) and **(B)** Significant stenosis at the level of anastomosis and suprahepatic vena cava on venography performed by transfemoral approach. **(C)** Transhepatic approach of the guidewire through the stenotic segment at the level of anastomosis and snare advanced by the transjugular way to capture the wire. **(D)** and **(E)** Insertion of self-expandable stent extending from anastomosis to suprahepatic inferior vena cava.

compatibility than a balloon-expandable stent and better coherence into vessels after stent placement (Figure 7). If stent placement is considered in endovascular treatment of the hepatic venous outflow problem, it should be placed without compromising the drainage of other hepatic veins.[50] Some recipients may require repeated intervention due to stent thrombosis or small-diameter stents.[20] Extension of the stent to the right atrium to be placed in the IVC may greatly complicate surgery in recipients requiring retransplant.[51]

Although angioplasty and stenting are considered the first-line treatments for inferior cava steno-torsion, many studies agree that angioplasty alone is not sufficient to provide adequate patency in the long term. Choosing the right stent characteristics, including diameter, radial force, low compressibility, and good resistance to pressure, is important in recipients considering stent placement.[41]

While stents are placed in the stenosis of the IVC, the recipient's preoperative tomography and inferior vena cavography before the stent procedure can be evaluated together to determine the stent size. Ideally, the stent diameter should be 15% to 25% above the unaffected vena cava.

In the case of stent placement in the hepatic veins, it may be necessary to extend the stent along the largest hepatic vein to maintain the stability of the stent and not affect the flow of other hepatic vein branches. In this case, the stent should be extended to IVC as little as possible.[5]

In the absence of large stents to be placed in the IVC, treatment can be performed using 2 stents advanced through a double guidewire passed through the stenotic segment (Figure 8).

COMPLICATIONS

Major complication rates in interventional procedures are often low.[38,44,52] The rate of minor complications such as transient hypotension due to balloon swelling in IVC and arrhythmia due to manipulation of the guidewire in the right atrium is around 10%.[45] Complications such

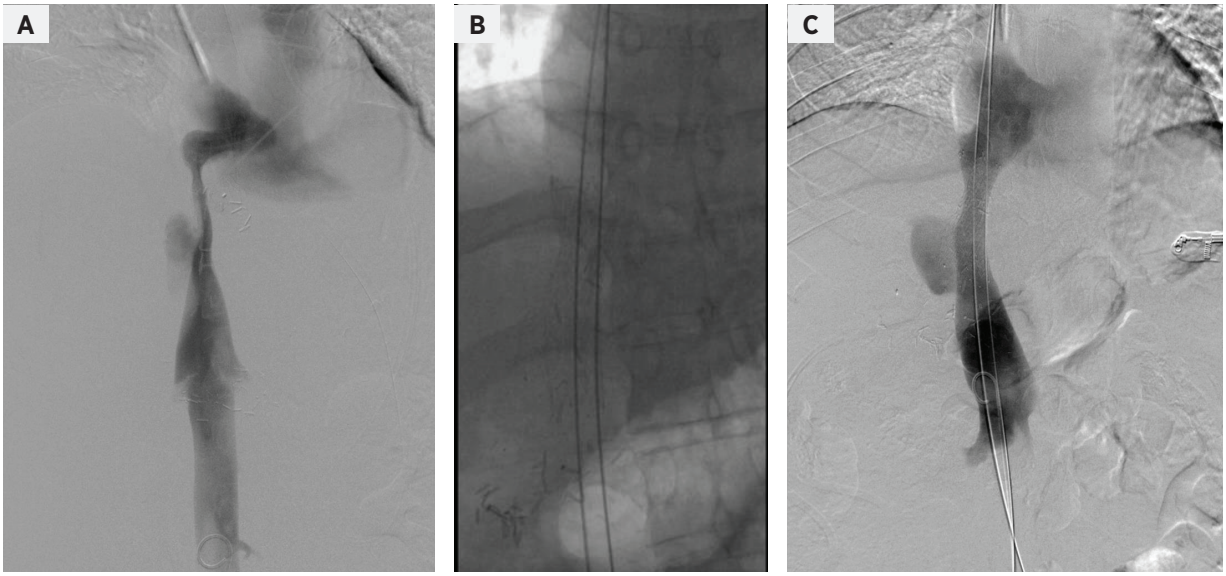


Figure 8. Transfemoral Venography of Inferior Vena Cava

(A) Significant stenosis in the suprahepatic inferior vena cava on transfemoral venography. **(B)** Insertion of 2 stents advanced over 2 guidewires in the stenotic segment. **(C)** Opening of stenotic segment and normalization of venous flow.

as stent migration, malposition, and occlusion of the hepatic vein ostium may occur during stent placement. Stent migration is a difficult complication, and there are several ways to resolve it during the procedure. Migration of the stent to the right atrium may cause disastrous results and may require surgery. For partial stent migration, a new stent may be placed in the migrated stent. In cases where the stent is markedly migrated, the stent can be taken to its normal localization using snare.[15,44,53]

FOLLOW-UP

It can be considered as technical success when the pressure gradient across a stenosis is 5 mm Hg on a postprocedural manometry or when stenosis is < 20% in postprocedural venography. Improvement of the recipient's symptoms and liver function tests, biphasic or triphasic waveforms in the hepatic veins on Doppler examination, and loss of geographic low attenuation area on computed tomography scan may be considered as clinical success.[50] After treatment of the hepatic venous outflow problem, the recipient's clinical condition improves rapidly. Improvements in symptoms such as ascites-edema and laboratory findings are decreased within a few days. If there is no clinical improvement despite the restoration of the venous patency, then there may be other conditions, such as acute rejection or permanent liver damage caused by hepatic vein congestion.[15] Recurrence would be defined as a relapse of clinical signs and symptoms or liver function deterioration associated with a hepatic venous outflow abnormality.[50]

Doppler ultrasonography findings together with decreased acid content and spleen size can also be used for follow-up. However, because the actual amount of acid cannot be measured exactly, it is considered a subjective criterion. There are reports that spleen size measurements provide more accurate results for follow-up.[17]

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Biliary Complications Following Liver Transplantation

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Liver transplantation (LT) has evolved to be the standard treatment for end-stage liver disease and for acute liver failure and liver tumors. Shortages of organs from deceased donors continue to be the main hurdle for LT. Long wait periods have resulted in wait list mortality rates of 20% to 25%; wait times due to organ shortages can cause liver disease progression and a lost chance for deceased-donor liver transplant (DDLT). The desperate search for organ sources has led surgeons to transplant a portion of the liver from a living donor.[1-4] Living-donor liver transplant (LDLT) can be an alternative option, especially for patients with acute liver failure.[5]

Biliary complications have been a challenging problem since the beginning of LT. Despite advances and improvements in immunosuppression, organ preservation, intraoperative management, and surgical techniques, 5% to 32% of LT patients present with biliary complications. The use of reduced-size grafts with more complicated surgery from living donors, the evolution of allocation rules, and the growing number of organs from donors after cardiac death (DCD) have influenced the epidemiology of biliary complications. The use of deceased and DCD donors has been associated with incidence of ischemic-type biliary complications. On the other hand, in the LDLT complexity of biliary anatomy, impaired vascularization of the bile duct during dissection can increase the risk of biliary complications.[6,7]

Although the most common biliary complications are biliary leaks and biliary strictures, there are others, including bile stones, hemobilia, and sphincter of Oddi dysfunction. The incidence and type of biliary complications are influenced by many factors, such as type of graft, donor type (deceased, DCD, or living donor), biliary reconstruction technique, ischemia-reperfusion injury, existence of vascular complications, and infections. According to onset time after LT, biliary complications are named as early (within the first 3 mo) or late. Most biliary complications occur in the early postoperative period of LT, which can become major causes of morbidity and mortality. Therefore, early diagnosis and management of biliary complications are critical priorities to ensure good graft and patient outcomes.[6-11]

Multiple risk factors have been detected for biliary complications after LT. The major determinant of risk of complications is the type of biliary reconstruction. The surgical construction of the biliary tree determines the intervention required when a complication occurs. The choice is made according to underlying liver disease, the number of bile ducts, the size of the recipient/donor bile ducts, and prior biliary surgery. The 2 most commonly used techniques for biliary reconstruction are choledochocholedochostomy (CC; duct to duct, with or without T-tube) and choledochojejunostomy (CJ; with or without stenting) with a Roux-en-Y loop. No exact rules

or guidelines exist for an optimal reconstruction technique.[12] Biliary anastomosis techniques such as "corner-saving suture technique" have improved complication rates. Haberal and colleagues described corner-saving suture technique as a way to produce secure anastomoses, especially at the corners of bile duct ends. This reconstruction technique can be performed both in CC and CJ anastomosis.[13]

Choledochocholedochostomy is the most common preferred procedure since it is much easier and preserves the function of the sphincter of Oddi, decreases ascending cholangitis, and allows endoscopic access.[13] When the donor and recipient ducts are of similar diameter and are sufficiently long, CC is preferred for reconstruction in LT and in selected LDLT patients. Choledochocholedochostomy can be performed with or without a T-tube. The T-tube allows postoperative follow-up of bile output, allows easy access for radiologic evaluation of the biliary system, and reduces the risk of biliary strictures. However, a T-tube can cause biliary leaks and cholangitis. T-tube usage in CC has different reported consequences.[14] Biliary strictures are reported to occur in 5% to 10% of biliary reconstructions with T-tubes and in 6% to 13% of biliary reconstruction without T-tubes.[15] T-tube use in bile ducts smaller than 7 mm or recipient-to-donor bile duct ratio of > 2 has been shown to decrease biliary complications from 23% to 12%.[10] Biliary leaks (5%-13%) and cholangitis (4%-6%) have also been reported in reconstructions with T-tubes.[16]

Choledochojejunostomy is the other reconstruction option for LT and is a preferred technique for patients with previous biliary surgery, biliary diseases like primary sclerosing cholangitis, and donor/recipient bile duct size mismatches. Choledochojejunostomy takes more time compared with CC. However, there are no differences in incidence of biliary complications between these 2 methods.[8]

Liver transplant patients with biliary complications may present with a variety of complaints, including right upper quadrant pain, abdominal distention, paralytic ileus, and fever. The clinical presentation can change from an asymptomatic patient to a patient with sepsis. The presentation time of biliary complications also varies; some occur early after LT and some occur weeks after LT. Therefore, a comprehensive examination is needed. Work-up should begin with laboratory evaluations followed by imaging studies. Abdominal ultrasonography (USG) shows biliary system and hepatic vascularization. The positive predictive value of USG is high and has a sensitivity of 38% to 68% for detection of biliary obstructions.[8] Despite clinical suspicion, if USG does not reveal biliary pathology, magnetic resonance cholangiopancreatography or endoscopic retrograde cholangiopancreatography (ERCP) can be applied. Magnetic resonance cholangiopancreatography is a noninvasive test with a sensitivity of 93% to 100% in detecting biliary strictures. On the other hand, ERCP or other interventions, such as percutaneous transhepatic cholangiography (PTC), are invasive and have risks.[8]

BILIARY LEAKS

After LT procedures, the incidence of bile leaks ranges from 2% to 25%. Biliary leaks that occur in the first 3 months after LT are classified as early; late biliary leaks occur at 3 months or later after LT. Early leaks are often caused by local ischemia or technical defects. The incidence of early postoperative biliary leaks is reported to be unrelated to the type of biliary reconstruction. Early biliary leaks occur at the anastomosis, T-tube insertion, or cystic remnant site and can occur at the cut surface of a reduced-size graft, split graft, or a graft from a living donor. The rate of occurrence is greater with LDLT than with DDLT (11.8% vs 7.1%). In addition, the rate of occurrence of biliary leaks in LT is less with deceased donors than with DCD in many reports (10.6% vs 30.6%).[6,15,17] In our series, we also reported more biliary leaks in LDLT than in DDLT. In addition, we found a higher incidence in pediatric LT than in adult LT.[7] Biliary leaks should be suspected in any patient with abdominal pain, fever, and peritonitis. When leaks

follow T-tube removal, initial management usually involves pain control with analgesics, intravenous fluids, and supportive care. Biliary leaks due to ischemia are difficult to treat because the cause is usually not corrected by endoscopic or radiologic interventions. The use of ERCP with stenting of the bile duct, sphincterotomy, nasobiliary drainage, or a combination of these techniques can result in high rates of success. Most studies have reported resolution of symptoms in 85% to 100% of cases. Percutaneous transhepatic cholangiography is commonly used in cases where ERCP cannot be performed or in patients with Roux-en-Y reconstruction. In rare cases, surgical intervention may become necessary.[8]

BILIARY STRICTURES

Strictures are seen as late complications of LT. The incidence of biliary strictures is reported to be 5% to 15% in DDLT and 28% to 32% in LDLT. Biliary strictures can be anastomotic or non-anastomotic. Anastomotic strictures can occur with both CC and CJ anastomoses. Inadequate mucosa-to-mucosa anastomosis, failed surgical techniques, ischemia, and healing processes can cause biliary strictures.[8] The clinical presentation is usually with jaundice, fever, and abdominal pain. Biochemical analyses can show cholestasis, and imaging studies can show dilatation of bile ducts. Recently, ERCP (stenting or balloon dilatation) has become popular in the treatment of biliary strictures, with reported success of 75%, especially in those with CC reconstruction. In patients with CJ reconstruction, the initial treatment usually involves stenting by percutaneous approach. If a stricture does not respond to endoscopic or percutaneous therapy, surgery may be indicated.[7] Non-anastomotic strictures (NAS) are frequently hilar but can also be diffusely intrahepatic. The incidence of NAS can range from 5% to 15% (mean presentation of 3.3-5.9 mo after LT). Prolonged cold ischemia time, hepatic artery problems, and immunologic causes are shown to be responsible for NAS.[8] Treatment of NAS is difficult. Endoscopic or percutaneous therapy is often attempted first. Repeated dilatation with stenting is mostly needed. Treatment success depends on stricture severity, number, and location. Different studies have reported variable treatment success rates, ranging from 50% to 70%.[7,8]

BILE STONES

Although the incidence of bile stones after LT is rare (2% to 6%), it causes various complications, such as recurrent cholangitis, biliary strictures, secondary biliary cirrhosis, sepsis, graft loss, and even mortality.[11] The pathogenesis of bile stones after LT has not yet been clarified, but it is thought to be multifactorial. Many variables like bile stones after LT, ischemia-reperfusion injury, hepatic arterial thrombosis, and long cold ischemia periods are possible predisposing factors for bile stones. In addition, immunosuppressive drugs that inhibit bile acid synthesis (such as cyclosporine), hyperlipidemia, and hypercholesterolemia increase bile stone formation. Abdominal ultrasonography is usually insufficient in bile stone diagnosis, but ERCP and PTC are techniques that can be used for both diagnosis and treatment of bile stones. More systematic and careful observations and treatment options are required for bile stones after LT because bile stones can cause graft loss and even patient mortality.[11]

SPHINCTER OF ODDI DYSFUNCTION

The incidence of sphincter of Oddi dysfunction is reported to be up to 7%. It can occur due to denervation and is suspected in cases with significant dilatation of bile duct with biochemical abnormalities but in the absence of cholangiographic evidence of obstruction. Endoscopic therapy with sphincterotomy with or without stenting is the treatment option.[8]

HEMOBILIA

Hemobilia is reported to be a rare complication with an incidence of 0.1%. It is mostly associated with liver biopsy or PTC. Treatment of hemobilia requires both hemostasis and treatment of any associated biliary obstruction.[8]

SUMMARY

Biliary complications have effects on both graft and patient survival due to the high incidence and need for repeated and prolonged treatment. Although standardization of reconstruction techniques and improvements in immunosuppression and organ preservation have reduced the incidence, biliary complications are still associated with high mortality and morbidity rates. Prophylaxis is the major issue. Although many risk factors (older donor age, marginal graft, prolonged ischemia time, LDLT, partial LT, DCD transplant, hepatic arterial thrombosis, organ preservation, chronic rejection, and other donor/recipient characteristics) do not directly affect biliary complications, they may pave the way to an accumulation of the factors mentioned above that should be avoided.

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Interventional Radiology in the Management of Biliary Complications After Liver Transplant

Özgür Özen

Complications of the biliary tract, a common source of morbidity and mortality, still occur in many patients after liver transplant despite the improvements in surgical techniques, graft preservation, immunosuppressive therapies, and medical management. It has been called the "Achilles heel" of orthotopic liver transplant (OLT) by some authors.[1-5]

In humans, solid-organ transplant began in 1954 with a successful kidney transplant between identical twin brothers.[6] In 1963, Starzl and associates[7] published the first 3 attempts at human liver transplant, but it was not until 1967 that the procedure resulted in an extended survival. This case involved a 19-month-old girl with hepatocellular carcinoma, who died 13 months after surgery for metastatic disease.[8] Roy Calne, in Cambridge, United Kingdom, joined Roger Williams in London, United Kingdom, in 1968, and reported 5 cases of liver transplant, detailing the technical difficulties encountered.[9] In 1984, Bismuth and associates[10] (France) reported the first left-lobe liver transplant in a child, and, in 1988, Pichlmayr and associates performed the first split liver transplant in Hannover, Germany.[11] The first living-donor liver transplant (LDLT) (adult-to-child) was carried out by Raia and colleagues[12] in 1988 but it failed. One year later, Strong and colleagues[13] managed to complete the first successful LDLT operation (adult-to-child). The history of liver transplant in Turkey starts in 1988. The first successful deceased-donor liver transplant (DDLT) was performed by Prof. Haberal and his team[14] in 1988. The first successful partial LDLT in children in Turkey and also in Europe was performed by the same team on March 15, 1990. That same year, a left lobe LDLT was performed in an adult patient for the first time in the world by Prof. Haberal.[15-17] In 1992, Prof. Haberal performed a simultaneous living-donor liver and kidney transplant to an adult from the same donor for the first time in the world.[18] After Haberal had paved the way for liver transplantation, a number of Turkish surgeons began to be closely interested in liver transplantation.

The most common biliary complications are biliary strictures (anastomotic, nonanastomotic) and leaks; in addition, sphincter of Oddi dysfunction, hemobilia and biliary obstruction from cystic duct mucocele, stones, sludges, or casts have also been observed.[19-22] Biliary tract complications can occur both in the immediate post-liver transplant period and also years after. Technical problems related to surgery and vascular insufficiency are the most common causes of the complications in the immediate posttransplant period, whereas recurrent disease (ie, the initial reason for the transplant), rejection of the graft, secondary neoplasms, stone formation, as well as vascular insufficiency are common causes often observed in the late period.[23,24]

It has been shown that early diagnosis and quick treatment of biliary complications following transplant can reduce morbidity and mortality and improve graft survival.[25] Various treatment modalities, including surgical, endoscopic, and radiological approaches, have been used to treat biliary complications. The treatment strategies differ between transplant centers. There are many series showing excellent results with transhepatic percutaneous biliary drainage (PBD) and endoscopic retrograde cholangiography (ERCP) procedures with low complication rates.[26] As nonsurgical interventions have been currently emerging as the most prominent treatments in biliary complications, the vital role of interventional radiologists in the long-term care of transplant recipients has increased significantly.[27]

BILIARY DUCT RECONSTRUCTION

Over the years, several modifications have been made for bile duct reconstruction during transplant. The surgical construction of the biliary tree determines the intervention required when a complication occurs. To have a background knowledge of the different types of reconstructions that occur during OLT is important while evaluating a patient with a potential biliary complication. Today, choledochocholedochostomy (duct-to-duct) and choledochojejunostomy (duct-to-jejunum) are the 2 standard biliary reconstruction procedures used. When the donor and recipient ducts are of similar diameter and are sufficiently long, choledochocholedochostomy is preferred for reconstruction in OLT and in selected LDLT patients. Biliary anastomosis techniques such as "corner-saving suture technique" have lowered the risk of complications throughout the years. Prof. Haberal described the "corner-saving suture technique" to produce secure anastomoses, especially at the corners of the bile duct ends. This reconstruction technique can be performed both in duct-to-duct and Roux-en-Y hepaticojejunostomy (duct-to-jejunum) anastomosis.[28,29]

Choledochocholedochostomy is the preferred technique for anastomosis because making a Roux-en-Y loop for hepaticojejunostomy (an additional operative procedure) is avoided, and it makes endoscopic treatment of ductal anastomotic stricture (ANS) in the future possible. Choledochocholedochostomy also prevents sepsis that can occur because of the contamination of the peritoneal cavity with bowel contents through the bile leakage from the anastomosis. However, duct-to-duct anastomosis is not the right choice for patients with sclerosing cholangitis, biliary atresia, and duct size mismatch, and also in cases in need of a repair for problematic choledochocholedochostomy anastomosis. If a complication occurs, then duct-to-duct anastomosis can be managed either by the percutaneous route (percutaneous transhepatic cholangiography [PTC] with percutaneous transhepatic biliary drainage [PTBD]) or by endoscopic route as ERCP, whereas Roux-en-Y choledochojejunostomy can only be managed by the percutaneous route. Some studies have suggested that endoscopic management is possible with the use of a double-balloon endoscope or variable-stiffness pediatric colonoscope.[30,31]

Liver transplant is also applicable in the case of children with end-stage chronic liver disease or acute liver failure. However, biliary tract complications are still as high as 12% to 50% and observed to be higher in recipients weighing less than 10 kg.[32] Therefore, despite recent progress in surgical techniques, the high rates of biliary complications are still a major challenge in pediatric liver transplant (PLT) cases both during and after surgery. Small duct diameter and split procedures are the causes of both high complication rates and also reoperation and retransplant.[33] In PLT, Roux-en-Y hepaticojejunostomy is usually chosen for biliary reconstruction because of the prevalence of biliary atresia. In addition, in pediatric LDLT, Roux-en-Y hepaticojejunostomy is still the main procedure even in patients without biliary atresia. There are also an increasing number of studies showing duct-to-duct biliary reconstruction in pediatric patients. Because of the Roux-en-Y reconstruction and small patient size, endoscopic biliary interventions are rarely possible in pediatric recipients. That makes PTC a very important

procedure in the evaluation and treatment of these patients, but it is still technically difficult because of the small caliber of the intrahepatic biliary tree. Still, biliary complications after PLT can be managed successfully with percutaneous interventions.[34-36]

PRESENTATION, EARLY EVALUATION, AND DIAGNOSIS OF BILIARY COMPLICATIONS

The biliary complication rate is highest in the first few months after transplant, and it decreases gradually thereafter. One year after transplant, the biliary complication rate is generally less than 4% per year.[19,37] Biliary leaks and strictures are the most widely seen complications. Usually, leaks tend to occur early, whereas strictures occur late. When a biliary complication is suspected, imaging studies of the liver, biliary tree, and hepatic artery are necessary for diagnosis, such as Doppler ultrasonography (US), magnetic resonance imaging (MRI), computed tomography (CT), and CT angiography. Noninvasive radiologic imaging begins with US examination, which is often used in combination with Doppler examination of the flow characteristics of the hepatic artery and portal vein. It is also useful in detecting fluid collections-bilomas adjacent to the liver and also has a slightly higher sensitivity rate than CT for determining bile sludge and stones. Hepatic artery thrombosis, along with hepatic artery stenosis, must be ruled out with Doppler examination or CT angiography. Hepatic artery thrombosis, which is an urgent complication post-OLT, often causing graft failure, can be determined by US with Doppler with a sensitivity and specificity of 91% and 99%, respectively.[38] If required, hepatic angiography should be used for final decision. Although US has a sensitivity rate of 38% to 66% in terms of detection of biliary obstruction, further investigation should be carried out when there is no bile duct dilatation on US but biliary tract complication remains highly suspect.[39,40] Today, magnetic resonance cholangiopancreatography (MRCP) is regarded as an optimal noninvasive diagnostic tool for assessment of biliary tract complications after OLT, and that is why MRCP is usually preferred before contrast cholangiography, which is an invasive procedure.[41-43] However, in certain situations, contrast cholangiography may be the only way to determine anatomic abnormalities as well as biliary sludge and cholelithiasis. Cholangiography may be done by either PTC or ERCP. It is easier to perform cholangiography in patients with an existing T-tube, and that has been one of the arguments for T-tube placement. Whereas duct-to-duct reconstruction can be managed endoscopically or percutaneously, duct-to-bowel reconstruction can only be managed percutaneously. Endoscopy uses the body's natural openings and conduits, which makes it safer, but unfortunately endoscopy cannot be used in patients with a Roux-en-Y hepaticojejunostomy.

Biliary strictures

Strictures are the most common cause of biliary obstruction, which can be multifactorial.[27] Strictures can be classified as anastomotic (ANS) or nonanastomotic (NANS). Approximately two-thirds to three-fourths of all biliary strictures are ANS, whereas the remainder are NANS. Nonanastomotic strictures can occur in hilar ducts, intrahepatic ducts, or the distal recipient duct.[42-45] Some studies suggest a higher rate of strictures in patients with hepaticojejunostomy; this is still controversial, although some researchers have suggested a higher incidence of both ANS and NANS in choledochojejunostomy or hepaticojejunostomy patients.[19,42,43,46-48] The incidence of biliary strictures is higher after LDLT than DDLT in various studies, which is due to the devascularization of the bile duct, technical difficulty of biliary reconstruction (small or multiple ducts), and bile leakage causing fibrosis around the anastomosis.[25,26] Occurrence of early-onset ANS after OLT is usually the result of surgical issues, whereas late-onset ANS can result from poor healing caused by primary ischemia.[49,50] Nonanastomotic strictures are often multiple and longer in length than ANS, and NANS also occur earlier. On the other hand, ANS are isolated, localized to the site of anastomosis, and short in length.[25,51] Inadequate mucosa at an anastomotic site, local tissue ischemia, localized edema, and

fibrosis at the site of healing may be the underlying causes of ANS.[44,52] Early diagnosis of strictures is facilitated by better response to short-term stenting, which is done in 3 to 6 months.[53] Recipients with ANS within 3 months after the transplant have the best prognosis.[54] After 12 months, the success rate of stent and dilation is low and the relapse rate is as high as 30% to 40%.[54] The risk of bile leakage increases if there is an ANS, and this is because of a rise in biliary pressure.

Elevated levels of bilirubin, alkaline phosphatase, gamma glutamyl transferase, and dilated intrahepatic biliary ducts at graft imaging can suggest biliary strictures. Magnetic resonance cholangiography followed by either PTC or ERCP will confirm the diagnosis of biliary strictures. MRCP has a sensitivity and specificity rate of nearly 90% for diagnosis of biliary strictures.[41,51] The size of the duct is not a reliable indicator to follow up with these patients or to assess response to treatment. Furthermore, there is also a lack of correlation between the ductal dilation seen on the US and both cholangiography and clinical features. It is still not clear why the transplanted livers display a different degree of dilation in response to obstruction compared with nontransplanted livers. Nevertheless, it is possible that the presence of variable degrees of fibrosis subsequent to the injury during surgery may cause less pliable ducts.

The most common biliary complications of liver transplants are ANS. The underlying causes of ANS are ischemia and/or fibrosis due to a suboptimal surgical technique and bile leakage in the postoperative period. Technical issues are more important factors for early onset: improper surgical technique, small caliber of the bile ducts, mismatch between the donor and recipient bile ducts, inappropriate suture material, tension on the anastomosis, excessive use of electrocautery, and infection.[51,55,56]

The etiology of NANS is more complicated than that of ANS, and it is associated with multiple factors. Moench and colleagues suggested that these be classified as follows: NANS secondary to macroangiopathy (arterial occlusion, stenosis, thrombosis) (Figure 1), NANS secondary to microangiopathy (preservation injury, prolonged cold and warm ischemia duration, donation after cardiac death, and prolonged use of vasopressors in the donor), and immunogenicity (chronic rejection, ABO incompatibility, autoimmune hepatitis, and primary sclerosing cholangitis).[57] Its association with hepatitis C and cytomegalovirus is less significant and indefinite.[21,58,59] Nonanastomotic strictures usually occur in the peritransplant period, which is earlier compared with that of ANS.[60] These complications are mainly seen in hepatic bifurcation, but multiple strictures involving both the intrahepatic and extrahepatic ducts are also frequent.[61] Since the main underlying cause of NANS is ischemia, many of these occur together with biliary sludge, necrotic debris, and leaks.

There are 3 therapeutic strategies for the management of biliary strictures after liver transplant, which are ERCP-guided therapy, PTC-guided therapy, and surgical revision including retransplant. The first choice for the treatment should be endoscopic and percutaneous methods. Surgery is preferred only when the noninvasive methods fail. Treatment strategies may differ between transplant centers. In the literature, there are many studies suggesting great results with PBD and ERCP with low complication rates. Most cases of ANS can successfully be managed by percutaneous dilatation. Biliary interventions can easily be performed with US and fluoroscopy, and, to reduce the complication rate, it is better to use both techniques together. Two to three percutaneous intervention sessions are usually needed for the treatment of these strictures.[27] The success rate is up to 75% to 85%.[62] With noninvasive methods, only 10% to 30% of patients will require reexploration or conversion to a choledochojejunostomy or hepaticojejunostomy.[42,63-66]

Management of anastomotic strictures

Broad-spectrum antibiotics should be started and coagulation profile should be kept under control before invasive procedures. Dilatation and stenting during the intervention may cause microscopic

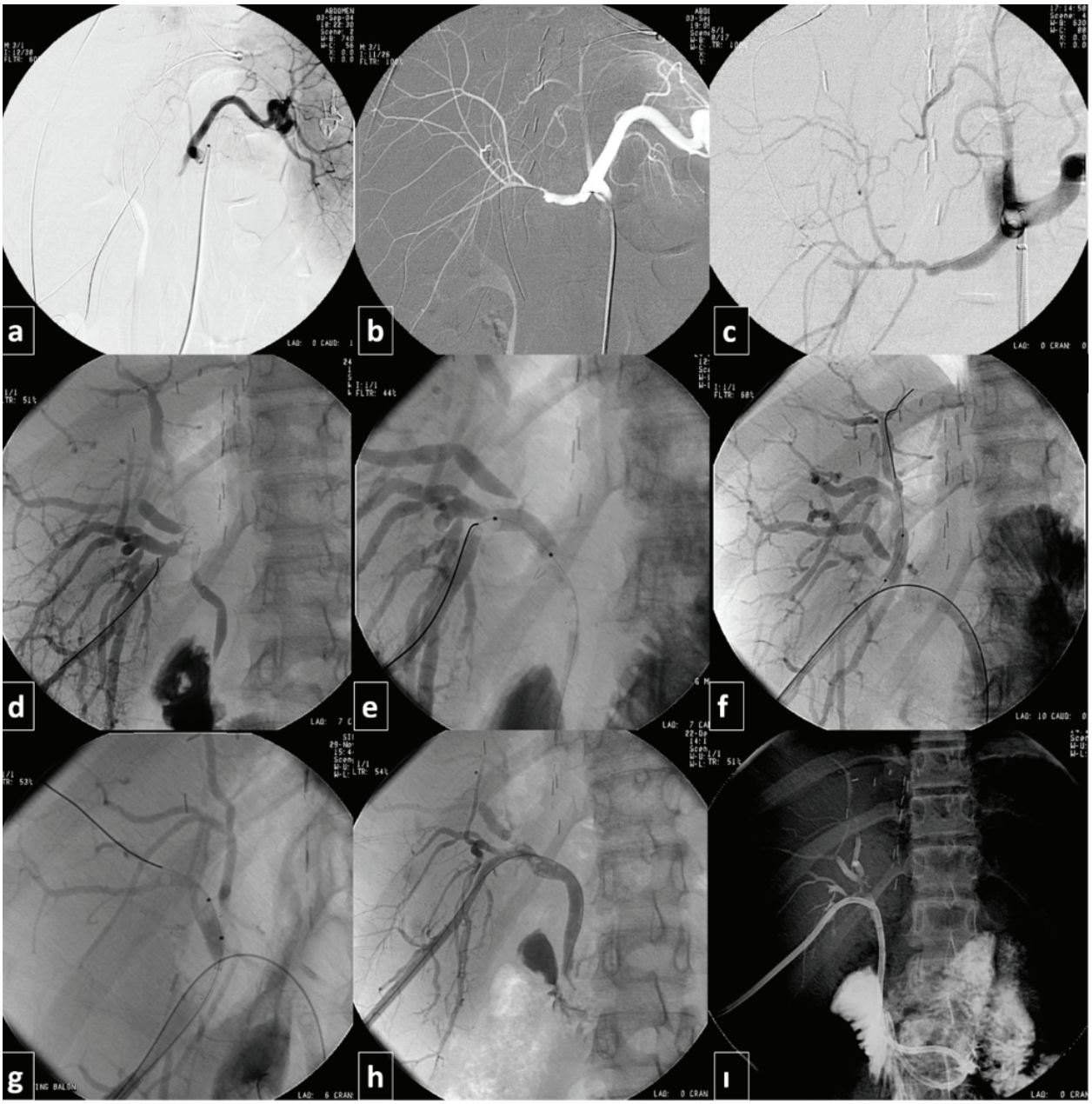

Figure 1. Anastomotic and Nonanastomotic Strictures in 12-Year-Old Right Lobe Orthotopic Liver Transplant Recipient

Abbreviations: ANS, anastomotic stricture; NANS, nonanastomotic stricture; PTA, percutaneous transluminal angioplasty; PTC, percutaneous transhepatic cholangiography

(a), **(b)**, and **(c)** The patient underwent 2 PTA procedures due to hepatic artery occlusion during the early postoperative period. **(d)** Postoperative PTC procedure on the 80th day revealed ANS and NANS of intrahepatic segments at hilus level (probably due to ischemia secondary to hepatic artery occlusion-stenosis). **(e)**, **(f)**, and **(g)** Multiple conventional and cutting balloon dilatation of the anastomosis level, proximal common bile duct, and intrahepatic NANS strictures were performed. The patient was followed up with internal-external biliary drainage catheter between these procedures. **(h)** and **(i)** Despite multiple percutaneous procedures, stenotic segments persisted.

fissures that may promote septic complications. Percutaneous procedures can be performed with aid of both US and fluoroscopy guidance in an angiography suite. Intravenous sedation and local anesthesia should both be used during all procedures. Complications of percutaneous

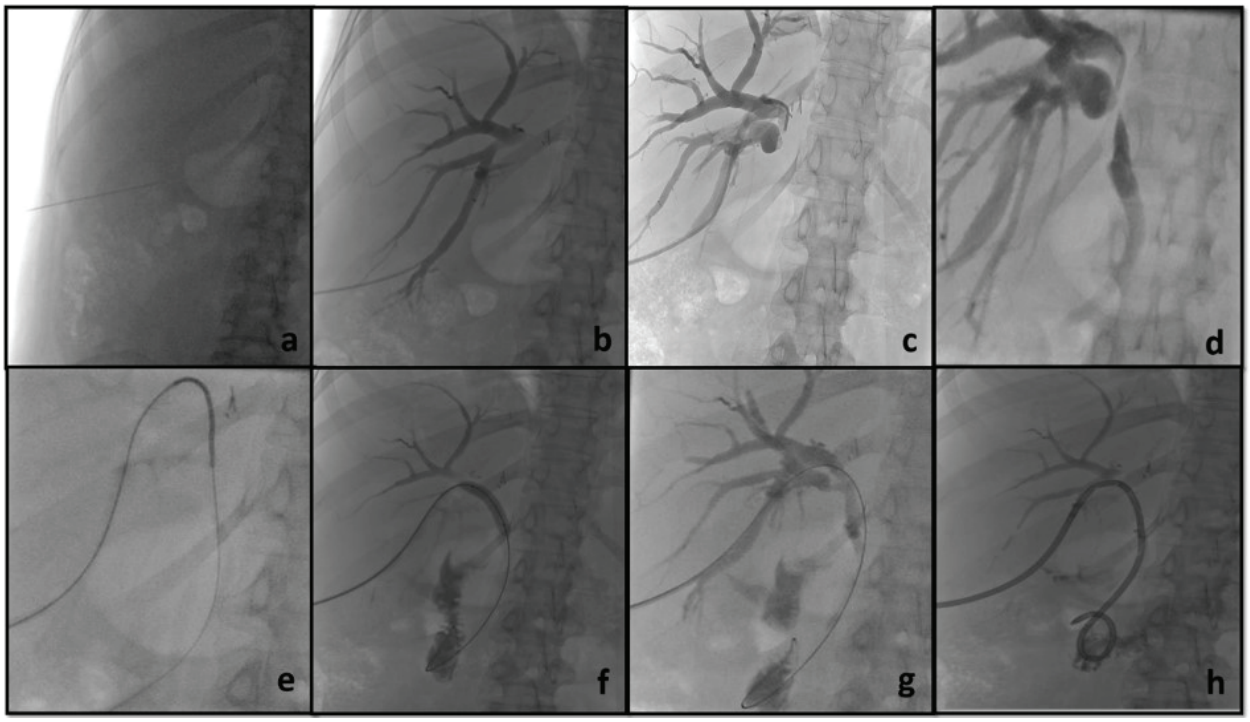

Figure 2. Steps of Percutaneous Transhepatic Cholangiography, Balloon Dilatation, and Biliary Drainage in Orthotopic Liver Transplant Patient

(a) After ultrasonography and fluoroscopy-guided puncture of bile duct with 21-gauge needle. **(b)** Cholangiogram after insertion of coaxial dilator. **(c)** and **(d)** Visualization of duct-to-duct anastomotic stricture after contrast administration through the 5F catheter **(e)** Crossing the structure with torqueable 0.035-inch hydrophilic guidewire and reaching the intestine. **(f)** Dilatation of stricture with 8-mm balloon. **(g)** and **(h)** Cholangiogram from the introducer sheath after balloon dilatation and insertion of an external–internal biliary drain over a stiff wire.

biliary interventions are decreasing, since fine-needle access sets are less traumatic. Usually, a 21-gauge Chiba needle is used for percutaneous cholangiography. A 0.018-inch guidewire is inserted into the duct through the Chiba needle, after obtaining the cholangiogram. Then, a coaxial dilator is placed. A 0.035-inch guidewire is then sent through the dilator, and a 6F introducer is inserted into the duct over the wire. A 4F or 5F catheter with a torqueable 0.035-inch hydrophilic guidewire can be used to traverse narrowed segments. Once the intestine is reached, balloon catheters over a stiff guidewire are used to dilate the narrowed segments. Different diameters of the balloons (4-10 mm) can be chosen according to the age of the patient and the size of the bile duct. The diameter of the balloon and the diameter of the intrahepatic bile duct on the hepatic side of stricture should be matched. Intrahepatic strictures should not be dilated more than their original size plus 1 mm. An external–internal biliary drain is placed (8-14F) right after the procedure and usually kept in place for a few weeks. To check the result of the dilatation, the drain can be changed with an introducer sheath, and cholangiography can be performed after a few weeks (Figure 2). These strictures usually require 2 to 3 balloon dilatation sessions. Repeated balloon dilatations are performed at 2- to 4-week periods; however, it is also possible to do it more frequently. There is no best method according to the evidence. There are particular advantages of transhepatic catheter placement across the stricture. First, the catheter enables maintaining the patency of the anastomosis; at the same time, the catheter provides repeated access to the stricture for its assessment and dilatation without increasing morbidity

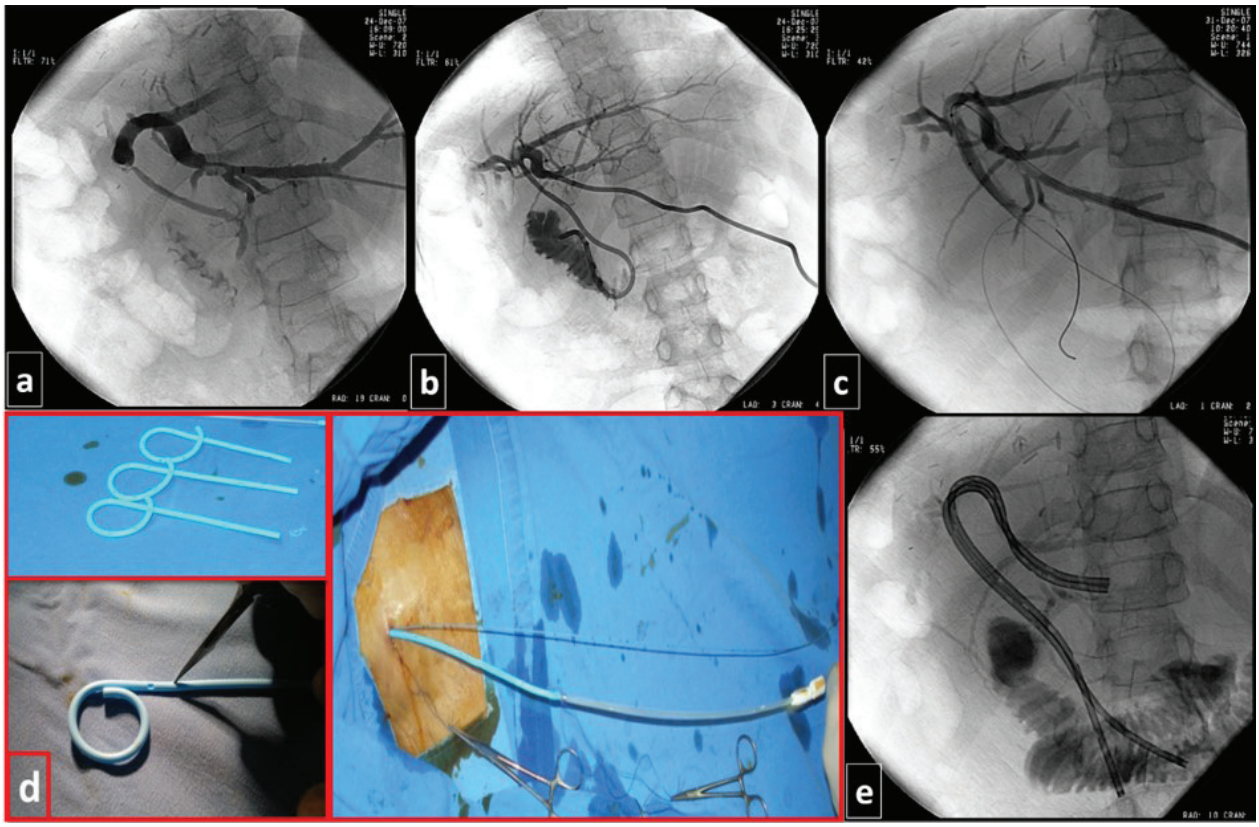

Figure 3. Left Lobe Orthotopic Liver Transplant in 10-Year-Old Patient

(a) Stricture of duct-to-duct anastomosis. **(b)** Insertion of internal, external biliary drainage catheter. **(c)** Conventional and cutting balloon dilatation in the subsequent sessions. **(d)** and **(e)** Stricture of the anastomosis line was successfully treated by percutaneous insertion of two plastic stents. At 5 months, the stents were removed by endoscopic approach.

significantly. Second, in strictures complicated with sludge, daily flushing of these catheters will move most of the sludge and small stones away; if this procedure is not sufficient, the catheter can easily provide access for percutaneous cholangioscopy to remove the stones or sludge. If cholangitis develops, then a catheter can be used for external decompression of the biliary system by opening it for gravity drainage, which will eventually improve the symptoms. To prevent restenosis between dilatations, long-term drainage through the dilated site seems to be the suitable choice. Use of cutting balloons, about which there are varying reports of success, is an alternative when traditional balloon catheter dilatation is not enough.[67] The percutaneous placement of double 8F to 14F plastic biliary stents is another method that can be used for biliary strictures (Figures 3 and 4).[27] Usually, metallic stents are not preferred in many centers, because, as a rule, permanent foreign bodies should not be placed. Still, in rare cases, self-expandable metallic stents (bare or covered) are shown to be useful as bridging therapy before retransplant. Also, in the near future, newly developed removable metallic stents and biodegradable stents seem to be promising as a solution in selected cases.[68,69]

If there is a high-grade stricture or occlusion that cannot be passed, external drainage should be used until the cholangitis and sepsis resolve. Another attempt to pass the stricture should be tried after the symptoms resolve and the patient is stabilized.

Transient hemobilia is the most common complication of PBD. After the procedure, hemobilia is sometimes seen but typically disappears within 12 to 24 hours. If transcatheter bleeding persists,

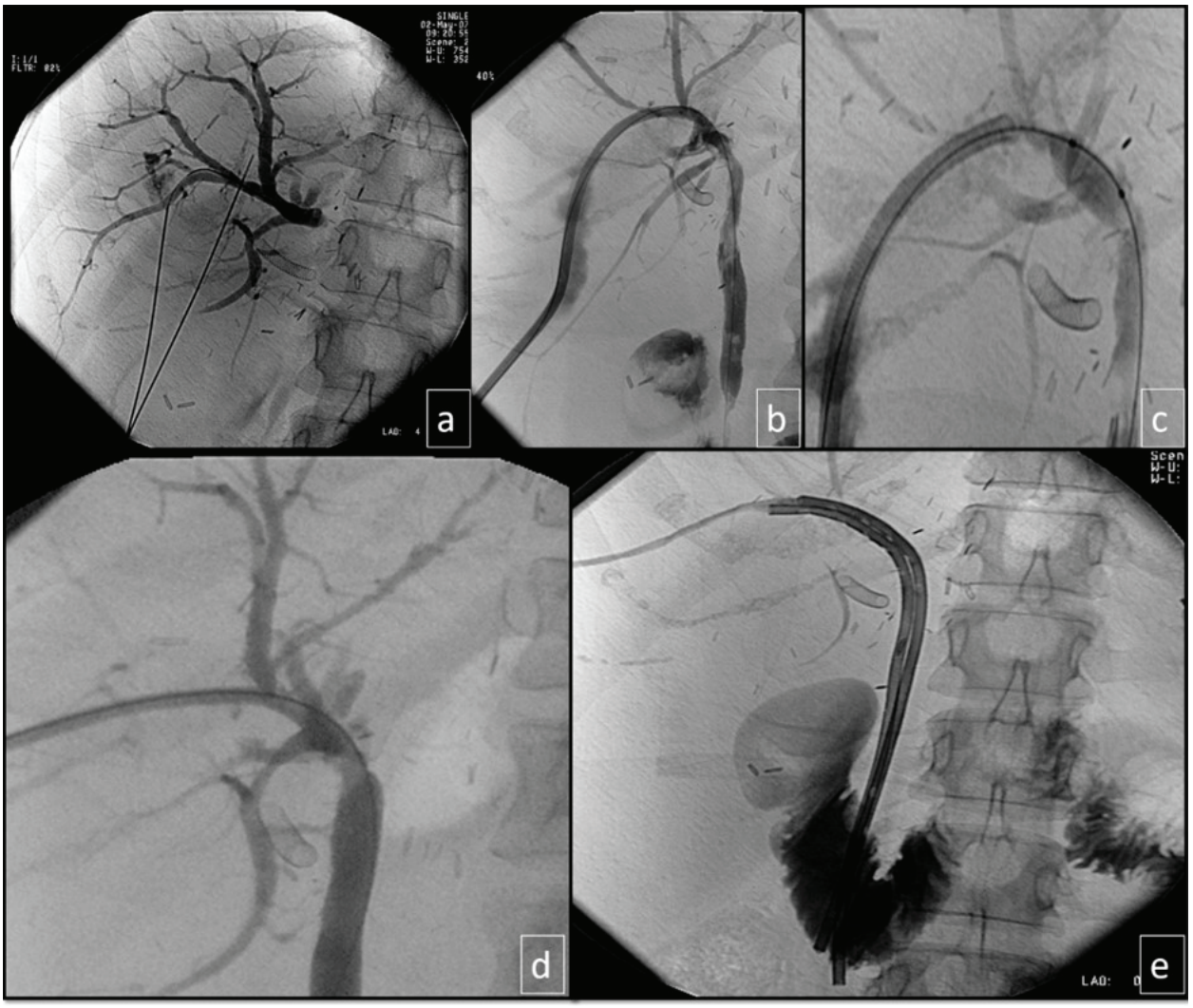

Figure 4. Postoperative 6th Month Stenosis-Occlusion of Duct-to-Duct Anastomosis in 30-Year-Old Right Lobe Liver Transplant Recipient
After failure of ERCP, treatment with balloon dilatation, biliary drainage, and double plastic biliary stents were performed, which were placed percutaneously. **(a)** PTC, occlusion of duct-to-duct anastomosis. **(b)** and **(c)** Balloon dilation after passing the occlusion. **(d)** Image after balloon dilatation. **(e)** Percutaneous insertion of 2 plastic stents. The stents were removed by endoscopic approach after treatment.

then other causes should be evaluated. One cause may be the placement of the side holes of the catheter adjacent to an injured portal or hepatic venous branch during the catheter placement; this condition can be diagnosed by catheter injection or by over-the-wire, pull-back sheath cholangiogram, which should reveal the injured vascular structure. For management, the side holes can be repositioned, and the drainage catheter can be replaced with a larger size so that the tamponade is improved. Hepatic artery injury should be considered if the bleeding continues to cause a decrease in hemoglobin levels. Angiography should be performed to diagnose the injured artery, which is usually seen adjacent to the drainage catheter where it crosses or lays near a hepatic artery branch at the bile duct puncture site. The drainage catheter can be removed over a wire if the injury cannot be seen while it is in place; the angiography is repeated afterward. Suggested treatment for arterial injuries is transarterial embolization. Occasionally, pseudoaneurysm may develop following arterial

injuries. Massive hemobilia may be observed if the pseudoaneurysm is connected with the biliary system. Another common complication of percutaneous biliary intervention is cholangitis-sepsis. To avoid this, proper antibiotics should be used, bile should be drained from the obstructed bile tree before contrast injection, and the bile tree should be manipulated minimally. If cholangitis occurs, it can be treated with antibiotics and catheter change.[70] Other possible complications are as follows: portal vein thrombosis, arterioportal fistula, pancreatitis, and pleural transgression. Although most complications tend to be minor and can be treated medically, they can also be life-threatening and a cause of death.

Endoscopic treatment can also be a choice in patients with duct-to-duct reconstruction. During conventional endoscopic treatment, first, the opening of the stricture is identified, and then it is crossed by a guidewire followed by balloon dilatation and plastic stent placement. The success rate of balloon dilation alone without stent is only 40%.[70] However, the long-lasting success rate of balloon dilation with additional stent placement is 75% in patients with ANS.[39,70] To prevent clogging, cholangitis, or stone formation, stents should be changed with larger ones every 3 months. The results with dual or multiple stents are better than with single stents because these provide greater dilatation than single stents. Stent occlusion or dislocation or restenosis can be a reason for recurrent endoscopic intervention in more than 40% of patients.[71-73] After approximately 2 to 3 interventions, the cumulative success rate is 85% to 90%.[73,74] Treatment often requires 1 year, with an average of 3 to 4 stent exchange sessions. There are some studies about the use of temporary placement of covered self-expanding metal stents to decrease the need for repeated stent changes. However, more research is required before any type of self-expanding metal stent is to be used in standard management of ANS.

If percutaneous or endoscopic methods are not successful, then surgical revision will be indicated as biliary reconstruction with the formation of a hepaticojejunostomy. After biliary reconstruction, in nearly 20% of patients recurrent ANS will develop, which can be treated successfully by balloon dilatation and/or stenting.

Management of nonanastomotic strictures

The prognosis for NANS (hilar or intrahepatic), which mostly occur at hepatic bifurcation and are often multiple and longer in size, is worse than for ANS. Luckily, NANS occur less frequently than ANS. Nonanastomotic strictures also develop earlier than ANS, with an average time of 3 to 6 months.[75] These strictures can be treated with percutaneous and endoscopic techniques, just as for ANS; however, depending on the causative factors, it is not uncommon to see graft dysfunction and multiple duct involvement (Figure 1). These strictures usually require surgery, because nonsurgical methods may not be successful.[37,62,76-78] PTC or ERCP treatment is less effective than that of ANS, and these strictures require a longer treatment time.[74] Unfortunately, 30% to 50% of patients with NANS either die or require retransplant due to this complication.[58,62,76,78-80]

BILE LEAKS AND BILOMAS

Biliary leaks are seen in 2% to 25% of patients after liver transplant and remain important causes of morbidity. The most common site of clinically important bile leak is the biliary anastomosis site (duct-to-duct or biliary-enteric). The cut edge, the T-tube exit site, and the cystic duct stump are the other possible sites for leaks. If the leak is small and self-limited, then clinical observation and percutaneous drainage of a biloma is usually sufficient (Figure 5). However, in patients with ongoing leaks, usually from the anastomosis, standard management entails the diversion of the bile away from the leak and maintenance of biliary drainage into the intestine.[70] In case of massive leaks, surgical revision should be preferred. Nevertheless, if the patient is clinically stable, an anastomotic leak can be successfully managed without surgery. Main causes of anastomotic leaks are issues related to surgical technique and/or ischemic necrosis at the end of the bile duct. The

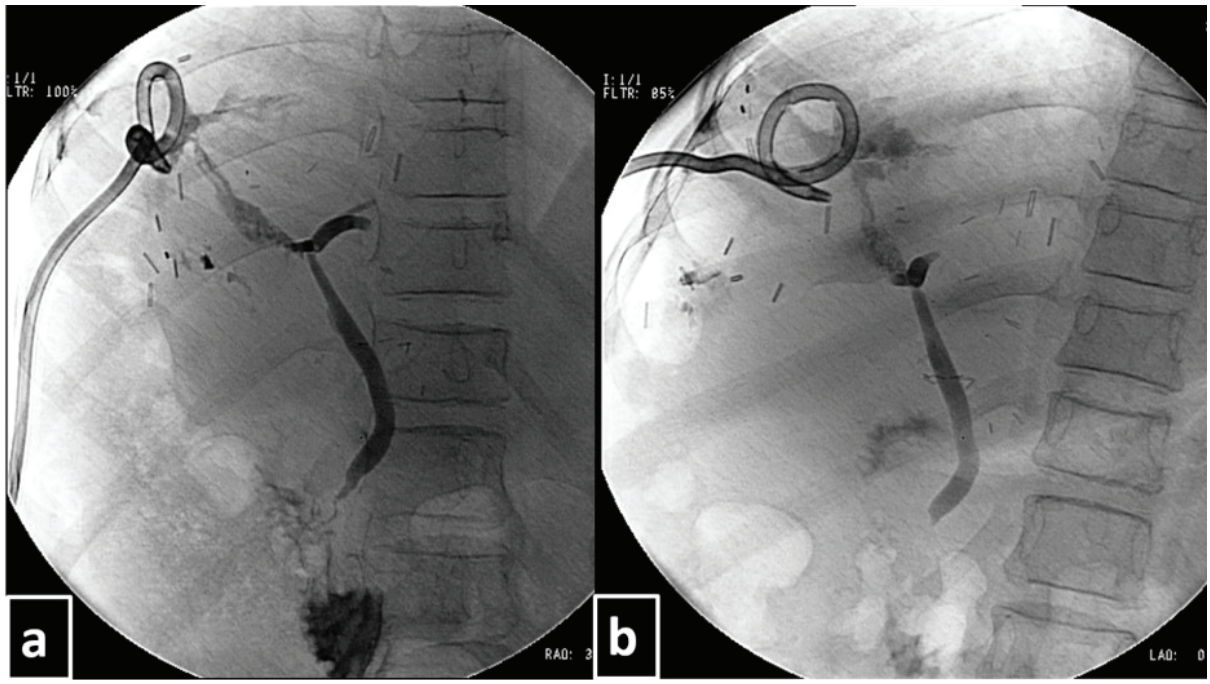

Figure 5. Bile Leak From Duct-to-Duct Anastomosis in 10-Year-Old Female Left Lobe Living-Donor Liver Transplant Recipient

Thirty days after the transplant, a drainage catheter was placed to the abscess, which was observed adjacent to the transplanted liver. **(a)** One day after the drain of the collection, the pouchogram revealed the connection between the biliary tract and the pouch. **(b)** Twenty-five days later, the pouchogram showed that the fistula tract between proximal common bile duct and pouch had shrunk. After no evidence of bile leak, the catheter was withdrawn several days later.

rates of bile leak after duct-to-duct and bilioenteric anastomosis are similar.[81,82] Ischemia and necrosis at the anastomotic site are usually the reasons for early bile leaks. These are often noticed in the peritransplant period. On the other hand, most of the late leaks are because of T-tube removal. Because of the high rate of catheter-related complications, many surgeons now prefer not to place a T-tube.

In patients with fever and signs of peritonitis, bile leaks should be suspected after liver transplant or after T-tube removal. It should be kept in mind that some patients may be asymptomatic because of immunosuppression. When there is a rise in bilirubin levels, a change in cyclosporine levels, or when bile is found in ascitic fluid, one should suspect bile leakage. If bile leak causing an extrahepatic collection is suspected, US or CT/MRI can be done. If the fluid collection is evident, then direct percutaneous drainage by interventional radiology should be considered. However, if no significant sign of fluid collection is detected with imaging modalities, then a hepatobiliary iminodiacetic acid (known as HIDA) scan can be considered, which has a sensitivity and specificity of 50% and 80%, respectively, for detecting a leak.

Management of bile leaks

Management of bile leaks differs among transplant centers. If there is a T-tube in place, then the diversion of bile flow often results in the resolution of the leak within the first 24 hours in one-half to one-third of the leaks (Figure 6). ERCP-guided or PTC-guided therapy is preferred for the rest of the patients. Ultrasonography and fluoroscopic-guided percutaneous transhepatic cholangiography and PBD are effective methods for treatment even when the biliary system is not dilated.[70]

With ERCP, extravasation is shown together with the site and the size of the defect in the bile duct. If the bile leaks are from the cystic duct or

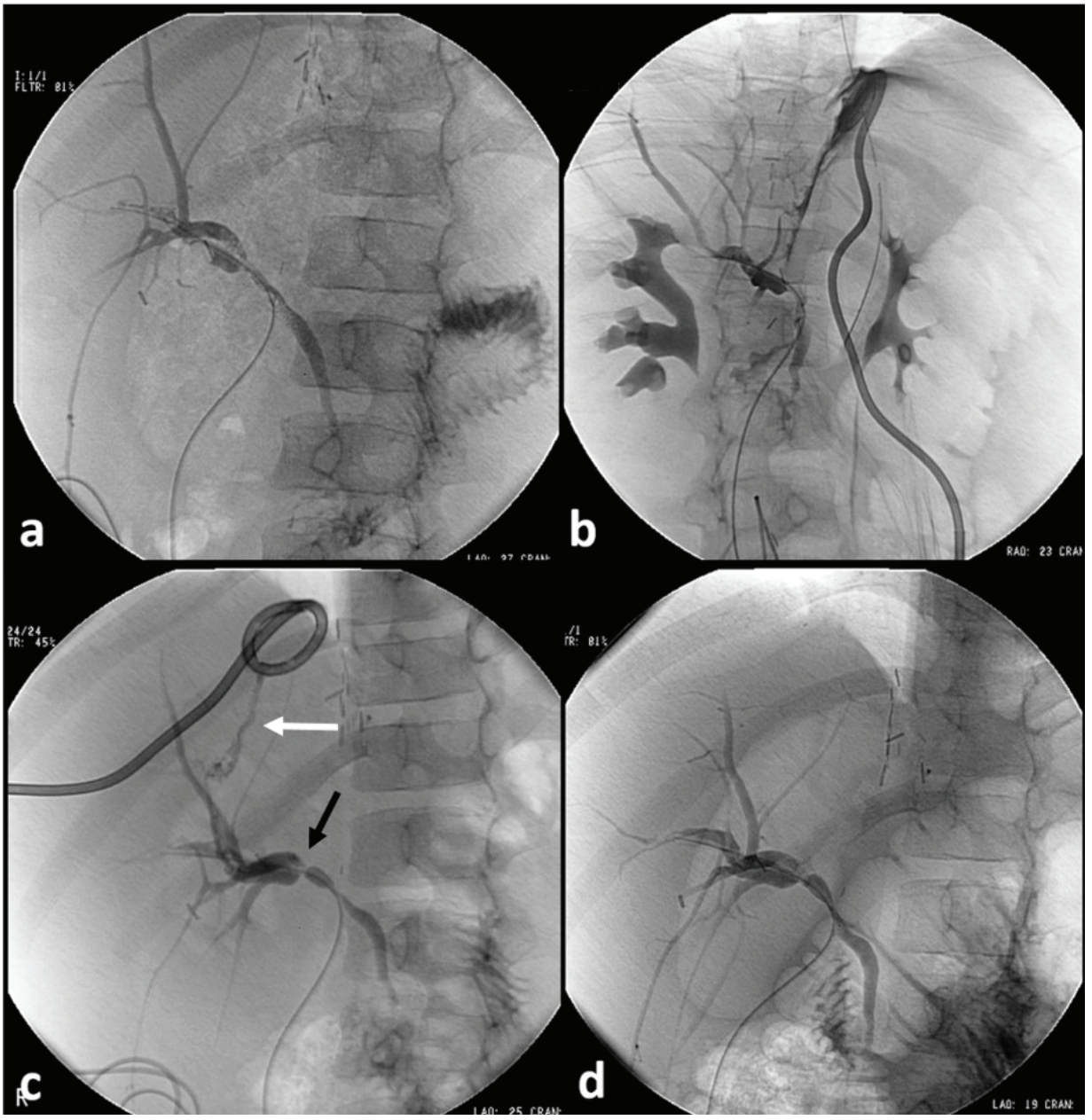

Figure 6. Duct-to-Duct Anastomosis and Bile Leak From Anastomosis and Intrahepatic Duct in 10-Year-Old Orthotopic Liver Transplant Patient

(a) One week after surgery, T-tube cholangiography revealed normal filling of intra and extrahepatic biliary tracts and no leakage. **(b)** On postoperative day 16, a drainage catheter was placed in the collection area between the stomach and liver. Simultaneously, T-tube cholangiography showed leakage in the common bile duct anastomosis. **(c)** On postoperative day 24, T-tube cholangiography revealed minimal stenosis at the level of anastomosis (black arrow). In addition, it was seen that the leakage in the anastomosis disappeared. However, minimal leakage was observed from the intrahepatic biliary tract into the pouch where the drainage catheter was placed (white arrow). **(d)** On the postoperative day 41, T-tube cholangiography showed complete disappearance of both anastomotic and intrahepatic biliary leakage.

if there is a minor injury of the common duct wall, then endoscopic sphincterotomy has been reported to be successful in most patients. If there is a large biliary duct defect, the biliary system should be decompressed by diverting the bile flow from the defect. This can either be done with the endoscopic insertion of an endoprosthesis or with a nasobiliary tube. In 90% to 95% of cases, early bile leaks resolve with the treatment by ERCP with plastic stent. Usually, a transpapillary stent is placed after sphincterotomy and left in place for 8 to 12 weeks to divert the bile away from the leak, which helps to decrease the transpapillary pressure gradient that can aggravate bile leaks. In OLT patients, when a stent has to be placed, it should be kept in place longer than the usual 4 to 6 weeks after standard cholecystectomy because the immunosuppressive state will compromise the healing. Nasobiliary tube is also effective in treating bile leaks which are placed proximal to the leak after the initial ERCP, which will allow frequent cholangiograms during follow-up (every 3–5 days) without repeating ERCP (Figure 7). As a result, endoscopic management is the preferred method for treating bile leaks; however, cannulation of the bile ducts proximal to the leak may be difficult and unsuccessful. In addition, in most patients with hepaticojejunostomy anastomosis, an endoscopic approach is also not possible.

Percutaneous therapy for bile leaks has been reported to be successful. Percutaneous techniques can be used regardless of the biliary anastomosis technique used. Percutaneous transhepatic cholangiography and PBD are effective methods

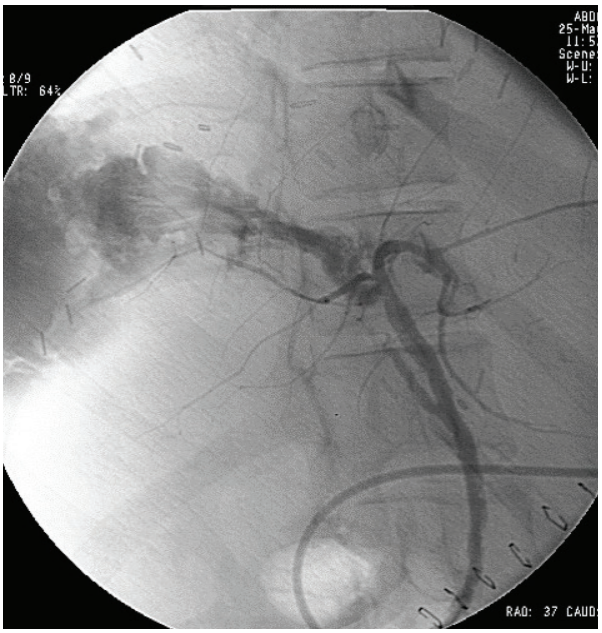

Figure 7. Contrast Administration Through the Nasobiliary Catheter in 14-Year-Old Orthotopic Liver Transplant Patient

There was a bile leakage from the proximal choledochus to the right medial extrahepatic space.

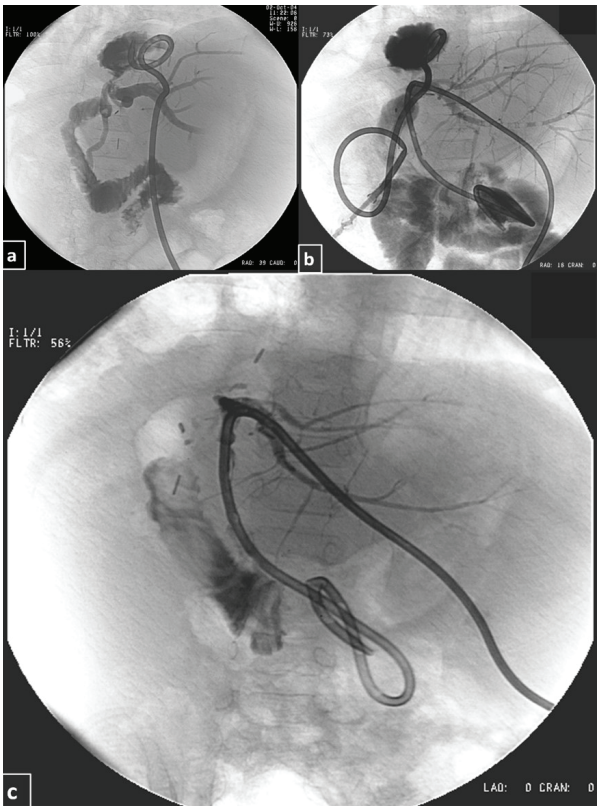

Figure 8. Bile Leak from Duct-To-Duct Anastomosis in 2-Year-Old Male Living-Donor Liver Transplant Recipient

A drainage catheter was placed in the subdiaphragmatic collection on day 107 after transplant. **(a)** Pouchogram was performed 7 days after the drainage catheter was inserted. It was observed that the contrast material filled the common bile duct and then intrahepatic bile ducts. Contrast material was also seen in the duodenum. **(b)** In the same session, an external-internal biliary drainage catheter was inserted through the bile duct of the left lobe. **(c)** After 40 days, cholangiography examination revealed complete disappearance of bile leak.

for treatment of biliary leaks (Figure 8). Once percutaneous bilioenteric access is accomplished, further interventions such as a catheter exchange in cholangitis patients or balloon dilatation in cases with coexisting stricture can easily be performed. In addition, control cholangiograms can be obtained from the catheter to follow-up on resolution of the leak. The most important limitation of percutaneous management is decompression of the bile ducts resulting from large leaks. In patients with marked leaks, which are usually from the anastomosis, massive bile leakage into the peritoneal cavity prevents dilatation of the bile ducts, which is essential for sonographic guidance. As a result, the puncture site may be more central than usual, which may explain the reason of higher risk of vascular complications in patients with nondilated bile ducts. When the biliary system is not dilated, puncturing the main bile duct near the hilum, then filling the entire biliary tract, including the peripheral bile ducts, with contrast is one of the techniques for achieving percutaneous biliary access. However, central bile duct puncture carries the risk of damage to the hilar vessels, and it may be also difficult to fill the peripheral bile ducts sufficiently in patients with massive leakage. A T-tube located at the choledochus or the catheter at the perihepatic biloma cavity, which is connected to the biliary system by the defective anastomosis, can be used for contrast injection to make the peripheral bile duct fluoroscopically visible, and this can be a valuable alternative method. Contrast material can be rapidly washed out of the biliary tree if the defect is large. In such cases, the puncture can be facilitated by the retrograde passage of a microcatheter from the biloma via the drainage catheter or T-tube tract. The microcatheter can be navigated to an ideal peripheral bile duct, and then contrast material may be injected through the microcatheter for opacification and distention of the targeted duct. An occlusion balloon catheter can be used to avoid duct decompression in the case of rapid emptying of the duct after injection. When the proximal part of the duct is occluded with the inflated balloon, a peripheral bile duct can be distended with contrast material. Alternatively, a snare can also be used to better facilitate the percutaneous puncture.

Biliary leakage due to anastomotic disruption generally requires surgery for treatment. It can be difficult to repair a disrupted biliary anastomosis, and in some patients neither percutaneous nor endoscopic approach effectively stents the biliary anastomosis. In this case, bile drainage can be accomplished by using combined percutaneous transhepatic and endoscopic transpapillary approach (the rendezvous technique). If the antegrade approach fails and the success of the retrograde approach alone is judged to be hopeless, then an antegrade-retrograde approach may be used in combination for biliary drainage and stenting. The rendezvous technique has been described to treat benign or malignant biliary obstruction or traumatic bile duct transaction, and it can also be used in selected liver transplant recipients complicated with an anastomotic leak.[83-86] Surgical revision may be needed for a severely disrupted anastomosis.

Intraabdominal bile collection (biloma) should be treated by either US-guided or CT-guided drainage. Secondary infections and late complications of adhesions associated with bile can be prevented by drainage of bilomas. Antibiotic therapy should be added to drainage if infection is suspected in bilomas. After a few days are allowed for drainage of this bile collection, a pouchogram can be performed by injecting contrast material through the drainage catheter, which usually shows the communication of biloma with the biliary system (Figure 5). As mentioned before, injecting contrast material into the biliary tract by this catheter makes peripheral bile ducts fluoroscopically visible and facilitates percutaneous access. A percutaneous approach can also be used to drain the bilomas among the biliary tree within the liver.

HEMOBILIA

Hemobilia can be seen after percutaneous interventions or biopsy. It can also be seen if hepatic artery pseudoaneurysm ruptures into the

bile duct. The patients may complain of right upper quadrant pain, upper gastrointestinal bleeding, and biliary obstruction. For significant hemobilia, to achieve hemostasis, selective embolization of the vessel should be done angiographically. If clot formation is suspected, ERCP or PBD and/or thrombus extraction can be used for clearance of the bile ducts.

CYSTIC DUCT MUCOCELE

Imprecise ligation of the cystic duct at both ends may cause a blind mucosa-lined sac, which can eventually become distended by accumulated mucus resulting in a mucocele. A mucocele can be sufficiently large to cause bile duct obstruction by extrinsic compression. The cystic duct stump is left open at one end or cystic duct lumen is united with the choledochal anastomosis to avoid this rare complication. Mucocele appears as a fluid collection in the porta hepatis, as observed with US. Abscess, biloma, or aneurysm must be considered and excluded before a firm diagnosis is possible, since these conditions will produce radiographic findings similar to mucoceles. Cystic duct mucoceles can be treated by either interventional radiology or surgery. The interventional radiological approach can be achieved by percutaneous drain placement and ethanol ablation, which is safe and effective. Endoscopic therapy is not recommended because it is not shown to be effective.[87]

STONES, SLUDGE, AND CASTS

After liver transplant, filling defects may appear, caused by stones, sludge, casts, or clots. Biliary stones and sludge formation occur in the same circumstances as in nontransplant patients. Predisposing factors for the formation of common bile duct filling defects are strictures, ischemia, and infections. Stones can be managed by either endoscopic or percutaneous methods; however, in case of an accompanying stricture, stricture has to be treated effectively to prevent recurrent stones and sludge (Figure 9). There are several advantages of PBD, including daily flushing of the drainage catheter, which helps to irrigate the biliary system and wash out the debris. The presence of multiple, hard, and pigmented brown casts causing obstruction is known as biliary cast syndrome.[39,88] This syndrome is thought to be caused by acute cellular rejection, ischemia, infection, and biliary obstruction from stasis.[25] Damaged mucosa of the biliary tree together with lithogenic bile can cause formation of desquamated epithelial cells (casts). Hepatic artery stenosis and strictures are the risk factors for this syndrome. The cast can be removed by percutaneous methods or ERCP.

SPHINCTER OF ODDI DYSFUNCTION

Sphincter of Oddi dysfunction is seen in 3% to 5% of liver transplant recipients; patients present with cholestasis and dilatation of the distal bile duct; also, no anatomic cause for biliary obstruction will be seen with cholangiography.[19,81,89] Denervation and devascularization during recipient hepatectomy might cause dyskinesia of the sphincter of Oddi.[90] Decreased cholestasis with T-tube unclamping, delayed drainage of contrast medium after cholangiography (> 15 min), delayed biliary emptying on scintigraphy, and elevated ductal pressures (biliary manometry) can confirm the diagnosis. This condition can often be treated successfully by endoscopic sphincterotomy and/or biliary stenting, but rarely, conversion to a hepaticojejunostomy may be required.[19]

SUMMARY

Biliary complications have decreased gradually due to improvements in surgical techniques. However, these are still significant causes of morbidity and mortality. It has been shown that early identification and aggressive treatment of these complications reduces morbidity and mortality and improves graft survival after liver transplant. Treatment strategies differ between different centers. No strong suggestion can be made for the initial treatment of biliary complications on the basis of the current literature. Many studies about ERCP-guided therapy and PTC-guided therapy have suggested excellent results with low complication rates. Today, surgical modalities are spared for patients

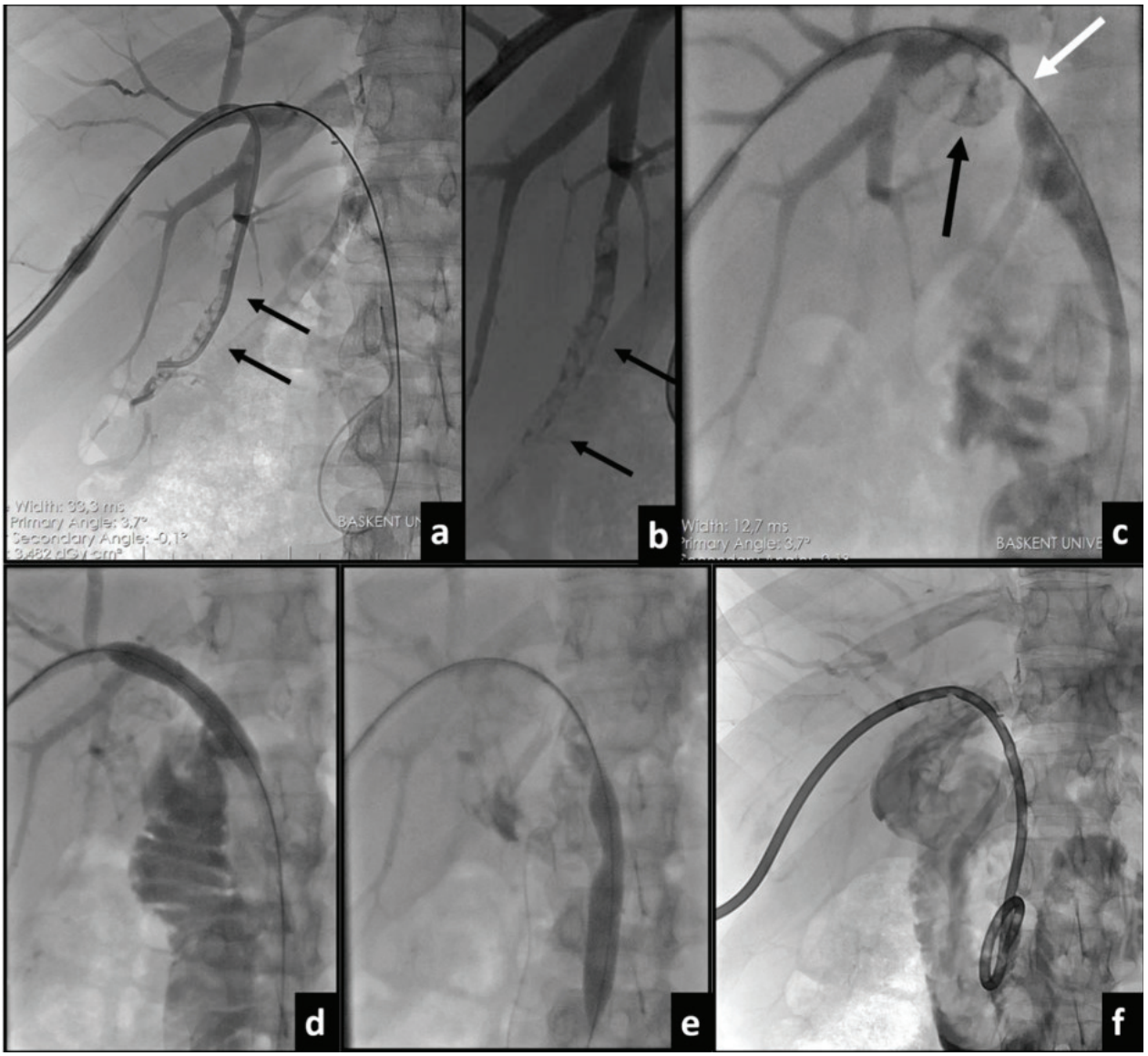

Figure 9. 30-Year-Old Orthotopic Liver Transplant Recipient

(a) and **(b)** Multiple stones and sludge in the segment VI bile duct (black arrows). **(c)** Anastomotic stricture (white arrow) and multiple stones in the proximal common bile duct (black arrows). **(d)** and **(e)** Balloon dilatation of stenotic segments in anastomosis and common bile duct. **(f)** Insertion of the external-internal drainage catheter after percutaneous removal of the stones and pushing the stones into the duodenum with a balloon catheter.

in whom percutaneous and endoscopic treatments fail. Treatment-related morbidity and mortality, recurrence rates, quality of life, and retransplant rates of the procedure should be considered while choosing the treatment modality. Management of biliary complications after liver transplant requires a multidisciplinary approach involving transplant surgeons, endoscopists, and interventional radiologists. The interventional radiologists are an important part of this multidisciplinary team and have an increasing role in the management of complications after liver transplant. Percutaneous interventional methods with low complication rates are effective therapeutic alternatives for the treatment of biliary complications after liver transplant.

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Other Complications After Liver Transplant

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Orthotopic liver transplant (LT) has become the treatment of choice for patients with end-stage acute or chronic hepatic disease. Over the past several decades, advances in surgical techniques, organ preservation, immunosuppressive therapy, and early detection of postoperative complications have increased rates of survival after LT. Early detection of postoperative complications is essential for graft and patient survival. The common complications after LT are vascular and biliary complications. Postoperative hemorrhage, gastrointestinal bleeding, gastrointestinal perforation, large-for-size syndrome (LFSS), and incisional hernia (IH) are also seen after LT.

POSTOPERATIVE HEMORRHAGE

Massive blood transfusion after LT negatively affects graft and patient survival. The underlying causes should be investigated. Despite advances in surgical technique, hemorrhage as an early complication can occur in approximately 20% of LT patients.[1] Delayed detection and treatment of postoperative intraabdominal hemorrhage can have fatal consequences. Liver transplant recipients already have 3 factors that affect coagulation function: **(1)** anomalies in thrombocyte function,[2] **(2)** thrombocytopenia that occurs because of increased thrombocyte sequestration in spleen or decreased thrombopoietin production,[3] and **(3)** decreased synthesis of plasmatic coagulation factors in the liver.[4]

The most important factor that can prevent hemorrhage after LT is the surgical technique. The most common cause of hemorrhage during the first week of surgery is surgical bleeding accompanied by coagulopathy. Postoperative hemorrhage can be life-threatening, and 10% to 15% of patients require reoperation to control hemorrhage and/or drain the hematoma. Reoperation due to hemorrhage contributes to overall mortality and to the financial burden of LT.[5] Therefore, determining the risk factors for hemorrhage and taking the preventive measures will increase posttransplant success. Moreover, hypotensive crises caused by uncontrolled active hemorrhage can have catastrophic clinical consequences. Causes of hemorrhage in the early postoperative period include preoperative status of the patient (such as severe coagulopathy and thrombocytopenia), early graft dysfunction or primary nonfunction, hemorrhage on the liver cut surface, vascular anastomotic hemorrhage, leaks due to surgical dissection, anticoagulation, hemobilia, hemorrhages in the gastrointestinal system, hemorrhages due to liver biopsy, and invasive interventions, including percutaneous biliary or endovascular procedures The most important risk factor for postoperative hemorrhage is the severe coagulopathy and/or thrombocytopenic preoperative status of the patient. In a study of 770 LT patients, Schrem and associates showed that postoperative hemorrhage was one of the most important risk factors for survival.[5] Patients with inadequate synthesis of coagulation factors and insufficient graft function have higher risk of postoperative hemorrhage. Ayva and associates retrospectively evaluated 408 LT patients and found that pretransplant thrombocyte

count of < 50 000/μL was directly associated with postoperative hemorrhage and survival. Although definitive incidence and mortality rates could not be determined in this study, postoperative abdominal hemorrhage was reported as the most important factor for patient survival.[6]

Early radiologic identification of potential sites of hemorrhage after LT determines the treatment method and increases the chance of success. Abdominal ultrasonography, computed tomography, and conventional angiography can be used as diagnostic methods (Figure 1). Although, most hemorrhages require surgery, during conventional angiography via transcatheter arterial embolization, hemorrhage can be treated without need for surgery.

GASTROINTESTINAL BLEEDING

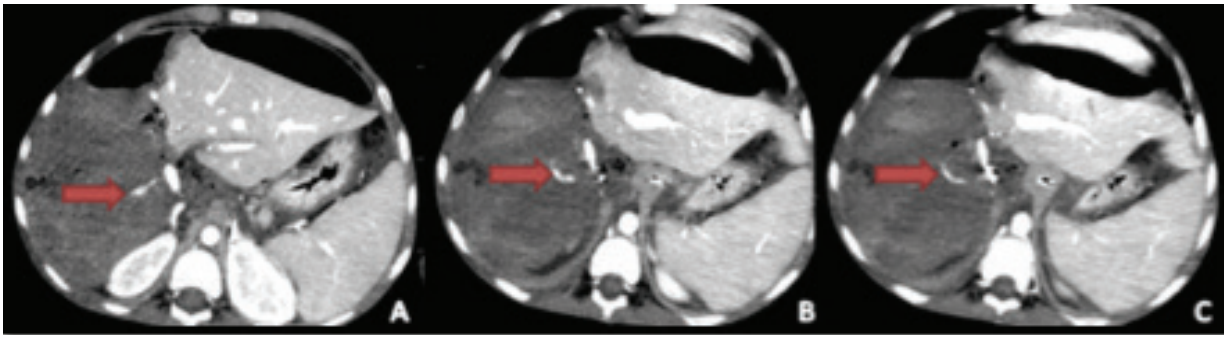
The reported incidence of gastrointestinal bleeding after LT is 13%; this complication can negatively affect patient and graft survival. It is more common in children than adults.[7] In the first 2 weeks after LT, gastrointestinal bleeding from a Roux-en-Y jejunojejunostomy anastomosis is due to a hemostasis defect in the mucosa and is associated with resorption of the sutures, weak blood supply, and presence of portal hypertension. In the late postoperative period, gastrointestinal bleeding can be due to cytomegalovirus gastroenteritis, liver dysfunction that causes bleeding diathesis, medication (eg, heparin, steroid), or stress-related ulcers in the upper gastrointestinal tract. Bleeding most frequently manifests with melena, hematochezia, and decreased hemoglobin levels. Diagnosis can be made with upper gastrointestinal endoscopy or angiography, allowing active bleeding (ie, varices, ulcers, mucosal lesions) or signs of bleeding (ie, attached clots) to be seen. Treatment involves medical support and, if possible, stopping the bleeding endoscopically. Surgical intervention is rarely required.[8]

LARGE-FOR-SIZE SYNDROME

The ratio between liver graft mass and recipient body mass (graft-to-body weight ratio) (GBWR) is important for LT. An ideal GBWR would be a graft of between 0.8% and 2.0% of the recipient's body weight. If this ratio is > 4%, the graft is large for size. The complication caused by large-for-size grafts is called LFSS. This condition is particularly observed in pediatric recipients who weigh < 10 kg. The incidence is 31% in children and 2.4% in adults.[9] A large-for-size graft disrupts the blood flow, leads to necrosis and graft dysfunction, perhaps even nonfunction, and results in a condition that threatens the patient's life. This syndrome is less common in adult LT recipients, and its effect on early and long-term consequences is controversial.[10]

Of importance is the identification of patients at risk of LFSS. Although there are various morphologic preoperative measurements that can be used, LFSS should be specifically evaluated for each patient during transplant. Allard and

Figure 1: Computed Tomography Angiography of Active Hemorrhage Taken in the Arterial Phase (red arrow)



associates reported that graft weight-to-right anteroposterior distance ratio is the best correlation to determine risk of LFSS. This is because this ratio takes the "depth" of the thorax into consideration, which can be the determinant of a large graft.[11] Not closing the fascia of these patients and only using temporary abdominal closure techniques can decrease mortality and morbidity. Moreover, monosegmental or hyperreduction of the graft can be a solution. However, due to increased surgery time and the increased risk of bleeding at the cut surface, this approach is not preferred by most centers.

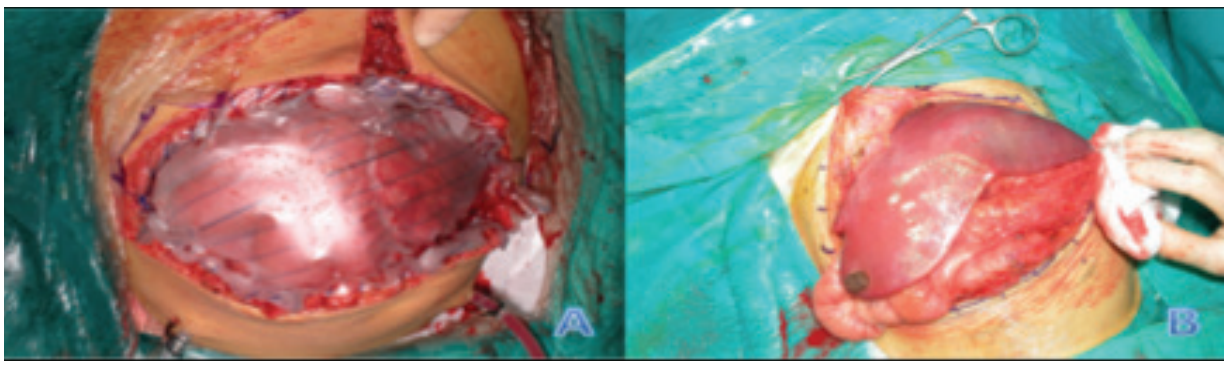
In children who receive a left lateral lobe graft, the main problem is the anteroposterior diameter of the graft. Graft liver volume estimation, which uses formulas based on morphologic parameters, can be useful, although significant discrepancies have been reported. These measurements should be considered, especially for organs from deceased donors. Akdur and associates retrospectively identified LFSS in 31% of 70 patients who were under 10 kg.[9] Although 50% of these patients were suspected to have LFSS during the operation and their abdomens were closed with temporary closure techniques, the remaining patients were suspected to have LFSS due to postoperative vascular problems, which required patients to be reoperated. To avoid the risk of LFSS, the Bogota bag technique or the skin closure technique as temporary abdominal closure techniques can be used to effectively treat LFSS (Figure 2). Complications of temporary abdominal closure techniques include development of hernia, which requires a secondary operation but does not affect graft survival.

The main problems in LFSS are the small abdominal cavity of the recipient, insufficient portal circulation, and development of abdominal compartment syndrome due to disrupted tissue oxygenation. In conclusion, in patients who are suspected to be at risk of LFSS, the use of the skin closure technique or the Bogota bag technique for abdominal closure can be safe and effective in avoiding vascular complications and abdominal compartment syndrome.

GASTROINTESTINAL PERFORATION

Gastrointestinal perforation is a rare but potentially destructive complication that occurs after LT. It can arise at any site in the gastrointestinal system, including stomach, duodenum, jejunum, ileum, and colon. The most important risk factor for gastrointestinal perforation after LT is previous gastrointestinal surgery. The incidence of gastrointestinal perforation has been reported to range from 10% to 15%.[12] Intraabdominal adhesions in patients with a previous history of surgery can make dissections during transplant more difficult. Isolating the stomach and colon from dense adhesions increases the risk of iatrogenic injury, which leads to gastrointestinal perforation. Other risk factors for gastrointestinal perforation are steroid treatment, prolonged anhepatic time, portal venous thromboembolism, and cytomegalovirus infection.[13]

Figure 2: Bogota Bag Technique for Abdominal Closure After Liver Transplant



The diagnosis of perforation depends on clinical symptoms, drainage characteristics, and radiologic examination. Most patients with perforations present with clinical symptoms such as fever, abdominal distention, and tenderness. Inflammatory markers such as white blood cell count, neutrophil concentration, and C-reactive protein level may be increased. However, some patients do not present with typical physical signs or high inflammation index. Administration of steroids and immunosuppressants can mask the characteristic symptoms and inhibit the inflammatory response. A cloudy stool drainage can indicate the presence of perforation. The use of ultrasonography or computed tomography is appropriate for evaluation of gastrointestinal perforation. Extravasation of oral contrast agent can help to correctly identify the site of perforation.[14,15]

After a perforation is identified, source control is the most important step. Patients with generalized peritonitis or an unstable condition usually require operation. If the lesion is benign and the surrounding tissue is healthy, well-perfused, and viable, small perforations can be mended with primary sutures. A large perforation usually requires partial resection and enterostomy in patients with severe abdominal infection. Because the risk of reperforation is high, regardless of whether the perforation is small or large, partial colectomy and colostomy are required in patients with colon perforation. On the other hand, these might not be required in relatively stable patients with microperforation but no significant disease or peritonitis symptoms.[13] Moreover, cessation of oral feeding and administration of fluid resuscitation and antibiotics are important in the treatment of gastrointestinal perforation.

Gastrointestinal perforation is a severe complication that leads to a significant increase in hospital stay duration and decreased survival rate and quality of life. Careful dissection and avoiding iatrogenic injury during surgical procedures are important to prevent gastrointestinal perforation. Perforation risk must be kept in mind when using high-dose corticosteroids. Early diagnosis, rational surgical intervention, and a combination of treatment may lead to better outcomes.

INCISIONAL HERNIA

Incisional hernia is reported to occur in 11% to 20% of patients with major abdominal surgery.[16] Median incisions have higher risk for IH than transversal or paramedian incisions. The development of an IH after LT comprises a potential complication that may seriously affect the postoperative course and quality of life. The rate of IH is reported to range from 1.7% to 43% in LT.[17-19] There are several predisposing factors for IH after major abdominal surgery that are similar to those shown with LT, including male sex, abdominal reinterventions, living-donor LT, postoperative respiratory complications, immunosuppressive agents (such as mammalian target of rapamycin [mTOR] inhibitors and mycophenolate mofetil), steroid usage, prolonged stays in the intensive care unit, acute rejection, severe ascites, viral hepatitis, obesity (body mass index > 25 kg/m^2), retransplant, and bilateral subcostal incision with midline extension (Mercedes incision). In addition to these, in infant LT recipients, discrepancies between the small abdominal cavity and a large graft can lead to insufficient blood supply to the liver graft, causing graft dysfunction. To decrease the tension of the graft, an IH is intentionally made in infant LT recipients who receive large-for-size liver grafts.

In a study of 290 LT recipients, the rate of IH was reported to be 17% over a 10-year follow-up. Advanced age of recipients (> 60 y), acute rejection, thrombocytopenia, and Mercedes incision were found to be risk factors. Obesity was also reported to be an independent risk factor for IH.[17,18] In another study, a Model for End-Stage Liver Disease score of > 22, use of an mTOR inhibitor, male sex, and high body mass index were identified as risk factors, with rate of IH reported to be 32.4%. A high IH rate (> 23%) was shown to be associated with use of an mTOR inhibitor and end-stage cirrhosis.[20,21] In another study of 1000 LT recipients that excluded the use of Mercedes incision, rate of IH was < 5%.[22] In a report of 600 LT recipients with bilateral subcostal incision, the rate of IH was 1.7%.[17]

Incisional hernias can be repaired primarily or with mesh (inlay/onlay) implementation. There are difficulties in hernia repair of LT incision, and the extent of incision to xyphoid process and costal margin, dense intraabdominal adhesions, multiple reoperations, impaired healing, and vulnerability of immunosuppressed patients to various infections can complicate the surgery. Mesh implementation in LT has been reported to diminish IH recurrence without increasing the risk of infection.[17,22] Polypropylene mesh may be the first choice.[23] However, biological prosthesis is also useful and safe. Recently, advanced use of laparoscopic techniques has changed the surgical repair options of IH, even for large ventral IHs. Despite the prolonged operative time, laparoscopic repair of IH has become more popular for post-LT IH repair due to shorter length of hospital stay (LOS), lower recurrence (3% to 10%), and lower complication and infection rates (1% to 3%).[24] In a study of 72 patients with large ventral IHs (an average hernia surface area of 125 cm^2), major complication and recurrence rates were significantly reduced in the laparoscopic group.[17] In another report of 27 LT patients with IH, laparoscopic repair (n = 13) had a lower risk of contamination and recurrence. However, postoperative LOS was longer.[25] A meta-analysis of 8 studies that compared open versus laparoscopic repair concluded that short-term complications were less likely to occur (14% vs 27%) after laparoscopy.[17] In a recent meta-analysis of randomized controlled trials regarding the management of IH, laparoscopic repair was found to have the same LOS and recurrence rate but lower postoperative infection rate than open hernia repair. The report concluded that laparoscopic IH repair was safe and reliable but required a longer intraoperative time.[26]

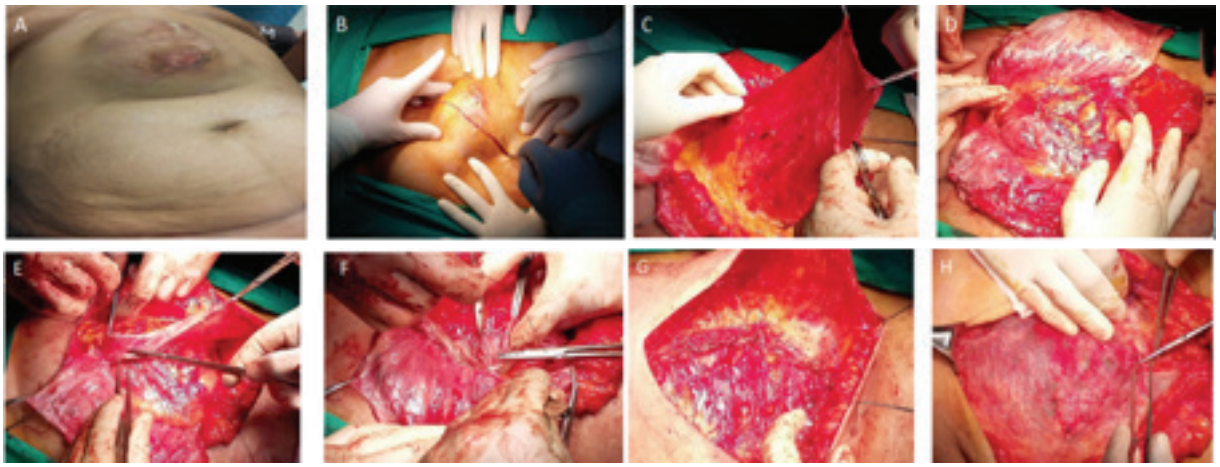
Intentionally made IH during infant LT procedures is a different entity. In pediatric LT, the use of large-for-size grafts (GBWR > 4%) may cause graft damage, including vascular complications and necrosis due to insufficient blood supply to the graft. Reduction of the graft has been used in several centers. However, it has some disadvantages for both the donor (in case of in situ reduction) and the recipient. For the recipient, there are increased risks of biliary leakage, impaired venous drainage, and longer cold ischemia time (in case of graft reduction at back table). The use of temporary abdominal closure using prosthetic materials in pediatric LT may be associated with increased risk of infection. Bioengineered skin equivalents have also been used for management of large abdominal skin defects. However, these are not available in many centers.[19]

At our center, in adults, we use a standard access for LT via the Mercedes incision. Exposure of the upper abdomen during transplant requires a retraction system, which causes compression of the incision margin. In infants, we use transverse bilateral subcostal incisions for laparotomy, and the retraction system is not required. Whenever possible, the incision in small infants is closed with interrupted sutures as a single layer. We base closure of the abdomen (both for fascia and skin closure, skin closure without fascial approximation, or closure with a Bogota bag) according to the intraoperative findings, perfusion of graft, and tension of the abdomen. Ultrasonographic examination of hepatic perfusion is done intraoperatively (twice daily during the first week after LT). All patients receive tacrolimus and mycophenolate mofetil-based immunosuppression. Methylprednisolone (10 mg/kg) is administered intraoperatively and tapered postoperatively from 10 to 0.1 mg/kg at the end of month 1, with stoppage at the end of month 3.

In our series of 452 LT patients (207 pediatric and 245 adult recipients),[19] IH was diagnosed in 29 patients (6.4%) (7 pediatric and 22 adult recipients). Most patients were males (77%) with Child-Pugh score of C (62%), moderate/severe ascites (81%), and serum albumin level of < 3.5 g/L (86%). Incisional hernia developed in 31% (16/51 LT recipients) of those with wound infection, 30% (12/40 recipients) of those with body mass index of ≥ 30 kg/m^2, and 18% (8/45 recipients) of those with repeated surgery. We repaired IH in 22 adult LT patients (age range, 31-62 y). Of 22 adult patients with IH, 5 (23%) had primary fascia repair and 17 (77%) had repair with Prolene mesh graft (3 sublay, 14 onlay).

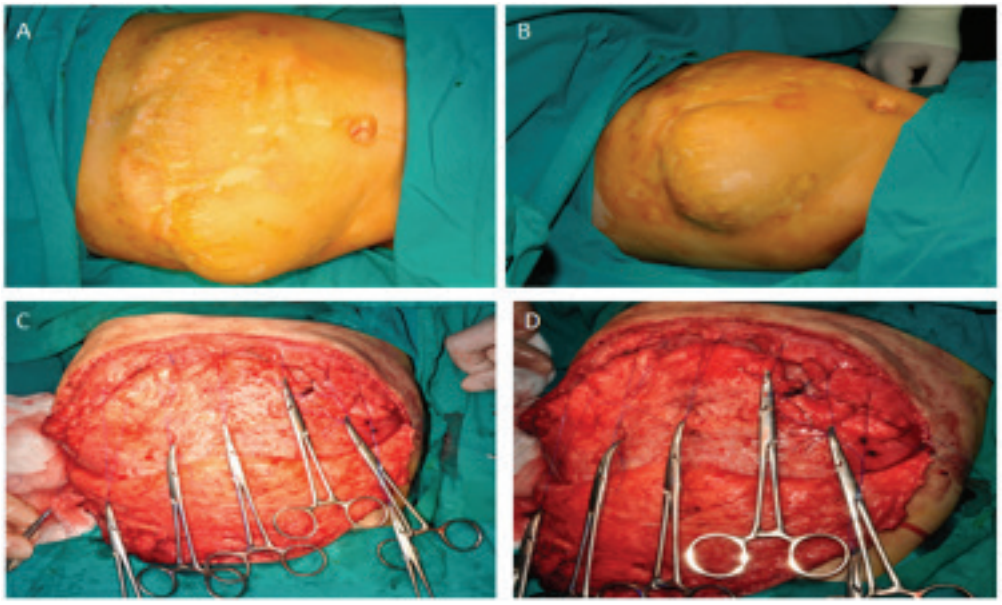
All 5 patients with primary fascia repair had midline and small IH (< 5 cm); therefore, these were repaired safely after fascia closure. However, in the 17 LT recipients with larger defects (12 IH between 5 and 10 cm, 5 IH > 10 cm), tension-free repair with Prolene mesh was preferred. We used Prolene mesh grafts in 83% of our patients (Figure 3). Three patients had seroma, and 1 patient had subcutane-

Figure 3: Incisional Hernia Repair in 53-Year-Old Female Liver Transplant Recipient



Patient developed hepatitis C virus cirrhosis at age 50 years, which resulted in transplant. **(A, B)** Incisional hernia was repaired 3 years after transplant. **(C, D)** Incisional hernia sac was dissected and excised. **(E, F)** Peritoneum was closed with absorbable suture. **(G)** Primary fascial repair was performed after edges of fascia approximated in the midline without tension. **(H)** Mesh was tailored according to defect so that at least 2 to 3 cm of mesh overlapped the edges of the fascia, with 15 × 15-cm Prolene mesh graft used for hernia repair.

Figure 4: Incisional Hernia in 3-Year-Old Male Liver Transplant Recipient Who Developed Biliary Atresia at 7 Months Old



(A) Intentional incisional hernia was made during liver transplant. **(B)** Incisional hernia was repaired 20 months after transplant. **(C, D)** Dissection of the skin layer, including subcutaneous tissue from the fascial layer, was extended sufficiently wide to the area peripheral to the hernia. After dissection, approximation of the fascia was primarily possible.

ous hemorrhage during the early postoperative period after IH repair (18%). We had no other complications and no hernia recurrence during patient follow-up (range, 51-181 mo).

Our data also showed 18 pediatric LT patients who received large-for-size grafts. After fascia was closed, all patients had graft perfusion complications; therefore, we intentionally implemented IH in all of these patients. We closed only skin in 11 patients, and we closed the abdomen with Bogota bag in 7 patients. All abdomens for Bogota bag patients were closed in 2 weeks. All patients received IH repair the first year after LT (range, 12-15 mo). Dissection of the skin layer, including subcutaneous tissue from the fascial layer, was extended sufficiently to the area peripheral to the hernia in all patients. After dissection, approximation of the fascia was primarily possible in all 7 patients. Of the 7 LT patients with intentional IH repair, 5 received primary fascia repair and 2 received onlay mesh repair. None of these patients had any complications or recurrence during follow-up (range, 55-103 mo) (Figure 4).

The incidence of IH after LT varies in the literature. There are several predisposing factors for IH after LT that are similar to those after major abdominal surgery. Primary repair of small and midline IHs can be done safely if fascia closure is possible; however, for larger defects and especially subcostal IH tension-free repair, use of Prolene mesh is preferred. Although the traditional approach consists of an open surgical repair with mesh implementation, recent reports also favor laparoscopic surgery. However, the pre- and postoperative management of LT cases should be handled studiously. Liver transplant recipients with IH require careful management by experienced transplant centers.

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Liver Biopsy in Liver Transplant Recipients

Behlül İgüs

A liver biopsy is a fundamental part of the management of liver transplant patients. A liver biopsy allows the histological evaluation of acute and chronic rejection and the degree of fibrosis/stage of liver disease, thereby facilitating the detection of the underlying cause of recurrent disease, as well as the monitoring of the response to treatment.[1,2] A liver biopsy can provide a diagnosis in 90% of patients with unexplained abnormal liver function tests.[3] Therefore, the timely diagnosis and management of the underlying cause of liver dysfunction are critical to preserve long-term graft function and to minimize adverse effects of the immunosuppressive medication in the worsening organ shortages.[4] Generally, in liver transplant patients, the main indication of liver biopsy is unexplained elevations of liver function tests. However, some transplant institutions advocate performing a liver biopsy on a protocol basis after liver transplant, even in patients with normal liver laboratory tests. In liver transplant recipients, liver function tests may be insufficient for assessment of the severity of rejection after the early period of transplant and diagnosis of important histological abnormalities, including chronic hepatitis after the later period of liver transplantation.[5,6] Therefore, protocol liver biopsies in transplant recipients with normal liver function tests provide important histological information about graft function and adjustment of immunosuppressive therapy.[4,7]

A liver biopsy allows the diagnosis of underlying liver histological disorders, even in healthy donors with normal laboratory tests and radiological findings, and it is the standard criterion for selecting optimal donors.[8,9] At our center, percutaneous liver biopsy (PCL) is a standard protocol during evaluations of living donors. As reported in a previous study, for diagnosis of liver disease, a specimen should have a minimum length of 15 mm and should include 4 to 6 portal areas.[10] Other studies have suggested that the ideal specimen should have a minimum length of 20 mm and include a minimum of 11 portal tracts.[11-14]

Liver biopsies can be performed with various techniques, including a percutaneous approach with ultrasonography (US) or computed tomography (CT) guidance, a transjugular approach, or surgical/laparoscopic approach. The surgical biopsy is usually performed when patients require a surgical procedure rather than as the primary procedure. Laparoscopic liver biopsy is no longer performed because there are less invasive procedures such as PCL and transjugular liver biopsy (TJLB).

PERCUTANEOUS LIVER BIOPSY

Patient preparation and technique

Percutaneous liver biopsy can be performed rapidly and safely in hospitalized patients and on an outpatient basis. Before the procedure, coagulation parameter testing (prothrombin time and international normalized ratio) and a baseline complete blood count should be performed. If coagulation defects are present (platelets < 50 000/μL and/or international normalized ratio > 1.5), then patients should be given appropriate transfusions of platelets and fresh-frozen plasma to correct the coagulopathy before the procedure. If the patient is receiving anticoagulant therapy, then the therapy should be discontinued 3 days before the biopsy.

The selection of the imaging modality depends on the best visualization of the lesion, as well as the operator's skill and experience. Ultrasonography and CT are the most commonly used imaging methods in PCL. Ultrasonography demonstrates the anatomy, identifies the abnormalities (such as dilated biller ducts and/or ascites), and allows real-time visualization of the biopsy needle to achieve safe access into the transplanted liver. Computed tomography-guided liver biopsy is preferred where the lesion is not well seen on US and helps to avoid transgression of the needle through other organs, such as interposed bowel and pleural, especially in split-liver and left-lobe liver transplant recipients.

The types of needles used in PCL are the fine aspiration needle, the core biopsy needle, and the coaxial needle. Aspiration needles typically are hollow needles of 20 to 22 gauge and used to obtain sufficient cells for cytological analysis. A core biopsy needle is used to obtain sufficient tissue for histological analysis; the core biopsy needle type is most often an automatic, spring-loaded, side-cutting needle. Usually, a needle of 18 to 20 gauge is of adequate size to obtain sufficient biopsy specimens; also, needles as large as 14 gauge may be used for large hepatic masses (Figure 1). The coaxial needle is usually used to guide the core biopsy needles in CT-guided biopsies. Typically, the coaxial needle is 11 to 19 gauge in size, depending on the size of the inner biopsy needle. Also, coaxial needles are used to minimize the number of passes through the liver, and these are used when the track embolization is planned after the biopsy procedure.

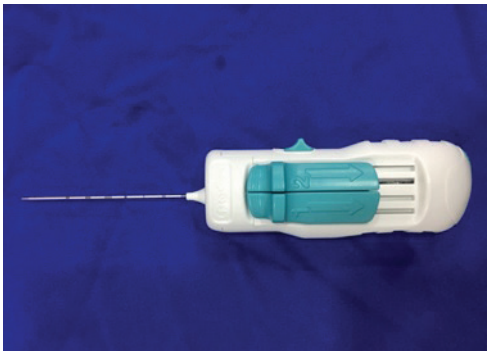

Figure 1. Fully Automatic 18-gauge, 15-cm-long Biopsy Needle

Ultrasonography-guided biopsy

Preprocedural full sonographic examination of the liver should be performed to plan a safe access route. Paracentesis should be performed before the biopsy if perihepatic ascites is present. The US-guided biopsy can be performed by using a freehand technique, with one hand controlling the transducer and the other hand manipulating the biopsy needle. Also, inexperienced operators can use a needle guidance system that attaches to the transducer to aid in the procedure. When planning the pathway, the shortest distance and the safest path between the skin surface and the target area should be selected. Generally, 3- to 5-MHz frequency transducers are used in the biopsy procedure. A higher frequency linear probe may be appropriate for subcapsular lesions or in pediatric patients. The US probe should be prepared sterile by placing it in the US cover. Biopsy is performed with a local anesthetic of 2% lidocaine. Sedation may be required for uncooperative and/or pediatric patients. The skin over the biopsy site should be prepared aseptically and covered with a surgical drape. Local anesthesia should be administered to the subcutaneous tissue and along the needle path to the liver capsule, aided by the real-time guidance. After adequate anesthesia, a 5-mm skin incision should be made for the biopsy needle entrance. The biopsy needle should be advanced within the sonographic field of view with transducer manipulations. Afterward, the needle should reach the target area, at which time the biopsy needle should be actuated, according to its design, to obtain sufficient tissue (Figure 2). The number of required needle passes is determined according to the quality of the specimen obtained. The subcostal or subxiphoid approach is preferred to reduce the risk of intercostal artery injury, pneumothorax, and hemothorax. However, in liver transplant patients, especially in living-donor transplant patients and sedated patients (involuntary breathing may cause to rise liver cranially), the only suitable approach may be an intercostal approach along the midaxillary line. After the biopsy, manual compression should be performed for approximately 15 to 20 minutes, and then the patient should be observed for 3 to 4 hours for vital signs.

Computed tomography-guided biopsy

Computed tomography-guided biopsy is preferred in cases where the lesion is not well seen on US, and generally, CT-guided biopsy is not used for parenchymal liver biopsy. Intravenous contrast may be used when lesions are not well seen on unenhanced images. Prior to the biopsy, CT scans of the upper abdomen should be performed to plan the safe pathway. After the skin access site is determined and sterile conditions are complete, the local anesthetic should be administered to the subcutaneous tissue and adjacent to the liver capsule. Then, a coaxial needle should be advanced in a stepwise manner while obtaining short-interval CT images as the needle is advanced toward the target area. When the target area is reached, the inner stylet of the coaxial needle is removed, and a smaller size cutting biopsy needle is placed into the lesion through the coaxial needle and actuated to obtain samples. The number of required needle passes is determined by the quality of the specimen obtained. After the biopsy, manual compression should be performed for approximately 15 to 20 minutes, and the patient should be observed for 3 to 4 hours for vital signs.

Complications

Complication rates for PCL have been reported to be between 1.4% and 9% in liver transplant patients.[15,16] Major complications after liver biopsy are possible, including bleeding, pneumothorax, abscess, bile peritonitis, and bowel injury. Bleeding after the liver biopsy is less frequent, but it is the most important complication in recipients. Bleeding can be localized as subcapsular, intraparenchymal, or intraperitoneal.[17,18] For hemodynamically stable patients, a small subcapsular or intraparenchymal hemorrhage can be managed with conservative and careful follow-up. A blood transfusion may be required in hemodynamically unstable patients; also, angiography and embolization should be considered in further management strategies. Hemobilia is a rare complication after the liver biopsy, which presents as a classic triad of right upper quadrant pain, jaundice, and upper gastrointestinal bleeding. Embolization is an effective treatment for hemobilia.

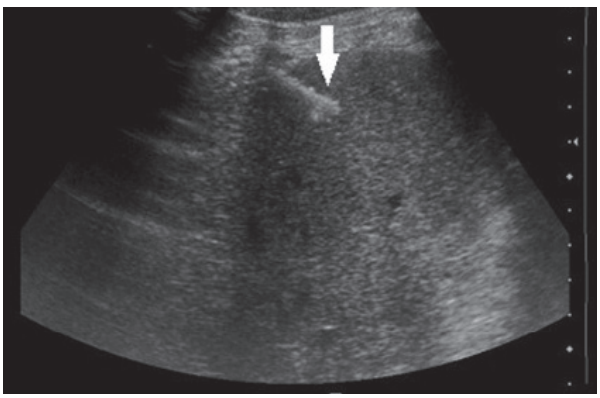

Figure 2. Ultrasonography-Guided Percutaneous Liver Biopsy
An automatic biopsy needle with 18-gauge needle (arrow) was applied under real-time ultrasonography guidance.

Infection is a rare complication after the liver biopsy, but it is a serious condition that may jeopardize the success of graft and/or the life of the patient. Infection-related complications such as bacteremia, cholangitis, and abscess have been reported after biopsy in patients with extrahepatic biliary obstruction.[11-21] Previous studies have reported risk factors for biopsy-related infections; for example, patients who had biliary tract abnormalities and choledochojejunostomy had a higher incidence of biopsy-related infections compared with patients who had choledochocholedochostomy.[22,23]

The most frequent complaint is reported to be pain at the biopsy site and/or at the right shoulder due to irritation of the right hemidiaphragm after the biopsy procedure.[18] Hypotension occurs frequently, as a vasovagal reaction, and usually resolves spontaneously.[24] Pneumothorax and hemothorax are rare complications that can occur in transthoracic approaches; chest tubes placement may be necessary for these patients. Despite the possibility of these complications, imaging-guided PCL is a safe and effective procedure when performed by an experienced operator. There are 4 key points to consider before proceeding with PCL (Table 1).

TRANSJUGULAR LIVER BIOPSY

Transjugular liver biopsy is used in liver transplant recipients to obtain hepatic tissue for histological

Table 1. Points to Consider Before Proceeding With Percutaneous Liver Biopsy

(1) If the patient has uncorrectable coagulopathy, then consider the use of track embolization after PCL or consider TJLB as the preferred option
(2) If the patient has ascites, then perform paracentesis prior to PCL
(3) To avoid intercostal artery injury, a subcostal or subxiphoid approach is preferred
(4) A specimen of at least 20 mm in length, containing at least 11 complete portal tracts, is required for sufficient diagnosis

Abbreviations: PCL, percutaneous liver biopsy; TJLB, transjugular liver biopsy

evaluation. Transjugular liver biopsy has been reported as a safe and efficacious procedure in liver transplant recipients.[25] Usually, it is a preferred method when there is a contraindication to PCL such as uncorrectable coagulopathy, lack of safe access, or ascites.[26,27] Also, TJLB provides concomitant pressure measurements to evaluate the hepatic venous pressure gradient and output. Although TJLB requires a longer procedure time, the participation of an experienced interventional radiologist, and a higher financial cost than PCL, in some transplant centers, TJLB is still a primary preferred method for liver biopsy because of the reduced risk of bleeding and the possibility of evaluating hepatic venous pressure gradient.[13,28] In patients with focal hepatic lesions, TJLB is not indicated. However, if there is a strong indication for biopsy and PCL is contraindicated, TJLB could be performed under external US guidance. There is no specific contraindication for TJLB; however, TJLB should be avoided when central venous access is absent or in cases with suspicion of cholangitis and uncontrolled sepsis. In liver transplant recipients, the hepatic vein angle is usually altered to some degree due to the extent or the type of transplant and vein anastomosis, and this is also the main cause of difficulty for TJLB procedures compared with nonliver transplant patients.[29-31] Nevertheless, in unsuccessful cannulation of the hepatic vein due to anatomic alterations of the hepatic vein, the transfemoral approach should be considered. In a literature review of TJLB, success rates of catheterization of the hepatic veins ranged between 87% and 99.5%, with a success rate for obtaining adequate specimens of between 86% and 94%. Most of the failed cases had occurred as a result of acute angulation of the hepatic vein, especially in recipients whose operation included the piggyback anastomosis technique.[32-36]

Patient preparation and technique

Before the procedure, CT scan is useful to evaluate the anatomic relationship between the inferior vena cava and hepatic vein and for planning the appropriate approach. The procedure should be carried out in the fully equipped angiography unit. Transjugular liver biopsy can be performed under local anesthesia and sedation. Patients should be in a supine position, and continuous hemodynamic and cardiac monitorization should be checked during the procedure. Right internal jugular vein (RIJV) is the most preferred access site, but the left internal jugular vein (LIJV), external jugular, subclavian, or even femoral veins can be used.[37] During the LIJV approach, great care is required to successfully advance the metal cannula and biopsy needle when crossing through the mediastinum and heart. All maneuvers should be carefully monitored by fluoroscopy, even though these are performed over a guidewire.

The vein puncture site should be prepared sterile, and adjacent skin should be covered with a sterile drape. A superficial high-frequency linear probe is prepared with a sterile cover. A local anesthetic agent (2% lidocaine) is used to numb the skin and subcutaneous tissue. A small skin incision is made with a disposable scalpel blade, and RIJV is penetrated with an 18-gauge vein needle under US guidance. When venous access is obtained, a 0.035-in (0.89-mm) J-shaped, angled guidewire is inserted into the vein. Afterward, the guidewire is advanced to the inferior vena cava under the fluoroscopic control; then the needle is withdrawn, and a 9F or 10F (11-cm long) introducer is inserted over the guidewire. The 9F TJLB sheath catheter with a curved tip is delivered with the TJLB kit over the guidewire and advanced through the introducer along the superior vena cava, right atrium, and

inferior vena cava into the hepatic vein or most adequate hepatic vein branch. In cases where it is difficult to catheterize the hepatic veins due to the acute angle between hepatic vein and inferior vena cava, a 5F multipurpose catheter with a J-shaped tip and guidewire should be used for catheterization of the hepatic vein. Also, the inferior vena cava can be traversed by asking the patient to perform a deep inspiration. This step may help to open the angle between the inferior vena cava and the right hepatic vein, making the procedure easier. A biopsy can be performed by Menghini (aspiration) technique or Tru-Cut technique.

For the Menghini technique, the position of the 9F sheath catheter into the hepatic vein should be confirmed by injecting contrast agent. The Colapinto needle (aspiration system needle) is advanced into the sheath through the hepatic vein; then the needle is moved forward 1 to 2 cm through the wall of the hepatic vein to puncture the liver parenchyma, and aspiration is applied with the syringe. The use of an aspiration system has been replaced by automatic needle systems. Aspiration technique is associated with inadequate tissue sampling in 12.5% to 29% of the cases, and multiple samples must be taken to obtain sufficient tissue.[38] The automatic biopsy devices typically obtain significantly longer, less fragmented, and more adequate specimens for histological diagnosis, compared with the less successful aspiration system.[13,39]

For the Tru-Cut technique, the following steps are required. After catheterization of the hepatic vein, the transjugular introducer sheath is advanced with the stiffening cannula over the 0.035-inch stiff guidewire into the hepatic vein. Hepatic venography is repeated throughout a side port of the stiffening cannula to confirm the exact position, and then a biopsy needle (18 or 19 gauge) is advanced through the stiffening cannula. Thereafter, the biopsy needle is actuated to capture tissue within the specimen notch. The number of needle passes is determined by the quality of the specimen obtained. During the biopsy, the direction of the needle should be oriented anteriorly if the right hepatic vein is catheterized or posteriorly if the median vein is catheterized. The starting point of the biopsy should not be far from the hepatic vein ostium. Generally, 3 to 4 cm from the ostium of the hepatic vein is appropriate because this provides a central position and decreases the risk of extracapsular puncture. At the end of the procedure, hepatic venogram is performed to rule out bleeding, fistulae, or capsule perforation. After the procedure, the puncture vein should be manually compressed for approximately 5 to 10 minutes, and patients should be hemodynamically monitored for at least 4 hours.

The key points to consider for TJLB are presented in Table 2.

Complications

Complication rates after TJLB have been reported to range from 0.8% to 7.1%.[13,33,37,40-44] The

Table 2. Points to Consider Before Proceeding with Transjugular Liver Biopsy

(1) Transjugular liver biopsy is a safe procedure by which to obtain tissue for histological evaluation when there is a contraindication for PCL, such as uncorrectable coagulopathy, lack of safe access, or ascites
(2) Although RIJV is the preferred access site, the LIJV, or even femoral veins, may be used
(3) The main limitation of TJLB is the possibility of unsuccessful cannulation of hepatic veins due to acute angulation; the hepatic vein may be catheterized by asking the patient to perform a deep inspiration
(4) Automatic Tru-Cut biopsy needles are preferred (instead of aspiration biopsy needles) to obtain sufficiently adequate samples

Abbreviations: LIJV, left internal jugular vein; PCL, percutaneous liver biopsy; RIJV, right internal jugular vein; TJLB, transjugular liver biopsy

bleeding complication depends on the number of passages performed during the procedures, and this usually occurs when the biopsy needle inadvertently passes through the cut surface of the graft or the liver capsule. Bleeding may present as intraparenchymal, subcapsular, and intraperitoneal hematoma. Exceptional complications, such as a biliary fistula or hepatic artery aneurysm, have also been reported.[13,37,45] Minor complications such as neck pain, hematoma in the neck, and inadvertent puncture of the carotid artery and pneumothorax are seen much less often when the internal jugular vein puncture is performed with US guidance.[13,46]

SUMMARY

Liver biopsy in transplant recipients remains the gold standard for the diagnosis and management of rejection therapy. Image-guided PCL in the liver transplant recipient population is a safe, efficacious, and relatively simple technique that can be performed on an outpatient basis. Compared with image-guided PCL, TJLB is a challenging procedure that requires a longer procedure time, an experienced interventional radiologist, and a costlier preparation. Therefore, TJLB should be considered if there is a contraindication for PCL.

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Fluid Collections, Hematoma, and Abscess Interventions After Liver Transplant

Behlül İgüs

Besides vascular complications in liver transplant (LT), a number of nonvascular complications can be seen with posttransplant fluid collections, which include hematoma, seromas, ascites, abscesses, and biloma, all of which may affect the survival of the graft and the patient. A timely diagnosis of these complications allows the patient to benefit from potential treatment options. These collections are common after LT, and small, noninfected collections usually resolve without complication; however, sometimes these are sufficiently large to compress vascular structures, which may affect the graft function.[1] Ascites after LT surgery is quite common and usually resolves within a few weeks. Hematomas are usually seen near areas of vascular anastomosis or the perihepatic/subhepatic space within a few days after the transplant. Liver abscess in the LT population is a life-threatening complication and is associated with various causes. Furthermore, bilomas may occur as a result of biliary or vascular anomalies.[2,3] Infected fluid collections and collections that compress vascular structures require percutaneous drainage treatment (PD) to ensure graft function and patient survival. Percutaneous drainage provides treatment for the most sterile and infected collections after LT, and it is a safe and efficient procedure that can be performed with local anesthesia and conscious sedation.

In LT recipients, lymphatic channels may get damaged during organ retrieval and surgery, which may cause lymphatic leaks, resulting in formation of chylous ascites. Management of chylous ascites has been shown to respond to *somatostatin* analogues, total nutrition, and PD.[4,5] Lymphoceles typically appear as an anechoic collection on ultrasonography (US) examination. Computed tomography (CT) usually reveals a sharply circumscribed collection with attenuation values similar to those of simple fluid, and magnetic resonance imaging (MRI) typically demonstrates a T1 hypointense and T2 hyperintense signal intensity.

Pleural effusions and minor amounts of ascites are common after LT and usually resolve with the recovery of the patient's hemodynamic status. On the other hand, massive pleural and peritoneal fluid collections occur occasionally but require prompt management to avoid any devastating consequences. In these patients, image-guided PD can stimulate the postoperative recovery. Formation of persistent ascites in LT recipients may depend on the following: use of reduced size graft, mismatch of donor and graft vascular size, and microvascular changes during acute rejection. Ascites formation may also depend on postoperative complications such as stenosis or kinking of the inferior caval vein anastomosis; in addition, ascites can occur without a definite cause.[6,7] The first aim of the treatment is to eliminate the underlying cause, if possible. Vascular outflow obstructions can be treated successfully with endovascular procedures such as balloons and/or expandable stents. The development of significant posttransplant ascites is associated with increased morbidity and mortality. Therefore, conservative treatment and drainage should be performed in massive fluid collections to preserve graft function (Figure 1).

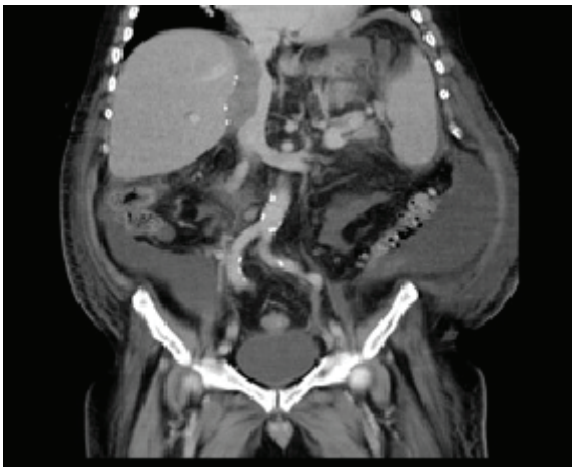

Figure 1. Collections at Liver Hilum and Right-Left Inferior Abdomen, Showing Collection in the Liver Hilum Compressing the Inferior Vena Cava

HEMATOMA AFTER LIVER TRANSPLANT

Hematoma is a predominant type of fluid collection after the first days of LT.[8] Hematomas may occur during the intraoperative, early postoperative, and later periods. Hematomas usually tend to be located in the vascular and biliary anastomosis, including the hepatic hilus and adjacent to the inferior vena cava, as well in areas such as the lesser sac, surrounding the ligamentum teres, perihepatic, and subhepatic spaces.[9] Hematomas that develop immediately are usually related to the handling of the graft during organ retrieval, preservation, transportation, and implantation.[10] Of particular concern, during living-donor liver transplant (LDLT), the graft volume is small and has a wide cut surface; therefore, a massive hematoma may develop from the expanding raw surface under the liver capsule, which may cause fatal consequences. Also, postoperative invasive procedures such as liver biopsy, percutaneous transhepatic biliary drainage, or even secondary to endoscopic retrograde cholangiogram may cause subcapsular and/or intraparenchymal hematoma. In addition, patients with LT may develop hematomas without risk factors, simply as a result of poor coagulation profiles. Regardless of the underlying causes, an immediate diagnosis and appropriate treatment strategy will determine the outcome of the graft and the recipient.

Surgical and nonsurgical approaches have been used to treat these hematomas; the optimal management strategy depends on the timing of diagnosis and hemodynamic state of the patient. Surgical exploration, PD of the hematoma, and transarterial embolization or a combination of these strategies are the available treatment options.[11,12]

Ultrasonography, CT, and MRI are helpful in detecting the underlying hematoma. Ultrasonography features of hematomas can be variable and may appear as completely anechoic, lobulated, or show fine internal echoes due to fibrin septa or blood components. Computed tomography appearance varies depending on the age of the hematoma and usually has higher attenuation than that of simple fluid. The appearance in an MRI changes depending on the time of hematoma, usually demonstrating areas of intrinsic hyperintensity in T1-weighted MRI. Also, CT imaging aids in demonstrating the source of hemorrhage if there is concurrent, active bleeding, by using arterial and delayed phase scans. If active bleeding is detected, then embolization should be performed with the super-selection of the bleeding branch of the hepatic artery.

Postoperative small hematomas can be managed conservatively and usually resolve without drainage. However, a massive hematoma may cause compression of the liver parenchyma, resulting in obstruction of the hepatic veins. Furthermore, outflow obstruction may occur, causing graft failure.[13] Percutaneous drainage should be performed in the case of massive hematomas, to reduce the pressure effect of the hematoma. Also, when significant stenosis is detected on venography due to external compression, stent insertion should be considered to maintain the graft patency. Percutaneous drainage can be performed under the selection of US or CT guidance, depending on which modality is better to demonstrate the hematoma and to provide a safe pathway to the hematoma. The "pigtail" catheters are used, with size range of 10F to 16F, depending on the internal structure of the hematoma. Selecting large-diameter catheters will provide effective drainage for dense hematomas. Percutaneous catheter

placement technique, catheter care, and removal criteria are explained later in this chapter.

LIVER ABSCESS AFTER LIVER TRANSPLANT

Despite advances in surgical technique, intensive care, immunosuppressive therapy, and effective prophylactic measures, infection is a still frequent cause of death and morbidity in LT.[14,15] Liver abscess is a rare complication with a reported incidence of between 1.4% and 8.9%, and the median interval of diagnosis after LT is between 2 and 39.7 months.[16-19] The most common predisposing risk factors for liver abscesses include hepatic artery thrombosis/stenosis, biliary strictures, choledochojejunostomy, cholangitis, LDLT, split liver, donation after cardiac death, endoscopic interventions, liver biopsy, and diabetes.[18,20-23]

Hepatic artery thrombosis is the most significant condition associated with hepatic abscess (HA) after LT, and it is reported in 13.3% to 66% of patients who developed liver abscess after LT.[16,18,19] Moreover, hepatic artery stenosis has been reported in 20% of LT patients with HA.[18]

Another important factor in HA formation is the underlying biliary anomalies. Biliary strictures that originate from a combination of scarring and ischemia or ascending bacterial infection from the upper limb of the small bowel may lead to abscess formation.[24,25] In previous studies, biliary reconstruction performed with choledochojejunostomy in LT recipients had a higher rate of infection than reconstruction performed with choledochocholedochostomy.[16,25,26]

Moreover, in cases of donation after cardiac death of the donor, the warm ischemia phase between cardiac arrest and cooling of the graft may cause ischemic cholangiopathy, which may result in biliary stricture in 40% of cases, and this can cause liver abscess formation.[27] In addition, during LT, nonreconstruction of a small accessory hepatic artery (usually right or left hepatic artery) or inadvertent occlusion of bile ducts during liver retrieval procedures increases the risk of HA development.[28]

The diagnosis of the HA is based on clinical findings (fever, chills, abdominal pain), abnormal laboratory tests (white cell count, prothrombin activity, and liver function), and confirmation with imaging modalities (US, CT, MRI). Ultrasonography is the primary imaging modality for the evaluation of liver abscess because it is safe, accurate, and a noninvasive method of demonstrating and evaluating the nonvascular complications concerning the hepatic parenchyma and extrahepatic tissues. The imaging appearance of HA changes over time and depends on 2 phases: presuppurative and suppurative. In the presuppurative phase, a liver abscess may appear heterogeneous, hypodense, with irregular contours, and poorly demarginated and may simulate a tumor-like appearance, especially when it is multiple and small in size. In the suppurative phase, the appearance can be hypo- or anechoic, sometimes multiloculated, with rounded contours, and can consist of a thin or thick capsule. At this phase, a typical "target" view can be visualized on sonographic images. In arterial phase CT images, peripheral enhancement forms a hyperdense border, which is called the "ring sign" without central enhancement. Sometimes this border is outlined by another hypodense ring, which is called the "target" image. The pathognomonic sign of liver abscess is the presence of internal gas. In addition, MRI can be useful to demonstrate the biliary anomalies as the underlying cause of HA.

Management of HA is complex and challenging and is usually managed with antibiotic therapy and PD, with retransplant being the final option in severe cases. Antibiotic therapy should be started initially after the diagnosis of the liver abscess to limit the systemic effects of septicemia.[29,30] A wide spectrum of pathogens may be related to the liver abscess, including Gram-negative bacilli (*Escherichia coli*, *Enterobacter*) or Gram-positive cocci (*Staphylococcus aureus*, *Streptococcus*).[16-18] Also, in LT recipients during antirejection immunosuppression therapy, various bacteria can be found, such as *Lactobacillus acidophilus* (Gram-positive), as well as fungi (resulting in candidiasis or aspergillosis) or viruses (cytomegalovirus), any of which may cause multiple HA formations.[31,32]

In LT patients with HA, blood and aspirate cultures usually consist of different pathogens; therefore, adjusting the treatment regimen according to blood culture may not be sufficient to control the abscess regression. For this reason, initial antibiotic therapy should be selected with a wide spectrum before a final culture result is obtained. Ultrasonography- or CT-guided needle aspiration is an effective tool for the identification of the causative germ in the abscess cavity to administer target medication. The duration of antibiotic treatment is dependent on the patient's condition and the resolution of the abscess cavity in imaging modalities. However, if there are improvements in the clinical condition and resolution of the abscess cavity, then oral antibiotic therapy should be continued for a few weeks after discharge because of the possibility of recurrence.

Despite advances in diagnostic and therapeutic radiology, there are arguments regarding the most appropriate time to add PD to antibiotic therapy. Studies indicate that antibiotic therapy alone is usually not sufficient to resolve a liver abscess entirely, unless it is small (< 3 cm). Therefore, it is recommended that a liver abscess greater than 3 cm should be routinely drained.[33-36] The other important point in liver abscess management is the selection method of percutaneous needle aspiration (PA) or percutaneous catheter drainage (PD). Both techniques are effective in the management of liver abscess, but with PA, patients are required to repeat the procedure more than once.[37]

In most cases, the common cause of unsuccessful treatment of a liver abscess is hepatic artery thrombosis.[20] If there is a persistent abscess or recurrent abscess, then hepatic artery thrombosis should be excluded and the treatment strategy should be rearranged. For liver transplant patients with small (< 3 cm) or multiple abscesses, antibiotic therapy should be selected as the primary treatment; however, PA or PD should be added for effective therapy. The mortality rate in liver abscess has been reported in different studies to range from 21% to 42%, and it is associated with sepsis, liver failure, respiratory insufficiency, and multiple organ failure.[16-18,20]

BILOMA AFTER LIVER TRANSPLANT

Bilomas occur in about 11% of adult patients and in about 8% to 16% of pediatric patients after LT; bilomas are associated with greatly increased hospitalization time, a high rate of graft loss, and high mortality.[16,38-41] Bile leaks may cause the formation of bilomas with the extravasation of the liver and the abdominal cavity. Bile leaks are usually seen in the anastomotic site or the T-tube entry point but may also be seen at the cut surface of the liver in LDLT.[42,43] Nonanastomotic leaks are usually related to hepatic arterial insufficiency (thrombosis/stenosis) in most cases. Signs and symptoms of bilomas are usually nonspecific in LT patients. Fever and abdominal pain are the most common clinical symptoms of biloma, as well as elevated laboratory liver enzyme levels. Ultrasonography is the primary modality to evaluate biliary anomalies, collections, and also liver arteries with the Doppler feature. Sonographic features of bilomas are round shape and hypo- to anechoic appearance, often with posterior acoustic enhancement. Computed tomography appearance is a round hypoattenuating lesion, and CT angiography should be performed to exclude underlying arterial disorders that may cause the formation of the biloma. In MRI scans, the appearance is usually hypointense on T1-weighted images and hyperintense on T2-weighted images. Magnetic resonance cholangiopancreatography (MRCP) T1-weighted imaging with hepatic specific contrast agents may help to demonstrate the relationship of bile leaks with the bilomas or perihepatic free fluid collections.[41-46] When the biloma is superinfected with various pathogens such as *Enterococcus*, Gram-negative bacilli, *Candida*, and anaerobic bacteria, its imaging features transform to an appearance characteristic of abscess.[47]

In the past, the traditional approach in the management of hepatic biloma was early retransplant.[48,49] Considering the recent advances in endoscopic imaging techniques and interventional procedures, there is now the opportunity to treat bilomas with nonsurgical methods.[50] Nonsurgical

management generally includes prolonged antimicrobial therapy and PD, and some cases may require insertion of a biliary stent, sphincterotomy, or a combination of these techniques; this sort of management has been shown to have high rates of success.[51,52] Ultrasonography-guided diagnostic PA for Gram stain and culture of the fluid sample are essential as anti-infective therapy in LT recipients. Percutaneous drainage should be performed under US and fluoroscopy guidance. If the cavity is linked with the biliary tree, biliary PD should be performed by advancing the drainage catheter through the abscess cavity into the bile ducts and duodenum. Drainage should be continued until the abscess cavity resolves. In exceptional cases, especially in those with underlying arterial stenosis and thrombosis, the successful resolution of a biloma with nonsurgical management is usually insufficient, and the last option for the survival of the recipient will be retransplant. The PD catheter placement technique, catheter care, and removal criteria are explained later in this chapter.

Table 1. Key points with regard to liver abscess are as follows.

(1) When a persistent or recurrent abscess is present, consider the underlying ischemic arterial complications.
(2) Percutaneous needle aspiration and PD catheter insertion are effective for liver abscess drainage, but repeated aspirations may be needed after percutaneous needle aspiration.
(3) This complication can be treated with antibiotherapy, with both blood and aspirate cultures (not only blood or aspirate culture).
(4) In the case of an abscess with a biliary connection, percutaneous biliary drainage should be added to percutaneous drainage.

Abbreviations: PD, percutaneous drainage

PATIENT PREPARATION FOR PERCUTANEOUS FLUID DRAINAGE

Before the procedure, coagulation parameter tests (prothrombin time [PT], international normalized ratio [INR]) and complete blood count should be evaluated. Liver transplant patients usually have poor coagulation profiles; therefore, coagulopathies should be corrected before drainage with fresh-frozen plasma or platelet transfusion. Patients with suspected infected fluid collections should receive broad-spectrum antibiotics at the time of PD requirement. Percutaneous drainage can be performed with local anesthesia and conscious sedation. General anesthesia is indicated for children and uncooperative patients.

Imaging guidance and access

The critical first step in the PD procedure is the selection of an appropriate imaging modality and planning a safe access route to achieve the catheter insertion. Ultrasonography, CT, and fluoroscopy are important imaging modalities for guidance. Ultrasonography guidance should be preferred whenever possible because it provides real-time guidance, best visualization of direct needle advancement and adjacent vascular structures (via Doppler imaging), is ideal for superficial collections or for angled access, and provides more information about collection content (septations, loculations). Fluoroscopy should be combined with US in select cases. Fluoroscopic guidance is useful for manipulating the wire and torqueing the catheter to insert the exact location, and it also demonstrates the association of the collection with the adjacent structures by injection of contrast material. Computed tomography is a preferred guide for deep collections that are difficult to access or invisible on US imaging; moreover, CT provides better visualization of bowel and pleura, which helps to avoid inadvertently transgressing bowel and pleura.

In planning the access route, the safest, straightest, and shortest route should be chosen between the skin and largest part of the collection. The selection of the skin access site is based on previous diagnostic studies (US, CT, MRI) and anatomic considerations (avoid large liver vessels, dilated bile ducts, large perigastric vessels, or transgression of bowel). When accessing the subphrenic collection, inadvertent transgression of pleura may occur, which may cause pleural infection. Therefore, low (subcostal) anterior extrapleural access should be selected to prevent inadvertent transgression. Also,

a combination of US and fluoroscopy can be useful in this setting. Some loops of bowel may interrupt the pathway when accessing the collection; in this situation, compression with the US probe can be used to displace the bowel to provide a safe pathway. Also, hydrodissection can be performed with an injection of 4 to 5 mL saline to create a safe pathway to avoid vessel or bowel injury on the access route.

At the beginning of the procedure, a wide area should be sterilized and covered with a surgical drape. Local anesthesia is applied to the skin and soft tissues where the needle and catheter will be inserted. Patients should be monitored for their heart rate, blood pressure, and oxygen saturation during the procedure, to reduce risk of complications such as sepsis, bleeding, and oversedation.

Catheter insertion technique

Diagnostic aspiration is useful to determine the nature of fluid (color, viscosity, turbidity, smell), and the selection of an appropriate drainage catheter depends on the nature of aspiration (eg, clear, viscous, particulate, clot filled). Generally, aspiration is performed with needles of 18 to 22 gauge in size. In diagnostic aspiration, the needle is inserted into the collection, and suction is applied with a 2- to 4-mL syringe. Excessive aspiration of fluid may cause difficulty of catheter insertion; therefore, diagnostic aspiration should not be excessive in small collections. The aspiration should be sent for Gram stain evaluation and culture. Occasionally, aspiration with a well-placed 18-gauge needle may be dry in the syringe; in that situation, PD of the lesion is not possible and biopsy should be considered for further evaluation. When proceeding with catheter insertion, regardless of the imaging modality used for guidance, 2 techniques have proved to be the best choices to aid in catheter placement: the Seldinger technique and the Trocar technique. The choice is often based on the physician's preference, experience, and comfort level.

The Trocar technique is preferred only for superficial and large collections. After aseptic preparation and local anesthetic infiltration, the shortest pathway is selected to approach the collection. Skin incision is made with a scalpel at the puncture point. The drainage catheter is mounted on a metal stiffening cannula/inner-stylet, and a central sharp needle is inserted directly under imaging guidance to penetrate the anterior wall of the collection cavity. Then, the central sharp needle is withdrawn, and a small amount of fluid is aspirated to confirm entry. The outer catheter is then moved further into the abscess cavity while the central stylet is held in place to feed off the catheter. This technique allows rapid drainage of the collection and minimal potential for spreading the infection because of absence of serial fascial dilatation. The principal disadvantage is the direct advancement of a catheter for serial fascial dilatation and a sharp stylet in an inadvertent, nontarget place, which can have serious consequences.

The Seldinger technique is the preferred method in daily practice. It is a useful technique to achieve catheter insertion for small collections and for difficult-to-reach collections. The procedure is performed under standard sterile conditions. The shortest distance between the skin and collection is selected by the evaluation of previous imaging. Local anesthesia is applied to the skin and along the needle pathway to the collection cavity. A small incision is made at the skin, an 18-gauage Chiba needle is penetrated into the anterior wall of the collection, and the aspiration confirms the exact needle position. Afterward, a 0.035-inch guidewire is inserted through an 18-gauge needle and coiled in the collection. The needle is then withdrawn, and the track is dilated over the guidewire with dilators under fluoroscopy or US guidance. After serial track dilatation, the catheter is advanced over the guidewire with the inner stylet. Subsequently, the stylet and wire are removed, and the catheter is locked as a pigtail. The final catheter position should be confirmed with imaging. The catheter should be sutured to the skin with 2 to 3/00 silk or other nonabsorbable materials for external fixation. The drainage catheter hub is attached with a 3-way connector and is connected to a bag. In general, catheter drainage is facilitated by gravity (Figure 2).

Catheter care

Patients should be seen in daily clinical rounds to evaluate the skin access site for leakage or infection, to monitor the catheter output, and to evaluate the patient for laboratory and clinical signs of the effectiveness of PD. In the viscous collection, catheters tend to occlude regardless of their size. Drainage catheters should be irrigated with 5 to 10 mL of normal saline every 4 to 6 hours to clear the tube of any adherent plugs or encrustations that might cause a blockage. When flushing the catheter, it should be done gently because over-distention of the collection site increases the intracavitary pressure, which may result in bacteremia and sepsis. Hematoma and loculated collections may have insufficient drainage. In these collections, treatment with tissue plasminogen activator (tPA) might be helpful for maintaining the catheter patency. The process of tPA installation consists of 4 to 6 mg tPA with 25 to 50 mL of 0.9% sterile saline installed into the catheter, which is clamped for 30 minutes; the clamp is then released, and the catheter is allowed to drain freely. This cycle can be repeated if needed. Catheter drainage setup should be checked in case of persisting collection in imaging and lack of catheter drainage. The most frequent cause of the catheter blockage or kink is usually outside the body or in the dressings. Flushing with saline or manipulating with a guidewire usually clears a blocked catheter. Occasionally, the catheter may fall out. In this situation, if the tract is a few days old, then it is possible to insert a new catheter using the existing tract by the aid of guidewire and 5F dilator. If this is not possible, a new catheter insertion should be performed with the Seldinger technique.

Catheter removal

Criteria for removal of the catheter depend on a few factors. (1) The most important is the clinical status of the patient. Successful drainage is usually associated with an improvement in the patient's clinical condition. (2) Signs of improvement in abnormal laboratory tests are important, including return of white blood cell count to the normal range and improvement in liver function tests.

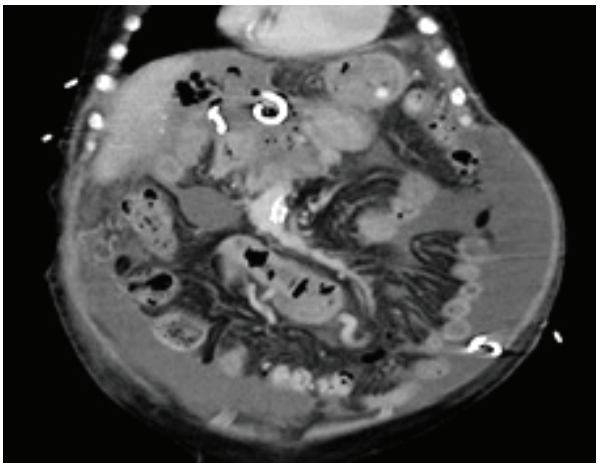

Figure 2. Percutaneous Drainage Catheters Were Inserted Into the Extensive Collection at the Hepatic Hilus, With Another Catheter Inserted in Left Lower Abdomen for Drainage

Table 2. Key points to consider for catheter insertion and care are the following.

(1)	Review the preprocedural imaging and plan the safe pathway to reach the collection.
(2)	Use color Doppler to avoid vessel injury.
(3)	Perform the diagnostic aspiration of 2 to 3 mL into syringe; select 6F to 8F drains for clear fluid, 8F to 10F for thin pus, 10F to 12F for thick pus, and 12F to 16F for abscesses with debris.
(4)	Avoid perforating the posterior wall of the collection when performing serial dilation.
(5)	If the collection is loculated, then consider multiple drains, with tPA installation.
(6)	Do not flush the catheter too vigorously (may cause septicemia).
(7)	Perform daily control of the catheter for outflow, skin infection, and leakage.

Abbreviations: tPA, tissue plasminogen activator

(3) Imaging features should clearly show a well-drained cavity. (4) Catheter output should remain below 10 mL/day for more than 24 hours.

SUMMARY

Liver transplant is becoming an increasingly routine procedure with an expanding list of indications. Besides vascular complications in LT, intraabdominal fluid collections are commonly seen at imaging as nonvascular complications after

LT. These collections are frequently uninfected and diminish in size without treatment. However, infected and large collections require aspiration or drainage. Timely diagnosis and proper management of these transplant recipients are crucial for maintaining graft and recipient survival. Percutaneous fluid drainage is an effective and safe procedure in LT patients when performed with the use of a complete range of imaging modalities in the hands of experienced radiologists.

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Complications of Living-Donor Hepatectomy

Sedat Yıldırım

Liver transplant is the most important and definitive treatment for end-stage liver failure. However, a lack of organs from deceased donors is the most important problem of this treatment. The idea of transplantation dates back to the third century BC, and this idea was realized at the end of the 20th century. Murray, an American plastic surgeon, was the first to perform successful human kidney transplant on identical twins on December 23, 1954.[1] In Turkey, the first living-related donor renal transplant from a mother to her 12-year-old child was performed on November 3, 1975, by Haberal and colleagues.[2] Strazl performed the first liver transplant in humans in 1963, with his first successful liver transplant in humans occurring in 1967.[3] On December 8, 1988, Raia and associates made their first attempt on a 4-year-old girl with biliary atresia. The donor of liver segments 2 and 3 survived, but the recipient succumbed on postoperative day 6 during hemodialysis to control metabolic disturbances and fluid overload. The group made a second attempt on July 21, 1989, and the recipient had delayed graft function and remained jaundiced on postoperative day 24. However, the further outcome of the recipient was not reported. No complications were observed in the donors of these 2 patients, and they returned to their normal lives.[4]

In the early 1970s, Haberal and his team began working on experimental liver transplant procedures in Turkey.[5] The group successfully performed their first deceased-donor liver transplant in Turkey in 1988 and performed the first living-related segmental liver transplant in Turkey and in the Middle East Region and Europe on March 15, 1990. For this procedure, a 10-month-old child received a transplant from his mother. One month later, on April 24, for the first time in the world, the team achieved success with adult living-related liver transplant (LRLT), grafting tissue from a father to his 22-year-old son.[2] On May 16, 1992, Haberal and his team performed the first in the world multiple-organ retrieval (segmental left liver and right kidney) from a living donor in a transplant from mother to daughter.[6]

Unfortunately, living-donor hepatectomy surgery does not provide any medical benefits to donors and exposes patients to some risks of complications. When evaluated in terms of the recipient, LRLT has some advantages over deceased-donor liver transplant (DDLT). Because of the low supply of organs from deceased donors, LRLT can reduce organ wait times for patients in decompensated stage. It is important to have elective and planned surgery, to transplant from a higher quality organ, to have a shorter period of cold ischemia, and to have a low rate of primary dysfunction or nonfunction. However, although LRLT is advantageous in the recipient, complicated surgical procedures for the donor and donor safety problems are frequently a concern. During donor hepatectomy, the rate of mortality is 0.1% to 1% and the rate of morbidity is 5% to 75% in healthy donors.[7-14] Most morbidities are minor complications. Overall, donor hepatectomy surgery is considered a feasible and acceptable surgical procedure because of the

low rates of major complication (2%) after donor hepatectomy. However, donor safety must remain a top concern before anything else.

LIVING-DONOR HEPATECTOMY

Living-donor hepatectomy is a completely different operation from hepatectomy performed for tumor surgery or for other reasons. It is imperative that the removed liver tissue be functional enough to meet the needs of the recipient, that the donor and the liver from the recipient do not have any other diseases, and that the remainder of the liver is undamaged and sufficient in volume. Moreover, the donor must understand the process well and be able to overcome its possible psychologic consequences. In general, the graft-to-recipient body weight ratio should not be lower than 0.8%; also, the remaining liver volume should not be less than 30% to 35% of the initial volume of the liver. If a fatty liver is suspected, a biopsy should be performed. If there is more than 30% macrovesicular steatoses, liver transplant should not be performed to avoid hepatic failure, remnant loss, and death after surgery.[15]

Before hepatectomy, informed consent must include full information on the potential surgical, medical, financial, and psychologic risks (including death). The potential outcomes for the recipient must also be explained to the donor.

DONOR PREPARATION

Donor safety is the center issue during the evaluation period. Before the operation, the donor candidate, the recipient, and their families are informed in detail about liver donation and liver transplant. In the first stage of donor evaluation, blood panel determination, complete medical history, physical examination, electrocardiography, chest radiography, and biochemical laboratory tests are performed by the general surgeon, hepatologist, and psychiatrist. The blood group of the donor candidate for liver transplant must be the same or compatible with that of the recipient. Exhaustive cardiovascular assessments should be done, and echocardiography should be routine. Additional investigations, such as stress echocardiography and/or coronary angiography, should also be performed, if needed. Transmissible disease is a contraindication for living donation. Appropriate blood tests should be used to systematically screen for asymptomatic inherited coagulation disorders involving liver synthesis (eg, Leiden factor V, protein C/protein S deficiency, and antithrombin deficiency).

After these tests, the donor then undergoes a second evaluation phase, which includes abdominal tomography and tomographic angiography, volumetric analysis with computed tomography, magnetic resonance cholangiography, and liver biopsy. Those who are between 18 and 60 years old, have ABO blood group (same or compatible), have graft-to-recipient body weight ratio > 0.8, have body mass index < 35 kg/m^2, do not have diabetes, and have liver macrovesicular steatosis rate < 30% are accepted as donors. Patients with predisposing factors for fatty liver (obesity, diabetes, dyslipidemia) and who have imaging findings consistent with fatty liver should undergo biopsy for macrovesicular steatosis during the pretransplant evaluation. At our center, all patients should have normal radiologic and clinical results, and histopathologic evaluations should be performed with liver needle biopsy. As mentioned above, the remaining liver volume after hepatectomy should be estimated to be at least 30% to 35%. Segments II and III for left lateral segment grafts; segments II, III, and IV for left lobe grafts; and segments V to VIII for right lobe grafts are used for transplant.[15]

POSTOPERATIVE CARE

Pulmonary embolism, myocardial infarction, peptic ulcer disease, and liver failure are the most common causes of mortality after donor hepatectomy.[5,6] Early identification and close follow-up of complications are important to reduce mortality. Daily liver and liver function tests should be conducted after the operation; if necessary, the condition of the liver should be evaluated with Doppler ultrasonography. Immediately after surgery, all donors should receive effective

prophylaxis against deep vein thrombosis and stress-related peptic ulcers. Appropriate analgesia is provided to all donors after surgery. The nasogastric tube is pulled in the first 6 hours after surgery, and clear fluid intake is started on the first day. Early mobilization and intensive spirometry should also start early. The drain is removed when there is no bile leak and fluid drainage is less than 50 mL. Donors are estimated to return to their previous physical performance and psychologic state within 1 year after surgery. After discharge from the hospital, all donors are recommended to have at least 2 years of regular clinical follow-up, but preferably for life.

COMPLICATIONS

Today, the main methods of evaluating surgical results in terms of quality assurance and control are the determination of mortality and morbidity. To measure morbidity, the definition of surgical complications must be made correctly. Today, there are no generally accepted surgical complication standards or definitions. Clavien and Dindo defined surgical complication as "any deviation in the ideal postoperative course that is not in the natural course of surgery," and a system consisting of 5 sections and 7 levels was published in this system (Table 1).[16] Grade 1-2 complications are considered minor complications, and grade 3 and above are considered major complications.

All complications that occur after other major abdominal surgeries can also be seen after donor hepatectomy; other complications include those related to liver function deficiency. The complications are classified as follows: (1) surgical complications (eg, surgical site infection, pulmonary embolism, incisional hernia) and (2) complications related to liver function (signs of liver failure).

SURGICAL COMPLICATIONS

Surgical complications seen after liver resection are similar to those seen with other major abdominal surgeries. Complication rates in donors during and after surgery vary between 5.5% and 78.3%, and these complications can be seen intraoperatively, early postoperatively, and late postoperatively.[7,10-12,14,17-22] There are many reasons why morbidity rates can vary. For example, differences may occur among LRLT

Table 1. Clavien-Dindo System for Classification of Surgical Complications

Degree	Description
1	Changes in normal postoperative follow-up. Any change that does not require medical treatment, surgery, endoscopic, and radiologic intervention. Accepted treatment regimens are drugs such as diuretics, antiemetics, antipyretics, analgesics, and electrolytes, as well as physiotherapy. Also wound infection that can be treated at the bedside in this group.
2	Drugs that are allowed to be used in grade 1 complications will not be used. These are conditions that require the use of other drugs, such as total parenteral nutrition and blood transfusion.
3	There is need for surgical, endoscopic, and radiologic intervention.
3a	Interventions that do not require general anesthesia.
3b	Interventions that require general anesthesia.
4	Life-threatening complications requiring treatment in the intermediate intensive care unit or intensive care unit (such as brain hemorrhage, ischemic stroke, and subarachnoid hemorrhage other than central nervous system complications).
4a	Single-organ dysfunction (including dialysis).
4b	Multiple organ dysfunction.
5	Patient death.
Appendix d	If there are complaints of a complication during the patient's discharge from the hospital, the letter "d" should be added at the end of the appropriate grade for this complication. This suffix indicates the need for follow-up to fully evaluate the complication

centers because of their level of experience, because complications are not fully reported, or because there is a lack of full agreement on the classification of complications.

The most common complications reported in the literature after donor hepatectomy are biliary tract complications, cardiopulmonary complications, and infections (Table 2). Major complication rates

Table 2. Complications After Living Donor Hepatectomy

Complication	Reference																
	10	11	12	15	16	18	19	20	22	24	25	26	32	36	40	41	56
Total percent	40	15.7	9.3	39	33.3	17.6	5.5	32.8		34	28.8	8.4	39.6	17	78.3		25.7
Biliary, %		2.8	1.7							5.3							
Bile leakage/biloma, %	8.3			2.3	6.5	3.8	2.4	8.2	15.3	2.4	7.0	2.6	2.5		13.2	4.9	9.3
Bile stricture, %	0.6			0	0.8		0.8	0.5		2.9	0.7	0.3	0.5				
Intrabdominal bleeding, %	0.9	0.8		1.7	0.4	2.2		1.3	0.4				3.5		3.6	1.6	0.7
Gastric ulcer, bleeding, %	0.2					1.8				4	0.7	0.2					
Intrabdominal abscess, %	1.2		1.0	2.3	3.2	2.4					0.7	1.7			1.2		
Ileus, %	3.3	0.8		12.1		1.0		1.0		1		0.2					
Intestinal obstruction, %	1.7	0.05		1.7							2.2		2.0				
Incisional hernia, %	7.2				0.4			0.7		0.9		0.1	4.0				0.35
Wound dehiscence, %	0.08		0.1										1.5				
Clostridium difficile colitis, %	0.2				0.4												
Surgical site infection, %			0.1	5.6	2.4		1.5	4.7			4.9	1.2	3.5		8.4	3.2	
Intraabdominal collection, %		0.8	0.2								4.2				20.5		
Chylous ascites, %					0.4							0.03				1.6	
Pancreatitis, %					0.8						0.3						
Change in bowel habit, %															2.4		
Diaphragm hernia, %					0.4												
Cardiopulmonary, %		2.2															
Pneumothorax, %	0.8									2		0.05	0.5				
Pleural effusion, %	11.2		0.1	2.8	8.1			6.1		1	1.7	0.2	7.5	1.6	37.4	9.7	2.5
Pulmonary edema, %	2		0.1														
Respiratory arrest, %	0.1			1.7													
Atelectasis, %								3.1				0.08		4.1			3.2
Aspiration, %	0.2																
Pulmonary embolism, %	0.9			0	1.2		0.8	0.7	0.8	0	0.8		2.0	0.5			
Pneumonia, %									0.2			0.03	1.0	2.1	2.4	3.2	1.7
Encephalopathy/coma, %	0.2																
Ascites, %	2.8	0.8			2.0	3.8					0.4						
Liver failure, %	0	5		0					1.6		0.01	0.08					1.8
Portal vein thrombosis, %	0.5	0.04	0.3		0.4		0.8	0.2	0.2	0		0.05				1.6	
Inferior vena cava thrombosis, %	0.4	0.06								0							
Deep vein thrombosis, %	0.8	0.02		0.5			0.8			0			1.0				
Neuropraxia, %	3.2			1.7						9		0.2					
Infection, %	15.1	7			1.6	2.4							6.0		1.2		3.9
Psychologic difficulty, %	7											1.4	2.0		2.4		
> Grade 3, %	1.4	4.65	1.9		13.8	3.6		8.2			8.5						

that may develop after donor hepatectomy also constitute 1% to 40% of all complications.[18,21,23] Major complications include biliary tract problems, cardiopulmonary problems, intraabdominal abscesses, intestinal obstruction, complex hernia, wound dehiscence, infection, intraabdominal bleeding, psychologic disorders and suicide, sepsis and multiorgan failure, inferior vena cava (IVC) thrombosis, drug overdose in the long term, intestinal obstruction, and acute liver failure.[10,11]

Complications related to the biliary tract are the most common. This complication occurs as bile leakage, biliary tract injury, biliary stenosis, and biloma. The rate of biliary tract complications is reported to range from 1.9% to 18%, and biliary complications are more frequently seen after right liver donations.[11,12,24-28] Less than 10% of patients with biliary complications require reoperation.[18,25] Biliary tract complications are lower at centers with high transplant speed and occur more frequently in the periods when centers first begin transplantation. Complications become less common as surgical experiences increase.[11,12,20,21,29] The rate of biliary stricture incidence after hepatectomy is < 1%.[7,30,31]

In the late period after donor hepatectomy (1 month after surgery), radiologic and clinical changes can also be seen in donors, which usually do not cause any complaints. Liver regeneration in patients is completed in the third month after hepatectomy.[32] Mild splenomegaly, minimal biliary dilatation, and thrombocytopenia are the most common clinical and radiologic changes.[32] Splenomegaly becomes apparent 3 months after hepatectomy and disappears after 1 year. Although the cause of splenomegaly is not fully known, it is thought that it may be due to temporary portal hypertension developed after hepatectomy.[33] Splenectomy and thrombocytopenia generally accompany it, but these complications do not constitute clinical significance in the donor.[33,34]

Keloid development at the wound site, small bowel obstruction, pneumonia, pulmonary embolism, pleural effusion, incisional hernia, wound pain and fullness, rectus muscle atrophy, change in bowel habit, depression, intraabdominal abscess, IVC thrombus, diaphragmatic hernia, gastroesophageal reflux disease, pancreatitis, and biliary stricture are late-term complications after hepatectomy.[18,30,32,35,36]

Cardiopulmonary complication rates after donor hepatectomy are between 2.2% and 14.5%.[17,37-40,41] These rates are similar to those for other major

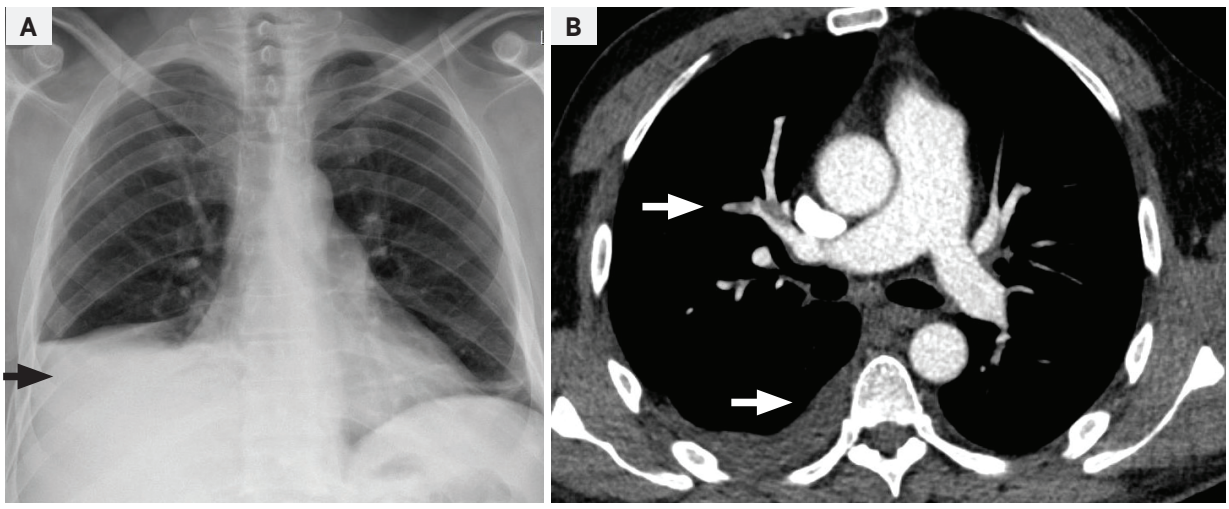

Figure 1. Pleural Effusion
(A) Chest radiography. **(B)** Axial computed tomography pulmonary angiography demonstrating chronic pulmonary emboli in the right upper lobar and segmental artery (white arrow) and right-sided pleural effusion (white arrow)

abdominal surgeries (Figure 1).[37] Cardiopulmonary complications are frequently observed after right hepatectomy.[11] These complications are pneumonia, atelectasis, pneumothorax, pulmonary edema, pleural effusion, and pulmonary embolism. Pleural effusion is the most common cardiopulmonary complication.

After hepatectomy, incidence of hyperbilirubinemia is between 3.7% and 18.7% without biliary obstruction; elevations in aspartate aminotransferase and INR levels can also occur.[17,38] These findings can be dangerous and sometimes fatal. Donor age, presence of different histologic changes (hepatocellular injury, balloon cell degeneration, steatosis, nonspecific histologic changes), and volume of the remaining liver tissue (< 40%) in the structural biopsy before hepatectomy can affect their occurrence and can be more common with right hepatectomy.[17,38]

Development of intestinal obstruction after donor hepatectomy, which has an incidence rate of 0.5% to 2%, can cause the emergence of a second surgical procedure.[6,7,9,13,23,31,37]

Incidence of postoperative bleeding into the abdomen ranges from 0.4% to 3.6%,[10,11,17,18,20,24,35,41-43] and incidence of surgical site infection can occur in 0.1% to 8.4% of patients. Although donor hepatectomy surgery is a clean contaminated surgical procedure, long operation time increases the rate of infection in the surgical field.[12,13,17,18,21,22,27,28,35,42] Intraabdominal collections that cannot be drained through drains placed after surgery can be seen in up to 20.5% of patients.[13] About 2.4% of patients may have changes in their bowel habits after hepatectomy.[13] Pancreatitis and *Clostridium difficile* colitis and diaphragmatic hernia are rarely seen after hepatectomy.[10,18,27] About 0.4% to 2.8% of patients develop ascites after surgery.[10,11,18,20]

As a result of the long operation time, improper patient positions, and excessive stretching of the extremities, neuropraxias are seen in 0.2% to 9% of patients.[10,17,26,28] Deep vein thrombosis is seen in less than 1% of patients.[10,11,17,21,35,37]

Psychologic difficulties can be observed in 1.4% to 7% of patients after hepatectomy.[10,13,28,35] Hepatic artery, portal vein, and IVC thrombosis are seen in less than 2% of patients.[10-12,18,21,22,28,33,42] With regard to incisional hernia, rate of incidence is 0.1% to 7%.[10,18,22,26,28,35,42] After right lobe donor hepatectomy, the rate of chyle leakage is 0.3% to 1.61%.[28,42] Stopping oral feeding and providing total parenteral nutrition support in these patients will ensure that the chylous leak will recover spontaneously. The lymphatic structures occurring during hilar dissection should be ligated to prevent the development of chilosis leak in donors postoperatively.

After donor hepatectomy, duodenal ulcer may develop in 0.2% to 5% of donors and 0.27% of donors may have ulcer bleeding. Therefore, giving proton pump inhibitors to patients after hepatectomy is a suitable treatment option.[10,20,26,27,34] Liver failure may develop in 0% to 1.8% of patients after hepatectomy.[10,11,24,27,28,43]

LIFE-THREATENING OR NEARLY LIFE-THREATENING COMPLICATIONS

Surgical and medical complications defined as life-threatening or nearly life-threatening complications include biliary complications requiring radiologic, endoscopic, or surgical intervention under general anesthesia; gastrointestinal hemorrhage requiring endoscopic, radiologic, or surgical intervention under general anesthesia; postoperative hemorrhage requiring relaparotomy; organ abscesses requiring relaparotomy or interventional radiology; organ injury/perforation requiring relaparotomy; progressive hepatic failure requiring liver transplant; transient hepatic failure; renal failure hemodialysis; multiorgan failure; cerebrovascular events; and all Clavien grade 3b/4 complications.[13,14,39] Other events that are considered life-threatening or nearly life-threatening include intraoperative hemodynamic instability requiring medical therapy, anaphylactic reactions, difficult to control bleeding episodes secondary to opening of hepatic or portal vein clamps, biliary tract injury requiring hepaticojejunostomy or T-tube drainage, vessel

Table 3. Complications According to Timing During Donor Hepatectomy

Intraoperative Complications	Early Postoperative Complications	Late Postoperative Complications
▪ Portal vein injuries ▪ Inferior vena cava injuries ▪ Bile duct injuries	▪ Bile leakage ▪ Postoperative bleeding ▪ Respiratory arrest ▪ Hepatic failure ▪ Infected biloma ▪ Liver abscess/necrosis ▪ Gastric volvulus ▪ Vascular thrombosis ▪ Transient liver failure ▪ Respiratory failure ▪ Gastric ulcer ▪ Transient ischemic attack with motor weakness ▪ Liver and kidney transplant	▪ Biliary stricture ▪ Intestinal perforation ▪ Postoperative bleeding

narrowing that limits blood flow developing after suturing the hepatic vein or portal vein stump, pulmonary embolism, and myocardial infarction.[14,17,39]

These complications can be divided into 3 groups per timing, as shown in Table 3. In general, these complications occur in 0.36% to 6.5% of patients that undergo living-donor hepatectomy,[12,14,18,30,39,44,45] with decrease in incidence as experience of the transplant center increases. Although these complications are more common in patients undergoing right lobectomy, multivariate analyses have shown no correlation between right and left hepatectomy and rate of complications.[12,13,30,39]

There is ongoing debate on whether a relationship exists between remnant liver volume (RLV) less than < 30% and > 30%.[12,45,46,47] The International Liver Transplant Society has recommended donor RLV to be no less than 30% to 35% of the initial volume of the whole liver. Donor age, the status of the middle hepatic vein (MHV), and presence of hepatosteatosis are also important factors.[15]

Opening the vascular clamps accidentally during surgery and injuries to the IVC are the most common causes of bleeding during surgery. Bleeding is an important predictive finding for postoperative complications.[18] Early identification of bleeding and good medical treatment during and after surgery are life saving for the donor.

Excessive rotation of the liver and external compression during hepatectomy must also be avoided. The falciform ligament should be sutured to the abdominal wall after right hepatectomy to prevent rotation of the left lobe. Adequate and appropriate analgesia, breathing exercises, and deep vein thrombosis prophylaxis after surgery can significantly reduce the development of complications. All vascular injuries should be repaired with primary or patch venoplasty with vein graft to prevent narrowing of vessels. Bile leaks can be treated with hepaticojejunostomy, T-tube insertion, drainage, and primary suture repair. Liver failure should be treated with supportive therapies or liver transplant.[39]

COMPLICATIONS RELATED TO LIVER FUNCTION

Posthepatectomy liver failure, which is classified according to the International Study Group of Liver Surgery,[48] manifests itself as hyperbilirubinemia, coagulopathy, and encephalopathy. This type of complication is fatal and results mainly from exaggerated loss of liver volume and insufficiency of remnant liver, especially in right donors.[40] In a

study of 11 553 donor hepatectomies, mortality was detected in 23 donors (0.2%). The cause of mortality in 8 donors was multiorgan/liver failure and right liver donor. Three of the 8 patients received liver transplant as treatment.[14] Type A liver failure can be followed. Type B failure is treated with fresh frozen plasma replacement, liver-protecting diet, and close liver function test monitoring. Type C failure needs invasive treatment, such as plasmapheresis, liver support system, or liver transplant.[11,14,40,49]

When causes of death after adult donor hepatectomy are analyzed, liver failure appears to be one of the main causes of complications.[14,40] The volume of liver tissue that will remain after hepatectomy, donor age, the need for blood during surgery, remnant liver volume, RLV-to-donor body weight ratio, complicated biliary and vascular variations, duration of surgery, quality of the liver, donor age, body mass index, insufficient portal flow of the liver, and outflow can affect development of sepsis liver failure.[49-54] For this reason, these conditions must be investigated and considered to prevent development of posthepatectomy liver failure before donor hepatectomy. Candidates who have liver fat < 30% by biopsy and whose remaining liver volume is more than 30% to 35% and RLV-to-body weight ratio > 0.6 are usually accepted as donors when calculated by computed tomography.

RISK FACTORS FOR COMPLICATIONS

Similar to that shown for any other major surgery, increased experience can reduce the complication rate. Many risk factors have been identified for the development of complications after donor hepatectomy. Right lobe surgery, amount of liver volume, blood loss during surgery of > 300 mL, age, sex, excessive weight, transplant rate and experience of the center, vascular anomaly, operation time of > 400 minutes, and hypotension during operation (< 100 mm Hg) are associated

Table 4. Complications in Right Lobe Versus Left Lobe Hepatectomy

Reference		Any Complication, %	Biliary Complication, %	Major Complication, %	Minor Complication, %	Liver Failure, %
11	RL	13	3.0	3	7	5
	LL	9.2	1.9	1.4	5.7	0.05
12	RL	9.4	1.8	2.1		
	LL	6.8	0	0		
15	RL	48	2.6	7.7	33.1	0
	LL	18	0	0	18	0
17	RL	13		0	13	
	LL	10		0	10	
18	RL	19.9	3.4	3.8	15.8	1.9
	LL	11.3	3.4	3.2	8.1	1.0
19	RL	10				
	LL	8.9				
24	RL	43.4	10.1			0
	LL	29.2	2.9			0
25	RL	44.2	12.2	17	27.2	
	LL	18.8	4.9	2.8	16	
26	RL	9.4		4.0	3.5	
	LL	8.7				

Abbreviations: LL, left liver donor hepatectomy; RL, right liver donor hepatectomy

with factors such as postoperative international normalized ratio of < 2, anatomic variations, early mobilization of the donor, and fatty state of the liver.[10,17,18,24,55] However, one study, the Adult-to-Adult Living Donor Liver Transplantation Cohort Study, found that operative time did not affect donor outcome; this study advocated meticulous and time-consuming dissection as a prudent approach to reduce complications during donor surgery.[10] Some studies found that donor type, portal vein, and biliary tract diversity are not associated with development of biliary tract complications.[24,30,31,56]

Injury to the vascular supply of the biliary tree is thought to be a risk factor for biliary complications. Because the biliary tree has a complex arterial supply, many surgeons attempt to minimize dissection around the duct as much as possible.[25,47]

As stated, a right hepatectomy can lead to more complications, with rate of complications shown to be 9.4% to 48% in right hepatectomy and 6.8% to 18% in left hepatectomy. Although minor complications (≤ grade 2) have been shown to be similar with both right and left hepatectomy, major complications (≥ grade 3) have been shown to be more common in right hepatectomy. These complications mostly belonged to the biliary system and were associated with bleeding (Table 4).[10,11,12,17] In a case-control study that compared results of right hepatectomy in living donors with right hepatectomy in patients with benign tumors, the complication rate was higher in right hepatectomy than in benign tumors (46% vs 21%). It was concluded that donor right hepatectomy may cause a more severe loss of liver volume than right hepatectomy for benign tumors, and the remaining liver regeneration effort after hepatectomy is important and this may increase the postoperative complication rate.[57]

Macrovesicular-type liver steatosis increases the rate of primary graft nonfunction in the transplanted liver. Each 1% change in fat reduces the functional liver volume in liver tissue by 1%. In an examination of the donor preparation process, liver biopsy showed a rate of 32% of unusual findings in 612 otherwise normal donor candidates, with 44% showing fat change and 12% showing portal inflammation. A limited volume of liver tissue remaining after hepatectomy and a high rate of lubrication can increase the rate of complications after hepatectomy or the possibility of developing liver failure.[58,59]

Morbidity rate correlates with the amount of liver tissue removed. The volume of graft from the living donor should be determined to ensure the absolute safety of the donor but also to meet the need of the recipient. Insufficient RLV has been reported to be a major risk factor for donor mortality and morbidity. The RLV should be no less than 30% to 35% of the initial whole liver volume according to International Liver Transplantation Society guidelines.[15] However, some studies have suggested that, if donor preparation is done with sufficient care, complications shown with RLV < 30% versus RLV > 30% in liver donors are the same.[12,45]

In right lobe hepatectomy, the use of a graft with MHV provides better venous drainage in recipients; however, it may increase the risk for donors. When the remaining liver volume is > 30%, the donor complication rate does not differ regardless of whether or not MHV is removed during donor hepatectomy. However, when the remaining liver volume is < 30%, the removal of MHV by graft can increase complications in donors. If the graft has a small right hepatic vein, it is estimated that excessive venous congestion may develop in segments 5 and 8, and MHV may be included in the right lobe liver graft.[60] When the remaining liver volume is above 30% and donor age is <50 years, hepatectomy with the right lobe can be safely conducted with use of MHV in cases of mild and no fatty changes.[47,61] Whether donor age affects the donor or recipient after hepatectomy is not clear; however, liver regeneration capacity decreases in elderly patients. In addition, mortality and morbidity rates are higher in patients who receive grafts from older donors and who undergo wide right hepatectomy or if MHV was removed. These findings suggest that MHV should not be removed for donor safety and the remaining donor

volume should be > 35% in older donors because the problem of venous flow in the remaining liver can reduce regeneration capacity and increase the risk of morbidity.[62]

Bleeding volume, which can depend on the surgeon's skill and experience, is also predictive of postoperative complications. The most frequent time of bleeding is during transection of the liver. Therefore, keeping central venous pressure low and having good muscle relaxation and inflow vascular occlusion are beneficial. On the other hand, excessive lowering of central venous pressure may be dangerous in older donors. Bleeding volume also depends on the anatomic arrangement of the hepatic vein at the junction with the IVC. If liver transection is done carefully and slowly, the amount of bleeding can be limited, regardless of prolonged surgery time. It is important to remember that excessive bleeding will cause major complications.[62]

Protecting the remaining liver tissue during surgery is important for donor recovery. Prolonged liver rotation and crushing of the liver with retractors should also be avoided.[39,62]

Inadequate pain control may lead to atelectasis; therefore, pain control is important. The Adult-to-Adult Living-Donor Liver Transplantation Cohort Study showed that there was a significant association between need for transfusion and development of a first complication, specifically with occurrence of bile leak and infection. Intraoperative hypotension is also associated with higher risk of any complication, and higher predonation serum bilirubin was associated with lower risk of any complication. The group also found that older age, male sex, and higher body mass index were independent significant predictors of hernia formation.[10]

TREATMENT OF COMPLICATIONS

The rate of repeat surgery for patients after donor hepatectomy varies between 1% and 2%.[11,63,64] The most frequent causes of reoperation are biliary reconstruction, biliary drainage, intestinal obstruction, postoperative bleeding, abdominal drainage, hernia repair, and pleural drainage.[18,28,39]

Biliary tract complications bring serious morbidity and mortality to donors. Therefore, it is recommended that surgeons perform magnetic resonance cholangiopancreatography to view the bile ducts in the donors before the operation to prevent bile leaks, that they perform cholangiography during the operation to detect bile leaks on the cut face, that they have increased clinical experience, and that they avoid donors with complex biliary anatomy if there is no emergency (Figure 2). Knowing the bile duct anatomy

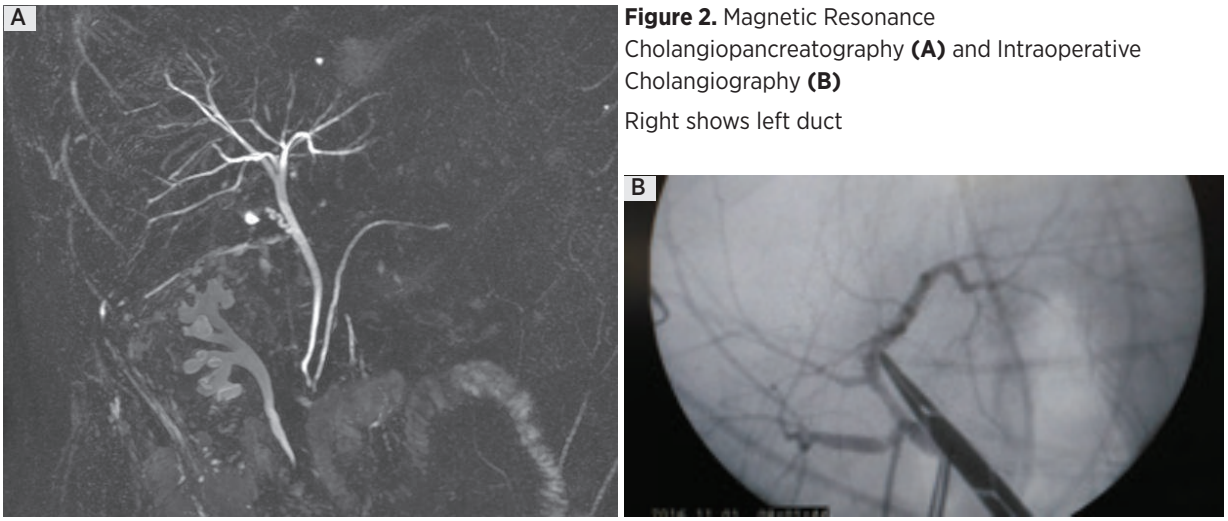

Figure 2. Magnetic Resonance Cholangiopancreatography **(A)** and Intraoperative Cholangiography **(B)**
Right shows left duct

preoperatively, carefully performing hepatectomy, detecting bile leakage from the cystic duct after hepatectomy, avoiding manipulations that may impair the blood supply of bile duct during hilar dissection, and repairing bile duct injuries that may occur during the operation all reduce biliary complications.

Although the incidence of biliary tract complications is high, most biliary complications are bile leaks or bilomas that resolve without requiring further percutaneous drainage or endoscopic retrograde cholangiopancreatography.[21,24,25,43] Treatment without surgery should be the first choice when biliary complications are encountered. Minor bile leaks can be drained with the drain placed during the operation. This option can be used when there is no spreading into the abdomen and if the patient is asymptomatic; these patients are expected to recover spontaneously.[24,43] The use of endoscopic retrograde cholangiopancreatography, percutaneous transhepatic cholangiography, and stent placement and sphincterotomy should be performed in bile leaks that do not improve spontaneously within 3 weeks. In addition, these options can be used in patients with increased bile drainage, increased cholestatic enzymes, and have an intraperitoneal spread. If there is any biliary tract injury that does not improve with this treatment and there are signs of peritonitis, the biliary tract injured by surgical treatment should be repaired and lavage should be performed with laparotomy (Figure 3).[24,25,43] If there are benign bile stenoses that cannot be corrected by interventional methods, these stenoses should treated with hepaticojejunostomy or duct-to-duct biliary anastomosis.[39,64]

Another important complication after donor hepatectomy is intraoperative and postoperative intraabdominal hemorrhage. During the intraoperative period, vascular injury at liver parenchymal dissection, IVC damage, and accidental opening of the portal and vascular clamps can cause bleeding. Bleeding is the most important indicator for postoperative complications. Bleeding should be carefully managed and proper medical or surgical treatment should be applied rapidly. Postoperative hemorrhage is frequently seen on the cut surface of the liver. Reoperation and hemostasis and conservative monitoring erythrocyte replacement are the treatment choices.[39,43]

Infection is one of the most common complications of hepatectomy. Infection may occur in the lung, urinary tract, and vascular structure. Access to

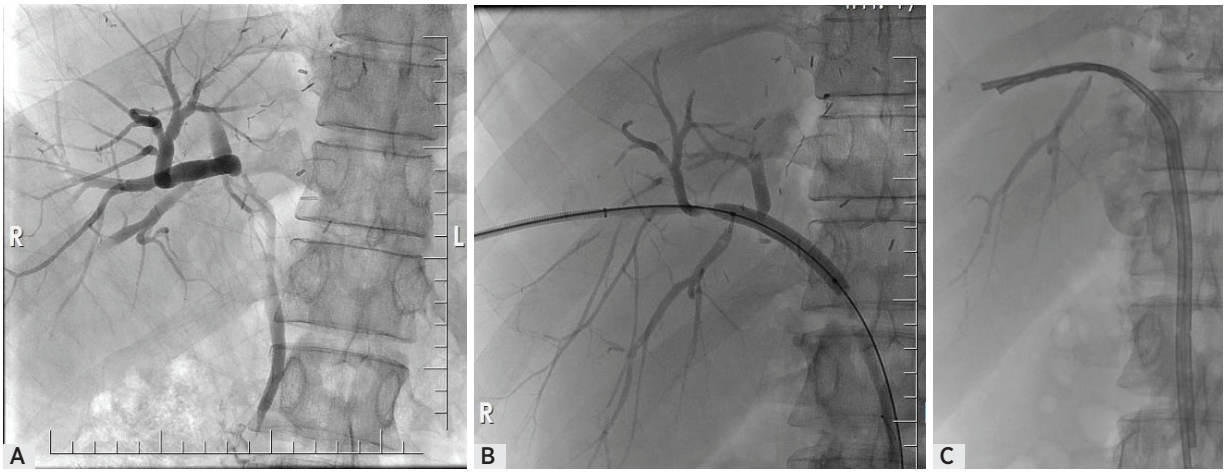

Figure 3. Treatment of Severe Stenosis at the Junction of the Right and Common Hepatic Ducts After Left Hepatectomy **(A)** Severe stenosis at junction of the right and common hepatic ducts after left hepatectomy. **(B)** Dilatation of the stricture using a 6-mm balloon. **(C)** Two plastic stents were inserted through the structure.

the abdominal cavity secondary to bile leakage or an infected necrotic liver on the transection surface may cause infections. Infection will cause liver failure and lead to deteriorating conditions in donors. Therefore, the donor should be closely monitored after hepatectomy.

MORTALITY

In a study of 23 patients who died after liver donation between 1999 and 2017, the biggest cause of death was postoperative sepsis in 7 donors (30%).[7,48] Although the mortality rate after hepatectomy for donation is low (0.3% to 0.5%), the death of the donor remains a tragedy for the families and transplant teams. In 2006, Trotter and associates[65] collected data on all deaths after donor hepatectomy. The group reported 13 donor deaths and 1 persistent vegetative condition after 4598 living-donor liver transplants in the United States and Europe that were directly related to surgery. Although 9 of the deceased donors had a right lobectomy, a single donor had a left lobectomy (with lobe not specified for 3 patients). In another study, most deaths occurred within 60 days of donation (ranging from an intraoperative death to suicide at 60 days).[14] In this survey, only 5 of the donors with mortality had left and lateral segment hepatectomy. Ringe and associates[8] also compiled all reported or known death cases in the world (from publications, conferences, communication, and personal correspondence) and identified 33 liver donor deaths, including 3 after recovery transplant; however, only 12 deaths were published in detail. The group concluded that the ratio of liver volume remaining after hepatotomy to body weight was more significant than the total liver volume remaining in predicting postoperative liver failure and death in < 0.5%.[54] In another study, among 4111 donor hepatectomies conducted between 1994 and 2011 in the United States, there were 7 donor deaths (4 right lobe hepatectomy, 1 left lobe hepatectomy, 2 left lateral lobectomy) and 4 donors who developed liver failure. Three patients who developed liver failure required liver transplant.[66] Although significant progress has been made worldwide since the first donor hepatectomy, donors are still at risk. Undeclared deaths should also be reported to provide a better estimate of donor mortality.

SUMMARY

Donor hepatectomy surgery for liver transplant is not a smooth surgical procedure for donors. All potential living donor candidates should be well informed about the risks of surgery, with donors carefully selected by the transplant teams. Donor hepatectomy should only be performed at well-established centers with surgical teams who have sufficient medical expertise and adequate institutional resources. Donor assessment, intense preoperative planning, and rigorous surgical techniques are essential to minimize complications and provide adequate grafts.

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Diagnostic and Interventional Radiology in Liver & Kidney Transplantation

PART III

Ultrasound Imaging of Renal Transplant Complications

Feride Kural Rahatlı

Renal transplant is the treatment choice for end-stage renal disease; transplant improves quality of life and increases survival rates versus those shown with long-term dialysis.[1] The kidney is the first and most often transplanted solid organ.[2] Despite advances in immunosuppressive drugs, surgical techniques for renal transplant patients can lead to complications that vary from vascular to miscellaneous.[3,4] Renal transplant complications can also be grouped as early (hyperacute and acute), intermediate, or late, according to the period of time that they are seen after transplant.[5]

Color Doppler ultrasonography is the first-line imaging modality to evaluate the transplanted kidney because of its lack of ionizing radiation, portability, rapidity, and the ability to assess the kidney vasculature without contrast material. It also provides some physiologic information about the kidney.[6]

ULTRASONOGRAPHY OF A NORMAL RENAL GRAFT

The morphologic appearance of a healthy allograft is similar to the appearance of the native kidney. According to its superficial localization in the iliac fossa, clearer detail is apparent. During grayscale ultrasonography, longitudinal and transverse dimensions and cortical thickness of the transplant should be measured with use of 4- to 5-MHz transducers. Echogenicity of the kidney should be evaluated (Figure 1a). The collecting system must be evaluated to understand whether hydronephrosis is present. The collecting system of a healthy transplanted kidney may be slightly dilated early after surgery according to the new anastomosis of ureterovesical junction and mild anastomotic edema.[4-6] The presence of perinephric collections should be checked with use of high-frequency (8- to 9-MHz) transducers.

Color and pulsed Doppler allow a detailed evaluation of the allograft's vasculature. The peak systolic velocity of the main renal artery and vein should be recorded at the anastomosis site and distal to the anastomosis, so that the renal artery and vein ratios to external iliac artery and vein can be calculated. If there is more than 1 main renal artery, each should be evaluated separately. Resistive indices (RI) should be calculated from interlobar and segmental arteries from the upper pole, lower pole, and interpolar region using both high- and low-frequency transducers (Table 1) (Figure 1b). Resistive index is calculated as follows: RI = (peak systolic velocity - end diastolic velocity)/ peak systolic velocity.

The renal artery vessels normally have low RI of < 0.70 m/s.[5,6] The most important point in calculating RI is not to apply pressure on the transducer during pulsed Doppler imaging. If pressure is applied to the parenchyma, diastolic blood flow is blocked, and the RI will be elevated.

The normal peak systolic velocity of the main renal artery should be smaller than 250 cm/s.[5] In the perioperative period, elevation of peak systolic velocity of the main renal artery can be seen accord-

Table 1. Data That Should Be Recorded During Doppler Ultrasonography of Transplanted Kidney

Transplanted Vessel	Evaluation
Main renal artery	Calculate peak systolic velocity at anastomosis and distal to anastomosis (hilum)
Main renal vein	Calculate peak systolic velocity at anastomosis and distal to anastomosis (hilum)
External iliac artery	Calculate peak systolic velocity proximal to the transplant
External iliac vein	Calculate velocity distal to anastomosis
Interlobar segmental arteries	Calculate resistive index from the upper pole, lower pole, and interpolar region

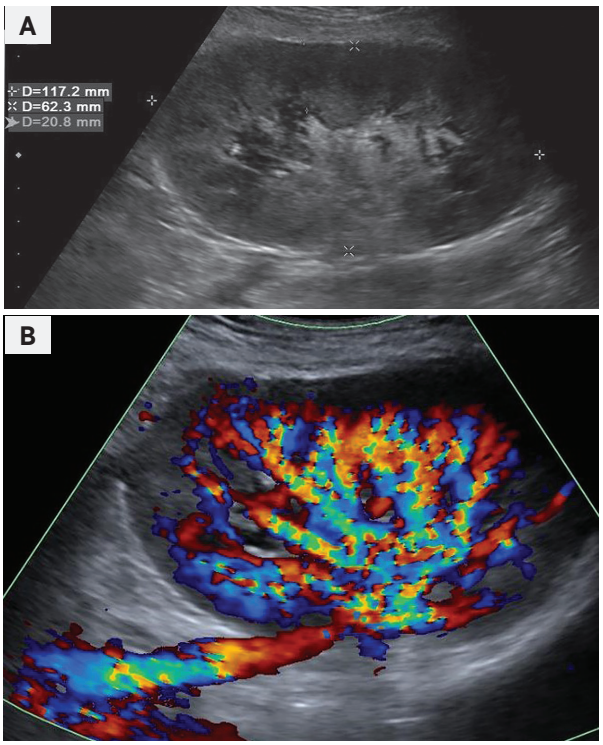

Figure 1. Normal Findings of Renal Transplant

(A) Craniocaudally and anteroposterior diameter measurement and cortical thickness measurement of normal transplanted kidney.
(B) Color Doppler ultrasonography of normal transplanted kidney.

Table 2. Renal Transplant Complications

Vascular
- Renal artery stenosis
- Renal artery thrombosis
- Renal vein thrombosis
- Pseudoaneurysm
- Arteriovenous fistula

Collecting System Complications
- Urine leak
- Obstruction

Perinephric Fluid Collections
- Hematoma
- Lymphocele
- Urinoma
- Abscess

Parenchymal Abnormalities
- Delayed graft function
- Rejection
- Acute tubular necrosis
- Drug nephrotoxicity

Neoplastic Complications
- Posttransplant lymphoproliferative disorder
- Renal cell carcinoma

ing to postoperative edema, and decrease in peak systolic velocity can be seen in days or months.[5,6]

ULTRASONOGRAPHY OF RENAL TRANSPLANT COMPLICATIONS

Complications of the transplanted kidney can be grouped as vascular and nonvascular, and the nonvascular complications can be grouped as parenchymal abnormalities, collecting system complications, perinephric fluid collections, and neoplastic complications (Table 2). Complications of the transplanted kidney can also be grouped depending on the time of onset (that is, early, intermediate, or late) (Table 3).

VASCULAR COMPLICATIONS

Transplant renal artery stenosis

Renal artery stenosis is the most common vascular complication in renal transplant; it has been thought to occur in up to 23% of transplanted kidneys[7-9]; however, recent evidence from larger studies have suggested a much lower incidence of 1% to 3%.[5,10,11] Renal artery stenosis occurs between 3 months

Table 3. Peak Onset of Renal Transplant Complications

Early		Intermediate		Late	
Hyperacute rejection	During surgery (minutes to hours)	Ureteral stricture or obstruction	Weeks to 6 mo	Chronic rejection	Months to years
Acute rejection	1 to 4 wk	Abscess	Weeks to months	Malignancy	> 1 y
Acute tubular necrosis	Immediately after transplant (< 2 d)	Drug-related nephrotoxicity	> 2 mo		
Renal artery thrombosis	Immediately after transplant (minutes to hours)	Renal artery stenosis	> 3 mo		
Renal vein thrombosis	Immediately after transplant (< 5 d)	Lymphocele	4-6 wk		
Hematoma	Immediately after transplant (< 5 d)	Urinoma	First 3 mo		
		Urinary leak	First 3 mo		

and 2 years after transplant.[4,10,12] Renal artery stenosis is mostly seen at the site of anastomosis, secondary to vessel perfusion injury, imperfect suture technique, or reaction to suture material. It can be seen before anastomosis because of the atherosclerotic disease of the donor or after the anastomosis because of rejection, arterial kinking, compression, or turbulent flow from a kidney's malposition.[13] Patients with severe hypertension refractory to medical therapy or coexistence of hypertension and graft dysfunction should be investigated for renal artery stenosis.[13,14]

The initial imaging method to evaluate renal artery stenosis is color and pulsed Doppler ultrasonography; these techniques are easy and noninvasive but depend on the operator. During ultrasonography, evaluation of the main renal artery from hilum to anastomosis is important. The insonation angle should be nearly 60° and must not be smaller than 40° during calculation of peak systolic velocity.[6] Color and pulsed Doppler signs of renal artery stenosis are elevated peak systolic velocity of the main renal artery, increased ratio of the main renal artery peak systolic velocity to the external iliac artery velocity, and color aliasing in the stenotic segment from increased flow velocity. Previous studies have reported that the threshold value of peak systolic velocity of the main renal artery should be 250 cm/s; however, recent data have stated that this may lead to a false-positive diagnosis of renal artery stenosis.[5,7] In the absence of other findings, peak systolic velocity of the main renal artery between 340 and 400 cm/s at the anastomosis has been suggested as a cutoff value for renal artery stenosis.[5,7]

Acceleration time is the time between the beginnings of systole and the early systolic peak. Increased acceleration time (≥ 0.08 to 0.1 s) and decreased RI (< 0.50) from the interlobar, segmental arteries are indirect signs of renal artery stenosis; tardus parvus waveform abnormalities can be observed in the renal parenchyma[4-6] (Figure 2). Doppler findings suggesting renal artery stenosis are shown in Table 4.

In the perioperative period, isolated elevated peak systolic velocity of the main renal artery may be related to postoperative edema or technical challenges, which can decrease within months, not days.[5,15] In cases of high peak systolic velocity without other Doppler findings of renal artery stenosis and clinical findings, a closer Doppler follow-up is recommended instead of intervention.[6,16]

Table 4. Doppler Findings Suggesting Renal Artery Stenosis

Doppler Findings of Renal Artery Stenosis
▪ Increased peak systolic velocity of the main renal artery > 350-400 cm/s
▪ Increased ratio of the main renal artery peak systolic velocity to external iliac artery velocity > 2
▪ Decreased resistive index from interlobar, segmental arteries < 0.50
▪ Increased acceleration time from interlobar, segmental arteries > 0.08 s

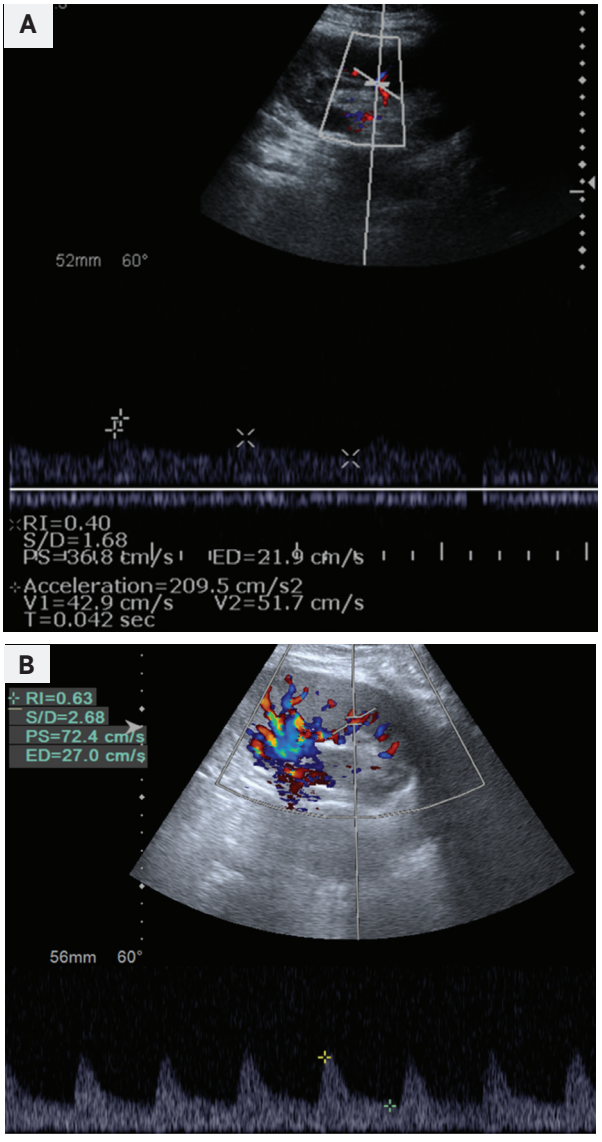

Figure 2. Male Patient With Worsening Hypertension After Renal Transplant

(A) 45-Year-old male patient with worsening hypertension after renal transplant has decreased resistive index (RI) from intraparenchymal renal artery branches and increased acceleration time compatible with renal artery stenosis. **(B)** After percutaneous transluminal angiography, patient has normal RI values and normal acceleration time.

Magnetic resonance imaging angiography can be used in the diagnosis of renal artery stenosis.

Renal artery thrombosis

Renal artery thrombosis is a rare complication with a prevalence of 0.4%; however, its occurrence is a serious event that can result in graft loss.[1,5] Arterial thrombosis develops in the immediate postoperative period; it can occur because of technical factors, such as arterial dissection, vessel kinking, hyperacute rejection, and hypercoagulable states.[4,13] Clinical signs are dead stop of urine output and worsening hypertension.[13]

In Doppler ultrasonography, renal artery thrombosis appears as an absence of flow in the main renal artery and branches. A fast and definitive diagnosis is important because immediate intervention is needed for recovering the graft.[1] Also, segmental renal infarction can be seen according to thrombosis of renal artery branches as hypoechoic mass-like regions at ultrasonography and avascularity at color and pulsed Doppler.

Renal vein thrombosis

Transplant renal vein thrombosis occurs in < 5% of adult patients but in up to 8% of pediatric patients, and it can lead to early graft failure in up to 35% of pediatric patients.[1,5,6,13,17,18] Symptoms include swelling, pain, and fever in the graft area and ipsilateral low extremity edema. It occurs in the early postoperative period within the first 5 days, but its peak incidence is in the first 48 hours. Donor and recipient risk factors are given in Table 5.

During grayscale ultrasonography, edematous enlargement of kidney, loss of corticomedullary differentiation, and perirenal fluid can be seen. With Doppler ultrasonography, the absence of flow in the main renal vein is diagnostic; in addition, high resistance waveforms with reversed diastolic flow in the graft's main renal artery and branches are seen[4,5] (Figure 3). An early and accurate diagnosis is important because immediate intervention is needed for recovering the graft.

Table 5. Donor and Recipient Risk Factors for Renal Vein Thrombosis

Donor Risk Factors
▪ Age less than 6 y
▪ Age greater than 60 y
▪ Allograft cold ischemia time greater than 24 h
▪ Renal artery atherosclerosis
▪ Right side allograft
Recipient Risk Factors
▪ Age less than 6 y
▪ Age greater than 60 y
▪ Peritoneal dialysis
▪ Hypercoagulable states
▪ Atherosclerosis
▪ Diabetes mellitus
▪ Hypovolemia
▪ Multiplicity of renal veins
▪ Blood vessel size dissonance between donor and recipient

A high resistance waveform with reversed diastolic flow in the transplanted kidney's main renal artery is not specific for renal vein thrombosis. These presentations can be seen in acute tubular necrosis, acute rejection, hydronephrosis, and extrinsic compression of the transplanted kidney.[5,19]

Pseudoaneurysm

Pseudoaneurysm is a complication of renal transplant biopsy. In grayscale ultrasonography, it appears as anechoic cystic lesion; in color Doppler, a yin-yang sign is seen.[4] These often resolve spontaneously; however, pseudoaneurysms with enlargement and those > 2 cm need intervention.[13]

Arteriovenous fistula

Arteriovenous fistula develops secondary to transplant biopsy due to laceration of adjacent arterial and venous structure and forming of a communication between them. Most cannot be seen with grayscale ultrasonography.[5] With color Doppler, aliasing is seen, and, with pulsed Doppler, the feeding artery shows high-velocity and low-resistance waveforms, with the draining vein showing arterializations[6,20] (Figure 4).

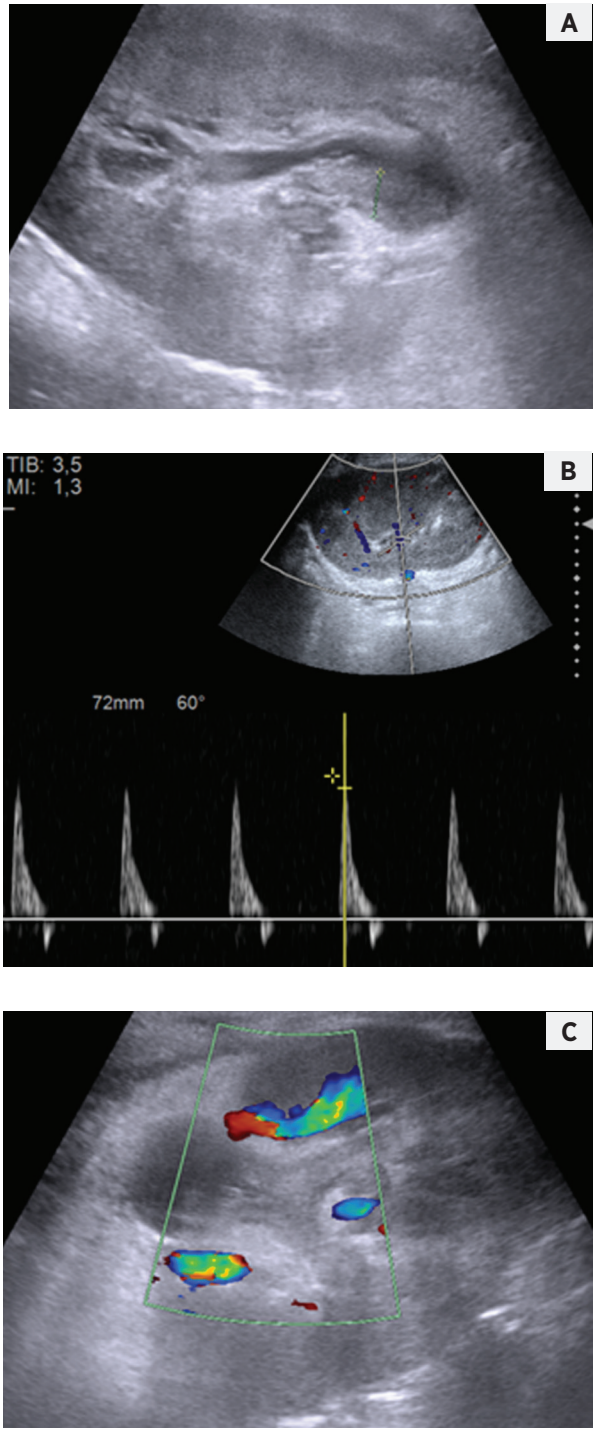

Figure 3. Female Patient With Anuria Just After Transplant

(A) 37-Year-old female patient with anuria immediately posttransplant has an edematous kidney with mucosal edema (4mm). Doppler ultrasonography shows resistive index > 1 and negative diastolic flow **(B)** and no venous flow **(C)**, with renal venous thrombosis determined surgically.

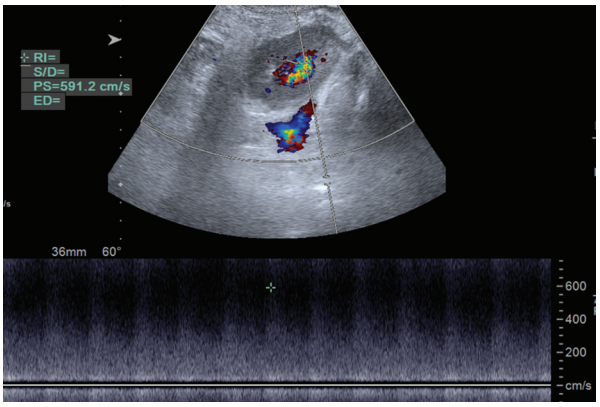

Figure 4. 41-Year-Old Female Patient After Tru-cut Biopsy
Patient has parenchymal lesion with yin-yang sign on Doppler ultrasonography and elevated peak systolic velocity with low resistive index on pulsed Doppler ultrasonography compatible with arteriovenous fistula.

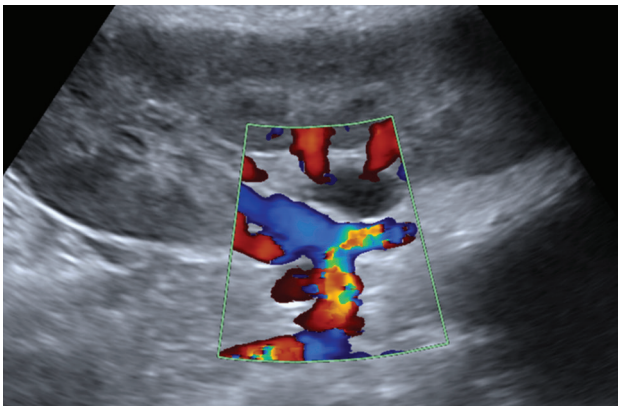

Figure 5. Mild Pelvicaliectasis Due To Enlarged Bladder

Table 6. Causes of Acceptable Pelvicaliectasis After Renal Transplant

Reasons of Mild Pelvicaliectasis
▪ Denervation of transplanted kidney
▪ Predisposition to vesicoureteral reflux
▪ Dependent orientation of renal transplant in iliac fossa
▪ Short ureter
▪ Loss of normal obliquity and submucosal tunnel due to ureteroneocystostomy

COLLECTING SYSTEM COMPLICATIONS

Because of the denervation of the transplanted kidney, elevated serum creatinine levels and decreased urinary output may be the only findings of collecting system complications.[4] Advanced surgical techniques such as preserving ureteral perfusion, using short ureter, and decreasing the dose of steroids can result in decreased incidence of collecting system complications, with rates ranging from 3% to 9%.[5,6,21] The most common complications of the collecting system are urinary obstruction and urine leak.

Urinary obstruction

A normal transplanted kidney may show a mild degree of pelvicaliectasis according to its denervation or vesicoureteral reflux (Figure 5). Renal transplant patients have a predisposition to vesicoureteral reflux because of short ureter and loss of the normal obliquity and submucosal tunnel within the bladder secondary to ureteroneocystostomy[5,22] (Table 6). The bladder must be evaluated with ultrasonography; if there is an enlarged bladder, a postvoid evaluation must be done. Most of these types of complications resolve after voiding. If an enlarged bladder persists after voiding, urinary retention should be considered.

Urinary obstruction occurs within 6 months after transplant. Hydronephrosis is shown in approximately 9.3% of transplant patients.[23] It can be seen because of primary ureteral abnormalities such as ureteral stricture or can occur from external compression from fluid collection.[4] Ischemia or scar tissue can lead to ureteral stricture. During surgery, a ureteral stent is often placed to reduce the urinary obstruction.[5]

During ultrasonography, the collecting system and ureter from the hilum to bladder should be evaluated. Investigations into periureteral fluid collection that can cause mass effects, intraluminal debris, and stones should be performed.[5]

Collecting system complications are higher in pediatric patients than in adults. Patients with a posterior urethral valve have increased risk of vesicoureteral reflux. In pediatric patients, worsening renal function is often the only sign of hydronephrosis and pyelonephritis could be also shown.[6,24]

Urine leak

Urine leaks mostly occur secondary to vascular insufficiency. Leaks are diagnosed in the first 2 weeks after transplant and have an incidence of 1% to 5%.[6,25,26] Urine leaks are commonly seen from the distal ureter because of ischemia; this presentation is followed by leak at the ureteroneocystostomy site due to obstruction or incomplete bladder anastomosis. Upper proximal ureter leaks are less common and are secondary to segmental infarction in patients with accessory renal arteries.[6]

At ultrasonography, leaked urine is seen as an anechoic, well-defined fluid collection mostly adjacent to the lower pole of the transplanted kidney. If the patient's renal function is available, intravascular contrast-enhanced computed tomography with delayed images (images taken 5-20 min after injection of contrast media) can be used to show urine leak.[4,6]

Small defects in the ureter and bladder can be managed with stent replacement and catheter drainage; however, larger defects may require surgery.[4]

PERINEPHRIC FLUID COLLECTIONS

There are 4 types of postoperative perinephric fluid collections: hematoma, urinoma, abscess, and lymphocele. Imaging findings, clinical symptoms, and time from surgery are used for the differential diagnosis of fluid collections; the final diagnosis may be made by percutaneous drainage.[5] Table 7 summarizes the characteristics of perinephric fluid collections.

Hematoma

Hematoma is the most common fluid collection; rates vary from 4% to 8%, mostly during the immediate postoperative period. They may also develop after biopsy or trauma.[6] On ultrasonography, acute hematomas are seen as hyperechoic heterogeneous fluid collections, subacute hematomas often contain hypoechoic clotted blood, and chronic hematomas are seen as hypo-anechoic septated heterogeneous fluid collections.[5] They can be perinephric or subcapsular, and small hematomas usually resolve spontaneously. Large subcapsular hematomas may show mass effect and alter the perfusion of the kidney.[23] Large perinephric and subcapsular hematomas should be drained surgically or percutaneously (Figure 6).

Urinoma

Urinomas from the urine leaks are seen in the first 10 days after transplant and are most commonly found between the kidney and the bladder.[5] On

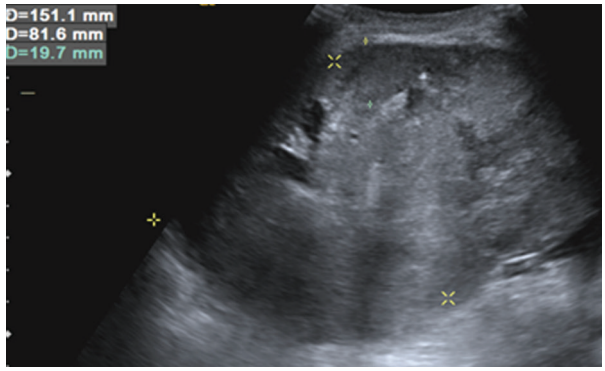

Figure 6. Subcapsular Hematoma After Renal Biopsy

Table 7. Characteristics of Perinephric Fluid Collections

Collection	Time Period	Ultrasonography Findings	Results of Fluid Analysis
Hematoma	First 5 d after transplant or after biopsy	Hyperechoic-heterogeneous fluid collection with septa and clot	Erythrocytes
Urinoma	First 10 d after transplant	Hypoechoic-anechoic simple fluid collection	Fluid creatinine > serum creatinine; fluid potassium> serum potassium
Abscess	First weeks to months after transplant	Hypoechoic heterogeneous fluid collection with irregular thick wall	Purulent material with polymorphonucleocytes
Lymphoma	2 wk to 6 mo after transplant	Anechoic simple fluid collection mostly medial to kidney	Fluid creatinine = serum creatinine; fluid potassium = serum potassium

ultrasonography, urinomas are seen as hypoechoic-anechoic fluid collections that cannot be differentiated from seroma or lymphocele.[5] Creatinine and potassium concentrations in urinomas are higher than those in the blood serum. Obtaining serum creatinine samples at the same time is important[23] (Figure 7).

Abscess

An abscess is a rare complication of renal transplant that is seen within the first weeks to months after transplant.[5,27,28] Abscesses arise as a complication of surgery, complication of pyelonephritis, superinfection of hematoma, urinoma of lymphocele, or infection of abdominopelvic organs or abdominal wall. On ultrasonography, a perirenal abscess is seen as hypoechoic heterogeneous fluid collection with irregular thick wall. On Doppler ultrasonography, increased peripheral blood flow is seen. Peritransplant fluid should be considered as infected in a febrile patient. Patients can also present clinically with pain and pressure on the transplant kidney[13,23] (Figure 8).

Lymphocele

Lymphoceles occur between 2 weeks and 6 months after transplant and are the most common collection resulting in pelvicalyceal dilatation.[13] Incidence ranges from 0.5% to 20%.[23] Lymphoceles result from leakage of lymph from damaged lymphatic vessels or from the lymphatics of the transplanted kidney.[5,29] On ultrasonography, a lymphocele is seen as an anechoic fluid collection, mostly medial to the transplanted kidney, between the kidney and bladder. Most patients are asymptomatic; symptoms are usually seen because of the mass effect. Lymphoceles are rarely seen in the scrotum (Figure 9).

PARENCHYMA ABNORMALITIES

Renal allograft parenchyma complications are delayed graft function, allograft rejection, acute tubular necrosis, and drug toxicity. Ultrasonography is not enough for differential diagnoses.[2]

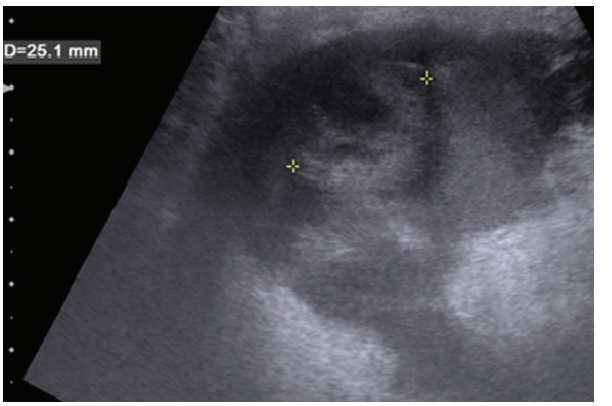

Figure 8. Patient With Pressure on Transplanted Kidney and Fever Has Hypoechoic Heterogeneous Mass With Elevated Vascularity on Ultrasonography Compatible With Renal Abscess

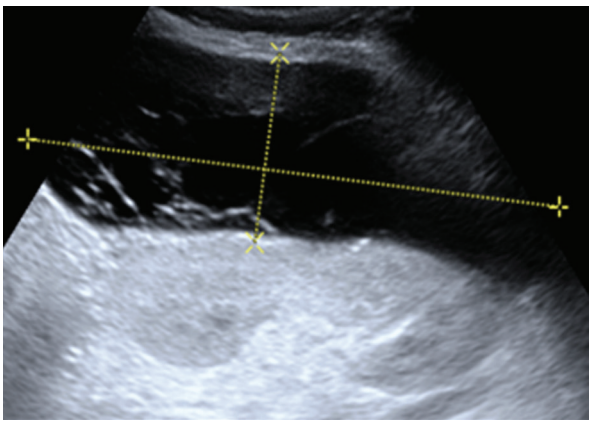

Figure 7. Anechoic Fluid Collection (130 x 50 mm) Anterior to the Kidney After Drainage, With Laboratory Results Compatible With Urinoma

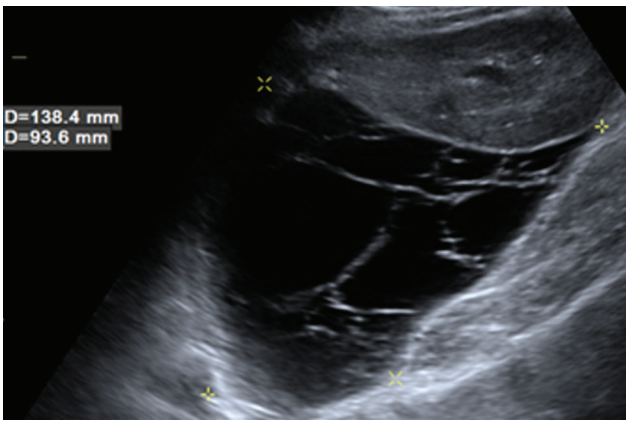

Figure 9. Septated Anechoic Collection After Drainage Laboratory Results Was Compatible With Lymphocele

Delayed graft function

Delayed graft function is defined as the need for hemodialysis in the first week after renal transplant. The greatest risk factor is cold ischemia time; other factors include rejection, acute tubular necrosis, and fluid collection.[23,30] Grayscale ultrasonography usually shows results that are within normal limits. On Doppler ultrasonography, elevated RI, which is a nonspecific finding, can be seen.[5]

Renal allograft rejection

Hyperacute rejection is a rare complication that can occur within minutes and is identified during surgery; nonperfusion of the transplant kidney and ischemia are seen immediately after the vascular anastomosis due to small vessel thrombosis.[2,5,23] When this occurs, the transplanted kidney is removed.

Acute rejection can be the result of T-cell activation, occurring between 1 and 3 weeks after transplant. Advances in immunotherapy have decreased the incidence of acute rejection over the years,[5,31] with incidence between 10% and 37%.[2] Clinical symptoms are graft swelling, tenderness, oliguria, fever, and increased laboratory serum creatinine levels. On grayscale ultrasonography, swelling and enlargement of kidney, heterogeneity of renal cortex, thickening of the renal cortex, loss of corticomedullary differentiation, and thickening of the pelvicalyceal system walls can be seen.[23] Ultrasonography findings are nonspecific and can be totally normal. On Doppler ultrasonography, increased intraparenchymal arterial RI is seen[5,32] (Figure 10). Increased intraparenchymal RI is a nonspecific finding, and rejection and other allograft dysfunction cannot be distinguished by use of RI alone. Pathologies with RI increase are given in Table 8. The definitive diagnostic method is ultrasonography-guided biopsy.[5]

Chronic rejection is seen months to years after transplant and results in late graft loss. Patients present with renal function abnormality and hypertension. The ultrasonography and Doppler findings are nonspecific; on ultrasonography, small kidneys with thin cortex, increased cortical echoge-

Table 8. Transplant Kidney Pathologies With Increased Intraparenchymal Resistance Index

Elevated Intraparenchymal Resistance Index
▪ Acute rejection
▪ Chronic rejection
▪ Acute tubular necrosis
▪ Cyclosporine toxicity
▪ Ureteral obstruction
▪ Mass effect on the allograft (from perinephric fluid collection)
▪ Renal vein thrombosis

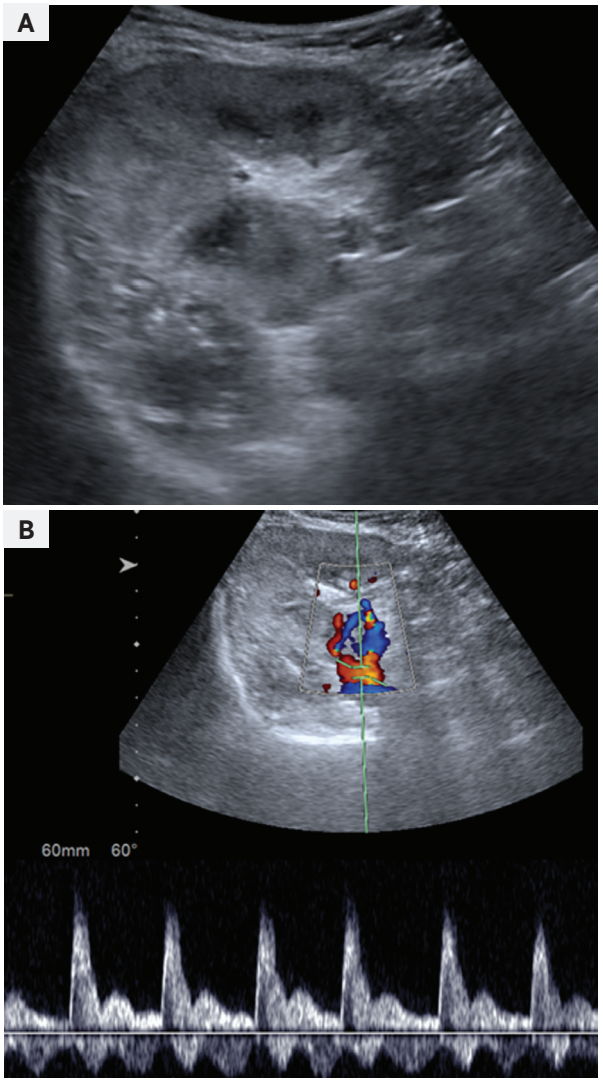

Figure 10. Patient With Acute Rejection

(A) Edematous kidney. **(B)** Increased intraparenchymal resistive index.

nicity, cortical lobulation, and mild hydronephrosis can be seen.[2,4] On Doppler ultrasonography, decreased vascularity of the transplanted kidney and increased intraparenchymal arterial RIs can be seen[5] (Figure 11).

Acute tubular necrosis

Acute tubular necrosis is an early postoperative (within the first 2 weeks) complication that causes renal allograft dysfunction.[2] The ultrasonography and Doppler findings are nonspecific and cannot be differentiated from acute rejection or drug-related nephrotoxicity.[5] The definitive diagnostic method is ultrasonography-guided biopsy.

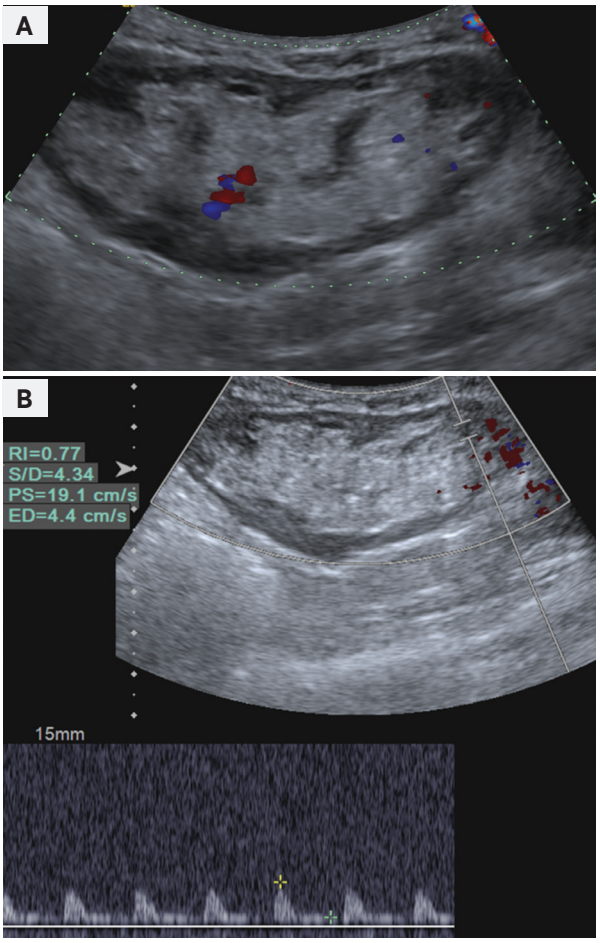

Figure 11. Patient With Chronic Rejection

On grayscale ultrasonography, kidney showed increased cortical echogenicity and decreased cortical thickness, with decreased vascularity on Doppler ultrasonography **(A)** and increased resistive index **(B)**.

Drug-related nephrotoxic effects

Calcineurin inhibitors are used in renal transplant immunosuppression. Cyclosporine, a calcineurin inhibitor, is nephrotoxic and causes a reduction in renal function.[5,33] The imaging findings of cyclosporine toxicity are nonspecific, and serum cyclosporine level and ultrasonography-guided biopsy are definitive diagnostic methods.[34]

INFECTION

Renal transplant patients have risk of infection greater than those in the normal population because of immunosuppression and donor-related infections. During postoperative month 1, infections are related to surgery. From the second to the sixth month, infections are opportunistic and occur because of immunosuppression. Cytomegalovirus and Epstein-Barr virus are the most common agents for infections.[5]

In the first year after transplant, acute pyelonephritis can be seen in up to 13% of patients. Female sex, history of prior urinary infections, diabetes mellitus, and urinary catheters are risk factors for pyelonephritis. In most cases, ultrasonography is normal; thickening of the pelvicalyceal system walls may be the only finding and is often nonspecific. Pathologies that can occur with pelvicalyceal system wall thickening are shown in Table 9. In some cases, diffuse or focal enlargement of the kidney, focal wedge-shaped hypoechoic areas, and focal wedge-shaped hypovascular areas may be seen. Evaluations of the pelvicalyceal system for the presence of any echogenic debris, pyonephrosis, and fungus ball with ultrasonography are important[5,23] (Figure 12).

Table 9. Allograft Pathologies That Accompany Pelvicalyceal System Wall Thickening

Pelvicalyceal System Wall Thickening
▪ Acute rejection
▪ Hydronephrosis
▪ Ischemia
▪ Ureteral stent
▪ Infection

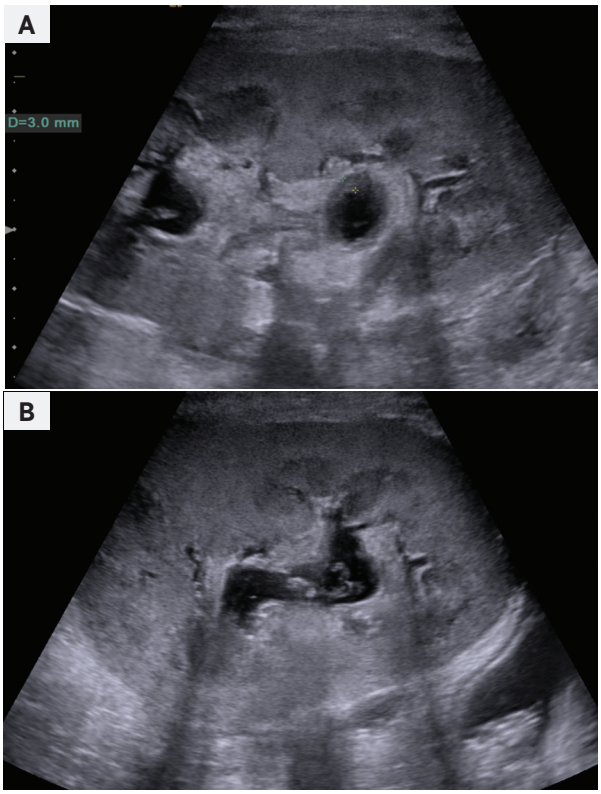

Figure 12. Patient With Pain, Fever, and Leukocytosis
(A) Thickening of the pelvicalyceal system wall. **(B)** Dilatation of pelvicalyceal system and debris.

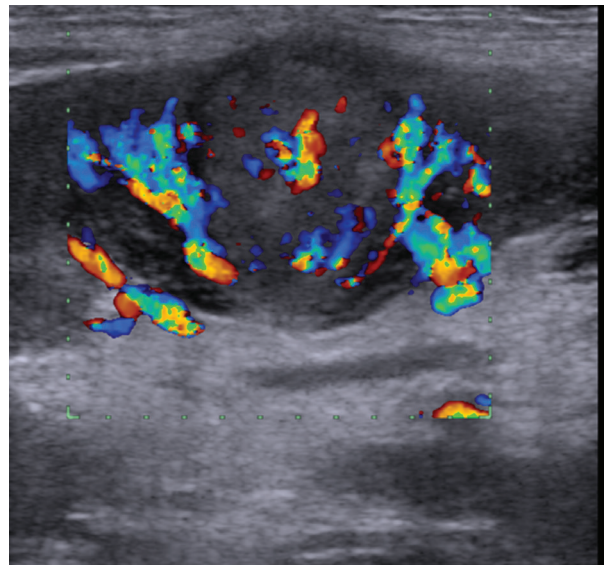

Figure 13. 55-Year-Old Male Patient With Incidental Renal Parenchymal Mass and Increased Vascularity
After surgery, pathology showed renal cell carcinoma.

NEOPLASTIC COMPLICATIONS

The risk of malignancy in transplant patients is 3 to 5 times higher than in the normal population.[5] New malignancy, recurrent malignancy in the recipient, and donor-related malignancy may occur. Recipients have an increased risk of non-Hodgkin lymphoma and non-melanoma skin cancers.[23,35] Renal cell carcinoma may occur in native kidneys as a result of hemodialysis duration and may occur in the allograft. Ultrasonographic evaluation of both the native and the transplanted kidney is important. Allograft renal cell carcinoma can be multifocal. Lesions are seen as hypoechoic masses with increased vascularity on ultrasonography (Figure 13).

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Computed Tomography Imaging: Complications of Renal Transplantation

K. Murat Haberal

Renal transplant is the preferred treatment for patients with end-stage renal disease. Advances in surgical technique, perioperative management, and immunosuppressive regimens have led to improved outcomes and patient survival rates.[1] Despite these advances, complications still occur (Table 1). Urologic complications occur in 4% to 8% of patients, and vascular complications occur in approximately 1% to 2% of patients.[2] Complications can be divided into nephrological, urological, vascular, and systemic complications or either can be divided into vascular and nonvascular categories. Nonvascular complications can be further divided into surgical and medical categories. Vascular complications include renal artery stenosis, infarction, arteriovenous fistulas, pseudoaneurysm, and renal vein thrombosis. Nonvascular complications include ureteral obstruction, urine leak, peritransplant fluid collections (hematomas, lymphoceles, abscesses, and infection), neoplasms, gastrointestinal and herniation complications, and posttransplant lymphoproliferative disorder (PTLD).[3-5]

Most complications occur at specified time intervals related to surgery, with posttransplant complications characterized as either early or late. Early complications appear in the first weeks after transplant and are usually attributable to surgical difficulties. Late complications appear some weeks after the procedure and are usually due to medical problems, such as those related to immunosuppression and toxicity. Early complications include acute rejection, acute tubular necrosis, hematoma, pyelonephritis, abscess, urinoma and ureteral obstruction, and vascular complications (eg, arterial stenosis and thrombosis, arteriovenous fistula and arterial pseudoaneurysm, renal vein thrombosis, graft torsion). Late complications include chronic rejection, other causes of ureteral obstruction, lymphocele, cyst, renal cell carcinoma, and transitional cell carcinoma of the graft and include complications due to immunosuppression (eg, lymphoma,

Table 1. Renal Transplant Complications

Vascular	Renal artery stenosis Renal artery occlusion Renal vein stenosis Renal vein thrombosis Complications of interventional procedures Arteriovenous fistula Pseudoaneurysm External iliac artery dissection Torsion
Urologic	Urine leak Obstruction Nephrolithiasis
Peritransplant collections	Lymphocele Hematoma Urinoma Abscess
Nephrologic	Rejection (hyperacute, acute, chronic) Delayed graft function Drug toxicity
Systemic	Infections Malignancy Hypertension Posttransplant lymphoproliferative disease

Kaposi sarcoma, opportunistic infections involving the transplanted kidney).[6]

Noninvasive imaging techniques, such as ultrasonography, computed tomography (CT), and magnetic resonance imaging, have developed considerably in recent years, allowing improved detection of vascular and nonvascular diseases in renal transplantation. Although ultrasonography and Doppler ultrasonography are the initial imaging methods for evaluating the transplanted kidney, CT is complementary in indeterminate cases.[7]

Computed tomography scans include 3 or 4 phases; precontrast series are used for depicting kidney stones and also for differentiating the nature of the perirenal collection. Series after intravenous contrast administration can be divided into early (after 20-25 s) for arterial phase and late (after 60-90 s) for corticomedullary phase. Both renal vein and artery can be evaluated at the same phase, and renal lesions (cysts, solid lesions), active bleeding, and the patency of renal arterial and venous vasculature can be depicted. Late series (scans performed 5 min after intravenous contrast administration) are used to depict pyeloureteral complications, such as urine leakage and urethral obstruction.[6,8] Administration of intravenous contrast material should be avoided in individuals with impaired renal function because of the risk of developing contrast-induced nephropathy.[9]

With unenhanced CT, the renal parenchyma demonstrates homogeneous soft tissue attenuation. Contrast material-enhanced arterial-phase CT is used to evaluate the renal graft artery and the iliac arterial system. In this phase, the cortex appears hyperattenuating and the medulla remains hypoattenuating because the contrast material has not reached it yet. Venous-phase (tubular nephrogram-phase) CT, the period when normal parenchyma is uniformly enhanced, is useful for demonstrating parenchymal masses. Late excretory-phase (pyelogram-phase) CT is used to evaluate the pyeloureteral system and demonstrates hypoattenuating, heterogeneous renal parenchyma and contrast material filling of the collecting system. To evaluate vascular and pyeloureteral anatomy in detail, postprocessing techniques, multiplanar and 3-dimensional maximum-intensity projection, shaded-surface display, and volume-rendered reformatted images can be obtained.

VASCULAR COMPLICATIONS

Renal artery stenosis/occlusion

The most common vascular complication is renal artery stenosis, with an estimated incidence of 19% to 23% in all transplant recipients.[10,11] In our centers, the rates are 0.5% to 0.75% (Figure 1).[12] This complication frequently appears with worsening or refractory hypertension, with or without graft dysfunction, in the absence of rejection, ureteric obstruction, or infection. Different locations and timing of disease onset may reflect different causes. For example, an anastomotic stenosis is most likely related to trauma to the donor or recipient vessels during retrieval, clamping, or suturing and usually arises early after transplant.

The complication of renal artery thrombosis usually occurs soon after the transplant procedure. It is destructive, usually resulting in graft loss, and its incidence is reportedly 0.2% to 7.5% or 0.5% to 3.5%.[12-15] The most important signs of renal artery thrombosis are instantaneous cessation of urine output, due to the absence of graft perfusion, and the presence of worsening hypertension. In preemptive patients and patients with preoperative urine output, this sign is masked, and postoperative bedside Doppler ultrasonography is recommended.[16] The most common causes of renal artery thrombosis are technical issues, such as a faulty suture technique producing an incomplete intimal reapproximation with secondary intraluminal fibrosis. Other factors predisposing to thrombosis are kinking or twisting of the renal artery, postoperative hypotension, a hypercoagulable state, atherosclerosis of the donor's or recipient's vessels, a wide disparity in vessel size, increased intrarenal pressure resulting from acute tubular necrosis, hydronephrosis, and cellular rejection.[4] Contrast CT shows absent nephrogram.

Renal vein thrombosis/stenosis

Renal vein thrombosis usually occurs within

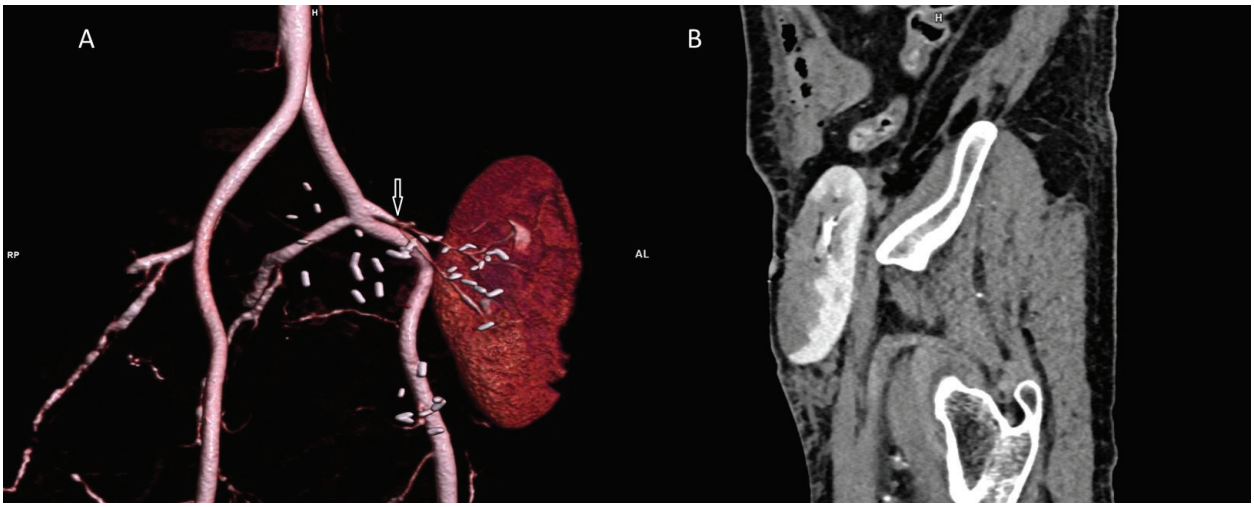

Figure 1. Renal Artery Stenosis

(A) Volume rendering technique image shows patency of the transplanted renal artery. There is diffuse narrowing after the proximal part from the anastomosis (white arrow). **(B)** Sagittal multiplanar planar reconstruction image; hypodense area is seen as an infarction in the anterior part of the transplanted kidney.

the first 7 days after transplant. The incidence of renal vein thrombosis ranges from 0.55% to 4% and usually causes early graft loss.[14] The clinical presentations of this condition are sudden oliguria or anuria accompanied by pain, hematuria, and life-threatening hemorrhage due to graft rupture.[17] If contrast-enhanced CT imaging is performed, non-opacification of the transplant main renal vein is seen with thrombus within it (Figure 2).

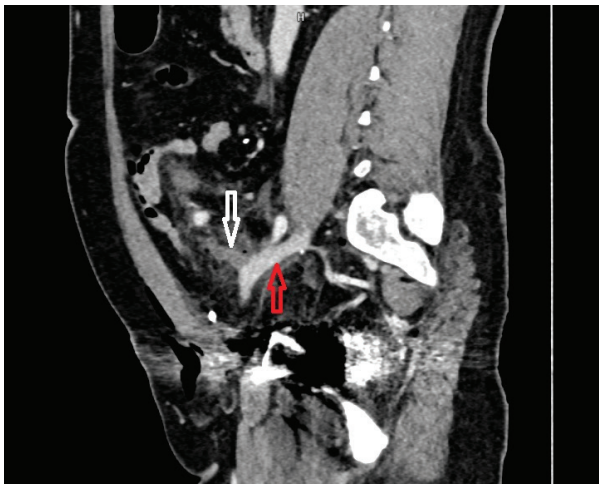

Figure 2. Renal Vein Thrombosis/Stenosis

Sagittal multiplanar planar reconstruction computed tomography shows common iliac vein (red arrow) and transplanted kidney renal vein (white arrow). The transplanted main renal vein is seen with thrombus within it.

RARE VASCULAR COMPLICATIONS

Pseudoaneurysms or arteriovenous fistulas may form as a complication of renal transplant biopsy.[18] The prevalence of extrarenal arterial pseudoaneurysm following renal transplantation is less than 1%. Extrarenal pseudoaneurysm is directly related to arterial anastomosis surgery and, rarely, to infectious causes. It is usually asymptomatic, but it can occasionally cause renal dysfunction or compression of adjacent structures.[6] Computed tomography scans show pseudoaneurysms as hypoattenuating (noncontrast) or hyperattenuating (contrast-enhanced) smooth-walled sacs adjacent to an artery, usually with a communication.[19] Computed tomography angiography may demonstrate arteriovenous fistulas as the anomalous renal arteriovenous communication with associated aneurysms and early opacification of the renal vein on the arterial phase.

Traumatic external iliac artery dissection following renal transplant is a rare complication, but it should be managed urgently due to its devastating effect on

graft and lower limb circulation. This complication is seen more often in recipients with diabetes mellitus and comorbid diseases.[4]

Torsion of the renal graft is a rare surgical complication that usually occurs in children with intraperitoneal transplants. Torsion occurs when the kidney rotates around the vascular pedicle, leading to vascular occlusion and parenchymal infarction.[20] Renal torsion can be an early or late complication. Prompt diagnosis permits graft detorsion and possible salvage. The most suggestive imaging finding is a change in the axis of the transplanted kidney. Both CT and magnetic resonance imaging can show changes in renal graft orientation and vascular pedicle kinking or secondary changes, such as swelling or abnormal enhancement of the graft, hydronephrosis, and sinusal and perirenal fat infiltration. Torsion may be incomplete and intermittent.[6]

UROLOGICAL COMPLICATIONS

Urine leak/urinoma/obstruction

Urologic complications after renal transplant occur in 2.6% to 13% of patients. Ureteral extravasation producing urinoma can be caused by graft rejection, ureteral necrosis due to ischemia, or inadequate surgical technique. Urine leaks usually occur in the second or third postoperative week and require surgical or percutaneous intervention. With unenhanced CT, urinoma manifests as a hypoattenuating collection. If the patient's renal function allows, contrast-enhanced CT imaging with acquisition of delayed images (5-20 min after injection of contrast material) can be used to noninvasively establish a diagnosis of urine leak because the excreted contrast material is a visible accumulation in the collection.

Urinary obstruction may be primary or secondary. Primary urinary obstruction is defined as an obstruction related to a primary collecting system stricture. Secondary urinary obstruction is caused by extrinsic compression, most commonly by a fluid collection or crossing vessel. Ureteral strictures occur in 2.6% to 6.5% of transplant recipients. Primary ureteral obstruction may present early in the recovery period if related to anatomic or technical factors. In comparison, ureteral obstruction related to ischemia becomes clinically evident at a median of 6 months. The use of CT with 3-dimensional image reformatting allows accurate imaging of the entire course of ureteral and periureteral diseases.[6]

Nephrolithiasis

Nephrolithiasis is seen in approximately 1.6% of renal transplant recipients.[21] Patients with kidney transplants are at higher risk of development of hypercalcemia because of disequilibrium of vitamin D and calcium metabolism. Renal calculi can also be donor derived, particularly in deceased-donor kidneys, and stones can be seen on early post-transplant ultrasonography. Clinically, obstructing stones may impair renal function. Unenhanced CT is a sensitive method for detection of renal calculi and will show a hyperattenuating focus within the transplanted kidney or ureter.[3]

PERITRANSPLANT COLLECTIONS

Postoperative fluid collections are common after transplant and include lymphoceles, hematomas, abscesses, and urinomas. The clinical significance of these collections is largely determined by their size, location, and possible growth. In the immediate postoperative period, small hematomas or seromas manifesting as crescentic peritransplant collections are almost expected. Their size should be documented at baseline examination, since any increase in size may warrant intervention. Growing collections may indicate a urine leak, abscess, or vascular injury. Different types of peritransplant fluid collections can be partially differentiated based on the time interval after transplant. Urinomas and hematomas are most likely to develop immediately after transplant, whereas lymphoceles generally occur 4 to 8 weeks after the surgical procedure.[21] The majority of these collections can be detected with ultrasonography, but their sonographic characteristics are entirely nonspecific. Computed tomography often delineates fluid collections and their anatomic relationship to adjacent structures better than ultrasonography, particularly in obese patients. In addition, puncture and drainage can

be performed with CT guidance in cases in which ultrasonography is inadequate for indicating access to the collection.

Lymphocele

Lymphoceles are the most common peritransplant fluid collection, with a prevalence of 0.5% to 20%. Lymphoceles form from leakage of lymph from the recipient's lymphatic channels. These fluid collections usually occur medially to the transplant, between the graft and the bladder.[21] With CT imaging, lymphoceles appear as well-circumscribed areas of simple fluid attenuation (< 10 HU at CT) (Figure 3).

Hematoma

Peritransplant hematomas are common in the early posttransplant period. A CT scan will show perinephric hematomas as fluid collections with attenuation values that vary depending on the acuity of the hematoma; however, the attenuation will usually be greater than 30 HU (Figure 4).[7]

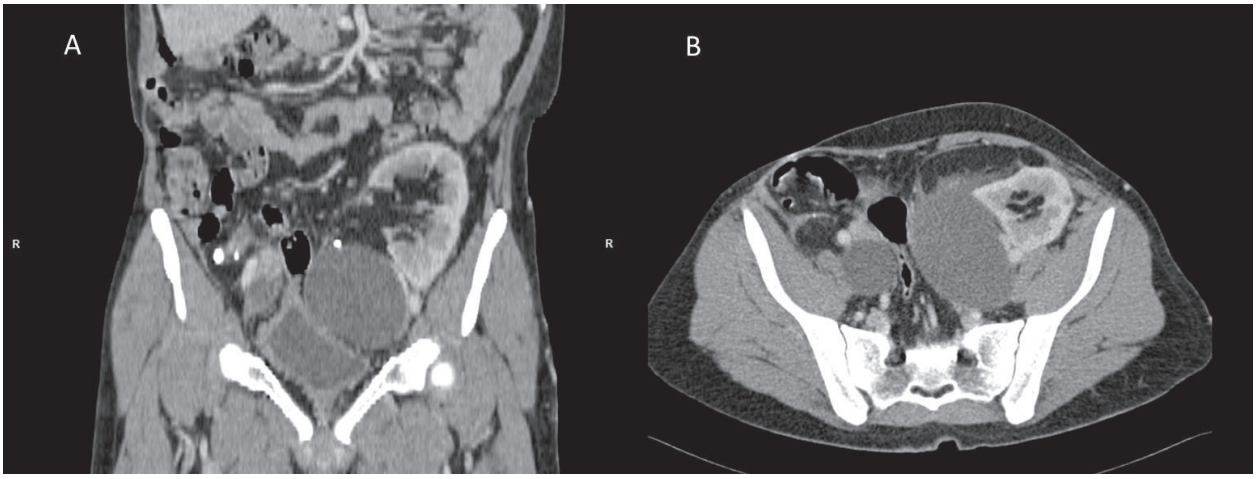

Figure 3. Lymphoceles

Portal venous phase coronal **(A)** and axial **(B)** computed tomography images show lymphoceles as well-circumscribed areas of simple fluid attenuation medial of the transplanted kidney.

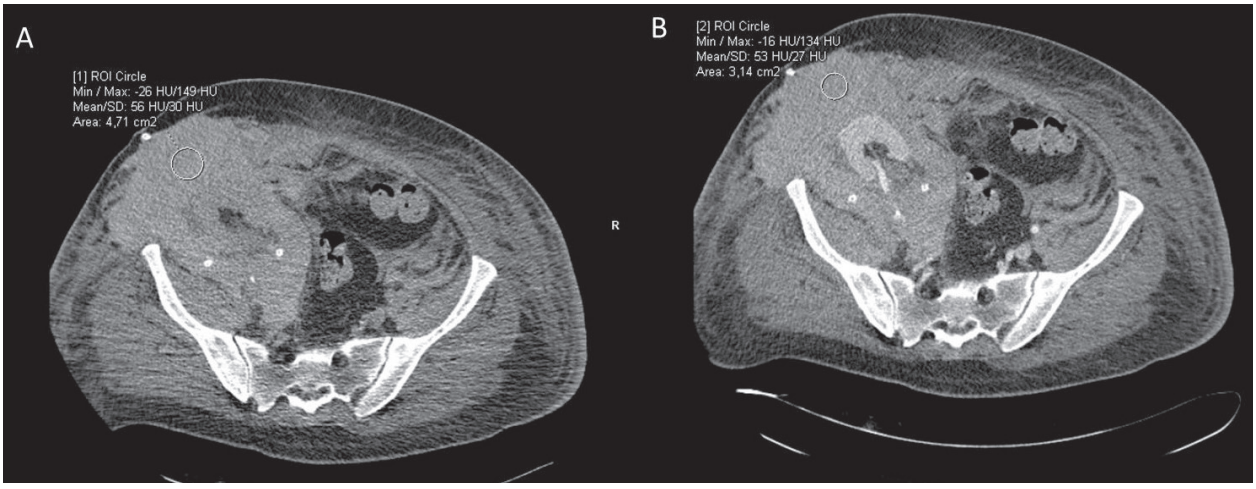

Figure 4. Hematoma

Precontrast **(A)** and late-phase **(B)** axial computed tomography images show high-density (> 30 HU) peritransplant fluid collections as perinephric hematomas. Lack of increased density in the late phase excludes active bleeding.

Peritransplant hematomas should be distinguished from subcapsular hematomas. Subcapsular hematomas may occur after trauma or transplant biopsy. Subcapsular hematomas appear as an area of blood products that exert mass effects on the underlying renal parenchyma (Figure 5). This mass effect may result in hypertension. Subcapsular hematomas typically resolve on their own.[22]

Abscess

Abscesses are an uncommon complication of renal transplant. When they occur, they usually manifest during the first few weeks posttransplant. Clinically, patients may present with pain and tenderness in the region of the transplanted kidney, fever, and signs of sepsis. Abscesses may develop as a surgical complication, as a consequence of superinfection of an existing peritransplant fluid collection, or as a complication of pyelonephritis.[3] On CT, abscesses are a hypoattenuating fluid collection. They may contain areas of hyperattenuation corresponding to internal debris and/or blood product. On intravenous contrast-enhanced scans, peripheral rim-like enhancement may be present. Sometimes there will be the foci of gas within the fluid collection, which could be from the abscess; however, in the immediate postoperative state, hemostatic agents such as Surgicel can also have a similar appearance.[3]

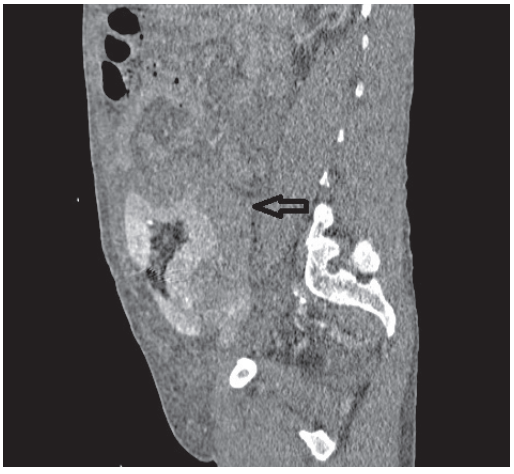

Figure 5. Subcapsular Hematoma Resulting From Renal Laceration (not shown) Products Exerting Mass Effect on the Underlying Renal Parenchyma

NEPHROLOGIC COMPLICATIONS

Renal parenchymal complications include delayed graft function, acute tubular necrosis, rejection (hyperacute, acute, or chronic), and damage caused by nephrotoxic drugs. When rejection is being considered, CT is rarely performed. The CT appearance of rejection and acute tubular necrosis are similar and nonspecific. In both pathologic conditions, CT demonstrates decreased graft enhancement with no contrast material excretion (Figure 6). The role of imaging is to rule out other potentially treatable causes of renal transplant dysfunction, including vascular and collecting system abnormalities. Transplant biopsy may be performed to establish a diagnosis.

Chronic rejection occurs months to years after transplant and is due to sclerosing vasculitis and extensive interstitial fibrosis. In the beginning stages of chronic rejection, the graft is enlarged and shows increased cortical thickness, which later changes to a thin cortex and mild hydronephrosis.[3,7]

SYSTEMIC COMPLICATIONS

Infections

After transplant, patients may present with increased infections as a result of immunosuppression. Acute pyelonephritis can be seen in up to 13% of patients within 1 year after renal transplant.[23] On intravenous contrast-enhanced CT, pyelonephritis of the renal allograft will have the same appearance as pyelonephritis occurring in native kidneys. Wedge-shaped areas of hypoperfusion or a striated nephrogram may be seen (Figure 7).[24] The kidney may be focally or diffusely enlarged, and there may be perinephric stranding. Most importantly, the role of imaging is to identify perinephric fluid collections or abscesses that could require percutaneous drainage.

Other infections include opportunistic pulmonary infections such as *Pneumocystis carinii*, tuberculosis, and fungal infections. High-resolution thorax CT can provide useful information and suggest a diagnosis in renal transplant patients with pulmonary infection.[25]

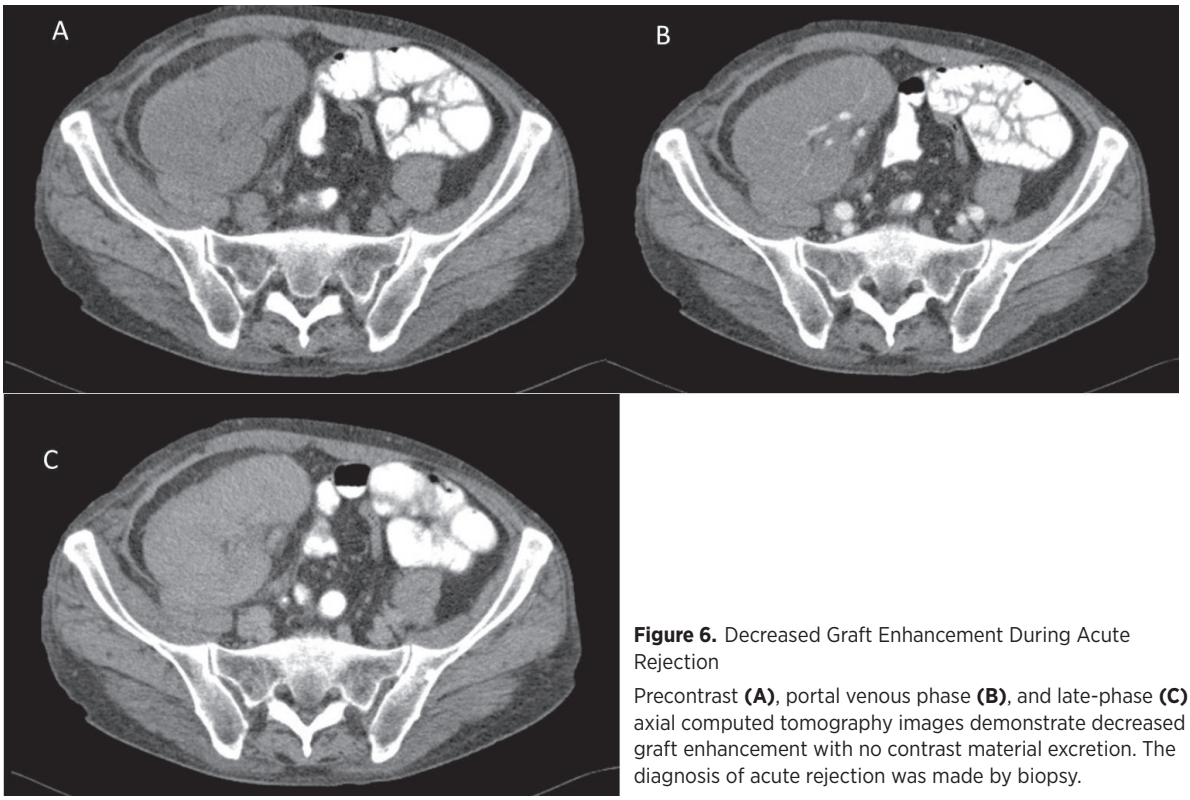

Figure 6. Decreased Graft Enhancement During Acute Rejection

Precontrast **(A)**, portal venous phase **(B)**, and late-phase **(C)** axial computed tomography images demonstrate decreased graft enhancement with no contrast material excretion. The diagnosis of acute rejection was made by biopsy.

Malignancy/posttransplant lymphoproliferative disorder

Immunocompromised patients have a higher prevalence of malignant neoplasms, the most common of which are neoplasms of the skin, cervix, and rectum; Kaposi sarcoma; and lymphoma.[6]

Posttransplant lymphoproliferative disorder is associated with Epstein-Barr virus and occurs in approximately 1% of renal allograft recipients.[26] Presentation of PTLD can range from a relatively benign lymphoid hyperplasia to aggressive lymphoma. At imaging, PTLD may appear as a solid mass or multiple masses with or without associated lymphadenopathy.

When CT demonstrates an infiltrating lesion in the sinus, the differential diagnosis should include lymphoma, sarcoma, transitional cell carcinoma, and postoperative fibrosis.

Hypertension

Hypertension can occur as a result of renal artery stenosis, chronic rejection, and primary disease affecting the native kidney and is a side effect of cyclosporine.[27]

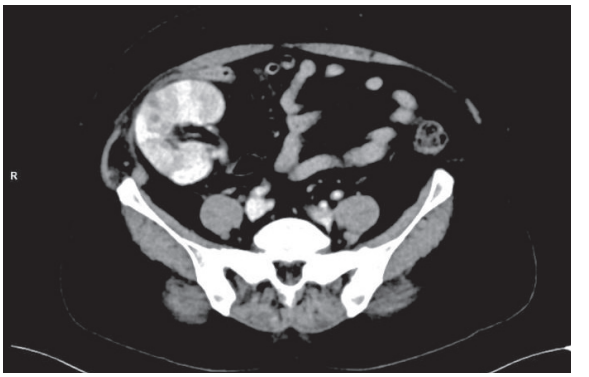

Figure 7. Portal Venous Phase Axial Computed Tomography Image Showing Wedge-Shaped Area of Hypoperfusion

SUMMARY

Many treatable renal transplant complications are diagnosed with imaging. Doppler ultrasonography is the imaging modality of choice to evaluate vascu-

lar patency, the collecting system, and perinephric fluid collections. Computed tomography can be used to depict parenchymal, perirenal, renal sinus, pyeloureteral, and vascular complications and plays a complementary role when ultrasonography is inconclusive. Accurate diagnosis of renal transplant complications is important because many complications are potentially treatable with early detection.

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Vascular Complications After Kidney Transplantation

Aydıncan Akdur,
Emre Karakaya

Since Murray and associates performed the first successful organ transplant between twins in 1954, the field of kidney transplantation has evolved considerably. Kidney transplant plays an important role in the treatment of end-stage renal disease, improving the quality of life and prolonging life itself. Despite surgical and medical advances, vascular complications are still among the major concerns faced after renal transplant, with a reported incidence of 3% to 15%.[1] Prophylactic correction during preoperative evaluation can obviate many problems; however, technical mishaps should be prevented at all stages of the transplant process, and careful postoperative monitoring is warranted. To minimize mortality and morbidity, all complications must be diagnosed early and managed appropriately.

Vascular complications can result from renal graft vessels (renal artery thrombosis, renal vein thrombosis), the native vessels (iliac artery thrombosis, pseudoaneurysms, deep venous thrombosis), or both.[2,3]

Vascular and hemorrhagic complications are related to various factors. These factors are dependent on donor or graft state (including living or deceased donor, organs retrieved from transplant pools, donor age, side of the graft, etc.), recipient conditions (including underlying diseases, recipient age, transplant site, etc.), or surgery (including hemodynamic stability, surgeon's experience, technical difficulties, etc.).[2]

Refinement of the operative technique for kidney transplant has greatly reduced rates of surgical complications, morbidity, and mortality in recipients. In particular, significant progress has been made with regard to methods of vascular anastomosis. The introduction of the Carrel patch vascular technique by Alexis Carrel in 1902 is considered one of the most important steps in transplant surgery.[3] Some vascular complications associated with renal transplant procedures can be managed with percutaneous techniques. Others call for urgent surgical intervention because of possible graft loss if treatment is not swift and appropriate. The incidence of vascular complications has been reported to be as high as 30% during early stages of transplant development, whereas, currently, the incidence rate is 0.8 to 6%.[4]

According to Clarke and associates,[5] 1 patient survived the removal of pulmonary embolus and complication of the vena cava for 2 months, during which the kidney functioned; however, at necropsy, the renal vein was occluded by a thrombus, which extended to its smaller branches. Another group (Smellie and associates[6]) attempted to visualize the renal vein by venography in 3 transplant recipients. In all 3 patients, the renal vein was thought to be patent, although only its terminal portion was demonstrated as such. Clarke and associates[5] also described arterial complications but did not mention thrombosis of the renal vein. In another study, Khastagir and associates[7] described 2

patients who developed thrombosis of the renal vessels as part of the rejection process, although the investigators did not specifically describe the renal veins. Finally, Owen and associates[8] suggested that, if diagnosed early enough, it was worthwhile to explore thrombosed anastomosis but that it was not often possible to obtain a viable kidney.

ARTERIAL COMPLICATIONS

Significant progress has been made with methods of vascular anastomosis. The introduction of the Carrel patch vascular technique by Alexis Carrel in 1902 is considered one of the most important steps in transplant surgery.[2] Some vascular complications associated with renal transplant procedures can be managed with percutaneous techniques. Others call for urgent surgical intervention because of possible graft loss if treatment is not swift and appropriate. The incidence of vascular complications has been reported to be as high as 30% during early stages of transplant development; currently, the incidence rate is 0.8% to 6%.[3]

In Turkey, the first living-donor kidney transplant was performed by Haberal and his team on November 3, 1975. Since then, Haberal has described different vascular anastomosis techniques. Between November 1993 and December 2003, he performed end-to-side or end-to-end anastomoses using the 4-quadrant running suture technique.[9] In early 2004, he defined the corner-saving renal artery anastomosis technique[10] (Figures 1 and 2). His group has reported arterial complication rates of 0.35% for thrombosis and 0.7% for stenosis.[10]

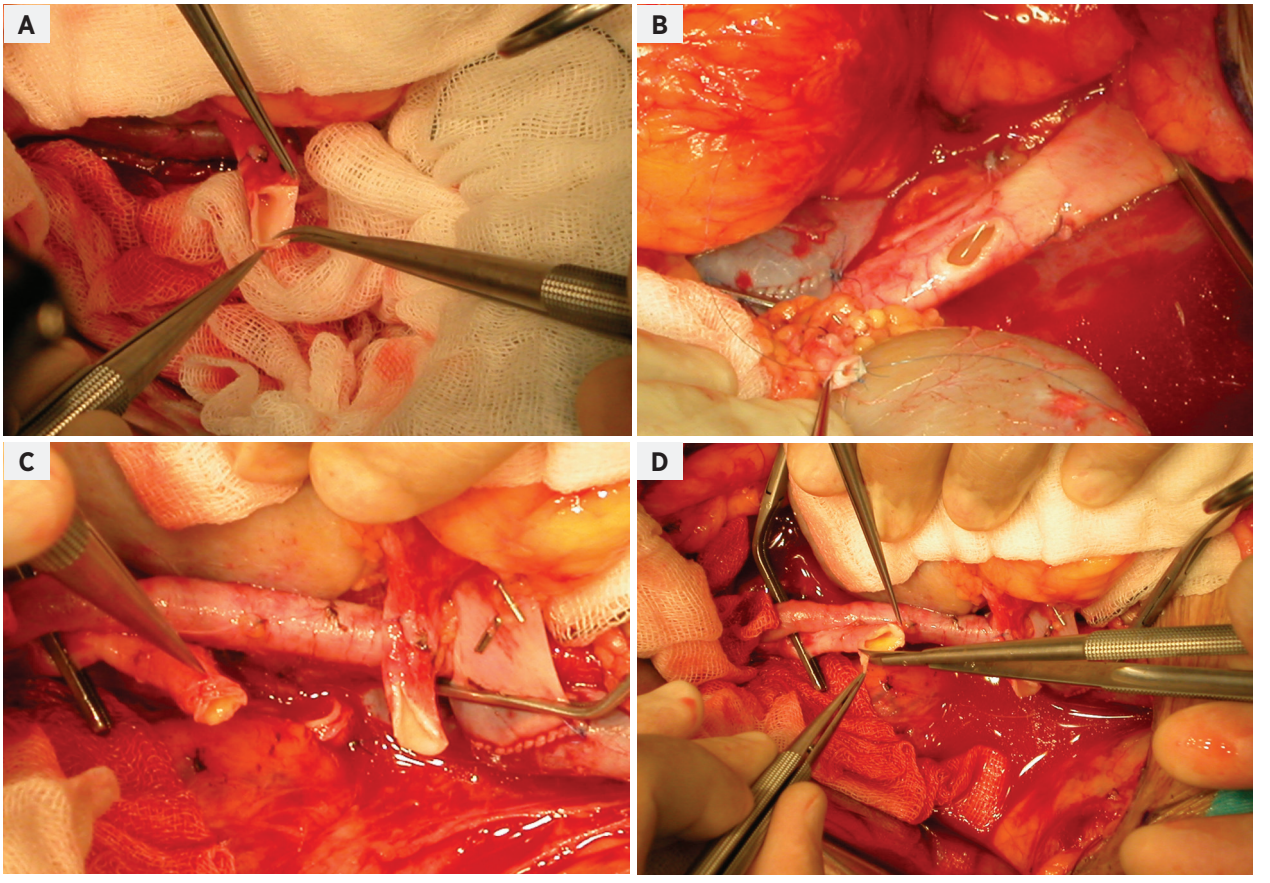

Figure 1. Preparation of Renal Artery and Iliac Arteries for Anastomosis

(A) Spatulating of renal artery. **(B)** Preparation of external iliac artery. **(C)** Preparation of internal iliac artery. **(D)** Spatulating of internal iliac artery.

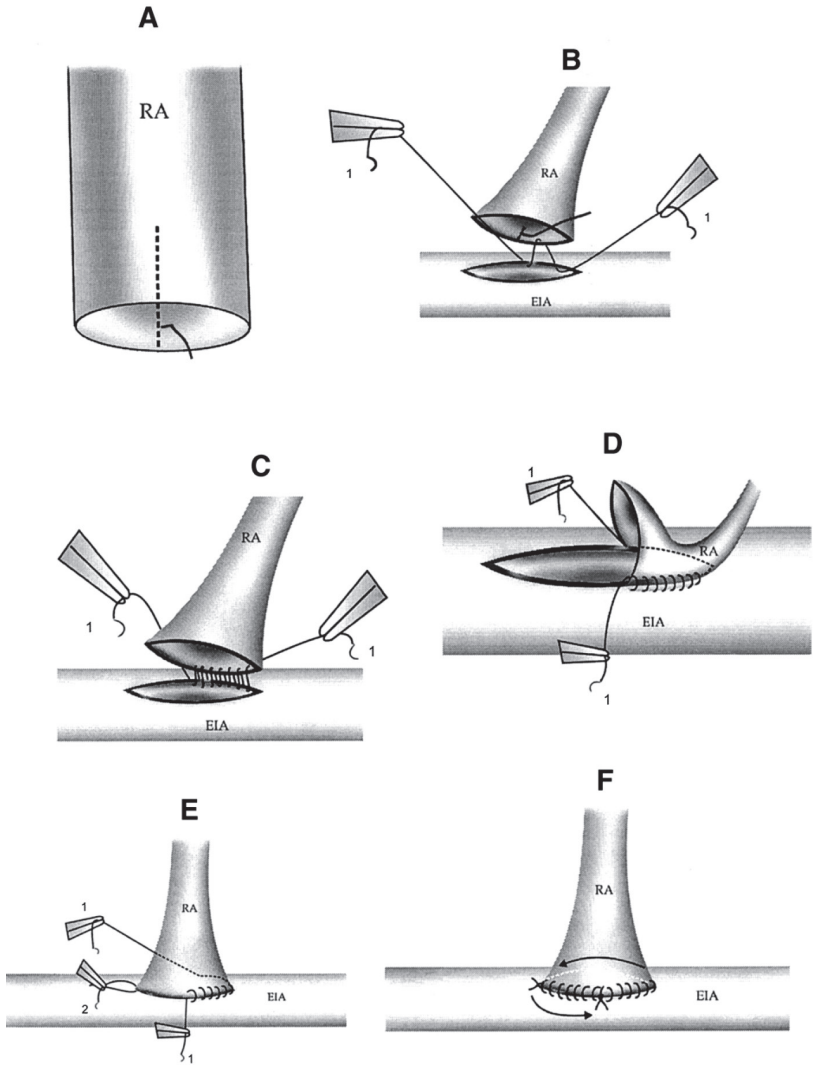

Figure 2. Corner-Saving Renal Artery Anastomosis Technique

(A) The posterior wall of the renal artery (RA) is spatulated. A running suture (number 1) is made beginning 3 mm ahead of the middle of the posterior walls of the renal artery and the external iliac artery (EIA) **(B)**, finishing at the anterior walls of the renal and external iliac arteries **(C)**. **(D)** After the last stitch, both ends of the suture material are pulled to decrease the excess, and the posterior walls of the renal and external iliac arteries are approximated tightly. **(E)** One retraction suture (number 2) is placed at the anterior corner of the external iliac and renal arteries. **(F)** The remaining wall is sewn with the same suture..

INTRAOPERATIVE COMPLICATIONS OF EXTERNAL ILIAC ARTERIAL DISSECTION

Traumatic external iliac artery dissection (EIAD) after renal transplant is a rare complication, but it should be treated immediately because of its devastating effects on graft and lower limb circulation. External iliac artery dissection is seen more in recipients with diabetes mellitus and comorbid diseases. Vascular atherosclerosis and cardiomyopathy are predisposing factors for EIAD. In addition to senility, hypertension, dyslipidemia, smoking, and diabetes, many other risk factors (like anemia, microalbuminemia, and oxidative stress) may play a role in EIAD in patients with end-stage renal disease.[11,12] External iliac artery dissection after renal transplant appears with hypertension,

sudden pain in lower limbs without pulse, oliguria, or anuria. Blood flow in the graft artery and femoral artery cannot be visualized by Doppler ultrasonography. Recipients with EIAD should be treated immediately by percutaneous angioplasty or surgical reconstruction. In the literature, some cases have been treated by percutaneous angioplasty and stenting and/or endarterectomy.[11-13] The other treatment option is a reconstruction with expanded polytetrafluoroethylene (ePTFE) graft.[13] In our center, EIAD complications have occurred in only 2 patients. Both cases were due to vascular clamping, and we treated the patients with the ePTFE graft reconstruction technique. The dissected part of the external iliac artery was resected and replaced with a 6- to 8-cm × 8-mm PTFE graft using 6/0 Prolene. The renal artery was then anastomosed to the PTFE graft with 7/0 Prolene continuously. Both patients were well at follow-up with normal kidney function (Figure 3, A and B). Creatinine levels of patients after transplant are shown in Figure 4.

POSTOPERATIVE VASCULAR COMPLICATIONS

Vascular complications can result from renal graft vessels (renal artery thrombosis, renal vein thrombosis), the native vessels (iliac artery thrombosis, pseudoaneurysms, deep venous thrombosis), or both.

Renal artery thrombosis

Although vascular thrombosis is a rare complication, it has become a major cause of early graft loss,

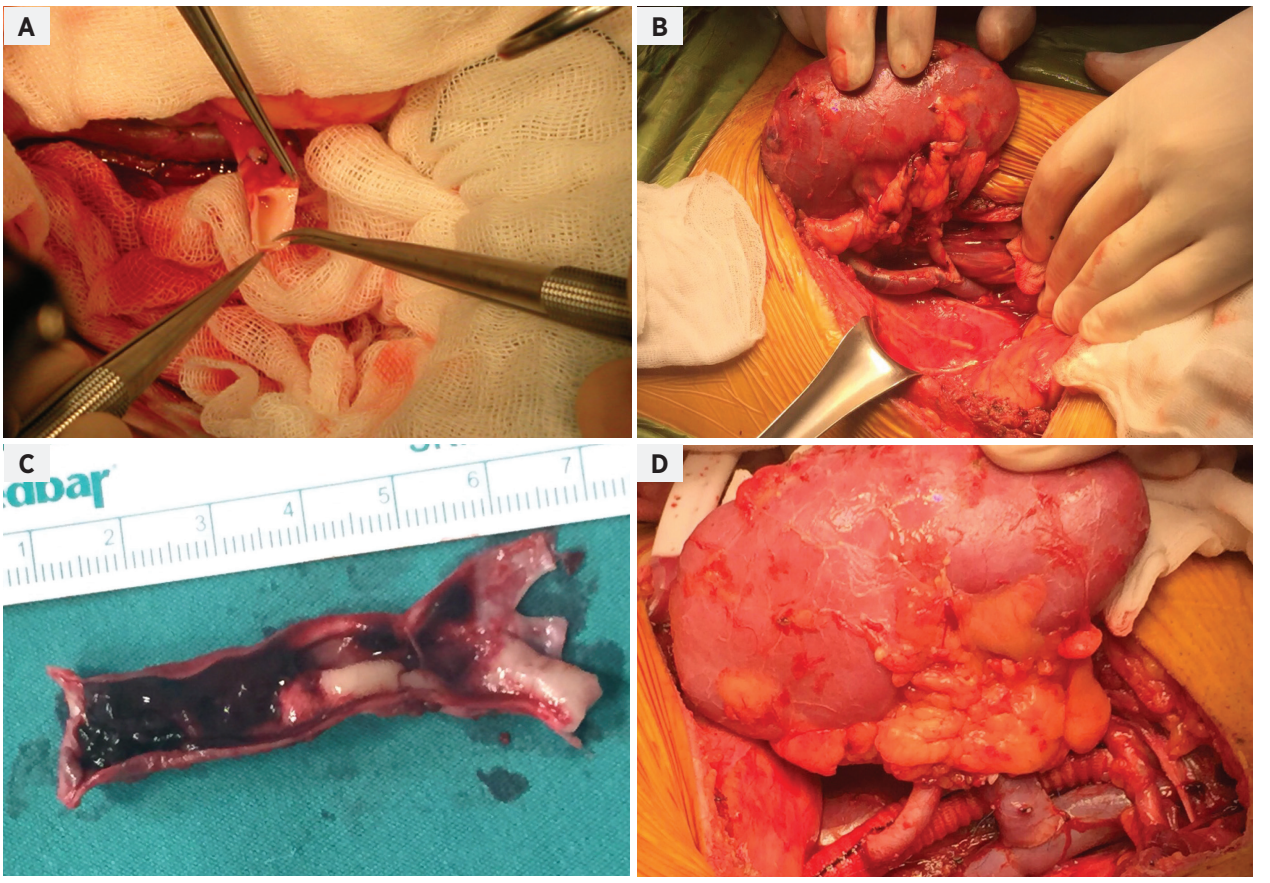

Figure 3. Reconstruction of External Iliac Artery With Expanded Polytetrafluoroethylene Graft

(A) Dissection of left common iliac artery and occlusion of the dissected external iliac artery. **(B)** Dissected external iliac artery. **(C)** Inside of dissected external iliac artery. **(D)** External iliac artery is replaced with expanded polytetrafluoroethylene graft.

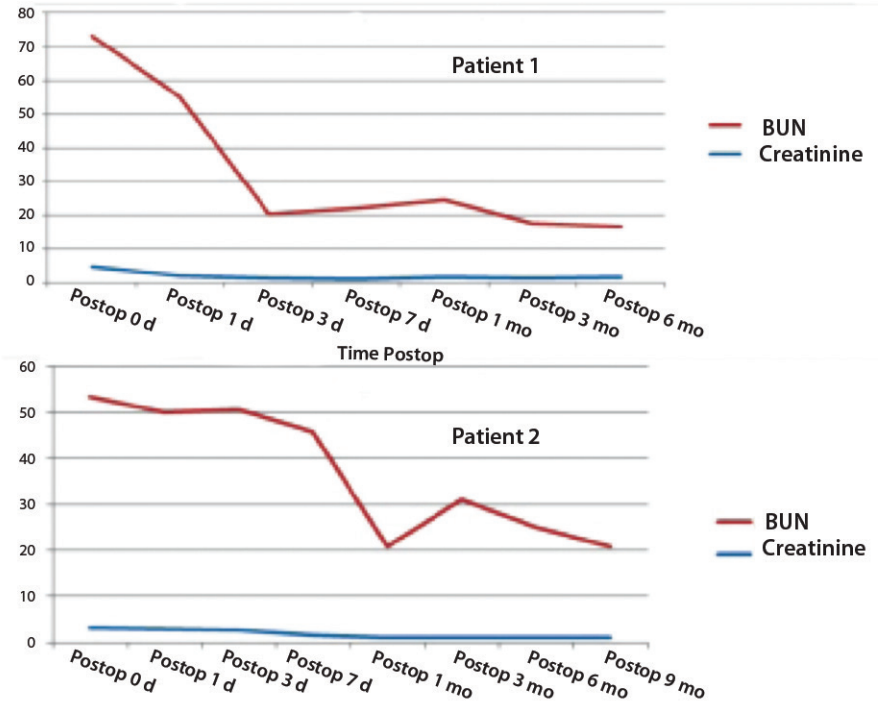

Figure 4. Improved Kidney Function After Expanded Polytetrafluoroethylene Graft Reconstruction Technique

Abbreviations: BUN, serum urea nitrogen; Postop, postoperative

accounting for up to one-third of graft loss within 1 month and up to 45% to 47% within 2 to 3 months. In the North American Pediatric Renal Transplant Cooperative Study cohort from 1996 to 2001, thrombosis was the most common cause of early graft loss.[2,13]

Renal artery thrombosis usually occurs soon after transplant and is a destructive complication, usually resulting in graft loss. Its incidence is reported to range from 0.2% to 7.5%[2] or from 0.5% to 3.5%.[14-16] Children have a higher incidence than adults. The most important sign of renal artery thrombosis is the instantaneous cessation of urine outflow due to the absence of graft perfusion and the presence of worsening hypertension. In preemptive patients and patients who have preoperative urine output, this sign can be masked. In these patients, postoperative bedside Doppler ultrasonography is recommended.[17] The most common causes of renal artery thrombosis are technical complications, including faulty suture techniques producing an incomplete intimal reapproximation with secondary intraluminal fibrosis.[18]

Since November 1975, our transplant team has performed 3094 kidney transplants. We currently use the four-quadrant running suture technique or the corner-saving renal artery anastomosis for arterial anastomosis.[17] During this period, 8 renal artery thromboses (0.35%) have been seen, with surgical exploration performed in 5 patients, which included thrombectomy, reperfusion, and reanastomosis. The other 3 patients who developed renal artery thrombosis were treated with percutaneous transluminal angioplasty, thrombolysis, and intraluminal stent placement. One of the 8 patients with renal arterial thrombosis died from a pulmonary embolism 9 days after transplant. The remaining 7 patients had normal renal function. Radiological findings of the renal artery thrombus are shown in Figure 5. In Figure 5A, Doppler ultrasonography shows decreased perfusion of the anterior segmental branch.

Angiographic findings from the same patients are shown in Figure 5B, and the first year Doppler ultrasonography findings are shown in Figure 5C.

Another surgical complication regarding renal artery thrombosis is the possible development of endothelial damage during donor nephrectomy and/or perfusion. The other factors for thrombosis are kinking or twisting of the renal artery, postoperative hypotension, hypercoagulable state, atherosclerosis of the donor or recipient vessels, wide disparity in vessel size, increased intrarenal pressure resulting from acute tubular necrosis, hydronephrosis, or cellular rejection.[15-17] In our center, 7 cases (0.3%) of renal artery kinking were seen, with patients treated via surgical exploration to rearrange the positions of their grafts. All patients had return of normal renal function.

Renal artery thrombosis is a surgical emergency, and its diagnosis is made by color Doppler ultrasonography or surgical exploration. To save the transplanted kidney, immediate exploration with restoration of the blood flow to the kidney is needed. A few cases of graft salvage in transplant renal artery thrombosis with endovascular catheter-directed thrombolysis with or without angioplasty have been reported. More commonly, by the time diagnosis is confirmed, it is already too late, and graft nephrectomy is the only remaining option.[17,18]

Renal artery stenosis

Renal artery stenosis represents the most common vascular complication, with an estimated incidence of between 19% and 23% of all transplant recipients.[18-20] In our centers, the rates are 0.5% to 0.75%. Renal artery stenosis is diagnosed first using ultrasonography and then angiography. Our preferred and initial option for treatment is the interventional radiologic approach. However, in cases where this is not successful, we have resorted to surgical reconstruction.[15-17,20-24]

Transplant renal artery stenosis (TRAS) is a relatively frequent, potentially curable cause of refractory hypertension and allograft dysfunction that accounts for approximately 1% to 5% of cases of posttransplant hypertension (renal transplant arterial stenosis).[17-19] In some series, the incidence of TRAS was reported to be 25%. It usually becomes apparent between 3 months and 3 years after renal transplant, but it can present at any time. Transplant renal artery stenosis can occur at the anastomosis, before the anastomosis, or after the anastomotic renal artery stage.[20-22] About 50% are located at the anastomosis, and end-to-end anastomosis has a 3-fold higher risk than end-to-side anastomosis.[23] It frequently presents with worsening or refractory hypertension and/or graft dysfunction in the absence of rejection, ureteric obstruction, or infection. Different locations and timing of disease onset may reflect

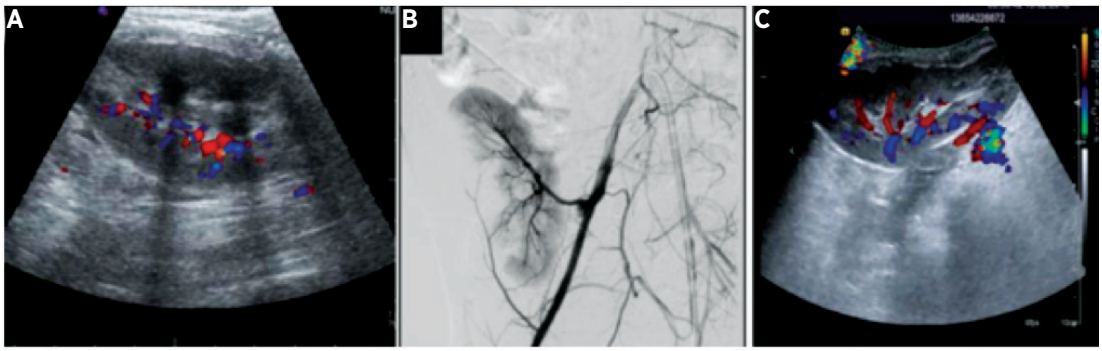

Figure 5. Segmental Renal Artery Thrombosis

(A) Doppler ultrasonography showing decreased perfusion of the anterior segmental branch. **(B)** Angiographic image revealing occluded segmental artery, with patient subsequently anticoagulated with Coumadin. **(C)** Doppler ultrasonography showing normal perfusion at first year due to hypertrophy of the remaining renal parenchyma.

different causes.[20-22] Thus, an anastomotic stenosis is most likely related to trauma to the donor's or recipient's vessels during organ recovery, clamping, or suturing and usually arises early after transplant. Small, subtle intimal flaps or subintimal dissections of the vascular wall precede intimal scarring and hyperplasia that result in a narrowing or occlusion of the lumen. The other predictors of TRAS include older donor and recipient age, expanded criteria donors (defined as any deceased donor over the age of 60 y or from a donor over the age of 50 y with 2 of the following: a history of hypertension, a terminal serum creatinine level ≥ 1.5 mg/dL, or death resulting from a cerebral vascular accident), delayed graft function, ischemic heart disease, and induction immunosuppression.[19-23]

Evaluation of TRAS may be performed with both noninvasive and invasive imaging techniques. Color flow duplex ultrasonography and magnetic resonance angiography have now become the primary noninvasive imaging modalities for diagnosis of TRAS, although catheter-based angiography has conventionally been held as the criterion standard in evaluation of arterial stenosis.[20,23]

Three different treatment options are feasible. If the kidney function and Doppler ultrasonography findings are normal, the first option for treatment can be medical therapy. In these patients, angiotensin-converting enzyme inhibitors should be used to control blood pressure.[19]

Intervention, either percutaneous or surgical, may be considered if refractory hypertension and/or worsening graft function as measured by increasing creatinine levels are present. Primary treatment with percutaneous transluminal angioplasty with or without stent placement has resulted in significant improvements in blood pressure and creatinine levels and can be considered as an initial treatment of choice[20-25] (Figures 6-8).

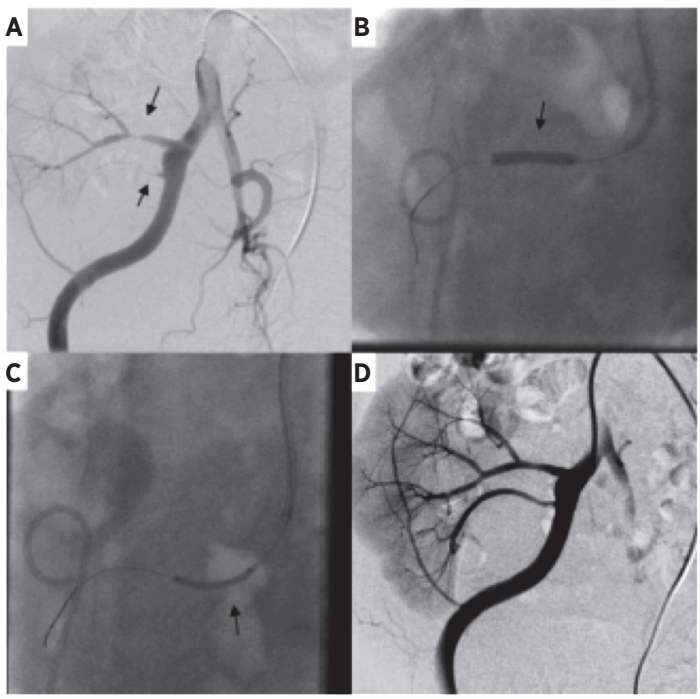

Figure 6. Renal Percutaneous Transluminal Angioplasty

(A) High-grade stenosis of the main and the polar arteries of transplanted renal artery. **(B)** and **(C)** Balloon dilation of both arteries. **(D)** Postballoon dilation showing good result percutaneous transluminal angioplasty.

RENAL VEIN COMPLICATIONS

Since Prof. Haberal performed the first kidney transplant in 1975 in Turkey for vein reconstruction technique, we have used the 2-quadrant running suture technique in our center. The external iliac vein, which is preferred for anastomosis, is dissected from distal to proximal until the common iliac vein and attached with nylon tape. Venotomy is performed into the external iliac vein as much as the diameter of the renal vein. After venotomy, corner sutures and sling sutures are placed. The back wall and then the front wall anastomoses are completed with continuous sutures. After anastomosis completion, the renal vein is clamped, with external iliac vein proximal and distal sides open, respectively[26] (Figures 9 and 10)

Renal vein thrombosis

Renal vein thrombosis usually occurs within the first 7 days after transplant. The incidence

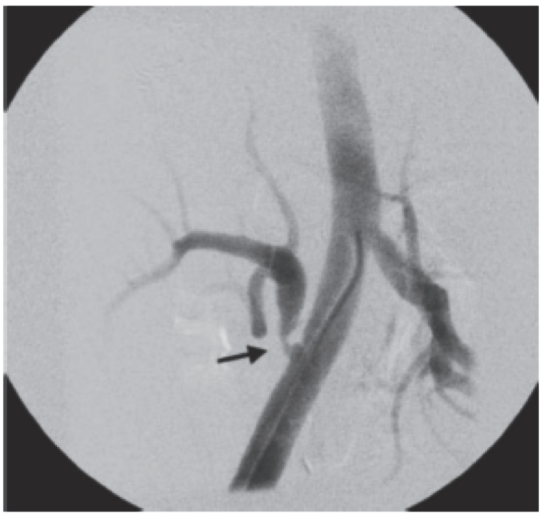

Figure 7. Anastomotic Stenosis of Transplanted Renal Artery at 9 Months After Transplant

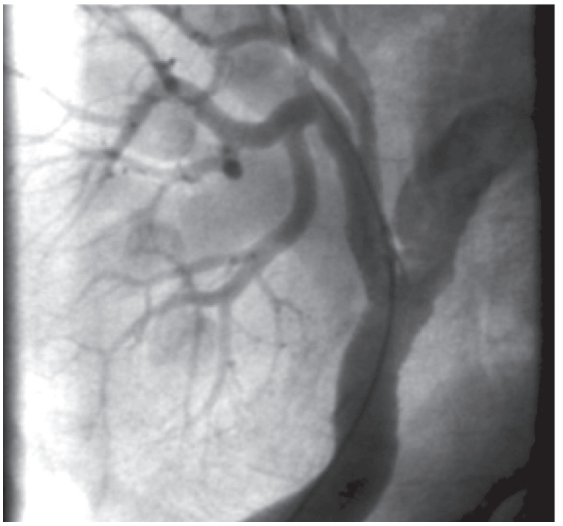

Figure 8. Stent Placement for Stenosis

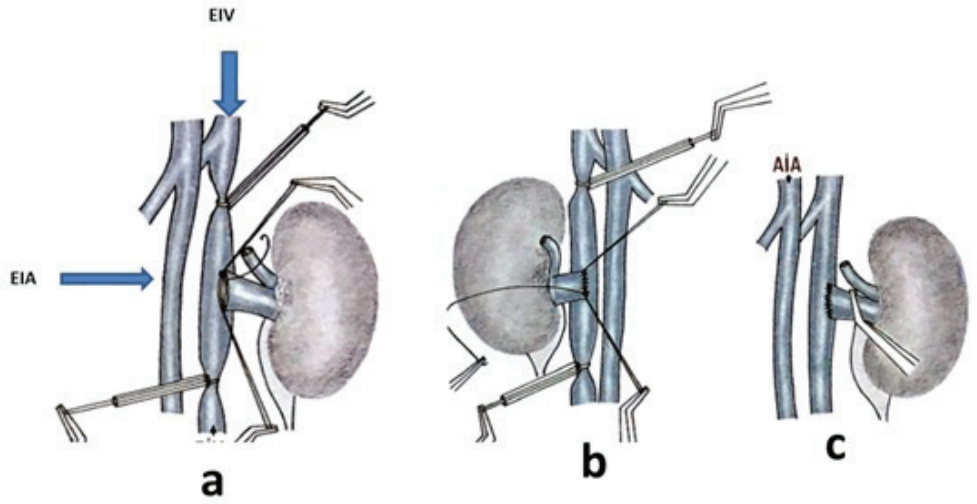

Figure 9. Renal Vein Anastomosis Technique
(A) External iliac vein is dissected from distal to proximal until the common iliac vein and hanged on with nylon tapes. **(B)** Back wall and front wall anastomosis. **(C)** Clamping of the renal vein.

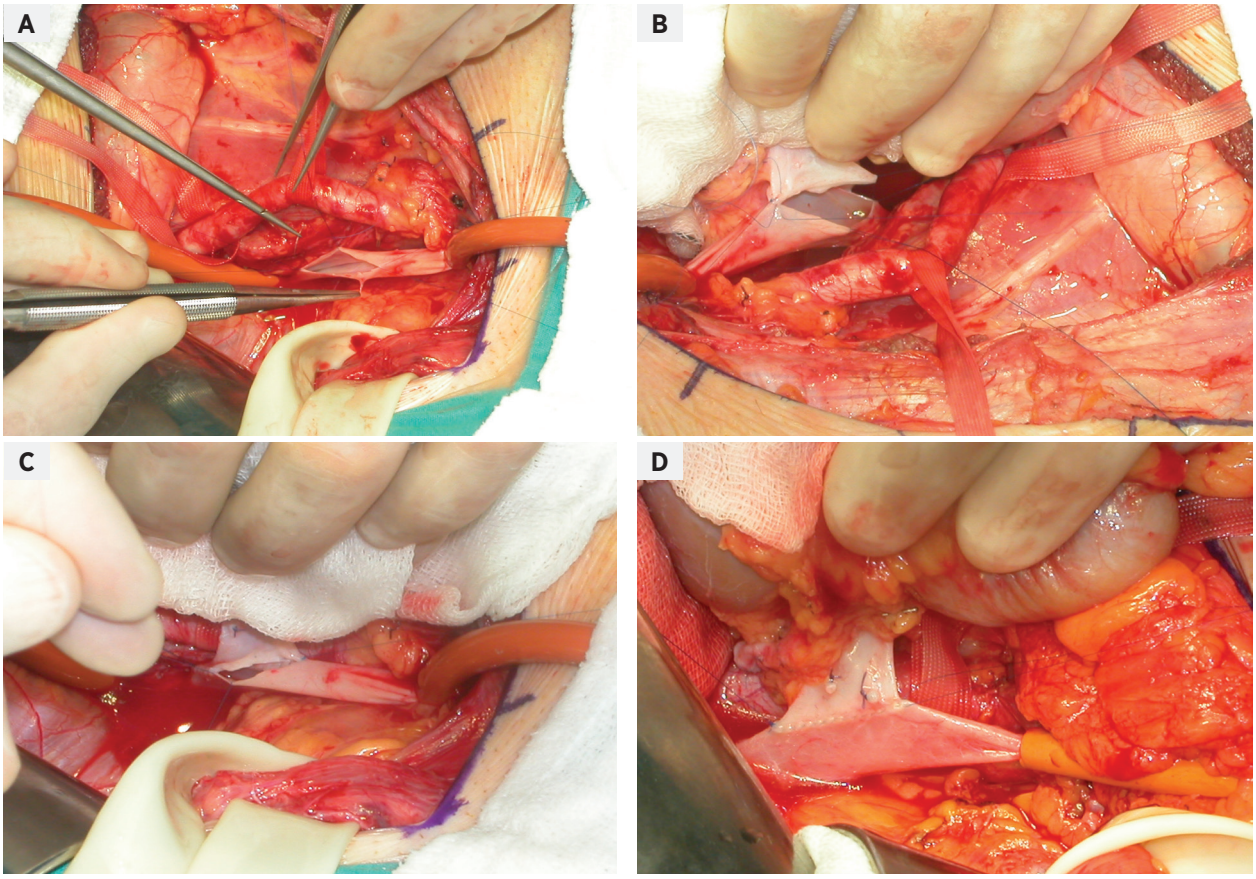

Figure 10. Renal Vein Anastomosis Technique
(A) Preparation of the external iliac vein for anastomosis. **(B)** Placement of corner sutures and sling sutures. **(C)** Front wall anastomosis. **(D)** View after anastomosis is completed.

of renal vein thrombosis ranges from 0.1% to 8.2%; this complication usually causes graft loss early posttransplant.[2,4,13] Risk factors for renal vein thrombosis are surgical technique errors; hypercoagulopathy states such as deficiency of antithrombin III, protein C, or protein S; right kidney transplant with kinking due to short renal vein; transplant in the left iliac fossa with kinking due to position of external iliac vein; dehydration; ipsilateral iliofemoral thrombophlebitis; deep femoral thrombosis; and vascular compression due to hematomas and lymphoceles. Clinical presentations of this condition include sudden oliguria or anuria accompanied by pain, hematuria, and life-threatening hemorrhage due to rupture of the graft. Depending on hemorrhage, patients may develop circulatory shock. For diagnosis, Doppler imaging studies are the best diagnostic tools.[17,20] In our clinic, we routinely apply Doppler ultrasonography examinations on postoperative days 3 and 7 for diagnoses of early vascular problems. Furthermore, Doppler ultrasonography must be performed during the immediate postoperative period on clinical suspicion and/or biochemical evidence of renal dysfunction. Evaluations of renal Doppler ultrasonography can confirm an increase in renal volume and an absence of venous flow.[16,20,23-25] An arterial view can show reverse diastolic flow. Perinephric hematomas and lymphoceles can also be seen with ultrasonography. External compression of the vessels (hematomas, lymphocele) produces vascular problems. These problems can be solved by percutaneous External compression of the vessels (hematomas, lymphocele) produces vascular problems. These problems can be solved by percutaneous drainage.

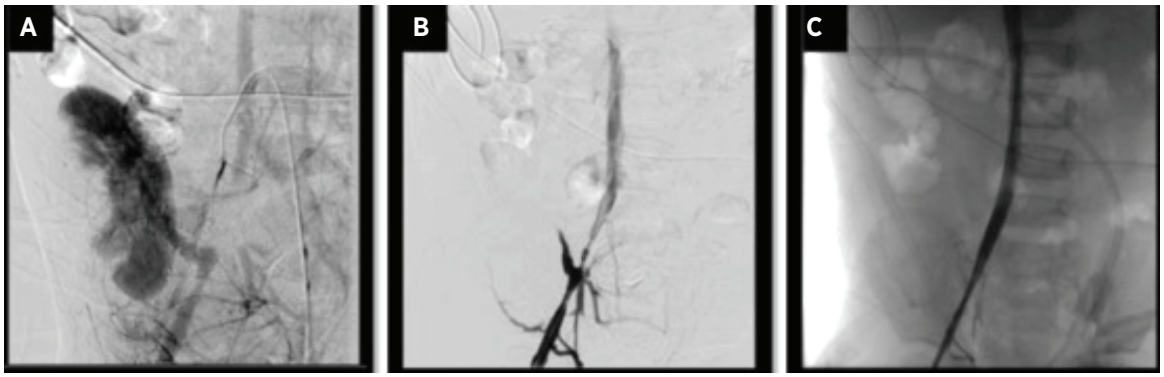

Figure 11. Renal Vein Complications Due to External Iliac Vein Thrombosis
(A) and **(B)** External iliac vein is blocked and causing venous congestion of the renal vein.
(C) Placement of self-expanding vascular stent in the external iliac vein.

Treatment includes emergency exploration for venous thrombectomy and to restore blood flow. If this treatment is not possible, nephrectomy is performed to save the patient. In our center, we had 4 patients (0.17%) who developed renal vein thrombosis after transplant, with all treated with urgent thrombectomy.[27] Unfortunately, 2 of the treatments were unsuccessful, and the grafts were lost. One patient had a renal vein problem due to external iliac vein thrombosis. Interventional radiologists placed a self-expanding stent to the proximal external iliac vein, and the graft was rescued. At recent follow-up, all patients maintained good graft function. The treatment technique for renal vein thrombosis is shown in Figure 11. In our center, 9 patients (0.4%) showed renal vein kinking, which was treated with surgical exploration to rearrange the graft positions.[27] At recent follow-up, all patients maintained normal renal function.

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Endovascular Treatment of Vascular Complications of Renal Transplantation

Erkan Yıldırım

Vascular complications after renal transplantation are seen in 3% to 15% of patients and accompany significant morbidity and mortality.[1-3] These complications include transplant renal artery stenosis (TRAS), transplant renal artery thrombosis (TRAT), and transplant vein thrombosis (TRVT), as well as pseudoaneurysms, arteriovenous fistulas, and hematomas due to miscellaneous surgery side vessels, renal artery, and vein kinking (Table 1). Early diagnosis and treatment of these complications are important for graft salvage and to reduce mortality and morbidity. Although Doppler ultrasonography (US) is the main diagnostic modality, computed tomography angiography, magnetic resonance (MR) angiography, or digital subtraction angiography (DSA) can also be used for diagnosis. Diffusion-weighted MR imaging of transplanted kidney may be used for additional diagnostic and follow-up modality after treatment of TRAS, TRAT, and TRVT.[4-9] The interventional radiologist has an important role in definitive and minimal invasive treatment of these patients. Interventional radiologic treatment options and methods to treat vascular complications are described in this chapter.

RENAL ARTERY STENOSIS

Transplant renal artery stenosis is a serious and the most common complication of renal transplantation, occurring in 0.8% of cases, which usually occur within the first 12 months after transplant.[10-12] Reported significant risk factors for TRAS are delayed graft function and cytomegalovirus infection.[13-16] Other risk factors are expanded donor criteria (mainly regarding age),[13] obesity,[15] and ischemic heart disease.[13] The origin of the graft is also an uncertain risk factor: a deceased donor is not significantly correlated with TRAS according to some series.[13,14,17] On the other hand, prevalence rates of TRAS in deceased-donor transplants have been reported to reach 4.1%, 4.5%, and 6.5%,[10,18,19] respectively, compared with 0.3%, 0.8%, and 1.7% in living related-donor transplants.[10,20,21] For early postoperative cases due to traumatic intimal injury or technical problems during vascular suture and suture type, Haberal and colleagues defined a new suture technique, the "corner-saving anastomosis," in 2008. With this technique, they reported low complication rates.[22]

Table 1. Vascular Complications After Renal Transplant

Complication	Treatment of Choice	Prognosis
Early postoperative		
Renal artery thrombosis	Surgery	Poor
Renal vein thrombosis	Surgery	Poor
Vascular kinking	Surgery	Good
Renal artery stenosis	Endovascular	Good
Hematoma	Both	Good
Iliac artery dissection	Both	Good
Late postoperative		
Arteriovenous fistulas and pseudoaneurysm	Endovascular	Good
Renal artery stenosis	Endovascular	Good

The main causes of late-onset stenoses are renal artery hyperplasia, endothelial damage related to immune response or renal disease,[23] and/or iliac atherosclerotic disease occurrences.[24] A higher rate of renal artery stenosis has been reported with end-to-end anastomoses (Figure 1), as well as with deceased-donor transplant procedures.[12,25] Clinical findings of TRAS are graft dysfunction with and or without new or refractory hypertension.

If renal artery stenosis is not addressed, it can lead to continued renal dysfunction, resistant hypertension, and eventual allograft deterioration.[25,26] Therefore, noninvasive imaging such as Doppler US, magnetic resonance angiography, and radionuclide renal scans are warranted to evaluate for renal artery stenosis. The most common Doppler US findings for TRAS are peak systolic velocity higher than 200 cm/s, resistive index < 0.5, and velocity gradient > 2:1 (Table 2).[27,28] The gold standard diagnostic modality for renal artery stenosis is transcatheter angiography. Treatment modalities for renal artery stenosis include both surgical and interventional radiologic options.

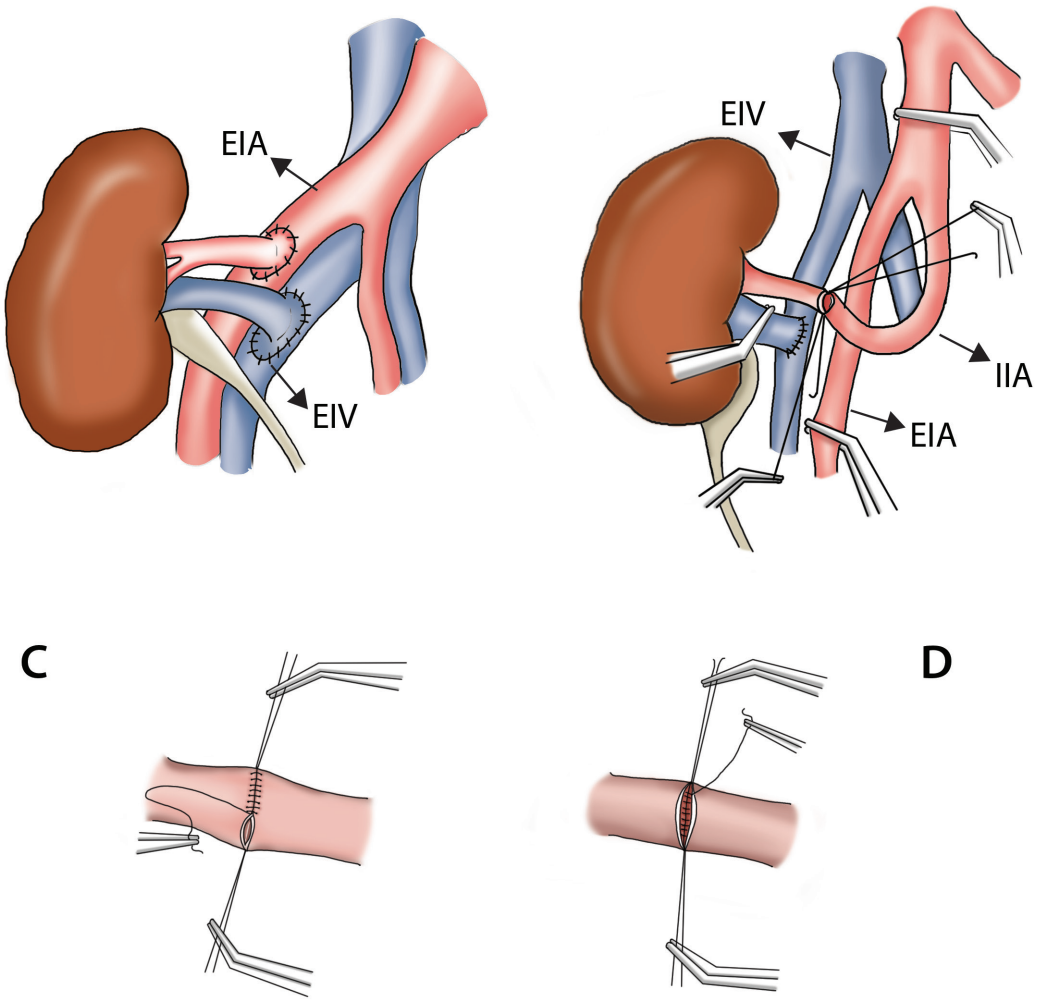

Figure 1. If the renal artery is single and internal iliac artery (IIA) is open **(A)** it is dissected; at the same time common iliac artery (CIA) and external iliac artery (EIA) are dissected distally. "Pots" clamps are placed to these dissected arteries. Stitches are placed by adjusting the lengths of renal artery and internal iliac artery **(B)**. Primarily, anterior wall anatomosis is performed **(C)**, then posterior wall is completed by twisting the artery **(D)**. According to the radius of the artery, these stitches can be placed either continuously or one by one.

Endovascular Procedures

All procedures can be done under local anesthesia with or without conscious sedation. Usually a 5F vascular sheath inserted through the ipsilateral or contralateral retrograde femoral artery with US guidance. Nonselective DSA images are first obtained to confirm diagnosis and to rule out iliac artery steno-occlusive disease. The C-arm orientation should be an ipsilateral oblique projection for better visualization of arterial anastomosis and the entire renal artery. After detection of ≥ 50% stenosis or ≥ 10 mm Hg gradient, 70 IU/kg intravenous heparin sodium should be administered. Stenosis measurement is made according to the ratio between narrowed segment diameter and normal vessel diameter adjunct to stenosis side. The transplant renal artery is then selectively catheterized with appropriately shaped catheter, and a 0.035-, 0.018-, or 0.014-inch guidewire is advanced to the intraparenchymal branches. Subsequently, a balloon catheter or balloon-expandable stent is inserted and deployed (Figures 2 and 3). Balloon and stent diameter must be chosen according to the adjunct normal vessel diameter. If there is ili-

Table 2. Vascular Complications of Renal Transplant and Treatment

Reasons for Performing Angiography
▪ Graft dysfunction
▪ Refractory or newly diagnosed hypertension
▪ Doppler ultrasonography findings; increased peak systolic
Main Steps of Endovascular Procedures
▪ Retrograde ultrasonography-guided femoral artery access
▪ Confirm diagnosis and make measurements (ipsilateral 30° oblique projection)
▪ Heparinize patient with 70 IU/kg
▪ Selective catheterization of renal artery with appropriate catheter
▪ Insertion of 0.014-inch or 0.018-inch guidewire
▪ Inflation of balloon or deploy balloon expandable stent
Renal Artery Thrombosis Incidence
▪ 0.5%-3.5% (less common complication)
▪ 80% in first month after transplant
Causes of Renal Artery Thrombosis
▪ Hyperacute rejection
▪ Postoperative hypotension
▪ Hypercoagulation
▪ Atherosclerosis
▪ Renal artery torsion
▪ Arterial injury during donation
▪ Cyclosporine
Causes of Transplant Renal Vein Thrombosis
▪ Donor factors: Using right kidney, short vein and long artery, multiple renal arteries, prolonged ischemia time, older age
▪ Recipient factors: Older age, inappropriate vessel size between donor and recipient, peritoneal dialysis, perioperative hypotension, and dehydration
▪ Operative factors: Kinking of the graft vein, long vein, wide disparities in vessel size, and injury to the vascular endothelium
▪ Mechanical causes: Kinking in renal vein, compression by hematomas or lymphoceles, anastomotic stenosis, extension of an underlying deep venous thrombosis, and compression of the renal vein by the renal artery
▪ Immunosuppression: Cyclosporine, OKT3 antibody, high doses of methyl prednisolone, and antithymocyte/antilymphocyte globulin

ac artery stenosis or dissections that do not extend or include the anastomosis site, then iliac artery lesions should be treated in the same session. In cases in which iliac artery stenosis and dissection involve the renal artery anastomosis site, surgical correction should be the treatment of choice (Table 2), but it can also be treated endovascularly (Figure 4).

Percutaneous transluminal angioplasty, with or without stent insertion, is the primary endovascular therapy. The goals of treatment are return of renal

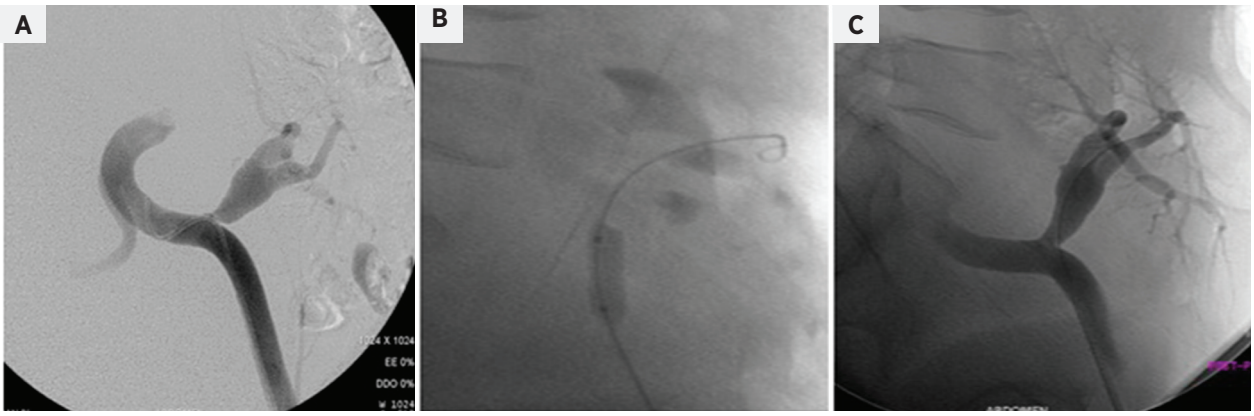

Figure 2. Severe Anastomotic Renal Artery Stenosis at Left Lateral Oblique Projection

Diagnostic transplant renal artery digital subtraction angiography image showing severe anastomotic stenosis at left lateral oblique projection **(A)** and balloon inflation over advanced 0.035-inch guidewire **(B)**. Completion angiography after angioplasty shows near complete correction of stenosis **(C)**.

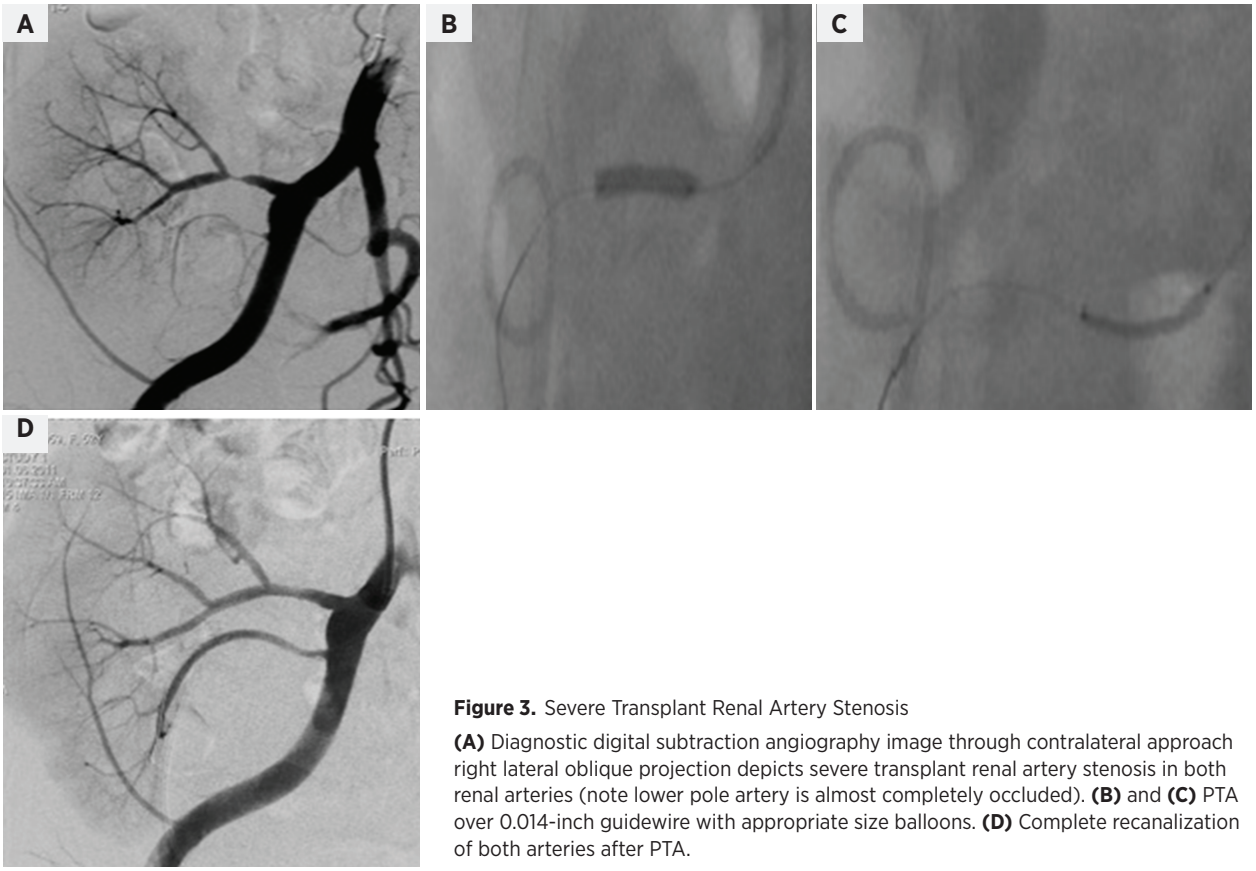

Figure 3. Severe Transplant Renal Artery Stenosis

(A) Diagnostic digital subtraction angiography image through contralateral approach right lateral oblique projection depicts severe transplant renal artery stenosis in both renal arteries (note lower pole artery is almost completely occluded). **(B)** and **(C)** PTA over 0.014-inch guidewire with appropriate size balloons. **(D)** Complete recanalization of both arteries after PTA.

function and control of blood pressure. Some have shown significantly decreased blood pressure and number of antihypertensive drugs,[27-30] whereas others have shown no significant changes in those values.[31,32] The impact on postoperative creatinine

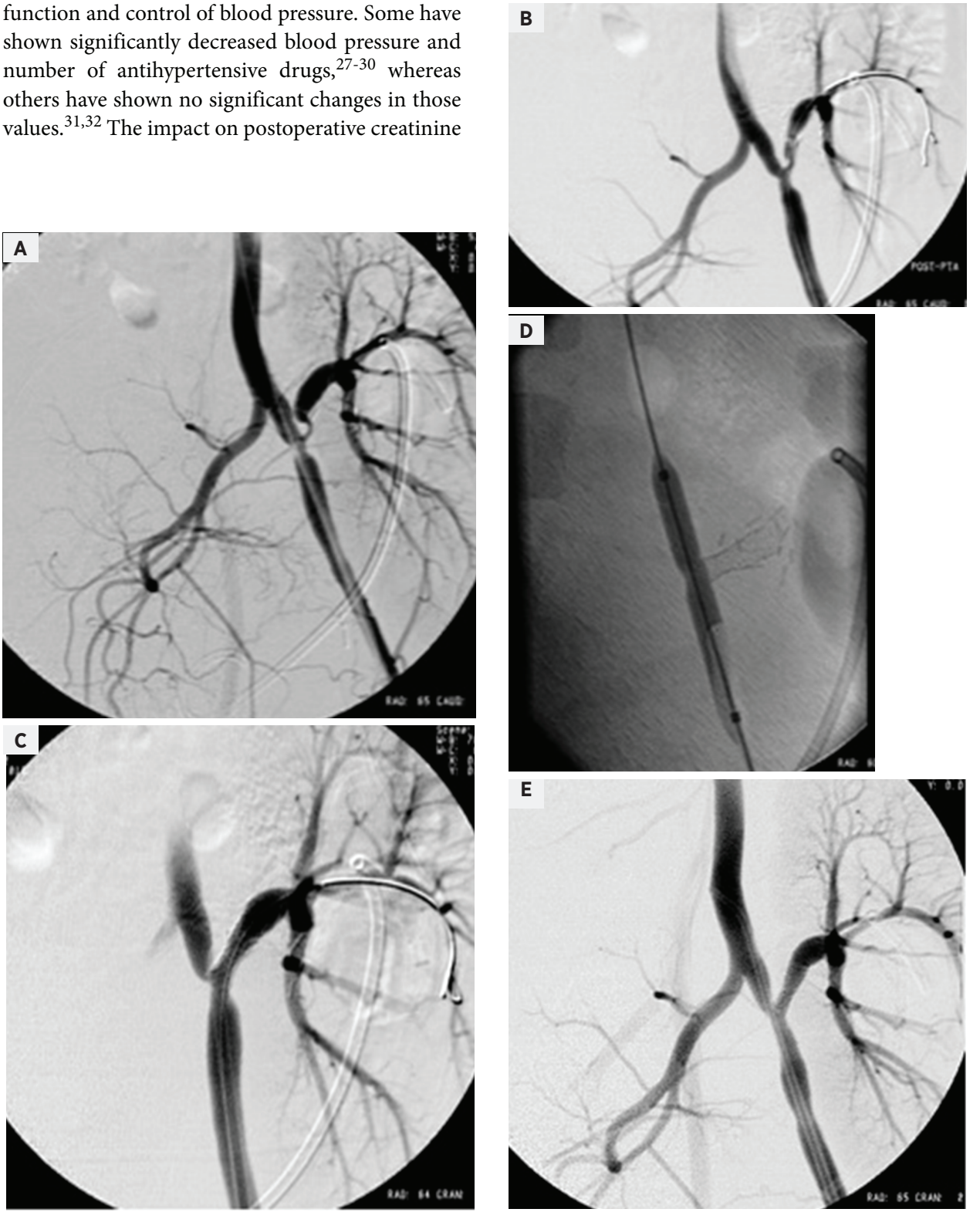

Figure 4. Severe Stenosis at Both Renal Artery Anastomosis and External Iliac Artery

(A) Diagnostic digital subtraction angiography through ipsilateral retrograde femoral artery approach left lateral oblique projection depicts severe stenosis at both renal artery anastomosis and external iliac artery. After stenosis was crossed with 0.018-inch guidewire **(B)**, balloon-expandable stent was deployed to renal artery **(C)**, with external iliac artery stenosis then dilated with balloon catheter over 0.035-inch guidewire **(D)**. **(E)** Image shows resolution of stenosis.

levels seems more consensual, with most reports citing a significant decrease following angioplasty with or without stent placement.[10,24-30]

The technical success and complication rates of endovascular procedures are 60% to 100% and 0% to 8.3%, respectively, with allograft loss rarely reported.[10,32-36] Recurrent stenosis (restenosis) is the main inherent complication of endovascular techniques, with no specificity regarding the particular location at the renal transplant artery. About 10% to 12% of endovascularly treated patients develop restenosis posttreatment, although the rate has been reported to be as high as 20% to 30%.[19,34,37,38] Balloon angioplasty alone entails from 10% to 56% of the incidences of restenosis.[10,14,20,26,39] This result seems to improve with stent usage, with rates of restenosis after primary stenting varying from 5.5%[27] to 20%.[26] Restenosis mostly occurs within the first 8 to 9 months postprocedure. Treatment options for restenosis include repeat percutaneous transluminal angioplasty and possibly deployment of an endovascular stent.[40,41] However, in-stent restenosis occurs in as many as 13% to 25% of patients after percutaneous transluminal angioplasty and stent insertion.[42] In our study, the prevalence of renal artery stenosis was 0.75%, which was lower than other studies. Effectiveness of angioplasty in terms of graft survival is equivocal. Multiple series have reported no differences in the survival curve of grafts without TRAS compared with those treated with stenting with TRAS.[27,42,43]

Despite the relatively high restenosis rate and some reports of better long-term clinical outcomes after surgical management of renal artery stenosis, most authors still recommend percutaneous transluminal angioplasty as the first line of therapy because it is less invasive and has low periprocedural morbidity.[19,34,35,44]

Surgery is mainly reserved for cases of unsuccessful endovascular therapy or with severe complicated stenosis because of the high reported rate of significant complications such as graft loss (15% to 20%), ureteral injury, and reoperation.[45] Reported surgical success rates range from 63% to 92% with stenosis recurring in 12% of patients.[35,39]

VASCULAR KINKS

Arterial and venous kinks form as a result of vascular redundancy or when shifts in graft and/or pelvic contents occur in time, causing torqueing of the artery or vein. It is important to identify an arterial narrowing to be a kink and not a simple stenosis. Surgery remains the primary treatment for vascular kinks. In cases where surgery is not feasible or patients refuse to have it, one can resort to higher-risk options of endovascular management. Kinks are notoriously refractory to balloon angioplasty, which may increase the risk of arterial vasospasm and/or dissection. All vascular kinks can be treated without graft loss with urgent operative management.[1]

RENAL VASCULAR THROMBOSIS

Renal graft vascular thromboses are serious complications that usually lead to graft loss if not treated in a timely fashion. Renal graft thrombosis is seen in about 0.3% to 1.28% of cases and usually occurs within the first 2 weeks after transplant.[1] In the early period posttransplant, TRAT usually occurs as a result of intimal damage during graft retrieval or the surgical technique.

Causes of TRVT are mainly technical factors, including torsion or kinking of the graft vein, a long vein, and injury to the vascular endothelium during surgical manipulation or back-table procedures.[46] Technical problems may also occur with right donor nephrectomy because of short or thin-walled renal veins.[47] At 1 month or more posttransplant, TRAT usually occurs because of rejection or high-grade renal artery stenosis, whereas TRVT usually occurs as a result of proximal propagation of deep venous thrombosis in the lower extremity or external compression from a perigraft fluid collection.[1] Sudden reduction or cessation of urine output and elevation of serum creatinine levels are usually the only clinical presentations of TRAT.[47,48] Clinical symptoms of thrombosis include oliguria,

hematuria, rising serum creatinine, and occasional graft pain.[49,50] Renal graft thrombosis is often treated surgically by laparotomy, thrombectomy, vascular polytetrafluoroethylene graft interposition,[51] and ultimately possible graft nephrectomy. There are multiple case reports describing endovascular therapy for renal thrombosis; however, the exact interventional radiologic treatment has not yet been well defined.[52,53] Because thrombosis is difficult to treat and graft loss is usual, preventive strategies are of paramount importance (Table 2).

Endovascular Techniques for Renal Artery Thrombosis

Because the underlying causes of thrombosis are intimal damage or stenosis, stent implantation is almost always performed after thrombolysis or mechanical thrombectomy. For mechanical thrombectomy, after gaining femoral access (preferably ipsilateral with a 5F or 6F vascular sheath), aspiration is done with 5F or 6F flexible tip guiding catheters. After removal of thrombi from the renal artery, the stenting procedure is performed. For thrombolysis, an infusion catheter is advanced over a guidewire into the main renal artery after passing the thrombosed segment of artery with a diagnostic catheter and guidewire (0.014 or 0.018 inch). The thrombolytic agent used for it is tissue plasminogen activator, with an infusion rate of 1 or 1.5 mg/hour. The infusion can be continued for up to 24 hours with controlled angiography every 6 hours and monitoring of serum fibrinogen levels. After successful thrombolysis, if stenosis or dissection or intimal damage is detected, the stenting procedure is performed as usual (Figure 5).

RENAL VEIN THROMBOSIS

Transplant renal vein thrombosis will lead to graft loss and nephrectomy in almost all cases,[54-57] even if a successful open thrombectomy procedure had been performed.[58-61] The prevalence of TRVT is higher in deceased-donor than in living-donor transplant procedures. This may be because living-donor transplant procedures are usually done under more favorable conditions and are not usually subjected to ischemic injury.[26,62]

Renal vein thrombosis can cause impaired microvascular perfusion and reduced blood flow, resulting in ischemic injury; if it is severe enough, it can lead to cortical necrosis.[63] The pathogenesis of this devastating complication is often multifactorial and includes donor factors, recipient factors, operative factors, and immunosuppression.[64] Higher doses of cyclosporine, common in the early years of its use, are also associated with higher incidence of venous thrombosis. Another important cause is hypercoagulopathies, such as deficiency of antithrombin III, protein C, or protein S. Renal vein thrombosis usually presents with sudden onset of oliguria and hematuria that is associated with intensive pain or discomfort over the graft area. Ipsilateral lower extremity edema, low-grade fever, and, in severe cases, massive hemorrhage may also be seen (Table 2).[65]

Doppler ultrasonography is the standard diagnostic radiological method for evaluation of renal vein patency.[65,66] Duplex US characteristically reveals reversed arterial diastolic flow, a spike-like systolic component, and nonvisualization of the renal vein. Although DSA is the gold standard diagnostic procedure, scintigraphy and MR angiography have greater sensitivity than Doppler US and can be used as alternative diagnostic imaging modalities.[4,10,67-69]

Endovascular Treatment of Transplant Renal Vein Thrombosis

In selected patients, endovascular thrombo-aspiration and thrombolytic therapy can be done for TRVT that occurs within 2 weeks after transplant because of hemorrhagic complications.[70-73] If there is no contraindication, combined percutaneous mechanical thrombectomy and localized catheter-directed thrombolysis can be done safely and effectively in TRVT.[50,70,72,74,75] Both jugular and femoral vein access can be used, but the ipsilateral femoral vein should be preferred if concomitant femoral and iliac vein thromboses are present.

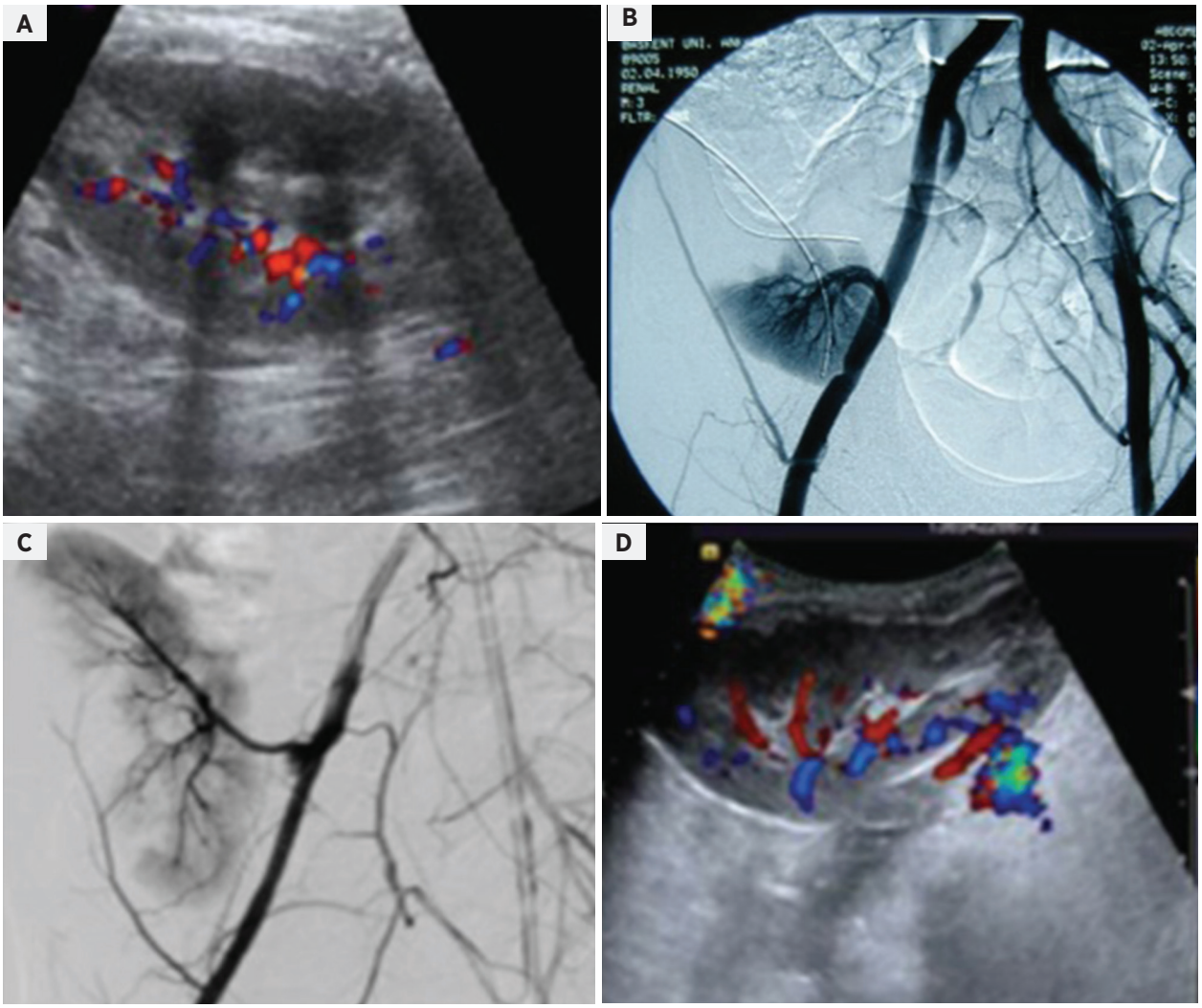

Figure 5. Flow Deficit at Anterior Portion of Transplanted Kidney

(A) Doppler ultrasonography reveals flow deficit at anterior portion of transplanted kidney. **(B)** Digital subtraction angiography confirms diagnosis and shows patent lower pole or polar artery and complete thrombosis of main renal artery. **(C)** and **(D)** Completion angiogram and Doppler ultrasonography after tissue plasminogen activator infusion depict complete arterial flow restoration of kidney.

For the procedure, a 6F vascular sheath is first inserted with use of US guidance and diagnostic iliac venograms are obtained. Next, after the diagnosis is confirmed and the entire venous vascular tree is visualized, the thrombosed renal vein is catheterized with an appropriate diagnostic catheter and guidewire (0.035 inch hydrophilic or 0.018 inch). For mechanical thrombectomy, a 6F guiding catheter with soft tip can be used. If iliac vein and/or inferior vena cava are thrombosed concomitantly, these should be recanalized either with catheter-directed aspiration or with thrombo-aspiration devices. In cases of failure or residual cloth in renal vein, a catheter-directed thrombolysis must be performed. For this purpose, a multiple side hole infusion catheter is inserted into the renal vein, and thrombolytic infusion (tissue plasminogen activator) is started with the dose of 1 to 1.5 mg/hour. The success rate for these interventions is variable among different studies. Unfortunately, there are no large randomized controlled studies that have assessed the relative efficacy of this management strategy.

RENAL ARTERY PSEUDOANEURYSM AND ARTERIOVENOUS FISTULA

Renal artery pseudoaneurysms can be either in the extrarenal or intrarenal parts of the renal artery. Extrarenal pseudoaneurysms are usually seen secondary to the surgical suture technique or because of immunologic factors and infections, whereas intrarenal pseudoaneurysms occur because of iatrogenic factors (biopsies) and infection. The incidence of renal artery pseudoaneurysms is about 1% of renal transplant patients.[76-80] Infectious pseudoaneurysms can be seen in any part of the transplanted renal artery and can be in multiple numbers.[81,82] The management of pseudoaneurysms can be done either with open surgical repair or interventional radiologic procedures (endovascular interventions or US-guided percutaneous thrombin).[83,84] Patients are usually asymptomatic, and pseudoaneurysms are incidentally found on Doppler US or computed tomography scan. Some patients present with pulsatile mass, hemorrhage, increased serum creatinine, pain over the transplant site, fever, and lumbosacral plexopathy.[82] Although in the absence of infection conservative management is recommended for small asymptomatic pseudoaneurysms,[85] pseudoaneurysms can lead to rupture and potentially lead to graft loss and even death of the patient.

Arteriovenous fistulas frequently occur as a complication of percutaneous graft biopsy, with 1% to 18% of renal allograft biopsies resulting in arteriovenous fistulas.[86,87] They can be asymptomatic or cause gross hematuria.[88] Other, less common presentations include renal insufficiency, hypertension, and high-output cardiac failure. Although up to 70% of arteriovenous fistulas are resolved spontaneously within 2 years, treatment is often indicated, especially if they are symptomatic. Embolization is the treatment of choice for symptomatic arteriovenous fistula.

Endovascular Treatment

With 100% technical and clinical success in all patients, endovascular treatment is the first-line management option for intrarenal pseudoaneurysms and arteriovenous fistulas while surgery is in anastomotic pseudoaneurysms.[82,89-91] For intrarenal pseudoaneurysms and arterio-venous fistulas, the commonly used embolic material is coils. After femoral access, catheterization of the renal artery with an appropriate catheter, and diagnosis, a microcatheter is advanced into the feeder artery of the aneurysm or arteriovenous fistula over an 0.014-inch guidewire until complete obliteration of the feeder artery (Figures 6 and 7). Endovascular repair of extrarenal pseudoaneurysms has been described in the literature using stent-grafts, fenestrated stent-graft and coil embolization, and thrombin injection with balloon remodeling technique in selected hemodynamically stable patients.[83,89,92-97] Thrombin injection without stent placement is useful only in a small set of patients in which the extrarenal pseudoaneurysm demonstrates a narrow neck and carries the risk of embolus in the more distal renal artery. Most reports on endovascular treatment involve the use of covered stents alone with good results.[89,93,94,97] Stenting across an anastomosis can be technically challenging, especially in cases of end-to-side anastomoses. However, endovascular repair has been shown to be feasible even in these cases using detachable coils with balloon remodeling technique.[81]

The optimal management for extrarenal mycotic pseudoaneurysm remains unclear. Although endovascular stent placement has been shown to be useful in these patients,[98] in the setting of active infection, there is concern for seeding the stent with the offending organism, leading to persistent infection.[97,99]

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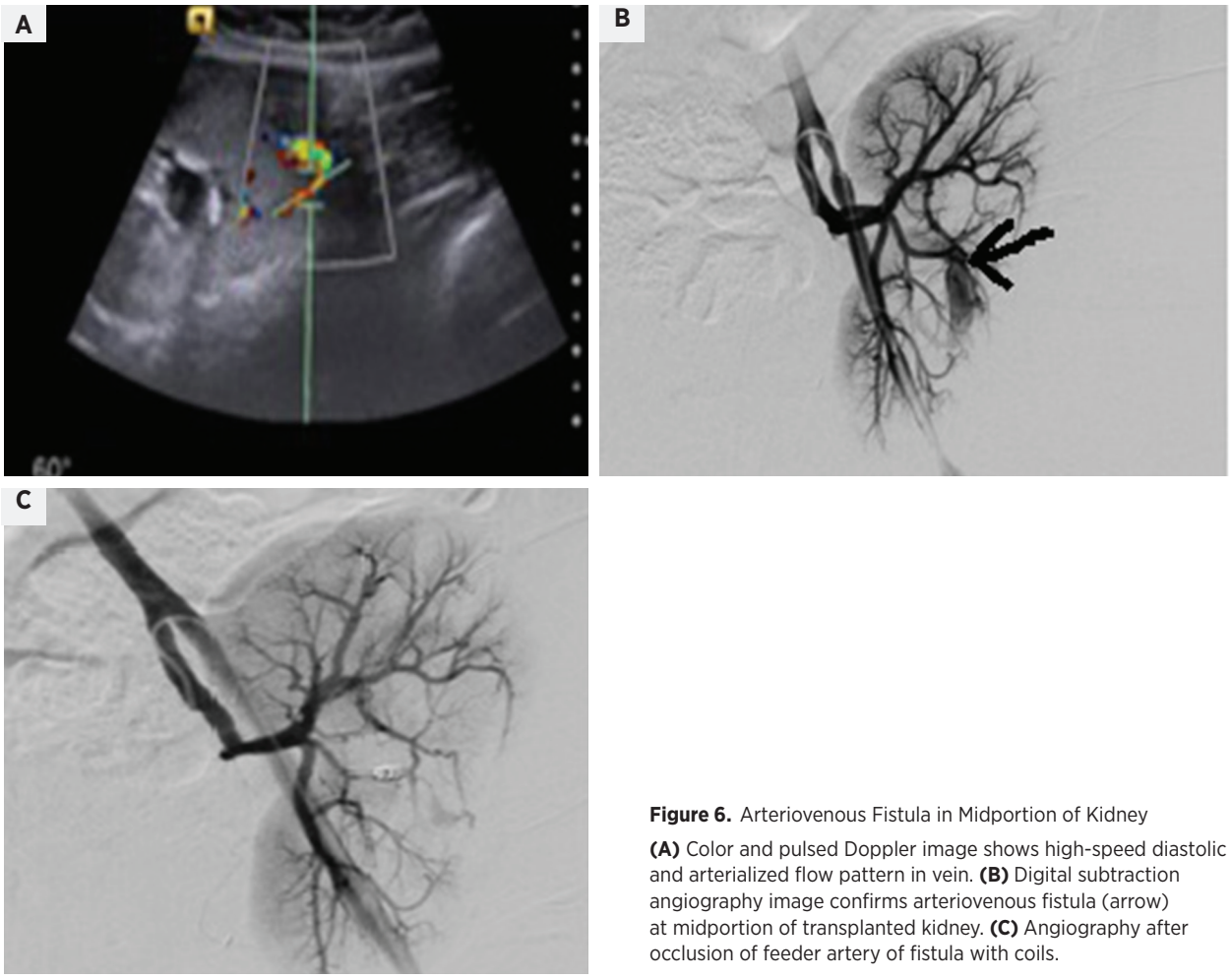

Figure 6. Arteriovenous Fistula in Midportion of Kidney

(A) Color and pulsed Doppler image shows high-speed diastolic and arterialized flow pattern in vein. **(B)** Digital subtraction angiography image confirms arteriovenous fistula (arrow) at midportion of transplanted kidney. **(C)** Angiography after occlusion of feeder artery of fistula with coils.

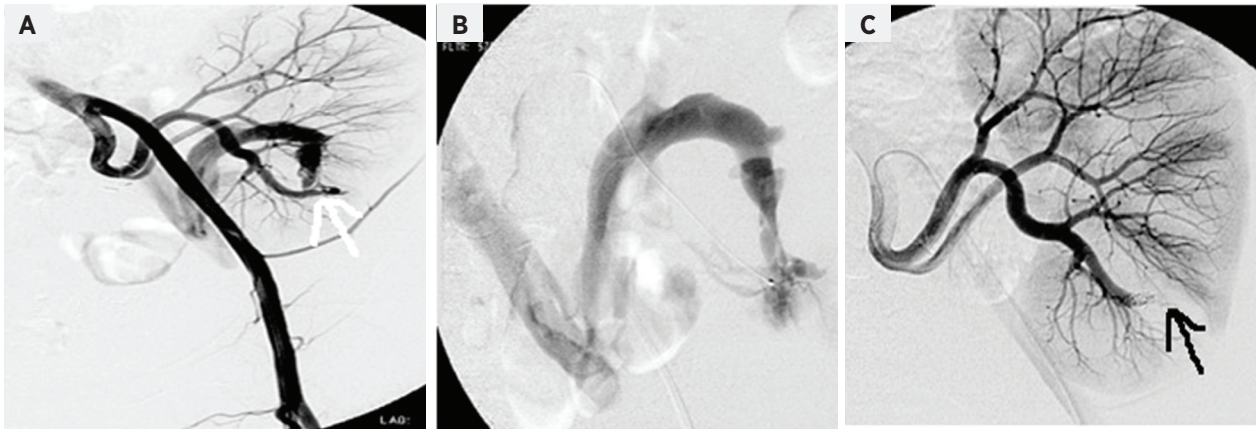

Figure 7. Arteriovenous Fistula in Lower Pole of Kidney

(A) Digital subtraction angiography image shows arteriovenous fistula at lower pole (white arrow) and early filling of vein during arterial phase. **(B)** A microcatheter is advanced into the feeder artery and positioned near the fistula location. **(C)** Image after coil (black arrow) embolization of the feeder.

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Posttransplant Urologic Complications

Aydıncan Akdur
Emre Karakaya

Urologic complications are the most common surgical complications encountered after renal transplant, causing significant morbidity and mortality.[1-3] Rates of urologic complications after kidney transplant range between 2.5% and 30% of all recipients.[1-4] Most complications occur within 3 months after the transplant.[5] A few studies have compared the incidence of complications between living-donor versus deceased-donor transplant but have found no significant differences in the complication rates.[6,7]

Complications are usually determined at the distal part of the ureter and especially at the site of the ureterovesical anastomosis.[5] Two common causes of complications are ischemia and technical problems.[6,7] During the donor nephrectomy, the normal blood supply of the ureter may be disrupted by the dissection of segmental artery branches. The renal artery and its branches that traverse in the periureteral tissue are the only blood supply of the distal ureter. For this reason, it is highly recommended to avoid extensive dissection in the "golden triangle" (the area between the ureter, kidney, and renal artery) in order to prevent ischemia and subsequent urologic complications.[8,9] In living-donor transplant, it can be more difficult to preserve the periureteric connective tissue compared with deceased-donor transplant. However, deceased-donor transplant is accompanied with longer cold ischemia time, which is also associated with ureteral obstruction. Other described risk factors for complications following transplant include donor age, male sex of the recipient, recipients of black race, delayed graft function, cytomegalovirus infections, and renal artery multiplicity or arterial reconstructions.[10]

Another important reason for complications is the ureter anastomosis technique. The most well-known anastomosis techniques in the literature are the Politano-Leadbetter technique and the Lich-Gregoir technique. Several studies have shown that the Lich-Gregoir technique significantly reduces the risk of complications compared with the Politano-Leadbetter technique.[11,12]

Since 1975, our transplant team has performed 3094 renal transplants. From 1975 to 1983, we performed 300 ureteroneocystostomies using the modified Politano-Leadbetter technique. From 1983, we began using the extravesicular Lich-Gregoir technique in combination with temporary ureteral stenting in 1141 patients. Then, in September 2003, we began using the corner-saving technique. Since we began using this technique, we have not used a double J stent or any other stent to prevent ureteral stenosis at the anastomosis site. Before suturing is started, the posterior wall of the ureter is spatulated, and in the corner-saving technique, the ureteral reimplantation is performed using a running 6-0 monofilament polydioxanone suture; this suture begins 3 mm ahead of the middle of the posterior walls of the ureter and bladder and finishes 3 mm behind. After the last stitch, both ends of the suture material are pulled to decrease the excess, and the posterior walls of the ureter and bladder are approximated tightly. The anterior wall is sewn either with the same suture or with another running suture (Figures 1 and 2).[2,3,13-16]

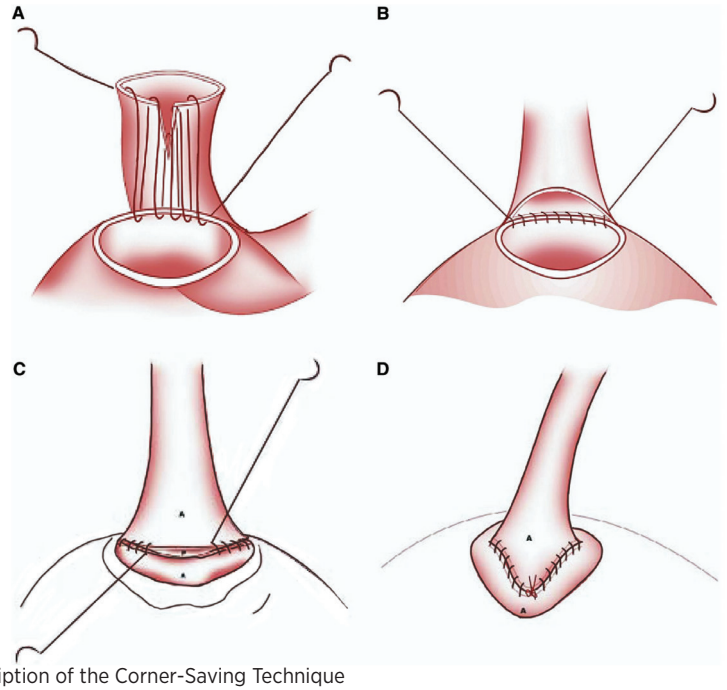

Figure 1. Schematic Description of the Corner-Saving Technique

(A) Running suture between posterior walls of the ureter and bladder. **(B)** The ends of the suture are pulled to approximate the posterior walls. **(C)** Anterior walls are approximated at the corner. **(D)** Anterior walls are sewn with a running suture.

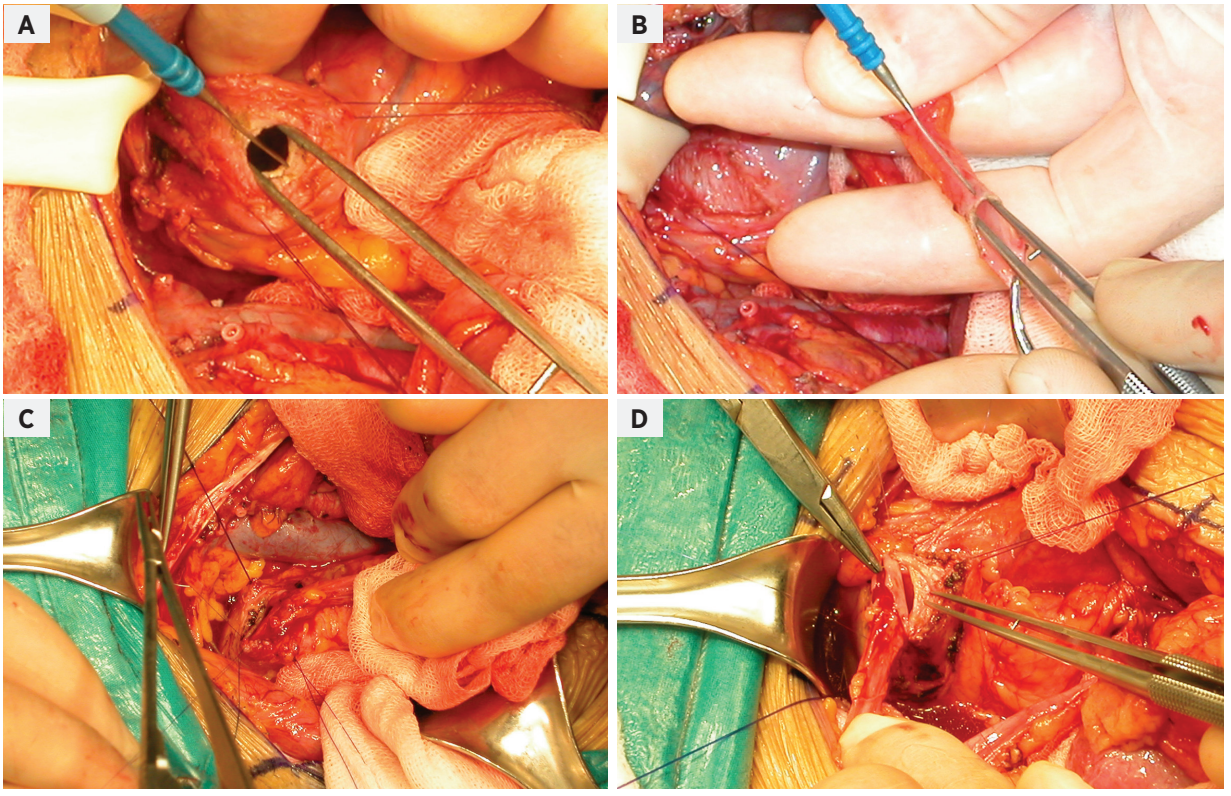

Figure 2. Corner-Saving Technique

(A) Preparation of bladder. **(B)** Preparation of graft's ureter. **(C)** The ends of the suture are pulled to approximate the posterior walls. **(D)** Anterior walls are approximated at the corner.

The gold standard for diagnostic imaging of urologic complications is an ultrasound examination to visualize perigraft collections or a dilated renal pelvis and ureter. In case of perigraft collections, aspiration followed by a biochemical test may confirm the diagnosis of urinary leakage. Other imaging techniques applied to diagnose urologic complications are conventional urography, computed tomography, and magnetic resonance imaging.[17]

URINE LEAKAGE

Urine leakage associated with ureterovesical anastomosis after transplant may cause graft loss and mortality. Incidences of urinary leakage in different transplant centers have ranged from 0% to 8.9%, with incidences of ureteric stricture reported to range from 0.1% to 12.4%. Major urologic complications, for example, leakage and stenosis, are often related to the ureteroneocystostomy.[18-20] To avoid urologic complications, clinicians at some transplant centers routinely prefer stenting, as this maneuver avoids anastomotic tension, kinking, and ureteral narrowing. At our center, because the double J stent increases the risk of postoperative urinary infection and removal of this device requires an invasive procedure, we prefer not to use a double J ureteral catheter routinely. Although there are many disadvantages of this catheter, we do advocate its use in select patient groups, such as those with thin graft kidney ureter walls or thin urine bladder walls, especially with transplants involving deceased donors. To evaluate the complications earlier, we use ultrasonographic and scintigraphic findings from days 1, 3, and 7 and creatinine levels on day 7 and at 1 month after transplant. In our series, 1% of patients developed urine leakage after transplant.

Risk factors that contribute to the prevalence of urine leakage need to be determined. So far, many factors have been described in the literature, including several donor and recipient characteristics. Furthermore, problems encountered during the graft recovery, prolonged ischemia times, type of ureteroneocystostomy, presence of accessory arteries, and stent placement may influence the incidence of urologic complications.[7,9,15,17]

It has been suggested that urine leakage is caused by insufficient blood supply to the ureter. Excessive dissection of the site known as the golden triangle (the site confined by the ureter, kidney, and renal artery) should therefore be avoided during graft recovery. Damage of this triangle may lead to necrosis of the distal ureter in 70% of cases.[15,16]

In most cases, these complications require placement of a percutaneous nephrostomy (Figure 3). Sometimes, even a surgical revision is required, leading to additional morbidity and cost. The methods for treatment of leakages or strictures of the ureter (including ureter torsion) are generally

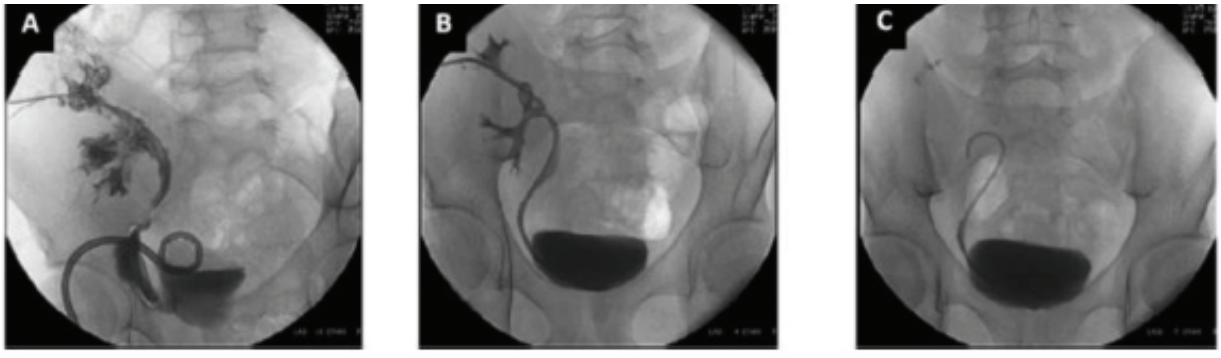

Figure 3. Double J Stent Was Removed at 2-Month Follow-up With No Sign of Leakage After Treatment

(A) Postrenal transplant ureteral anastomosis leak. **(B)** Treatment with percutaneous nephrostomy and double J stent replacement. **(C)** At the 2-month follow-up, the leak had disappeared completely and nephrostomy catheter was removed.

similar, consisting of insertion of a double J ureteric stent or reanastomosis. In small leakages, conservative treatment or suture over a ureteral stent can be considered, whereas, in larger leakages caused by necrosis, reanastomosis is necessary.[5,6]

URETERAL OBSTRUCTION

Ureteral obstruction occurs in 2% to 10% of renal transplant patients postoperatively, usually presenting within the first few weeks or the first year.[13,14,17,19] Prompt diagnosis and remedial treatment are vital to prevent the graft loss. Ureteric ischemia is the most common cause, accounting for around 90% of occurrences.[17,19] The other causes are more than 2 arteries, long cold ischemia time, tumor, calculi, lymphocele, hematoma, abscess, kinking, and technical problems. Some occurrences of transplant ureteric stenosis may be associated with ureteric leak or necrosis (Figure 4).

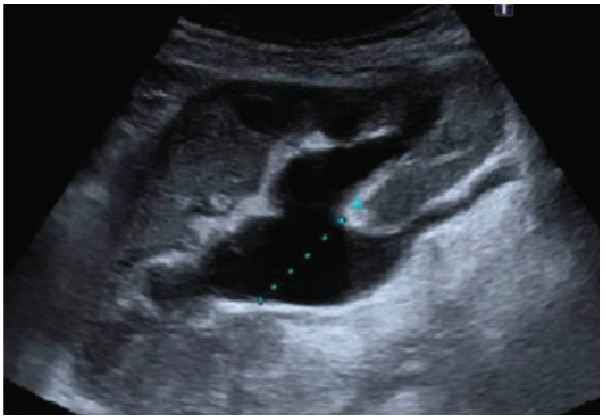

Figure 4. Ultrasonographic Image Showing Hydronephrosis Due to Distal Ureteral Stricture

Percutaneous therapy of ureteral strictures consists of balloon dilatation with or without temporary stenting (Figures 5 and 6). Balloon dilatation should be repeated to achieve adequate results, especially in patients with resistant strictures. A cut balloon may also be applied in fibrotic strictures in which a standard balloon dilatation would usually fail. After the successful dilatation, most authors suggest temporary stenting of the ureter with a double J stent. Metallic stents have been used to treat ureteral stenoses after a failed balloon dilatation, but uroepithelial ingrowth has been a major issue with these devices.[20]

If all of these methods are unsuccessful, surgical treatment should be applied. The options are to perform either a ureteral reimplantation or an ureteroureterostomy using the native ureter (side-to-side or end-to-end) through an abdominal or a kidney incision.

There are 3 different surgical techniques for ureteral stricture management occurring after the renal transplant: (1) proximal transections of the anastomosis after anastomosis stricture and performing ureteroneocystostomy; (2) excision of the

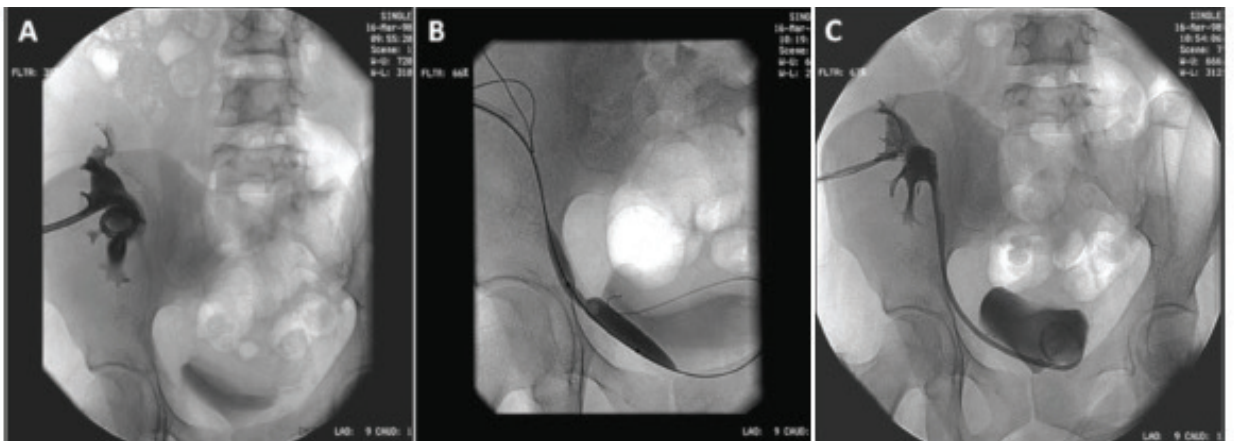

Figure 5. Distal Ureteral Stenosis and Balloon Dilatation and Double J Stent Placement
(A) and **(B)** Distal ureteral stenosis and balloon dilatation. **(C)** Double-J stent placement.

strictured part and end-to-end ureteroureterostomy; and (3) ureteroureterostomy using the native ureter (ipsilateral or contralateral native ureter). At our center, we have performed 4 revisions after ureter strictures. In 2 patients, the old ureteroneocystostomy was terminated and a new ureteroneocystostomy was performed. In 1 patient, we performed native nephrectomy and end-to-side anastomosis between the native ureter and graft's renal pelvis (Figure 7). Figure 8 shows the same patients

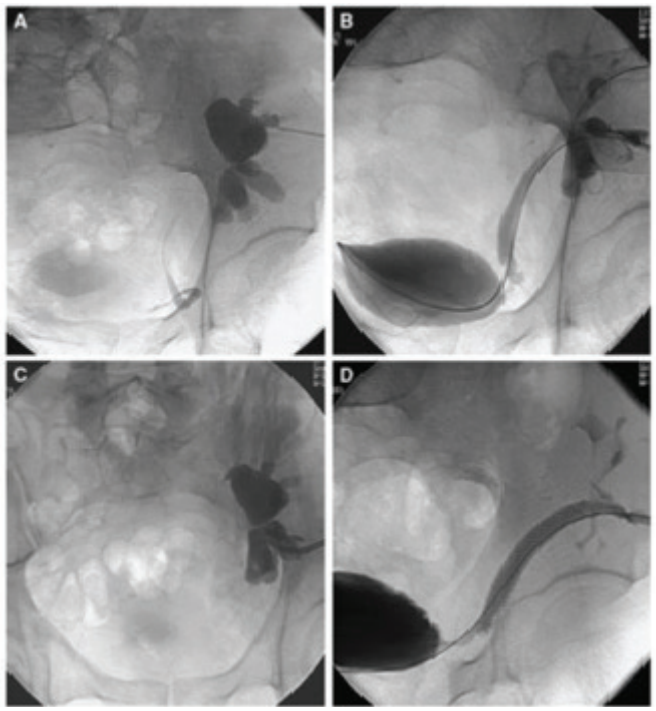

Figure 6. Interventional Radiological Treatment of Ureteral Stenosis

(A) Hydronephrosis and proximal ureteral stenosis. **(B)** After balloon dilatation of ureter, infundibulum and pelvis with 2 percutaneous access points to the kidney. **(C)** Complete obstruction developed at 2-month follow-up, and again percutaneous nephrostomy was placed. **(D)** Resistant stenosis of ureteral anastomosis, treated with metal stenting.

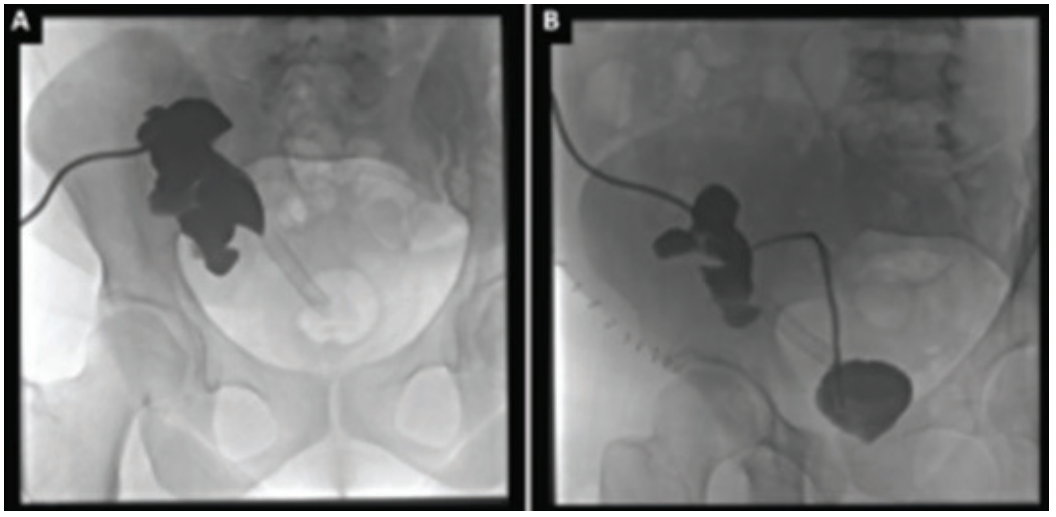

Figure 7. Interventional Radiological Control After Ureteroureterostomy Surgery

(A) Antegrade pyelography was performed via nephrostomy catheter revealing occlusion of the ureter (previously a metal stent had been placed and was also occluded). **(B)** Successful surgical result after uretero-ureterostomy pyelography.

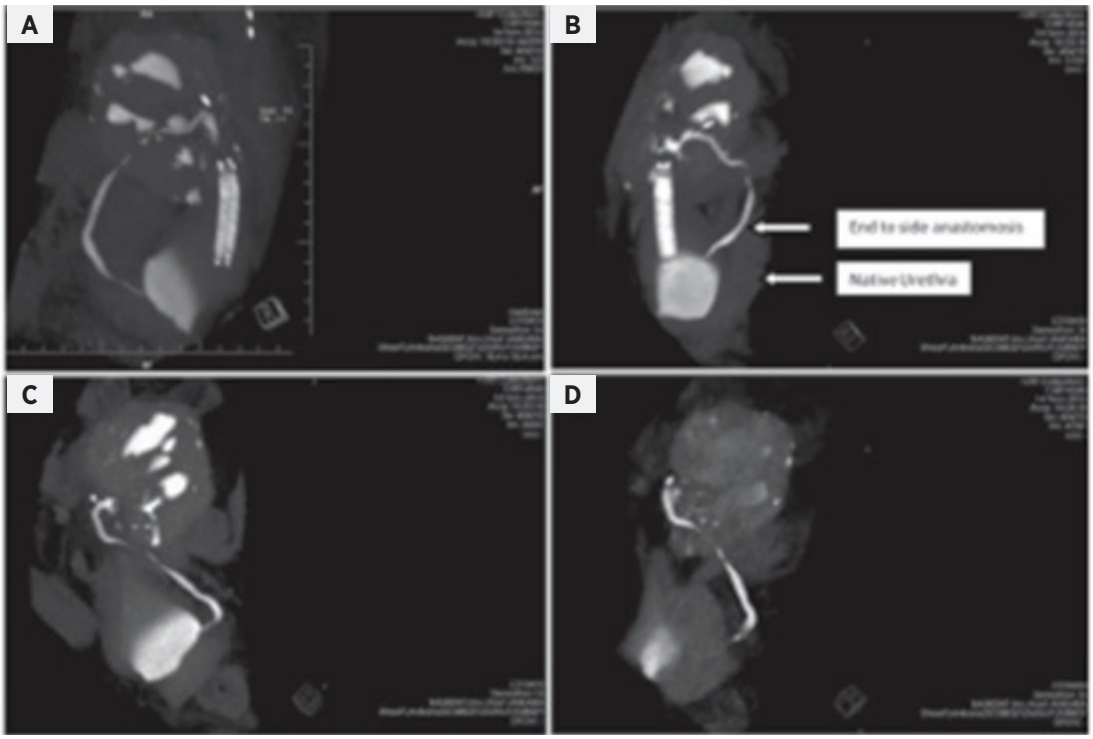

Figure 8. Ureteroureterostomy Anastomosis Seems Normal and Preoperative Pelvicalyceal Dilatation Has Disappeared

(A-D) Six-month posttransplant tomography images of patients with native nephrectomy and end-to-side anastomosis between native ureter and graft's renal pelvis.

at their postoperative 6-month evaluations. In the other patient, we performed end-to-side anastomosis between the graft's ureter and native ureter.

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Interventional Radiology in the Management of Urologic Complications After Renal Transplant

E. Umut Özyer

Although advances in surgical techniques such as intraoperative double J stent placement in selected cases and corner-saving ureteroneocystostomy technique defined by Haberal and colleagues have led to reduction in urologic complications, these complications still constitute the most frequent surgical complications after renal transplant.[1-6] In parallel with the evolution of minimally invasive percutaneous techniques and acquired experience, there has been a major shift from surgery to interventional radiologic procedures in the management of these complications, because these procedures have shown high technical success, acceptable long-term outcomes, and important advantages over surgery, such as easy repeatability and lower morbidity.[7-9]

This chapter addresses interventional radiologic management of ureteral obstructions and leaks after renal transplant surgery. The management of perirenal collections is mentioned in detail in another chapter in this book.

PERCUTANEOUS MANAGEMENT OF URETERAL OBSTRUCTIONS

A diagnostic ultrasonographic examination is the primary step for successful percutaneous management. Besides pelvicalyceal dilatation, any perirenal collection and distention of the bladder should be checked before an intervention. In case of bladder distention, it is necessary to repeat the ultrasonographic exam after emptying the bladder to rule out dilatation secondary to vesicoureteral reflux. If a perirenal collection is the cause of obstruction, then pelvicalyceal dilatation and serum creatinine will regress shortly after drainage of this collection.

In case of a fibrotic stricture or intrinsic ureteral obstruction, management gets more complex. Certainly, there are some technical variations among interventional radiologists according to their experience with the procedure and equipment. Nevertheless, the general routine is placement of a percutaneous nephrostomy catheter succeeded by follow-up with a double J stent for a certain period of time (Figure 1).

Before the procedure is started, the patient's international normalized ratio (INR) level and platelet count should always be checked. An INR level over 1.5 and platelet count < 50 000/μL constitute contraindications to percutaneous interventions and should be corrected before the intervention. Local anesthesia is adequate for performing antegrade pyelogram and nephrostomy placement. However, conscious sedation-analgesia with intravenous midazolam and fentanyl is usually required for further interventions. Antibiotic prophylaxis is mandatory before all interventional procedures concerning the urinary system.[10]

The common approach is to start the management with an antegrade pyelogram to gather anatomic

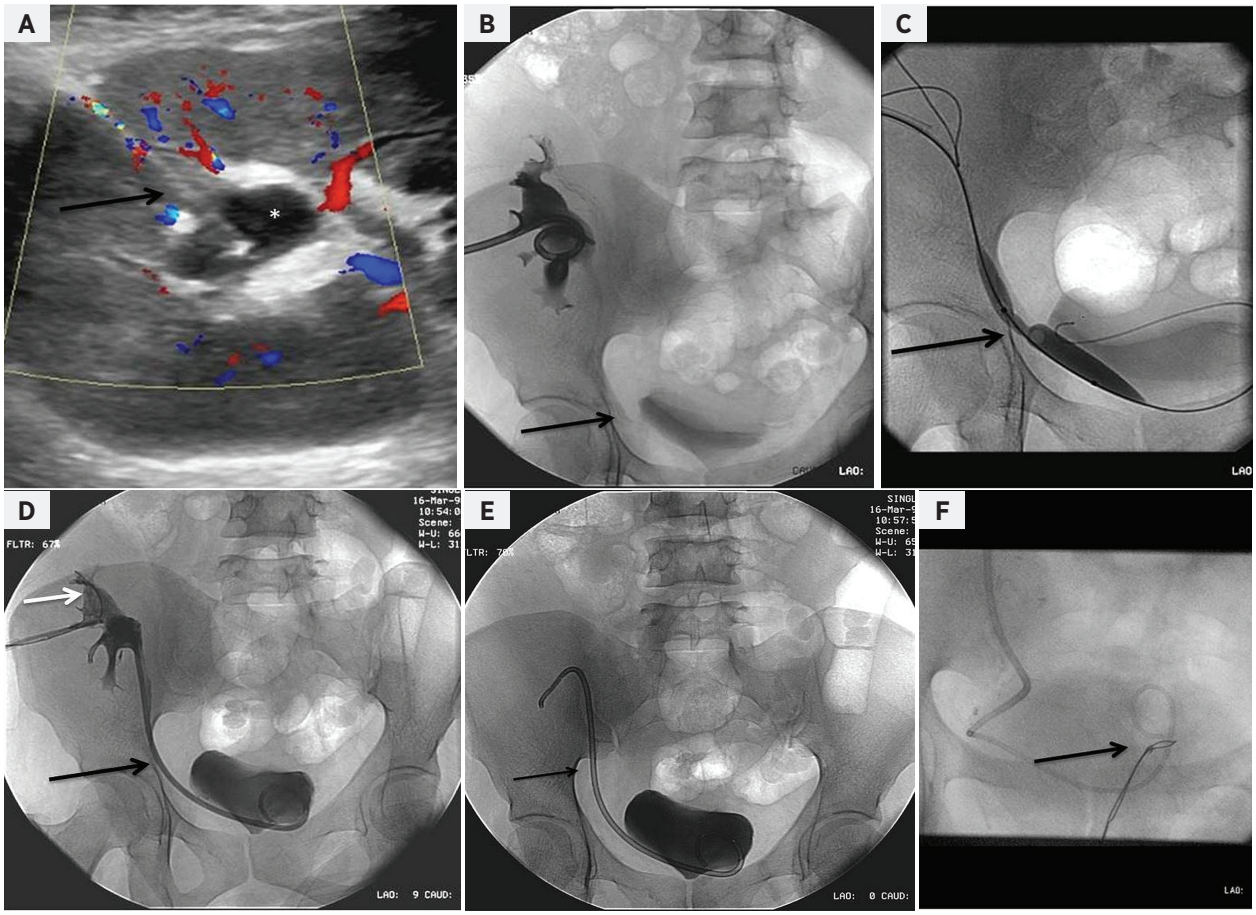

Figure 1. Oliguria and Hydronephrosis 6 Months After Transplant in 43-Year-Old Recipient

After puncture of the midpole calyx under color Doppler ultrasonographic guidance, a nephrostomy is placed. **(A)** Dilated superior calyx (*) puncture with a 21-gauge needle. Under color Doppler ultrasonographic guidance, the needle is advanced into the calyx through a vessel-free zone (arrow). **(B)** Nephrostogram 1 week after nephrostomy placement shows stenosis of the distal ureter (arrow). **(C)** Waist on the balloon (arrow) indicates the site of stenosis. **(D)** An 8F double J stent is placed (black arrow). The safety wire (white arrow) at the upper pole is to provide access for safety nephrostomy placement. **(E)** Safety nephrostomy removed after 24 hours. The patient is followed for 3-6 months with the double J stent (arrow). **(F)** Removal of the stent with the gooseneck snare (arrow) after 5 months.

information, to assess the flow along the ureter, to confirm the diagnosis of obstruction, and to demonstrate the precise location of it. Careful calyceal targeting is important as the direct puncture of pelvis or infundibulum may result in posterior division artery damage that may be complicated by persistent hematuria.[11] To prevent complications, the operator should prefer calyceal puncture under color Doppler ultrasonographic guidance (Figure 1A).[12] A superior and lateral calyx puncture should be performed whenever possible (Figure 2A).[10,11] The superior calyx approach provides optimal support while crossing the ureteral obstruction and placing an antegrade double J stent, whereas the lateral calyx approach minimizes the traversed cortex distance and avoids traversing the peritoneum and bowel segments.

Pelvicalyceal dilatation is the primary finding in ureteral obstructions; however, it should not be considered as a decisive sign of obstruction. It should be kept in mind that mild hydronephrosis is normal in some grafts due to denervation, and it can also be secondary to reflux.[7,13] For this reason, a less traumatic 21-gauge fine-needle system should be preferred over an 18-gauge needle to perform antegrade pyelogram.

After the ideal calyx is punctured with a 21-gauge needle under real-time ultrasonographic guidance, urine is aspirated and an antegrade pyelogram is performed with injection of contrast medium. If unobstructed passage of the contrast medium along the ureter and into the bladder is monitored, then the 21-gauge access needle can be removed without significant risk of bleeding, and the patient may be investigated with biopsy for rejection. When there is clinical suspicion of infection, antegrade pyelography using a large amount of contrast medium is deferred to avoid septicemia, and the routine management is the placement of a 10F to 12F nephrostomy catheter via the same access and follow-up for 1 week before further interventions are performed.[1,14,15] The nephrostomy catheter relieves tension by decompressing the upper urinary tract, recovers deteriorated renal function secondary to obstruction, provides safe access to further interventions, and confirms the diagnosis of obstruction and/or leaks by performing nephrostogram on follow-up (Figure 1B). Depending on the operator's choice, calyceal puncture can be performed with an 18-gauge needle to directly place a nephrostomy catheter. This approach is preferred when there is high suspicion of infection, pyonephrosis, or moderate to marked hydronephrosis with previous history of obstruction. In case of obstruction secondary to ureteral edema or ureteropelvic hematoma, percutaneous nephrostomy is almost always sufficient for management, and no further interventions are necessary.[15]

As previously mentioned, prior decompression of the pelvicalyceal system with the nephrostomy catheter and intervention to cross the obstruction via this access after resuming renal function is the common approach (Figure 1). The decision to primarily cross the obstruction instead of waiting for nephrostomy decompression and renal function recovery is an acceptable alternative when there are no signs of infection, hematuria, or pain (Figure 2). The focal strictures may be attempted to cross gently with a 0.035-inch hydrophilic guidewire and 4F to 5F angled catheter manipulations (Figure 2B). In case the operator encounters an impassable stricture, coaxial 2.4F to 2.7F microcatheters and 0.014- or 0.018-inch guidewires can aid crossing the lesion.[14] However, it should be kept in mind that an approach without decompression bears risk of sepsis and should not be performed aggressively. The obstruction crossing technique is the same for patients managed with primary decompression.

Obstructions are passable most of the time. Should there be a failure of crossing the obstruction despite all attempts, a nephrostomy catheter is placed for decompression, and surgical revision is indicated. After the crossing of the obstruction with the aforementioned catheter-guidewire manipulations, the operator may choose to place either a double J stent with a safety nephrostomy catheter or a nephroureterostomy catheter (Figures 1 and 2).[7,10,14] Balloon dilatation is advised before placement, as it ensures easier advancement of the stent/catheter and durable primary patency (Figures 1C and 2C).[7,18,14]

With regard to optimal balloon size and inflation pressure or the effect on recurrence, there are no current recommendations. Balloon diameter is selected according to adjacent normal ureter diameter. In common practice, 5- to 6-mm diameter high-pressure (> 20 atm) conventional balloons provide satisfactory results without any significant morbidity.[8] For better results, the fully dilated balloon is kept inflated for 2 to 3 minutes, and preferably dilatation is repeated 2 to 3 times.

Although no residual stenosis may exist on postdilatation pyelogram, the preference is to shield the obstruction site from recoil, which is achieved by placing a double J stent or a nephroureterostomy catheter (Figures 1 and 2).[1,7,14,16] Before placement of a double J stent, it is necessary to place a second safety guidewire in the renal pelvis to provide access for placing a safety nephrostomy catheter after double J stent placement (Figure 1D). Because there are various manufacturers, double J stent placements vary among different brands. Therefore, the stent with which the operator is most familiar should be used, or the instructions of the manufacturer for an unfamiliar stent should

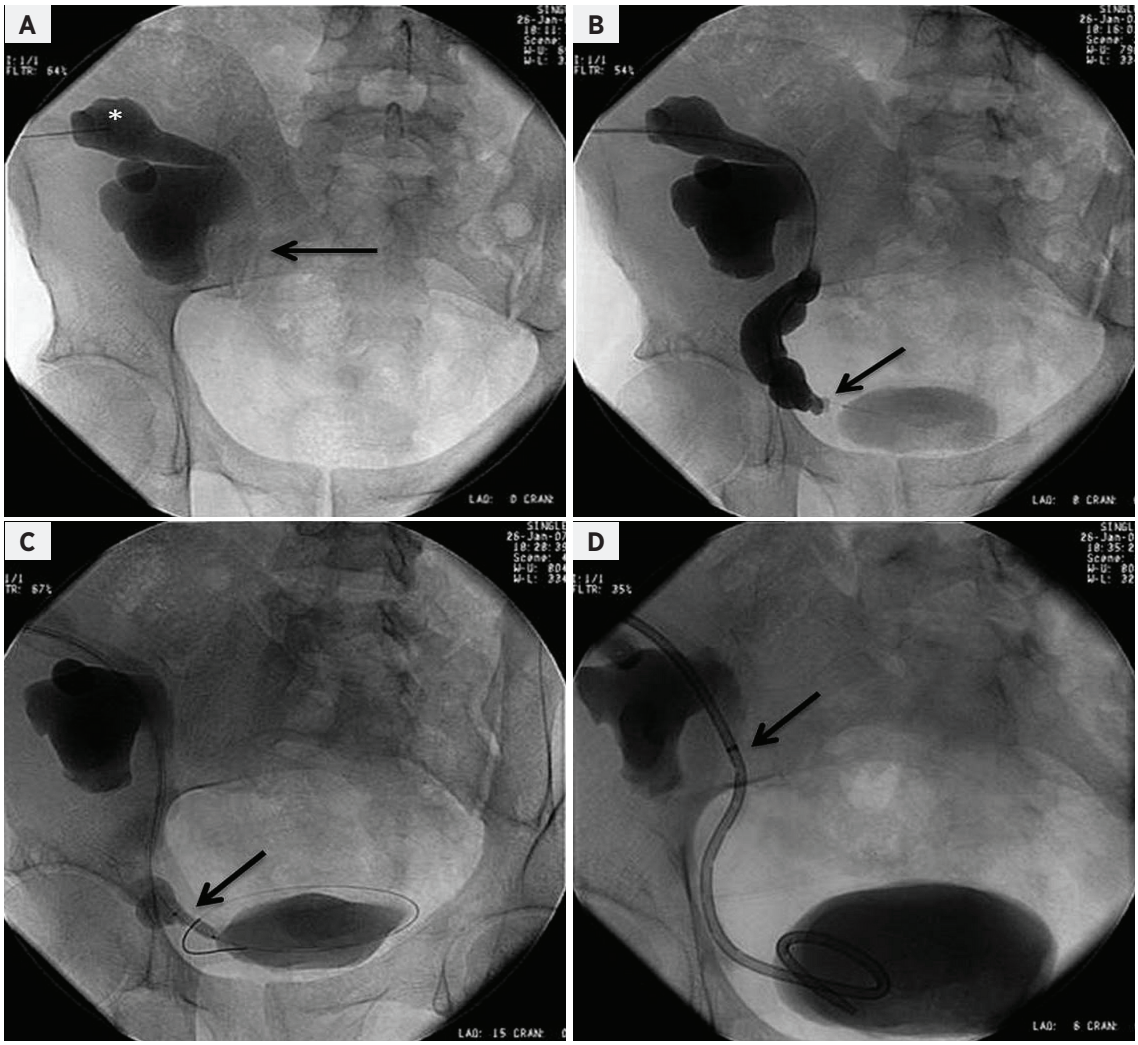

Figure 2. Oliguria and Marked Hydronephrosis 5 Months After Transplant in 50-Year-Old Male Recipient

(A) Antegrade pyelogram performed via the needle after superior lateral calyx puncture (*) reveals pelvicalyceal dilatation and poor ureteral passage (arrow). Further contrast medium injection is deferred to prevent septicemia. **(B)** A 5F Kumpe catheter is advanced to the stricture site at the distal ureter (arrow). **(C)** Balloon dilatation with a 5-mm balloon (arrow) after crossing the stricture. **(D)** Nephroureterostomy catheter (arrow) is placed after balloon dilatation.

be read carefully before the procedure. In general, the stent is loaded on the super-stiff guidewire and advanced by a pusher to the bladder under fluoroscopy guidance. After that, the pusher and a looped string traversing the proximal loop of the stent are used to form a proximal loop of the double J stent, which is then placed in the pelvis.

After placement of the stent, the procedure is completed with placement of a safety nephrostomy catheter over the safety guidewire (Figure 1D). The nephrostomy catheter is attached to gravity drainage if hematuria complicates the procedure. After the clearance of blood from urine, the nephrostomy is clamped and removed in case of uneventful follow-up and normal passage of contrast medium on nephrostogram after 24 to 48 hours. In case of uneventful follow-up, ureteral stents are generally removed at 6 months (Figure 1E).[1] Removal is routinely performed with flexible cystoscopy. Alternatively, removal with a snare via transurethral approach may be performed

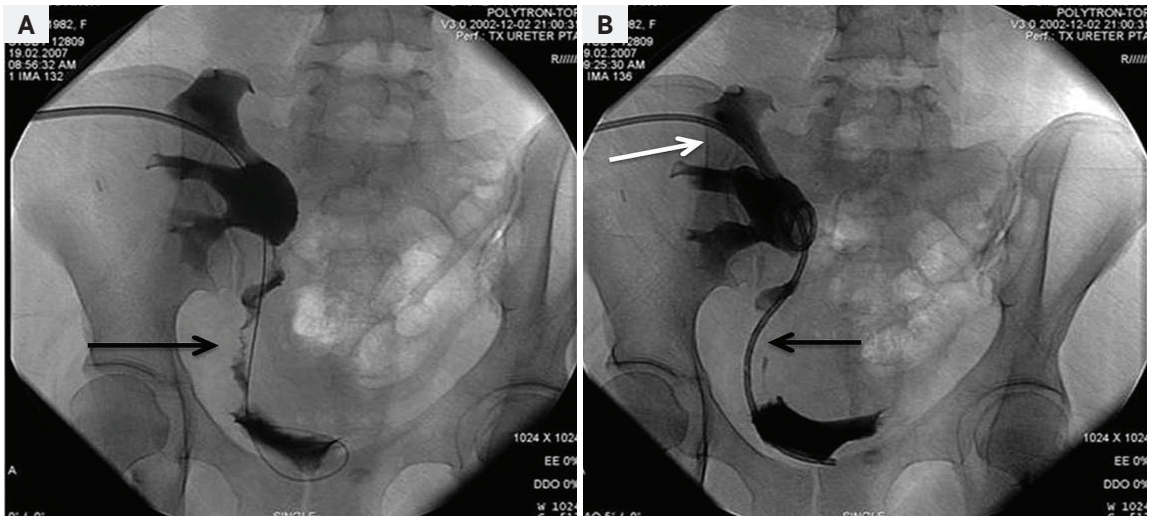

Figure 3. Obstruction at 8 Months After Transplant in 24-Year-Old Male Recipient

Patient was managed with nephroureterostomy and had balloon dilatation 3 times. **(A)** Antegrade pyelogram performed after removal of the catheter demonstrates patent but irregular ureter (arrow). **(B)** After balloon dilatation was performed for the fourth time, a 10F custom-made double J stent (black arrow) and a 10F safety nephrostomy catheter (white arrow) were placed.

under fluoroscopy guidance. After transurethral catheterization of the bladder, with the aid of a 6F guiding catheter and a gooseneck snare or flexible forceps, the distal loop of the double J stent can be grasped and removed (Figure 1F).

An alternative to placement of a double J stent is the placement of a nephroureterostomy catheter, which provides both external urinary diversion and internal bladder flow at the same time (Figure 2). This catheter has the advantage of providing permanent access for repetitive ureter balloon dilatations in 1- to 2-week intervals before the placement of a double J stent; however, it also bears a higher risk of infection.[7,14,15] The operator can perform an antegrade pyelogram to assess ureteral flow after exchanging this catheter over the wire. Balloon dilatation can be performed in case of poor flow, or a double J stent can be placed in absence of persistent stricture (Figure 3). In case the conventional balloons fail while attempting to dilate the tight strictures, then a cutting balloon angioplasty is a viable alternative to provide fissuring of the tight fibrous tissue.[7,10,14] In the case of cutting balloon failure, the only alternative left for the management is surgical revision.[16]

On nephroureterostomy follow-up, 2 to 4 dilatation sessions are carried out in 1- to 2-week intervals using this access. After demonstration of normal flow on nephrostograms, the treatment is maintained with temporary placement of an antegrade double J stent.[7,14] The optimal time interval for retaining double J stents is still controversial. The generally accepted practice is removing or replacing the double J stent with a new one every 3 to 6 months.[14]

In patients with prophylactic protection of the anastomosis with intraoperative double J stenting, one of the most common causes of obstruction has been malposition or occlusion of double J stents.[14-17] Fluoroscopy-guided percutaneous techniques provide a viable alternative to cystoscopic management of these complications with no requirement for general anesthesia. The percutaneous approach also allows assessment of the ureter and provides access for further procedures if necessary.[18] Before the procedure is started, ultrasonographic and fluoroscopic evaluations should be performed to choose the most convenient access calyx for greatest ease of grasping the stent. The aforementioned antegrade

access technique is applicable to gain access to the pelvis. After decompression of the system, the dysfunctional stent is removed using a gooseneck snare or flexible forceps. For this purpose, an 8F vascular introducer sheath can be advanced into the pelvis and, with aid of an angled-tip 6F guiding catheter and a gooseneck snare, the loop of the dysfunctional stent may be grasped and removed (Figure 4). An antegrade pyelogram performed after stent removal is beneficial to diagnose and treat any persistent ureteral obstruction.[18]

A relatively high recurrence rate of strictures is the most important drawback of percutaneous interventions.[8,14,19] The routine management of recurrence is surgical revision. However, percutaneous reinterventions may be more feasible in situations where surgical revision is complicated. The most common percutaneous reintervention for recurrence is long-term follow-up with double J stents. Many studies have shown that the longer the double J stent retains, the better is the outcome.[20] In common practice, the double J stent is retained for 6 months if it does not complicate with infection.[14,19] The duration of double J stents may be prolonged in resistant strictures, as reported by Pappas and colleagues, who found 90% recurrence-free patency with mean stenting duration of 15 months.[20]

Long-term follow-up with the placement of 2 parallel stents rather than a single stent may be a viable alternative to improve outcomes in resistant strictures (Figure 5).[19,21] The rationale behind placement of 2 double J stents is to provide healing in a wide-open configuration.[19] In this so-called "tandem stenting technique," two 8F to 10F double J stents are placed simultaneously over 2 super-stiff guidewires that were placed through the same point of access via an 8F long introducer sheath reaching the bladder. There have been reports revealing the benefits of tandem stents in malignant obstructions, yet their use in posttransplant benign strictures has not been well documented.[22] A few case series have revealed long-term patency of 83% in primary strictures and 58% in strictures resistant to balloon dilatation and double J stent placement.[19,21]

Although it has not been generally accepted, metallic stents can be used for recurrent strictures

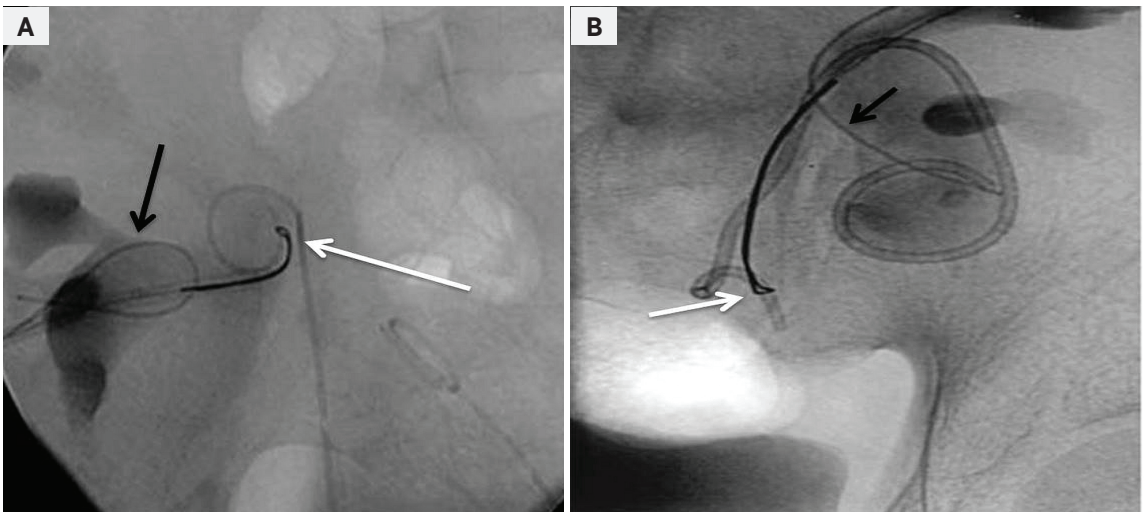

Figure 4. Two Patients Presented with Dysfunctional Double J Stents Secondary to Obstruction and Dislocation of the Stents

Injected contrast medium demonstrates moderate pelvicalyceal dilatation in both patients. Safety wires (black arrows) are looped in the pelvis to continue with the intervention after removal of the stent. **(A)** A snare (white arrow) through a 10F introducer sheath is used to grasp the proximal loop of the occluded double J stent. **(B)** The distal loop of the proximally migrated stent is grasped in the ureter using a snare (white arrow).

unresponsive to reinterventions with long-term double J stents.[1,14] An issue with bare metal stents is that they can get obstructed over time due to uroepithelial ingrowth, and therefore bare metal stents are not preferred.[1,2] Graft-covered stents can be used as an alternative to overcome the issue of uroepithelial ingrowth (Figure 6).[23] In addition to occlusion, metal stents bear risks such as encrustation, hemorrhage, and, most importantly, complication of further surgical revision.[7] To overcome these issues, removable long-term metallic stents such as the Memokath 051 (PNN Medical A/S, Kvistgård, Denmark) can be preferred over routine self-expandable stents (Figure 7). In only a few case series reported, this stent has been shown to have a high long-term patency, but strong evidence is lacking.[1,24] A brief summary of percutaneous management for ureteral obstruction is summarized in Figure 8.

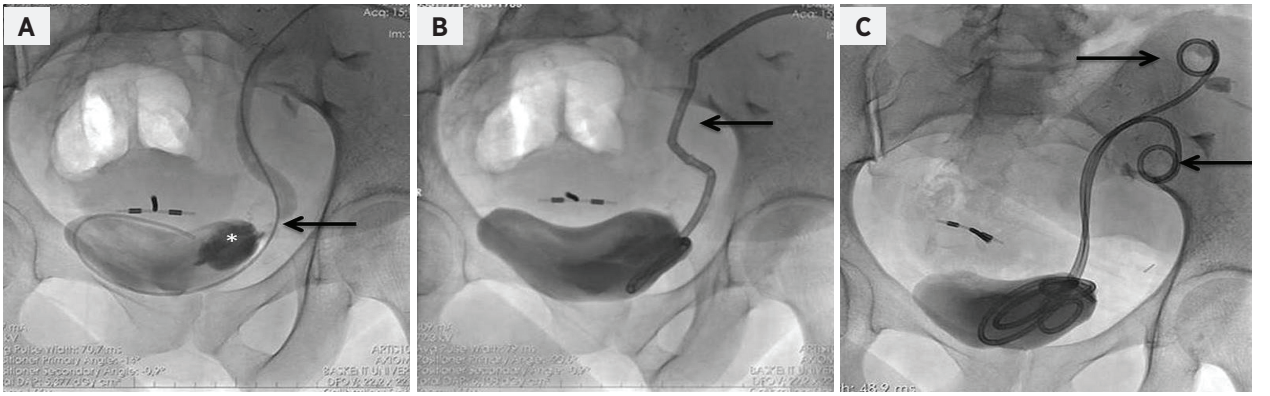

Figure 5. Distal Ureter Stricture Presented at 4 Months After Transplant in 33-Year-Old Recipient

(A) Antegrade pyelogram shows traversed distal ureter stricture (arrow) and perforation (*) secondary to catheter-guidewire manipulations. Perforations that occur during stricture crossing heal with nephroureterostomy or double J stent placement for the obstruction and do not necessitate further interventions. **(B)** A nephroureterostomy catheter (arrow) is placed after balloon dilatation. **(C)** Tandem double J stents (arrows) are placed 3 weeks after the nephroureterostomy.

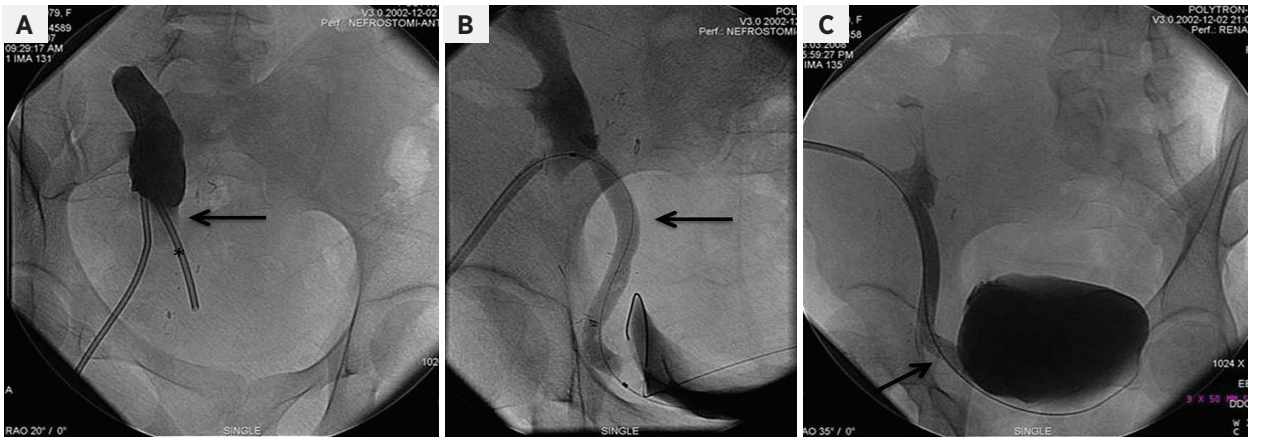

Figure 6. Multiple Recurrent Ureteral Obstructions in 28-Year-Old Female Recipient

Multiple balloon dilatation and double J stent treatments failed in the long term. Ten months after retrievable thermo-expandable stent placement, she presented with reobstruction again. Due to lack of thermo-expandable stents, a graft stent placement was planned. **(A)** Nephrostogram shows obstruction at ureteropelvic junction (arrow). Thermo-expandable stent (*) is dysfunctional and migrated proximally. **(B)** After removal of the retrievable thermo-expandable stent, a graft-covered stent (arrow) is placed. **(C)** Another stent (arrow) is placed at the distal ureter after 8 months of graft-covered stent placement due to a new stricture formation.

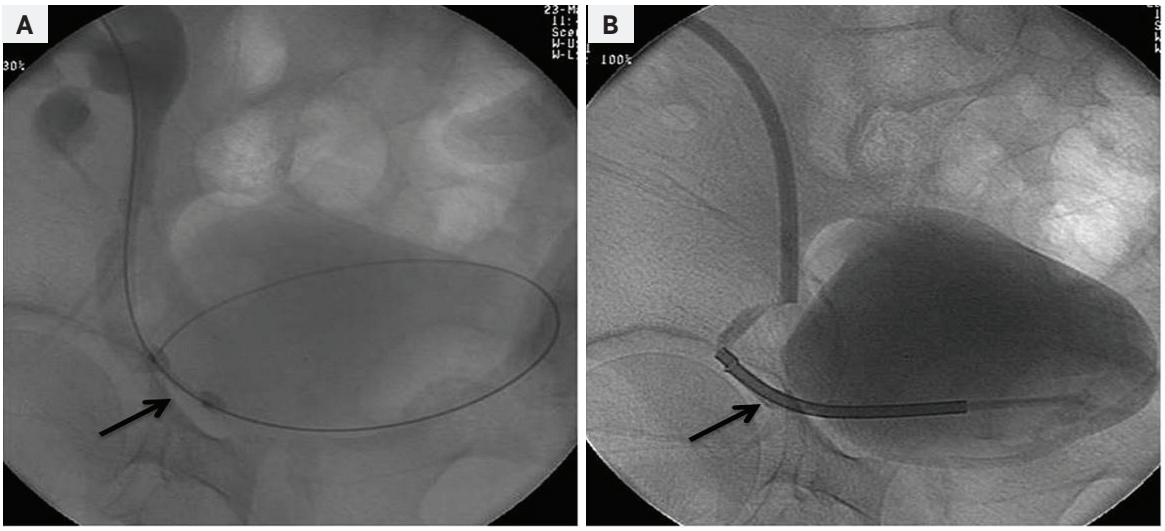

Figure 7. Third Recurrence of Distal Ureter Stricture After Treatment With Double J Stent in 49-Year-Old Recipient
(A) Waist on the balloon (arrow) indicates the site of stricture. **(B)** Retrievable thermo-expandable stent (arrow) is detached from the catheter and provides passage to the bladder.

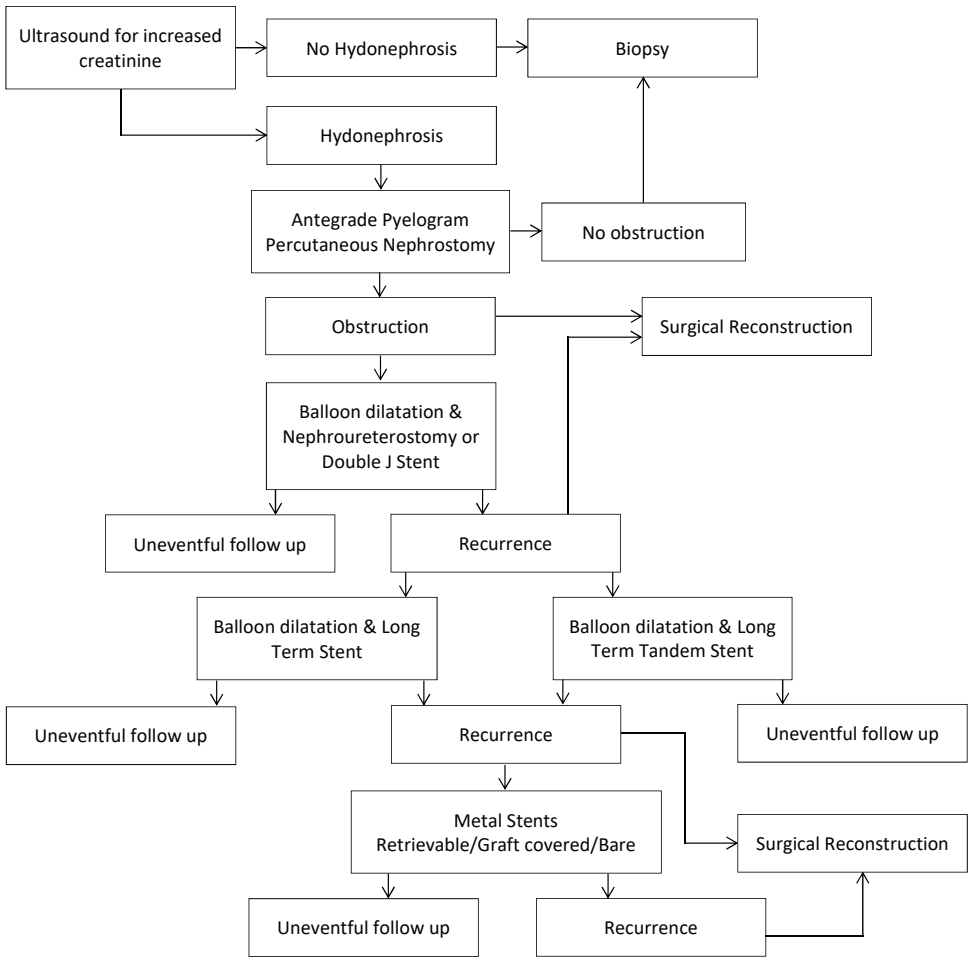

Figure 8. Management of Ureteral Obstructions

A rare cause of late ureter obstruction is renal stones. The recommended management for obstructive stone disease is decompression with a percutaneous nephrostomy or a retrograde double J stent. After that, treatment involves shock-wave lithotripsy or ureteroscopy for stones smaller than 15 mm and percutaneous nephrolithotomy for stones larger than 20 mm.[17] Existing percutaneous nephrostomy access may also be used for basket extraction of small stones.[14]

Obstruction secondary to intraluminal blood clot is also rare and is easily manageable with sole placement of a nephrostomy catheter and saline irrigation.[15] The routine management of urinary retention is Foley catheterization. In case of failure in the placement of a transurethral Foley catheter secondary to urethral strictures, percutaneous cystostomy placement under ultrasonographic guidance may be used as an alternative. However, the percutaneous cystostomy procedure may not be applicable in patients with ileal neobladder. In these patients, it is possible to place a Foley catheter after crossing the urethral strictures with catheter-guidewire manipulations under fluoroscopy guidance (Figure 9). A 4F angled tip catheter and a 0.035-inch hydrophilic guidewire are usually sufficient to cross the urethral strictures. After that, the stricture is treated with repetitive balloon dilatations in 2-week intervals, either with conventional or cutting balloons, and Foley catheterization to secure the passage is feasible.[25]

Percutaneous treatments with reinterventions offer patency comparable to surgical revision.[8] The reported success rates with early obstructions range between 48% and 100%, whereas these rates are between 16% and 60% in late obstructions.[7,10,14,15] In addition to these various results among early- and late-onset stenosis, the key result of these studies is that graft survival similar to early obstructions can be maintained with percutaneous reinterventions in late-onset obstructions that utilize percutaneous interventions as a viable alternative.[8]

There is no strong evidence concerning the effects of balloon dilatation on long-term patency; however, the use of repetitive balloon dilatations before stenting seems to be the best approach for the moment. Most reports in the literature

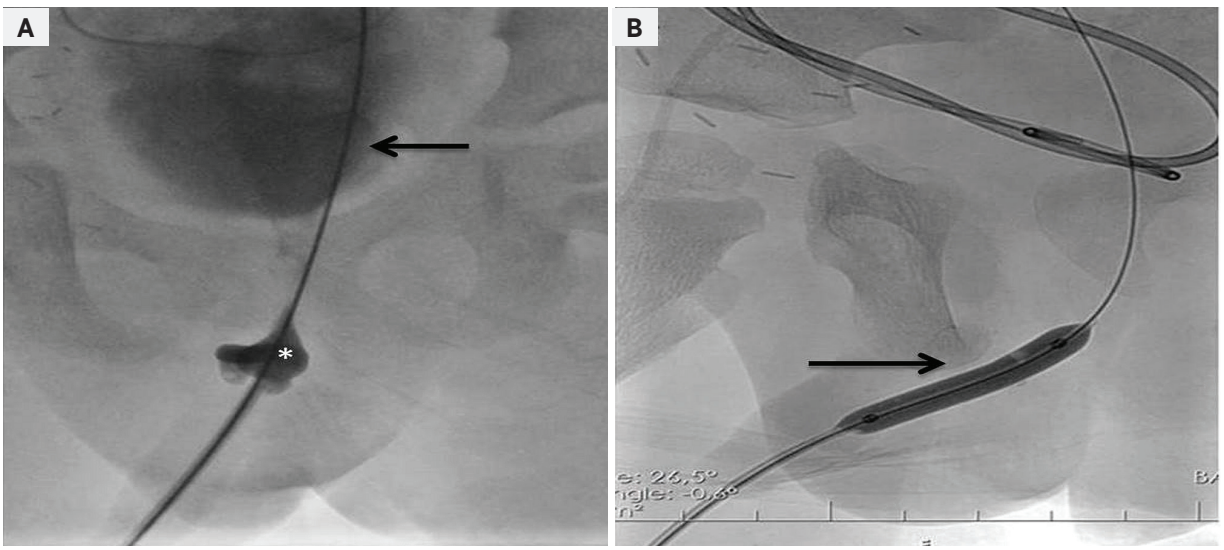

Figure 9. Ileal Neobladder Presented With Urinary Retention at 7 Months After Transplant in 5-Year-Old Recipient

Foley catheter placement failed. **(A)** Urethrogram after passage to the neobladder (arrow) shows a sac proximal to the urethral stricture (*). **(B)** Second balloon dilatation session. After balloon dilatation (arrow) of the urethra, a Foley catheter will be placed over the guidewire and will provide patency and access for further urethral dilatations.

presenting high patency have preferred repetitive balloon dilatations before stenting. Some studies have also revealed that repetitive balloon dilatations could provide similar patency among late and early obstructions.[1,7,8,14,19,26]

Major complications of percutaneous treatment are loss of graft, septicemia, hematuria requiring intervention, and damage to surrounding organs. These major complications are extremely rare, with no cases reported in most series. However, minor complications such as obstruction, encrustation, or dislocation of the stents, ureteral perforation, mild hematuria, self-limiting subcapsular hematomas, and infections treatable through antibiotherapy are common and have a reported incidence of between 14% and 52%.[7,10]

PERCUTANEOUS MANAGEMENT OF URINARY LEAKS

The most common sites for urinary leak are anastomosis and distal ureter. Calyceal leaks are far less common than ureteral leaks.[3,7] Ultrasonographic examinations will demonstrate an anechoic fluid collection without calyceal dilatation in leakage. However, these fluid collections may compress the ureter, and calyceal dilatation may develop in time. Aspiration under ultrasonographic guidance and analysis of fluid with high creatinine levels allow diagnosis of leaks.[10,11]

Diagnosis of urinoma requires timely and prompt treatment because infections in these immune-suppressed patients are life threatening.[15] Placement of a drainage catheter into the urinoma is the first step in management (Figure 10A).[7] Ultrasonographic guidance is almost always suitable for this purpose. After the collection is punctured with an 18-gauge needle and fluid is aspirated for diagnostic purposes, usually an 8F to 10F drainage catheter is placed by the Seldinger technique.

The main purpose of percutaneous leak treatment is to divert urine away from the defect. The presence and precise site of leakage should be demonstrated to plan the appropriate management. A cystogram carried out with the urinoma drainage catheter may demonstrate the leak tract and the site of leakage, and a cystogram performed from the urinary bladder may demonstrate the leaks from the ureterovesical anastomosis.[3] Antegrade pyelography is the optimal imaging technique to demonstrate the presence and precise location of urinary leakage[27] (Figure 10A); also, it is the primary step in the percutaneous management of urinary leaks. The aforementioned antegrade pyelogram technique used for urinary obstructions is also valid for urine leaks. However, absence of calyceal dilatation may create complications for the operator when conducting the calyceal puncture. Thus, entry with a 21-gauge Chiba needle and a 3-part coaxial introducer system is almost always recommended to reduce complications in these patients. If not contraindicated, intravenous administration of diuretics and fluids before the intervention may help in visualizing calyces on ultrasonography.

After successful calyceal puncture and demonstration of the pelvicalyceal system and the leak with contrast medium injection, a 10F to 14F nephrostomy catheter is placed in the pelvis to divert the urine flow. Nephrostomy placement provides primary healing of the leaks with reported success rates of between 63% and 83%.[11] However, ureteral leaks may persist despite the nephrostomy drainage and also possess the risk of ureteral stricture during the healing process.[2,3,14] Therefore, it is preferred to place an antegrade double J stent in addition to the nephrostomy catheter or place a 10F to 14F nephroureterostomy catheter across the site of leak to help close the defect and to prevent fibrotic stricture formation during the healing process (Figure 10B).[2,7,14,15]

The expected duration of complete leak cessation ranges between 2 and 6 weeks.[14] After complete cessation of the leak and demonstration of uneventful passage of contrast medium on nephrostograms, the nephrostomy catheter is withdrawn, and the patient is followed-up with a double J stent for 3 to 6 months to allow uroepithelial growth over the leak site (Figure 10, C and D).[19,27]

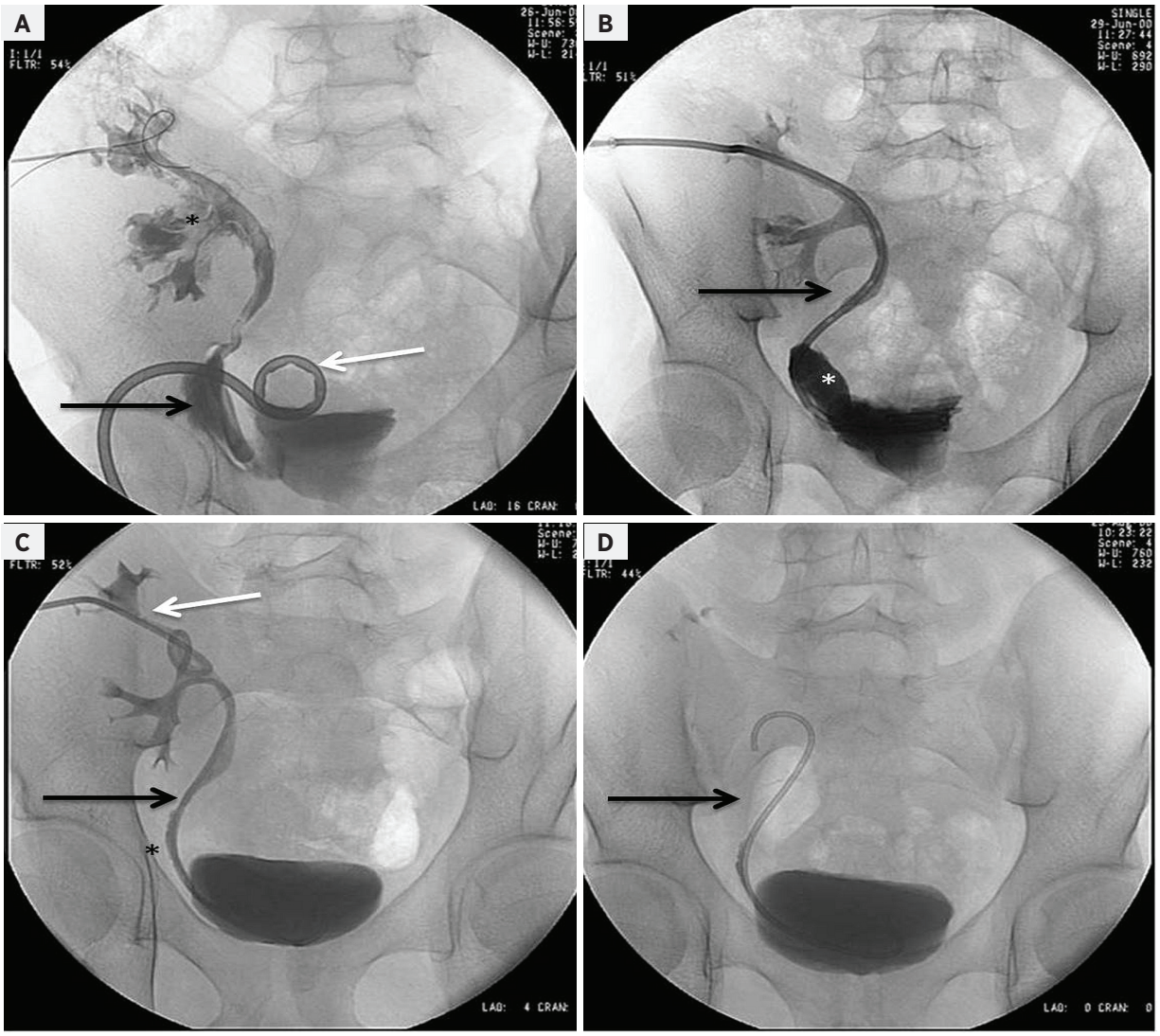

Figure 10. Urinoma at 23 Days After Transplant in a 20-Year-Old Patient

(A) Antegrade pyelogram shows hemorrhage in the collecting system (*) and contrast extravasation at the distal ureter (black arrow). Passage to bladder is conserved. Urinoma drainage catheter (white arrow) was placed earlier. **(B)** A nephroureterostomy catheter (arrow) is placed, and follow-up is started. Control nephroureterostogram after 3 days shows persistent leak (*) and resolved hemorrhage in the collecting system. Urinoma drainage catheter is removed after cessation of urine. **(C)** Complete absence of leak on day 25 (*). An 8F double J stent (black arrow) and a 10F safety nephrostomy catheter (white arrow) are placed. **(D)** Two days later, safety nephrostomy is removed after nephrostogram control and the patient is followed-up with a double J stent (arrow) for 3 months.

Surgical revision is the choice of treatment in case of leak recurrence.[14,17]

Calyceal leaks are far less common and require surgical revision in most cases. Drainage of the urinoma and diversion of urine by percutaneous nephrostomy placement provide less complicated surgery. When surgery is contraindicated, follow-up with nephrostomy and urinoma drainage catheters until the cessation of leakage may be of use.

Percutaneous interventions for urinary leaks possess the same previously mentioned complication risks with the same rates versus those of ureteral obstructions.[7] These techniques

have high reported success rates, ranging from 58% to 95%. The best results in the literature have been achieved by following up with a nephroureterostomy until complete resolution of the leak on nephroureterostograms and by placing a double J stent that remained in place for 3 to 6 months after that.[7,14] Technical failure of percutaneous management is rare and is commonly due to complete absence of ureteral continuity, which requires surgical revision.[10,14]

SUMMARY

Percutaneous management has become the treatment of choice for ureteral obstructions and leaks after renal transplant; it is a viable alternative to surgical revision with high technical success and lower morbidity than other treatments. Repeat interventions are usually necessary to maintain long-term success. Percutaneous reinterventions and further surgical revision are not precluded in case of failure.

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Renal Biopsy

Çağrı Kesim
Çağatay Andiç

OVERALL CLINICAL RELEVANCE OF RENAL BIOPSY

Renal biopsy is an integral part of the diagnosis and management of renal diseases. The technique was introduced in 1951[1] and generally employed after further development in 1954.[2]

Percutaneous biopsy has become one of the most commonly performed image-guided interventional procedures in radiology practice today. With refinement in imaging guidance (Figure 1), biopsy devices, and techniques, previously inaccessible and difficult-to-biopsy lesions are now routinely diagnosed. Paralleling the advances in image guidance has been the development of histopathologic, cytopathologic, and immunologic stains to further characterize tissue specimens[3] (Figure 2).

The minimally invasive nature of current outpatient biopsy techniques allows rapid diagnosis and formulation of treatment plans. Collaboration with cytopathology and histopathology departments is useful to determine the optimum needle choice for improved tissue adequacy and diagnosis and can provide valuable quality assurance feedback[3].

BIOPSY DEVICES

The various devices used for soft-tissue biopsy of abdominal, thoracic, and other lesions can be classified based on sampling mechanisms and needle-tip configurations. Such devices include aspiration needles and small and large cutting core biopsy needles.[4]

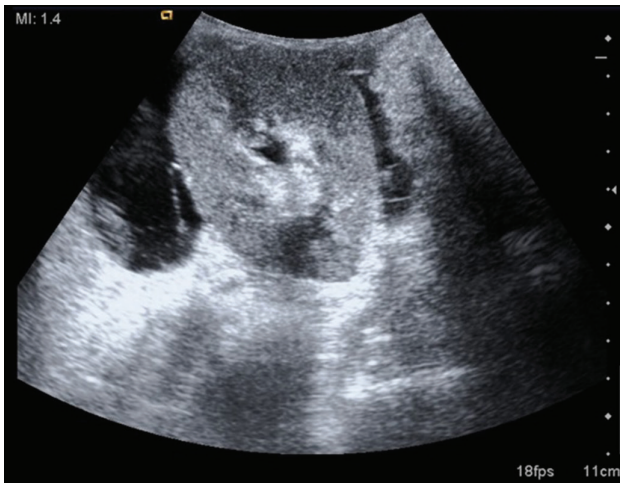

Figure 1. Axial Ultrasonography Image of a Transplanted Kidney with small lymphocele around it

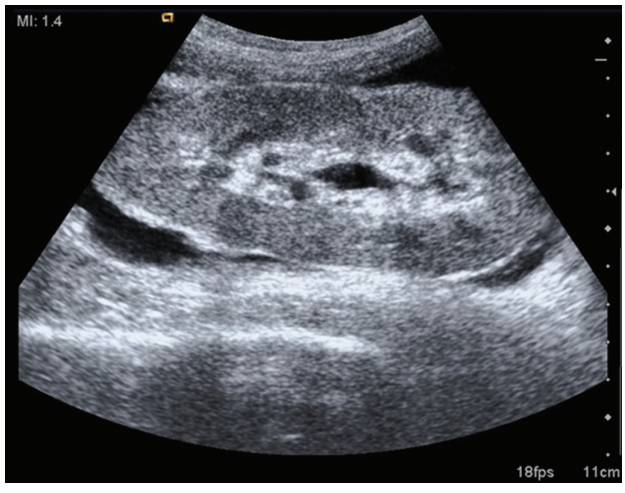

Figure 2. Sagittal Ultrasonography Image of a Transplanted Kidney

The selection of the biopsy device is based on patient history, location of the lesion, imaging appearance of the mass, intended trajectory of the needle, and, more importantly, the type of information sought from the pathologic sample. Coagulation status, proximity to vital structures, and expertise of the radiologist also play roles in needle selection. The needles can be used alone or coaxially with guide needles when multiple specimens are needed. Needle size is typically designated by gauge, in which the larger the gauge number, the smaller the needle size. An 18-gauge needle is approximately 0.05 inches or 1.27 mm in outside diameter, and a 22-gauge needle is 0.028 inches and 0.77 mm in outside diameter. Histologic diagnosis can be ascertained in most situations with an 18- to 20-gauge biopsy needle.

PERCUTANEOUS RENAL TRANSPLANT BIOPSY

Clinical relevance

Despite advances in noninvasive diagnostic tests and techniques, a core needle biopsy is still considered the standard technique for diagnosing renal transplant dysfunction. Although the procedure is relatively simple to perform, it carries a risk of complications, especially those related to bleeding and vascular injuries. Therefore, radiologists should be familiar with the proper biopsy technique to minimize these complications.[5]

Before biopsy, coagulation profiles should be obtained to exclude bleeding disorders. An uncorrectable coagulopathy is an absolute contraindication to biopsy.

If the patient is scheduled for hemodialysis, we routinely postpone dialysis until at least 24 hours after biopsy to facilitate hemostasis. Little or no heparin should be used for the first postbiopsy dialysis treatment.[6]

Real-time ultrasonography (US) guidance is most commonly used for these biopsies (Figure 3) because it allows precise localization of the allograft and the renal cortex, which contains the glomeruli to be targeted. A tangential approach at either the upper or lower pole of the allograft yields the largest biopsy area within the renal cortex and avoids major intra- or extrarenal vessels.[6,7] The needle track within the kidney should traverse only the renal cortex (Figure 4). Major vessels can easily be identified with additional color Doppler flow US.

Although core needle biopsies performed with 16- to 18-gauge automated or semiautomated needles are the most common, some centers also per-

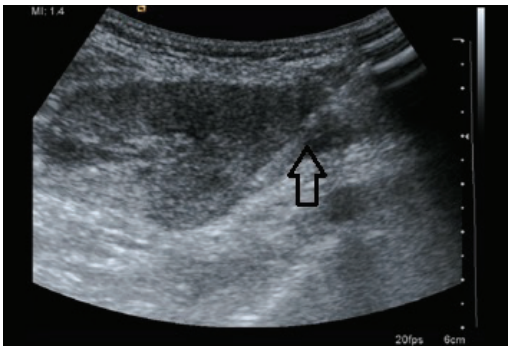

Figure 3. Renal biopsy is performed mostly on the lower pole of the kidney (Black arrow).

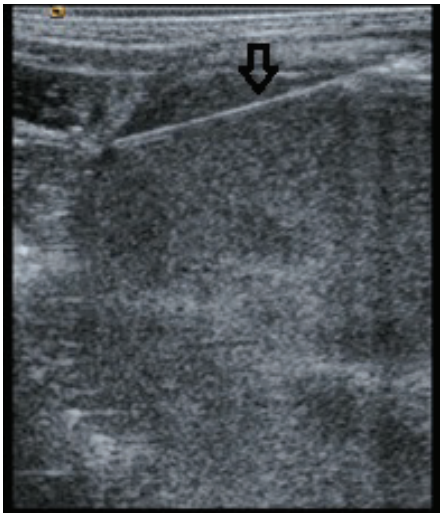

Figure 4. Biopsy of a renal transplant under real-time ultrasonographic guidance.

An 18-gauge core biopsy needle (black arrow) was advanced into the allograft cortex.

form fine-needle biopsy, which can help detect the presence of rejection but not the degree or type.[8] Ultrasonography is performed after the biopsy to identify any acute bleeding complications.

The reported prevalence of complications, including macroscopic hematuria, ranges from 0.06% to 13%.[7] Macroscopic hematuria is reported to occur in 5% to 8% of patients.[9,10] The wide variation in the complication rate may depend on multiple factors, including the use of imaging guidance, the gauge of the biopsy needle, and availability of follow-up imaging. Major complications of biopsy that lead to allograft loss are quite rare.[8,11] Complications that potentially require intervention include perirenal hemorrhage and development of arteriovenous fistulas (AVFs), pseudoaneurysms, and arteriocaliceal fistulas. These complications can be managed with transcatheter embolization techniques.

Biopsy-induced vascular injuries

Arteriovenous fistulas and pseudoaneurysms are the 2 most common types of vascular injuries resulting from percutaneous needle biopsy, occurring in conjunction with 1% to 18% of renal allograft biopsies.[12] An AVF occurs when an adjacent artery and vein are lacerated simultaneously; a pseudoaneurysm occurs when only the artery is lacerated. These vascular complications are easily detected with color Doppler flow and duplex Doppler US. Characteristic US findings in patients with AVFs include focal areas of disorganized color flow outside the borders of the normal renal vasculature.[13] Spectral analyses may show increased arterial and venous flow, with high velocities and low impedance, which is the classic waveform of AVFs. A dilated draining vein may also be visible.

Pseudoaneurysms appear as simple or complex renal cysts on grayscale US images, but the intracystic flow and alternating jets at the neck can be appreciated on color Doppler flow images. Magnetic resonance angiography can be a useful adjunct when US findings are inconclusive.[14] Although about 70% of all AVFs resolve within 1 to 2 years, 30% persist or become symptomatic.[15] Persistent or symptomatic AVFs can result in persistent hematuria or transplant dysfunction as a result of marked arteriovenous shunting stemming from an intrarenal "steal" phenomenon. Enlarging pseudoaneurysms can rupture.

Transcatheter embolization is the treatment of choice for both symptomatic AVFs and enlarging pseudoaneurysms. Superselective embolization performed with a coaxial catheter and metallic coils minimizes the loss of functioning allograft tissue. It also allows the occlusion of targeted vessels in a precise and definitive manner, unlike embolization with particles that may reflux into nontargeted branches. Because of the end-arterial supply of the kidney, a proximal occlusion is adequate to exclude AVFs or pseudoaneurysms from the circulation.[16]

In AVFs with high blood flow, temporary balloon occlusion of the draining vein may be necessary during coil embolization to prevent coils from making their way into the systemic circulation.[17] Pseudoaneurysms with a narrow neck may be embolized with coils tightly packed within the sac itself. This technique allows the preservation of flow in the distal renal artery. Surgery is the treatment of last resort because partial and total nephrectomy are the only two options.[18]

TRANSVENOUS RENAL BIOPSY

Clinical relevance

Renal histopathologic examination remains the diagnostic gold standard for most renal parenchymal diseases[19,20] and is therefore essential for clinical management of renal diseases such as proteinuria, hematuria, and renal failure.[21,22] The conventional technique for obtaining renal tissue involves percutaneous puncture of the kidney. This is a safe technique when performed in low-risk patients by experienced operators.[23] The first description of renal tissue sampling by percutaneous needle biopsy was published in 1951.[1] Improved technology and US guidance have considerably reduced the risk of complications with renal biopsy techniques and improved safety and efficacy.

Nevertheless, a significant risk still attends renal biopsy, and serious complications have been reported. Even under ideal circumstances, overt complications occur in up to 3.5% of cases,[24] and the incidence of perirenal hematoma has been reported to range from 57% to 85%.[25,26] Percutaneous renal biopsy is therefore considered a high risk in patients with abnormal clotting or low platelets. Furthermore, several other clinical conditions such as solitary, small, or obstructed kidneys, uncontrolled hypertension, horseshoe kidney, mechanical ventilation, and uncooperative patients present relative contraindications to the percutaneous approach. An aging population, diabetes, and more widespread use of anticoagulant and antiplatelet drugs have led to more frequent clinical encounters with high-risk biopsy candidates.

Some novel techniques have been developed over the past decade as alternatives to percutaneous biopsy in patients with contraindications.[27,28] These include performing renal biopsies through an open surgical approach, transvenous approaches using transjugular and transfemoral access, and laparoscopic techniques. The development of a cutting core biopsy needle has made transjugular renal biopsy the most important of these. Open biopsy has the added risk of general anesthesia and its associated morbidity and mortality. Transjugular biopsy is theoretically safer because the needle is advanced as distally as possible into the medullary interlobar veins; the needle then passes through the vein wall into the surrounding parenchyma, directed away from the larger blood vessels. When bleeding does occur, it will do so back into the venous system, limiting extravascular blood loss.[29] Another theoretical advantage of the transjugular approach is a lower likelihood of capsular perforation with the inside-out approach, in comparison to the 100% capsular perforation rate with percutaneous biopsy. Furthermore, if capsular perforation occurs and there is significant extravasation, elective coil embolization of the biopsy track can be performed during the same procedure.

The transjugular renal biopsy technique was developed as a modification of the classical transjugular liver biopsy[30] and described in 1990 by Mal and associates.[31] The authors first reported using a modified 9F liver core biopsy needle in 50 patients for transjugular renal cortical biopsies[31] and then in 200 patients with contraindications to percutaneous biopsy.[27] In a recent comparison of 400 transjugular transvenous renal biopsies versus an equal number of percutaneous biopsies, similar results were reported for both.[24] This is a significant finding because 75.8% of patients in the transjugular renal group had bleeding disorders.[32]

In clinical practice, the proportion of patients with contraindications to percutaneous biopsy is small (about 7%).[33] In high-risk patients, transjugular renal biopsy provides clinicians with expanding opportunities for obtaining renal histologic samples. The clinical utility of this procedure is also emphasized by the fact that patients with diabetes who undergo renal biopsy frequently have nondiabetic renal disease.[34,35] It has been established that transjugular renal biopsies, especially in patients with acute renal failure, affect patient care. The initially feared potential disadvantage of low diagnostic yield (owing to the need to first traverse the medulla to reach the cortex) was shown to be unfounded in various studies.

Indications

Indications for transjugular renal biopsy include the following: (1) patients with a bleeding diathesis or on oral anticoagulation that cannot be stopped; (2) concomitant hemodialysis catheter placement[32]; (3) patients with concurrent renal and liver disease who warrant both renal and hepatic biopsies; (4) morbidly obese patients; (5) patients on mechanical ventilation; and (6) failed percutaneous renal biopsy.

Relative contraindications

Contraindications for transjugular renal biopsy include the following: (1) absent right kidney and (2) occluded central veins such that venous access from above is not possible.

Equipment

Initially, a modified Colapinto aspiration needle had been used for the biopsy. More recently, the transjugular 19-gauge Quick-Core side-cut biopsy needle system (Cook Medical, Bloomington, IN, USA) has become popular with good cortical sampling.[24,36] However, there is a higher incidence of capsular perforation.[36]

The Quick-Core side-cut biopsy needle system consists of a 7F, 50.5-cm transjugular sheath with a 14-gauge inner stiffening cannula; a 5F, 80-cm multipurpose curved catheter; and a 60-cm, 19-gauge biopsy needle with a 2-cm throw length. The biopsy needle has an inner stylet and a 2-cm specimen notch with a beveled end. The biopsy needle is enclosed in a 5F straight angiographic catheter and cut to length to ease advancement through the transjugular sheath. An Arrowflex vascular sheath (Arrow International Inc, Reading, PA, USA) can be used as an alternative to the Quick-Core transjugular vascular sheath. The stiffness of the Quick-Core system makes a left jugular approach challenging. The blunt-tipped Quick-Core biopsy needle is a modification of the device that has been shown to not only provide sufficient cortical tissue for histopathologic diagnosis but also to possibly reduce capsular penetration and hence significant bleeding in an animal study[37] and in a subsequent study of 7 patients.[38]

Technique

The procedure is usually performed in a supine patient in an angiographic suite with a biplane or single-plane fluoroscopic machine. Prothrombin time (or international normalized ratio), partial thromboplastin time, platelet count, and serum creatinine level should be obtained before the procedure. Attempts should be made to correct any coagulopathy (international normalized ratio > 1.5, platelets < 50 000/μL) before the procedure. The patient's head is turned away from the side of puncture. The skin is cleaned with an iodine solution or chlorhexidine. The patient is then covered with a surgical drape. Right internal jugular vein access is preferred to the left because the former has a relatively direct continuation into the superior and inferior vena cavae. The right internal jugular vein is punctured after local anesthesia under US guidance. A 7F to 9F transjugular vascular sheath (or Arrowflex sheath) is inserted. A hydrophilic guidewire (Terumo Medical Corp., Somerset, NJ, USA) or standard Bentson wire (Cook Medical) is then advanced into the inferior vena cava. The renal vein is then selectively catheterized using a 5F Cobra (Cordis Corp., Hialeah, FL, USA) or multipurpose curved catheter introduced through the sheath. The catheter is manipulated into the posterior lower branch of the right renal vein. The hydrophilic wire or Bentson wire is then exchanged for a 145-cm Amplatz Super Stiff Wire (Boston Scientific Corp., Natick, MA, USA). Subsequently, the vascular (or Arrowflex) sheath is advanced over a stiff guidewire into the renal vein under fluoroscopic guidance.

Once the sheath is advanced into the renal vein, a transvenous Quick-Core biopsy needle with its protective outer straight catheter sheath is inserted. This catheter should be gently advanced as distally as possible into a peripheral cortical vein of the lower pole of the right kidney. An optimal peripheral position is confirmed by flushing with a small amount of contrast medium through the vascular sheath. The position is judged to be satisfactory when a wedge of cortical parenchyma is enhanced. In such a position, there is little likelihood of damaging a large central vein or artery. Furthermore, more glomeruli are obtained per pass when parenchymal enhancement is obtained.[24]

When the straight catheter is withdrawn, it exposes the 19-gauge biopsy needle. Tissue samples can then be taken with the aid of a spring-loaded gun. Alternatively, the inner stylet with the specimen notch can be advanced first into the renal cortex, and then the outer cutting cannula can be advanced over it. The straight catheter is then advanced back over the needle into the biopsy track. The needle containing the tissue specimen is removed. Contrast is injected through the straight catheter to identify any capsular perforation.

If capsular perforation is present, the biopsy track can be prophylactically embolized with coils at the discretion of the operator. Although embolization coils are used in general, some operators prefer Gelfoam to plug the tract.[39] Usually, only a small volume of contrast is used during the procedure (< 30 mL of iodinated contrast [strength 300 mg/mL]), which should reduce the risk of any renal dysfunction. Tissue samples are processed in a standard manner for evaluation by light microscopy, immunofluorescence, and electron microscopy. An average of 4 to 6 passes are made to obtain a sufficient sample for histologic analysis.[33,40]

The right kidney is preferentially biopsied because the right renal vein is shorter, and its angle allows for easier access to the kidney. The left renal vein is longer and tends to form a right angle with the inferior vena cava. The left may be biopsied in the case of a single kidney or unfavorable venous anatomy of the right kidney.

The critical step in performing a transjugular renal biopsy is positioning the needle in a subcortical location and allowing enough distance from the capsule to avoid capsular penetration.[37]

All biopsy devices are then removed. The catheter, its stiffeners, and sheath are all removed, and hemostasis is obtained with manual compression.[24,27,39]

Outcomes

The transjugular biopsy provides renal tissue in 92% of patients.[33] Tissue adequacy for histologic examination (ie, the number of glomeruli obtained) is excellent (range, 94%-100%). The average number of glomeruli per sample ranges from 10 to 19, which is comparable to results with percutaneous kidney biopsies.[33,40,41] The overall diagnostic success of the procedure ranges from 89% to 97%.[40,41] This is comparable to the yield of percutaneous biopsy, which generally ranges from 95% to 98.8%.[24,23,42] Furthermore, transjugular biopsies yield better samples for immunofluorescence. The amount of tissue retrieved increases with the number of passes (up to 3 to 4 passes) and decreases thereafter with poorer quality samples.[29,39]

It is a safe procedure in patients with coagulopathy.[41] The small amount of iodinated contrast (< 30 mL) used for the procedure is unlikely to result in contrast-induced nephropathy.[32,43] As opposed to percutaneous biopsy, perforation of the renal capsule and therefore the risk of perirenal hematoma is less likely.

However, transjugular renal biopsy may not be feasible in the following conditions: (1) congenital absence or thrombosis of the right internal jugular vein, (2) thrombosis of the inferior vena cava and/or renal vein, and (3) recurrent course of the renal vein.

A transjugular renal biopsy requires relatively high operator skills, technical equipment, and occupation of the radiology fluoroscopy suite. In inexperienced hands, it can be a time-consuming and costly procedure compared with percutaneous biopsy. These limitations mean that percutaneous renal biopsy will not be routinely replaced by transjugular biopsy. However, transjugular biopsy has a vital role in providing tissue samples to clinicians when a percutaneous route is contraindicated.

Complications

The rates of complications with transjugular kidney biopsy are likely to be influenced by patient selection and local policy regarding contraindications to percutaneous biopsy and operator experience. The complication rate of transjugular renal biopsy performed in patients with clotting disorders is comparable to that shown with percutaneous biopsy.[43]

Major complications with transjugular renal biopsy, such as bleeding requiring resuscitation or intervention, occur in only 1% to 2% of patients.[24,40] It is important to appreciate that these patients are, in general, at high risk of bleeding due to their coagulation status. More commonly, patients experience transient microscopic hematuria.

Major bleeding into either the perirenal space or pelvicalyceal system can occur. Gross hematuria due to puncture of the renal pelvis or calyces is a recognized complication of transjugular kidney

biopsy. Puncture of the renal pelvicalyceal system can result in a fistula between a blood vessel and renal calyx. Patients might need resuscitation, blood transfusion, transarterial embolization, or surgery, similar to patients with major bleeding into the perirenal space.

An arteriocalyceal communication may be identified by injection of contrast through the protective catheter immediately postbiopsy. Performing peripheral cortical biopsies may avoid this complication.

Capsular perforation occurs in 74% to 90% of cases.[33,39] The overall incidence of perirenal hematoma is less than 30% compared with 57% to 85% reported for the percutaneous approach.[25,26,41]

Postprocedure and follow-up care

The procedure is usually well-tolerated, and most patients return to their baseline activity the day after the procedure.[40] In view of evidence reporting delayed bleeding 8 hours after percutaneous biopsy in up to 20% of patients,[44] caution is required with regard to the length of postprocedural observation. After the procedure, patients remain on bedrest for 12 hours, and standard hemodynamic monitoring is carried out for 24 hours. Vital signs should be monitored every 15 minutes in the first 6 hours postprocedure. Hematocrit is usually assessed within 4 to 6 hours postbiopsy. The patient is usually discharged the next day.

Summary of transjugular renal biopsy

Transjugular renal biopsy is a useful procedure in patients with contraindications to conventional percutaneous renal biopsy. A combination of advanced technology and increased experience with the technique in the past decade has enabled transjugular renal biopsy to become an efficacious, well-tolerated, and relatively safer alternative to percutaneous renal biopsy in certain clinical situations.

Transjugular renal biopsy, at least in current practice settings, is unlikely to become a high-volume procedure, although this procedure is effective and safe when done by interventional radiologists with transjugular liver biopsy experience and equipment.

The role of this procedure is to enable histologic diagnosis in patients with contraindications to percutaneous biopsy. The tissue sample obtained is adequate in over 90% of cases to make a confident diagnosis and to influence management[33] by excluding important factors from differential diagnosis, instilling confidence in instituting specific treatments, and providing valuable prognostic information. Transjugular renal biopsy should be reserved for patients in whom the biopsy result could influence the therapeutic strategy, particularly those with rapidly progressive renal disease and contraindications to percutaneous biopsy.

SUMMARY

In several studies that compared conventional techniques with the biopsy gun technique, the latter has been superior with regard to adequacy and quality of the specimens, "crush" artifacts, number of passes required to obtain adequate specimens, rate of complications, applicability, procedure time, patient comfort, and the average length of stay in hospital.[45-52]

To secure enough tissue for histologic diagnosis, it may be necessary to perform more than 1 biopsy pass. Some authors have advocated that at least 2 specimens be routinely obtained,[53-58] whereas others recommend that the number of needle insertions be kept as few as possible to minimize the frequency of complications.[45,59,60]

With regard to considerations of different needle sizes in various biopsy techniques, reports have agreed that the rate of complications decreases when the size of the needle is reduced.[45,46,48,50,51,59,61-65] However, this reduction is often at the expense of a lower diagnostic yield.[47,51,59,61,62,64,66,67] Moreover, some studies have emphasized that the ability to obtain a satisfactory diagnostic yield using smaller needles is dependent on experience.[45,66,63,68]

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Perigraft Fluid Collections, Abscess, Hematoma Management

Çağrı Kesim

INTRODUCTION

Organ transplantation is indicated for patients with end-stage visceral disease, and kidneys are the most commonly transplanted major organ. Living related kidney donation has gained widespread acceptance; this is mainly because the overall incidence of severe perioperative morbidity is low and the long-term graft survival is superior.[1] Renal transplant has become the preferred treatment for end-stage renal disease. Advances in surgical technique, perioperative management, and immunosuppressive regimens have led to improved outcomes and patient survival.[2] However, despite continuous progress in surgical procedures and immunosuppressive therapy, a wide variety of vascular and nonvascular complications can arise postoperatively.

Nonvascular complications include urologic complications (eg, ureteral obstruction and urine leak) (Figure 1) and perigraft fluid collections (eg, lymphocele, abscess, hematoma, and urinoma). These postoperative complications can be diagnosed and managed with minimally invasive techniques; however, an understanding of renal transplant anatomy and the risks of posttransplant immunosuppressive therapy unique to this patient population are essential to their successful application. Clinicians should also be familiar with the indications for and limitations of these techniques. Finally, collaboration between the radiologist and the transplant surgeon is vital for maximizing the chances of renal allograft survival.[3]

Renal transplant confers long-term survival and a better quality of life than does either hemodialysis or continuous ambulatory peritoneal dialysis.[4] However, the success of the transplant procedure depends on the preservation of renal graft function. Although there has been ongoing progress in surgical techniques, immunosuppressive regimens, and supportive therapy to help preserve renal transplant function, many challenges remain, including the vascular and nonvascular complications that can arise postoperatively.[3] Postoperative complications occur in approximately 12% to 20% of renal transplant recipients.[5] A delay in treating any of these complications may lead to the loss of renal graft function or even to patient death.

With regard to urinary collecting systems of transplanted kidneys and peritransplant fluid collections, interventions can be complicated and require an understanding of current surgical techniques, image-guided interventional techniques, and multidisciplinary management strategies. Key surgical considerations include the donor renal anatomy (pediatric vs adult), the location and orientation of the kidney within the recipient pelvis, and the type of surgical ureteral anastomosis employed (donor ureter to the recipient bladder or ureter). Complications such as urinary obstruction or leaks can be identified by antegrade pyelography and managed by percutaneous nephrostomy and ureteral stenting. Peritransplant fluid collections, including urinomas or lymphoceles, can be definitively treated by percutaneous image-guided drainage-with or without adjunctive sclerosis.[6]

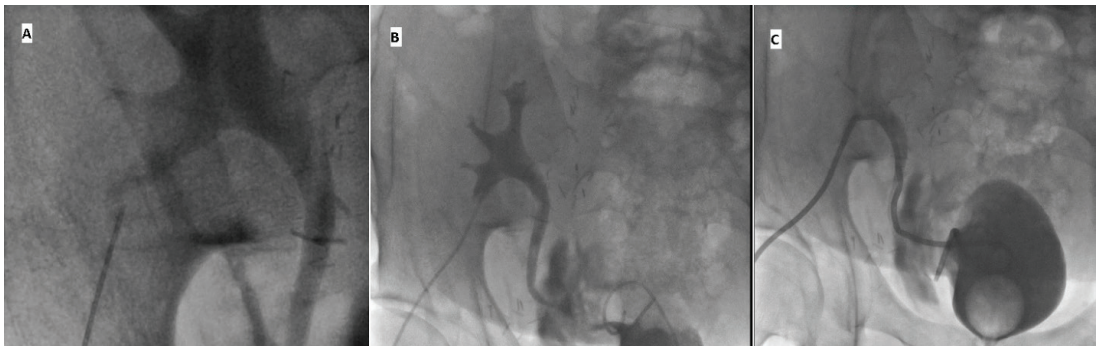

Figure 1. Antegrade Pyelography

(A) A 21-gauge needle is directed into a peripheral renal calyx under ultrasonographic guidance. The renal pelvis and ureter are opacified. **(B)** Fluoroscopic imaging shows the prompt filling of the bladder with obvious leakage at the ureterovesical junction. **(C)** A nephroureterocystostomy tube can be placed, and the patient's renal function can be monitored to see if percutaneous drainage results in improved renal function

Interventional radiologists can play a pivotal role in the prompt diagnosis and percutaneous treatment of postoperative complications by performing endovascular treatments, percutaneous urinary interventions, and drainage of abscess or fluids. These minimally invasive procedures can either obviate open surgery or stabilize the patient's condition prior to open surgical reintervention. In this chapter, we comprehensively review the renal transplant anatomy, the underlying causes of postoperative complications, and the required diagnostic work-up for patients before treatment. We also discuss and illustrate current approaches to the interventional radiologic management of renal transplant dysfunction, with emphasis on indications, limitations, and technical aspects of these minimally invasive procedures.

ACCESS AND ANTEGRADE PYELOGRAPHY FOR UROLOGIC COMPLICATIONS AND URINE LEAK

Among all ureteral complications, urine leaks are the most frequently encountered complication in the early posttransplant period.[7] These complications can cause high morbidity, increased hospitalization time, and subsequent increased costs. Therefore, the use of ureteral stents during kidney transplants as prophylaxis to prevent such complications seems logical.[8] Routine ureteric stenting for a kidney transplant is widely regarded as beneficial. However, in-dwelling stents in an immunocompromised patient can lead to risk of urinary tract infections.[9]

Urologic complications can play a significant role in patient outcomes, quality of life, graft loss, cost-effectiveness, and hospital stay. Double J ureteral stents have become one of the most basic and valuable tools in urologic practice.[10] In-dwelling ureteral stents provide direct drainage of the upper urinary tract to the bladder without the need for external diversion. Double J stents are inserted in patients with ureteral obstruction and for the prevention of complications after open or endoscopic procedures. However, their use is not free of complications and problems.[10]

Although many centers exclusively use double J stents, and some centers only use these with selected patients. Routine intraoperative use of double J stents is controversial and still debatable. There are many factors that call for their use, including surgical technique, graft retrieval, ureteric ischemia, patient sex, and graft source (deceased or living donor). The insertion of a stent does not eliminate the risk of complications, particularly urinary leak, but may alter the approach to managing them.[7] Because patients require immunosuppression posttransplant, double J stents in transplant patients can increase the risk of urologic or blood infections. Consequently, opinions continue to

be divided between those who routinely conduct stent placement and those who only do so selectively based on clear indications.[11] A ureteral stent after kidney transplant will usually be removed after 4 to 6 weeks, but it should be noted that the optimal length of time for retaining ureteral stents is controversial and is not yet specified.[12]

Urine leaks occur in approximately 1% to 5% of renal transplant patients.[13] Because of the risk of infection in patients who are in an immunosuppressed state, urine leak is a potentially life-threatening complication requiring prompt intervention. Most leaks occur (1) at the distal ureter, possibly as a result of necrosis due to ischemia or rejection, or (2) at the ureteroneocystostomy site, stemming from problems at the time of surgery. Leaks occur less frequently in the proximal ureter or pelvicalyceal system secondary to distal ureteral obstruction.

Patients with urine leaks may present with pain, swelling, discharge from the wound, or urinoma. Ultrasonography (US) and computed tomography (CT) can demonstrate a perigraft fluid collection.[3] The pelvicalyceal system may be dilated as a result of ureteral obstruction by the urinoma. Radionuclide imaging can suggest a urine leak by showing abnormal uptake around the transplant.[3] A definitive diagnosis can be made based on the creatinine level in the fluid from the wound or in the peritransplant fluid obtained with US or CT-guided needle aspiration. The urinoma should be drained percutaneously to relieve the extrinsic compression (and hence the associated symptoms) and to prevent infection.

Antegrade nephrostography can accurately demonstrate the site of a leak, and percutaneous nephrostomy can divert urinary flow, permitting ureteral healing.[3] In patients who have a suspected urinary bladder leak, which usually develops at the site of the cystostomy or ureteroneocystostomy, the leak can be demonstrated with cystography.[3] A Foley catheter is left in the bladder for urinary drainage.

Surgical revision is required in some cases; however, the placement of a nephroureteral stent or a double J stent with a nephrostomy catheter for external drainage, can constitute definitive treatment. Percutaneous approaches have been reported to be successful in closing the urinary leak in 36% to 100% of cases.[14,15] Substantial bladder leaks are generally managed with the primary surgical repair; however, most bladder leaks can be managed conservatively with bladder drainage alone.[3]

When ureteral obstructions or urine leaks do not respond to percutaneous interventions, various surgical treatments, including ureteropyelostomy, ureteroureterostomy, and revision of a ureter-oneocystostomy, are options for treatment, depending on the cause of the complications and the length of viable ureter available for urinary tract reconstruction.[16]

EVIDENCE-BASED MANAGEMENT OF URINARY LEAKS

Treatment of urinary leaks depends on its cause, site, and the presence of complications caused by the leak.

Prevention of urinary leaks

The following considerations should be followed to prevent urinary leaks. First, the shortest ureter as possible should be used, with efforts to preserve the tissues between the lower pole of the transplanted kidney and the ureter (the golden triangle) to prevent ureteral necrosis. Second, in accordance with 2005 and 2013 Cochrane database reviews, although placement of double J stents will reduce major urinary complications, these stents are associated with a high risk of infections and excess surgical cost. Third, according to a meta-analysis by Alberts and associates, the Lich-Gregoir technique for ureterovesical anastomosis has shown a lower rate of urologic complications with or without double J stent.[17-20]

Conservative management of urinary leaks

Foley catheter placement is suggested once a urinary leak is suspected. This is usually enough to control a small anastomotic leak due to incomplete

bladder healing by reducing intravesical pressure. Endoscopic placement of a double J stent for ureteric fistulas is considered if not placed at the time of transplant. Percutaneous antegrade nephrostomy tube placement is suggested if the leak is relatively small and associated with hydronephrosis. It is used to maximally decompress and divert urine away from the leak site to allow healing. This procedure can also be used to diagnose the location and severity of the fistula and guide further management. The short-term success rate is 69%, whereas the long-term success of this procedure is 58% due to the recurrence of stenosis. This concludes that surgical repair remains the best treatment for ureteric fistulas.[21-23]

Surgical management of urinary leaks

The type of surgical repair depends on the level of the leak and the viability of the tissues. If the ureteric leak is caused by a simple anastomotic leak, resection of distal ureter and reimplantation of the urinary bladder are recommended. If ureteric necrosis is the cause of the urinary leak, necrotic ureter resection is required and the ureteral implantation depends on the length of the ureter and adequacy of blood supply. If the ureteric length and blood supply of the ureter are sufficient, then the preserved transplanted ureter is reimplanted into the bladder. If the length of the transplanted ureter is insufficient and vascularity is weak, then the native ureter, not the bladder, is used for anastomosis or the bladder is fixed superiorly by a psoas hitch or extended by Boari flap. If no native ureter is available, in the case of bilateral nephrectomy, the ileal conduit may be used as a neoureter.[24]

The caliceal leak is treated by the removal of the obstructive cause and conservative management if the leak is caused by segmental renal infarction secondary to ligation of the polar artery. Partial nephrectomy is rarely needed for management.[25]

PERIGRAFT FLUID COLLECTIONS

Perigraft fluid collections are quite common, occurring in approximately 50% of renal transplant patients.[26] Of these collections, 15% to 20% become clinically significant. Local pain is typical in these patients, and compression of the transplant vascular structures or the ureter can result in transplant dysfunction.[26,27] Fluid collections occurring in the early postoperative period include urinomas, hematomas, and abscesses. Lymphoceles, which are the most common fluid collections, usually occur weeks to months after transplant.[3]

Ultrasonography usually depicts perigraft fluid collections, but the findings are frequently nonspecific. For diagnosis, US-guided fluid aspiration is essential. Computed tomography is also useful for assessing the anatomic relationship of the fluid collection with adjacent structures and can also demonstrate a route for needle guidance and catheter drainage, even when the US has failed to do so.

Incidence and etiology

The development of fluid collections adjacent to renal transplants is not uncommon, occurring in nearly 50% of renal transplant recipients.[27] Hematomas, abscesses, and urinomas tend to develop early after transplant. Lymphoceles are more commonly discovered weeks to months after transplant, with a peak incidence at 6 weeks posttransplant.[27] Patients with peritransplant fluid collections may be asymptomatic, in which case, the fluid collection is discovered by noninvasive imaging performed for other purposes. Alternatively, patients may present with pain, swelling, fever, or symptoms related to mass effect on organs such as urinary frequency or constipation. Renal transplant function may be abnormal if the fluid collection exerts sufficient mass effect on the renal transplant, the ureter, or vascular structures.[6]

Diagnostic and therapeutic percutaneous interventions that may be performed to treat peritransplant fluid collections include percutaneous aspiration, percutaneous drainage, and percutaneous sclerotherapy. The indication for each is based on the clinical situation and the contents of the fluid collection.[6]

Lymphocele

Lymphocele formation after kidney transplant has been attributed to open lymphatics in the recipient created by dissection around the iliac blood vessels or disrupted lymphatics in the donor kidney, with a resultant collection of lymphatic fluid in the retroperitoneal space.[27-32] Other suggested contributory factors include heparin, corticosteroids, early patient mobilization, extensive dissection around the external iliac artery, and acute rejection.[28,30,33] Treatment options for symptomatic lymphoceles include percutaneous aspiration with or without sclerotherapy or operative internalization of the lymphocele into the peritoneal cavity (by open laparotomy or with laparoscopy); however, these can become complicated if the lymphocele is associated with deep vein thrombosis, necessitating anticoagulation or placement of a vena cava filter.[34-38]

Rate of diagnosis of lymphoceles after renal transplant ranges from 10% to 51% of patients, depending on the criterion and method of detection.[27-31] Flechner and associates showed that, at their center, 31% of patients present with lymphoceles after renal transplant; these results include a review of all available imaging studies rather than clinical diagnoses alone and are similar to a previous report from their center, which gave a lymphocele rate of 33.9% for a nonoverlapping series of 450 consecutive adult renal transplants between January 1993 and August 2002.[39] The overall variability in previous reports can be attributed to the definition of lymphocele, duration of follow-up, and, more recently, the routine use of ultrasonography, which can identify small asymptomatic fluid collections. Symptomatic lymphoceles have been reported in up to 22% of patients treated with cyclosporine-based immunosuppression.[28,30,31]

Postoperative lymphoceles are caused by lymphatic leakage from the allograft bed or from the allograft itself, with a reported prevalence of 0.6% to 18%.[40] Renal transplant patients are predisposed to prolonged lymphatic leakage as a result of graft rejection, the use of steroids or diuretics, or retransplant.[28] Lymphoceles have levels of protein, urea nitrogen, creatinine, and electrolytes that are similar to serum, and chemical analyses can help differentiate lymphoceles from urinomas, seromas, and abscesses.

Most lymphoceles are small and asymptomatic, and intervention is not necessary. However, some lymphoceles compress adjacent structures and may cause hydronephrosis, edema, or deep venous thrombosis in the ipsilateral lower extremity. When examined with CT, they appear as rounded collections with or without septa (Figure 2).

Simple percutaneous aspiration of a lymphocele is associated with an 80% to 90% recurrence rate.[41] In-dwelling catheter drainage alone has been used with some success,[42] but the combination of in-dwelling catheter drainage and sclerotherapy is more effective, with a reported success rate of 68% to 100%.[3] Sinography is performed prior to sclerotherapy to help exclude communication between a lymphocele and adjacent vital structures.[3] Septa within the lymphocele should be broken with gentle wire manipulation. Various sclerosing agents, including povidone iodine,[43] doxycycline,[44] alcohol,[45] and bleomycin[46] have been used to a similar effect. Multiple treatments

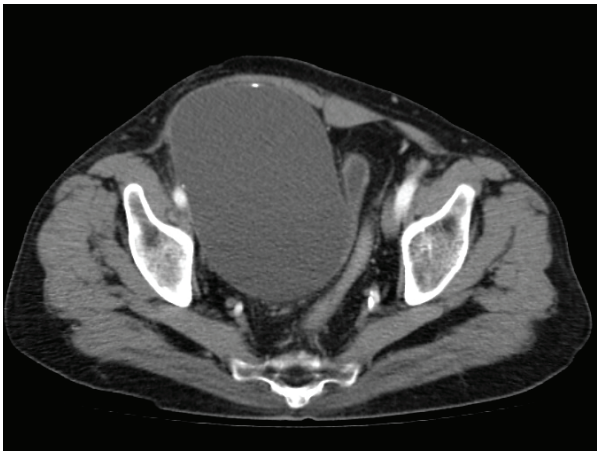

Figure 2. Lymphocele in a patient who had undergone renal transplant and presented with increasing serum creatinine level
CT image shows peri-allograft fluid collection. Ultrasonography-guided aspiration of the fluid helped confirm a lymphocele.

are required in most cases, with the catheter left in place for anywhere from 4 to 35 days.[27]

Whether to use surgical or percutaneous techniques for lymphocele treatment remains somewhat controversial, with preferences varying by institution. Comparable success rates have been reported for the 2 methods; however, surgical procedures are more invasive. Surgical marsupialization of lymphoceles into the peritoneal cavity has been performed using both open and laparoscopic surgical techniques. The former is associated with greater morbidity and a higher rate of symptomatic recurrence, whereas the latter is associated with a higher prevalence of iatrogenic injury to the urinary tract.[47]

Abscess

Abscesses may occur in isolation or may represent the superinfection of a preexisting peritransplant fluid collection. Urinomas occur because of urine extravasation, most commonly near the ureteral anastomosis due to surgical complications or ischemia. If there is clinical uncertainty as to the underlying contents of a fluid collection, needle aspiration may be undertaken, with samples sent for culture and creatinine level examination of fluid. If a Gram stain or culture is positive (abscess) or the fluid sample creatinine level is higher than the serum creatinine level (urinoma), percutaneous drainage is conducted. If the fluid collection is a confirmed urinoma, urinary diversion via percutaneous techniques described earlier or via retrograde ureteral stent placement should be undertaken where possible. Surgical revision of the ureteral anastomosis may be necessary if the urinary leak does not seal with these techniques.

Any perigraft fluid collection can become infected; usually, the affected patient presents with fever or local pain. The US or CT findings are nonspecific, but the air within the perirenal fluid collection can strongly suggest a perirenal abscess.[48] Prompt surgical or percutaneous drainage combined with systemic antibiotics is mandatory because of the immunosuppressed state of transplant patients. Percutaneous drainage under US or CT guidance is associated with a high rate of success and a low complication rate (Figure 3).[3]

Hematoma

Small hematomas are often seen after transplant and usually resolve over time. When the presence of an acute hematoma causes sufficient mass effect to impair renal transplant function or when superinfection is confirmed by diagnostic aspiration

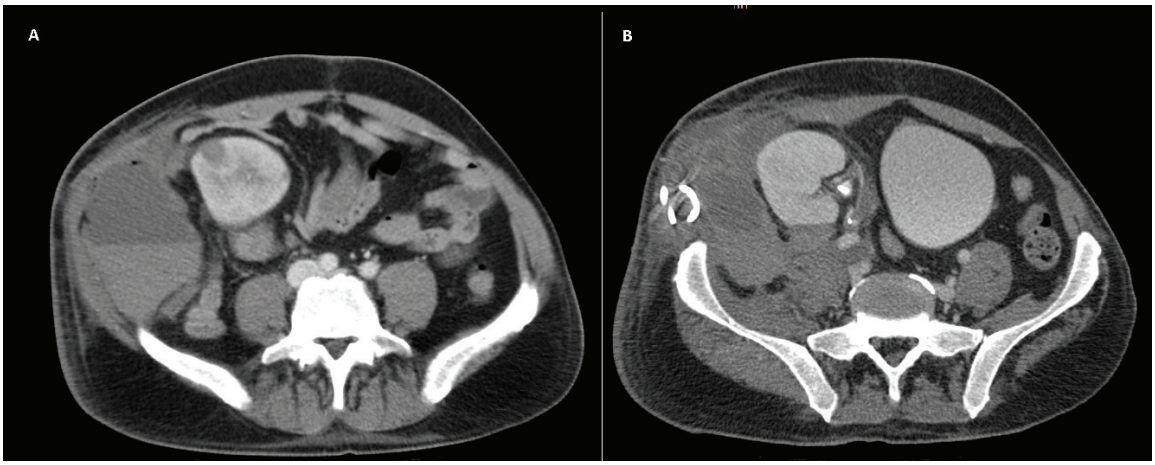

Figure 3. Perirenal abscess is seen as thick-walled, loculated collection and extensive inflamation in the soft tissue around the abscess **(A)**, which was treated with percutaneous drainage cathater, as seen in computed tomography scan **(B)**.

or highly suspected on clinical grounds, surgical evacuation is usually performed. Hemostasis of the surgical bed can also be ensured at the time of reoperation. If active bleeding is suspected, in particular, if the hematoma has occurred because of prior percutaneous intervention or an arterial pseudoaneurysm or fistula has been identified by US, renal transplant angiography and possible embolization are usually performed. If the superinfection of a peritransplant hematoma is suspected, needle aspiration can be performed for diagnostic purposes. Acute hematomas are not adequately evacuated via percutaneous methods because of the viscous nature of acute blood products. On occasion, percutaneous drainage of a subacute or chronic hematoma with a liquified (hypoechoic) component seen on US is performed. This is only undertaken if the hematoma is confirmed as superinfected by prior needle aspiration or if the mass effect is felt to impair renal transplant function.

Postoperative hematomas occur frequently, but they are generally small and asymptomatic and do not require intervention. On US, acute hematomas are typically highly echogenic, whereas resolving hematomas are hypoechoic or anechoic.[49] On CT, acute hematomas appear as hyperattenuating areas that do not enhance with contrast material administration, whereas older hematomas appear as heterogeneous fluid collections with liquefied serous components (Figure 4).

An infected hematoma, which is usually suspected based on clinical and laboratory findings, can be successfully treated with percutaneous drainage using 12F to 14F drains and periodic irrigation with saline solution to prevent drain clogging. Hematomas that form in the immediate postoperative period and then enlarge can result from disruption of a vascular suture line, vessel injuries in the graft bed, or spontaneous graft rupture.[3] Hypovolemic shock can occur rapidly in this setting, and emergent surgical exploration is mandatory in these cases.

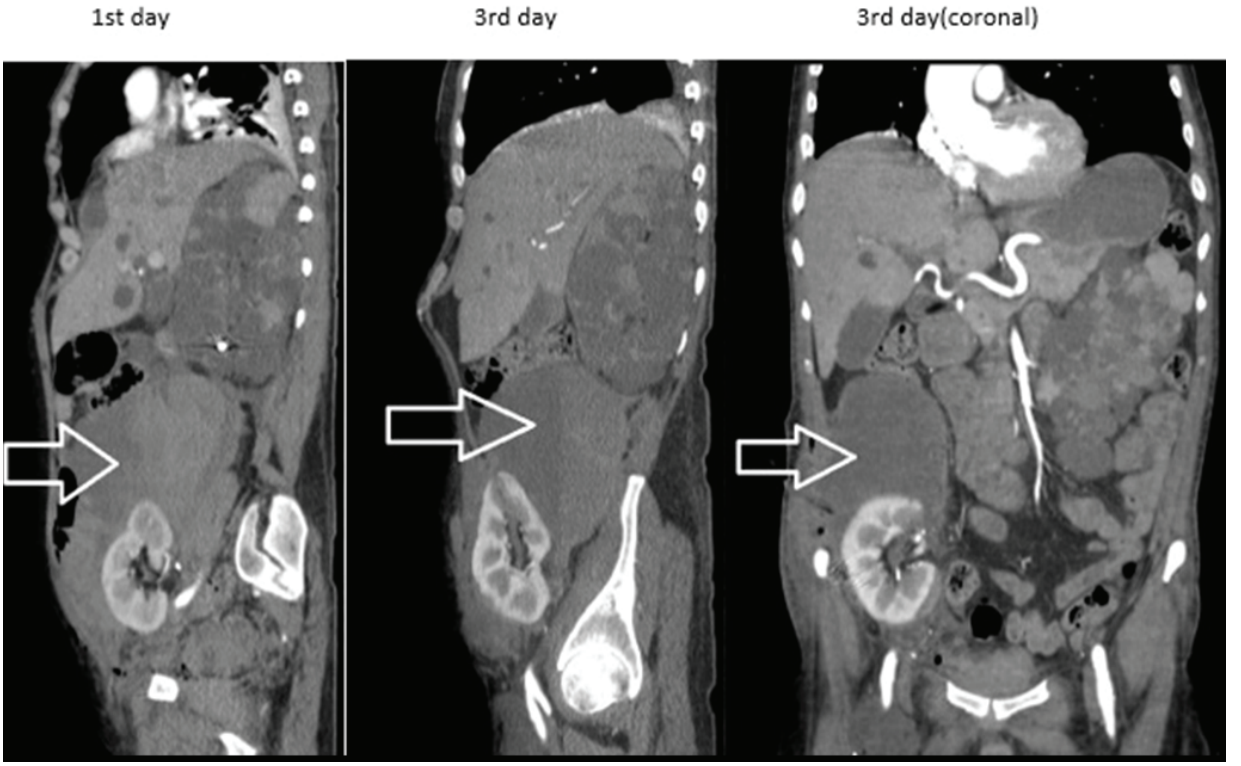

Figure 4. Perirenal hematoma is seen as fluid-fluid levels due to blood components, which became more visible over time.

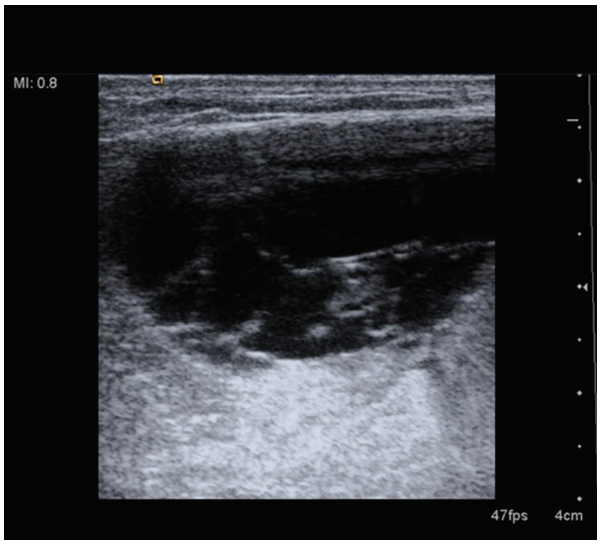

Figure 5. Septated Collections

Septated collections are mostly associated with lymphoceles, but sometimes urinoma and lymphocele can exist together. Therefore, septa in a loculated collection does not always exclude urinoma existence.

Urinoma

Urinomas are caused by the extravasation of urine from the renal pelvis, the ureter, or a ureteroneocystostomy. The most frequent site of the leak is the distal ureter, which is susceptible to ischemia. Other causes include postbiopsy injury, severe ureteral obstruction, or disruption of the ureteroneocystostomy.[14] On US and CT, appearances of urinomas are nonspecific (Figure 5), but a finding of internal septa usually excludes a urinoma.[13] Large urinomas can rupture, and free peritoneal fluid can be seen in such cases.[49]

As discussed earlier, once urinomas are definitively diagnosed on the basis of findings at imaging-guided fluid aspiration followed by antegrade nephrostography, they can be managed with percutaneous interventions.

SUMMARY

A wide range of postoperative complications of renal transplant can be diagnosed and managed with minimally invasive techniques; however, the increasing role of percutaneous management is still being defined. In this chapter, we reviewed transplant anatomy, the diagnostic work-up of renal transplant dysfunction, and technical considerations that are crucial to success for interventional radiologic management. Familiarity with the indications for and limitations of these techniques as well as collaboration between the radiologist and the transplant surgeon are crucial for maximizing renal allograft function.

Interventional radiologists play a vital role in the diagnosis and management of nonvascular complications after renal transplant. Renal transplant anatomy can be complex, and percutaneous interventions may be complicated and challenging. For successful image-guided interventions, true knowledge of the current surgical techniques and mastery of a wide range of percutaneous image-guided catheterization skills are required. Improvement in long-term patency after ureteral stricture dilation is an important area for future research.

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Other Complications After Kidney Transplant

Murat Kuş
Kenan Çalışkan

POSTOPERATIVE BLEEDING AFTER KIDNEY TRANSPLANT

Postoperative surgical site bleeding after kidney transplant occurs in the early postoperative period and generally within the first 2 weeks after surgery. The incidence of bleeding after kidney transplant varies between 0.2% and 14% according to the center's system for assessing hematoma size ranges. Bleeding may occur from renal parenchyma, vascular anastomoses, renal hilar vessels, retroperitoneal tissues, or iliac vessels. Postoperative bleeding after kidney transplant is associated with increased risks of long-term graft function, graft loss, or death. Although the mechanism is not clear, it is possible that bleeding around the graft site early after transplant may have a negative impact on long-term graft function by causing early graft dysfunction from mechanical compression or complications such as hypotension, anemia, need for blood transfusions, or sepsis from infected hematomas.[1-3]

Reasons for hemorrhage after kidney transplant

Donor type and recipient factors are important risk factors for development of postoperative bleeding. Graft procurement from living versus deceased donors may play an important role. Careful hemostasis in the perinephric tissues is achieved during mobilization of the living-donor kidney before extraction, whereas deceased-donor kidneys are usually procured en bloc with perinephric and retroperitoneal tissues. Moreover, the kidney is subsequently prepared for transplant using cold sharp dissection on the back table. Long ischemia time can cause endothelial cell injury and can reduce vessel integrity, thus increasing susceptibility to bleeding. The relation between increased cold ischemia time and bleeding risk may also be a result of the effects of deceased-donor kidneys on bleeding. Kidneys from expanded-criteria donors may have poor vessel integrity and tissue quality. This factor may become important during the perioperative period, potentially increasing the susceptibility to bleeds from the anastomotic site or hilar tissues.[1,4]

Recipients of deceased-donor kidneys are more susceptible to bleeding

Deceased-donor kidney transplant recipients often wait longer to receive a transplant than living-donor kidney transplant recipients. The prolonged exposure to dialysis prior to transplant may increase bleeding risk because of its negative effects on tissue and vessel integrity. High body mass index is associated with an increased risk of complications, including increased intraoperative and postoperative bleeding, delayed wound healing, and cardiac complications. Patients on chronic preoperative or postoperative anticoagulant or antiplatelet therapy have increased risks of hemorrhage.

It is important to distinguish between early and late postoperative bleeds because the latter are

not commonly caused by surgery but instead are characterized by distinct risk factors, including biopsy procedures or therapeutic systemic anticoagulation.[5,6]

Posttransplant hematomas can be located lateral or medial to the renal allograft. The lateral location suggests a venous etiology, and the medial location is often associated with anastomotic issues. Hematomas may be perirenal or subcapsular in location when viewed with ultrasonography, and acute bleeding produces echoes that are homogeneously echogenic. Subacute and chronic hematomas often contain clotted blood that is hypoechoic to anechoic. Computed tomography is often useful for assessment of patients with clinically suspected hematomas whose ultrasonography study is negative.[7] Subcapsular hematomas exert a mass effect on the kidney, flattening the cortical margin of the kidney. The mass effect of clinically significant subcapsular hematomas will alter the perfusion of the kidney such that pulsed Doppler shows increased arterial resistive indexes of the intrarenal and arcuate arteries. Acute hematomas are not adequately evacuated via percutaneous methods because of the viscous nature of acute blood products. On occasion, percutaneous drainage of a subacute or chronic hematoma with a liquefied (hypoechoic) component seen on ultrasonography is performed. This is only performed if the hematoma is confirmed to be superinfected by previous needle aspiration or if the mass effect is felt to impair renal transplant function. Significant hematomas requiring reoperation for evacuation may also be associated with poor long-term outcomes.[8,9]

LYMPHOCELE

Lymphoceles usually result from transection of recipient and donor lymphatic system that leads to nonstop drainage of the afferent lymphatics after renal transplant. This typically develops 2 weeks to 6 months after kidney transplant and is located in the pelvis, between the peritoneal and iliac vessels. Lymphoceles are usually asymptomatic; however, depending on their size and position, these may cause palpable mass, fever, wound dehiscence, leg edema, iliac vein thrombosis, and graft dysfunction (compression of graft vessels, ureter, and bladder).[10,11]

The incidence of lymphoceles varies between 0.6% and 49% in past decades. The reported mean incidence of symptomatic lymphocele ranges from 0.03% to 26%.[12]

During mobilization of the recipient iliac vessels, ligation of lymphatic trunks is crucial. Both meticulous dissection and ligation of perirenal lymphatics of the graft kidney either during the time of organ procurement surgery or during back table work are important to prevent lymphoceles. If these fragile lymphatic tissues are not clipped or sutured, then these may remain open and become an important source of lymphatic leakage. Different surgical techniques that require less lymphatic dissection of the recipients, such as the implantation of the graft kidney in the omolateral iliac fossa with anastomoses of the renal artery and vein on the common iliac vessels, will lower the rate of lymphocele incidence. Surgical dissection of the renal lymphatic vessels has been identified as a cause of lymphatic complications, such as laparoscopic procurement of the graft from living-donor recipients who received kidney grafts procured laparoscopically from living donors compared with recipients who receive transplants from deceased donors. It is possible that grafts with multiple arteries are associated with a higher incidence of lymphoceles. A higher occurrence of lymphoceles in transplant recipients with multiple artery grafts depends on the presence of more abundant lymphatic vessels likely caused by insufficient ligature.[13]

The combination of lymphocele incidence and diabetes in patients treated with calcineurin inhibitors has been found to be associated with a higher relative risk of lymphocele development. This correlation indicates that the microangiopathy caused by diabetes, a well-known risk factor for wound healing complications after kidney transplant, could be responsible for lymphatic complications.[14]

Obesity (a body mass index > 24 kg/m^2), recipient age, acute tubular necrosis/delayed graft function, warm ischemia time, duration of dialysis treatment before transplant, and retransplant have been associated with a greater risk of lymphocele incidence. It is known that some immunosuppressive drugs such as rabbit antithymocyte globulin, high dose of mycophenolate mofetil (> 2 g/day), and steroids increase the risk of lymphatic complications. Diuretics could increase the lymphatic flow, and this may also cause lymphoceles.[15,16]

Transplant recipients who develop lymphatic complications are usually asymptomatic. Therefore, lymphoceles must be discovered by methods such as ultrasonography examination, intravenous pyelography, computed tomography, and lymphangiography. However, large lymphoceles may manifest by edema in the inguinal regions and cause deterioration of graft function, abdominal discomfort, urgency, vesical tenesmus, compressive syndrome of the vena cava or the portal vein, and fever.[17]

Percutaneous aspiration and percutaneous drainage of peritransplant fluid collections are technically straightforward and may be performed under ultrasonography or computed tomography guidance, depending on the location of the fluid collection. If the drain output has been < 10 mL/day, then the tube check will demonstrate a patent tube without significant residual fluid cavity; if the patient shows no signs of infection, the drain tube can be removed. Otherwise, percutaneous sclerotherapy techniques to treat symptomatic lymphoceles may be used; such techniques vary with regard to the sclerosing agent used, intervals between repeat sessions, and criteria for removal of percutaneous drainage catheters. The use of dehydrated ethanol, povidone iodine, doxycycline, bleomycin, and fibrin glue has also been described.

Fluoroscopic guidance is a method that may help to ensure that there is no communication with the urinary collecting system, bowel, or vascular system during sclerotherapy. A volume of approximately 50% of the estimated cavity volume is instilled into the cavity, and the drainage catheter is capped at 30 to 60 minutes. When tolerated, we ask patients to vary positions between supine and prone and upright and recumbent over the course of the dwell time to maximize sclerosant contact with all portions of the lymphocele cavity. Patients return for weekly sessions until the drainage is < 10 mL/day. If percutaneous sclerotherapy proves unsuccessful after 6 to 8 weeks, then the patient undergoes surgical treatment.

Laparoscopic or open surgery to fenestrate the lymphocele into the peritoneal cavity is associated with a lower overall rate of recurrence. Compared with open surgery and aspiration therapy, laparoscopic surgery seems to be the better overall treatment option for symptomatic lymphoceles occurring after kidney transplant.[18-20]

SURGICAL SITE INFECTIONS

Surgical site infections after renal transplant are not as common as in other transplant procedures. However, this complication results in increased patient morbidity and mortality and has the potential to increase health care costs and length of hospital stay or may require readmission for an additional operation. In certain situations, wound infections may also be associated with inferior graft survival rates.

Wound infections generally occur earlier than other posttransplant wound complications and may affect either superficial (subcutaneous tissue or fascia) or deep surgical sites (retroperitoneal space). Deep infections are generally related to other complications such as urinary leaks. Superficial infections are more common than deep infections. The incidence of wound infections after kidney transplant is about 5%.[21,22] However, rapid advances in surgical techniques and medical treatment during recent years have been associated with a progressive decline in infection rates and severity. Posttransplant surgical site infection mainly develops within the first 2 weeks after kidney transplant.

The renal transplant procedure is generally considered a clean contaminated case: when the bladder is opened during surgery, some urine is usually spilled in the operative field. A posttransplant surgical site infection caused by *Staphylococcus* spp. suggests that endogenous skin flora is the infecting inoculum. However, contamination with coagulase-negative *Staphylococcus* may be the reason of surgical site infections in some cases. Colonization with nonfermenting gram-negative bacteria during the period of hospitalization or hemodialysis may occur before the transplant surgery. Fungal infections rarely occur in kidney transplant recipients and may be related to prolonged hospitalization and immunosuppressive drugs.[23,24]

Patients with diabetes have an increased risk of infection. Diabetes mellitus causes delayed wound healing and infection relapses during the posttransplant period. Increased serum glucose levels early after transplant are correlated with increased frequency of surgical site infection.

The quality of surgical technique, technical challenges, and intraoperative complications could lead to an increased operative time and/or cold ischemia time. Long cold ischemia time of more than 30 hours and operative time of longer than 200 minutes may increase the risk of surgical site infection. Reoperation causes contamination as a result of repeated handling of the surgical site.[23]

The incidence of surgical site infection is higher among patients who receive kidneys from deceased donors than among those who receive kidneys from living donors, which is probably caused by the long cold ischemia time associated with deceased-donor transplants. Preoperatively, better control of previous infections in living-donor kidney recipients and the need for more potent immunosuppression in recipients of kidneys from deceased donors may be other risk factors.[25]

Transfusion itself plays an immunosuppressive role and, in the case of infection, is an indirect marker of an intraoperative complication. Patients who receive sirolimus-based immunosuppressive regimens have a higher incidence of surgical site infections. Sirolimus inhibits growth factor production in response to tissue injury and antiproliferative effects on fibroblasts related to impaired wound healing. This feature has previously been observed and has been associated with a higher number of bacterial infections.[26]

Acute rejection episodes have also been identified as a risk factor, which is associated with using potent immunosuppressive drugs such as antithymocyte globulin for induction therapy for acute rejection episodes.

Obesity is probably the biggest risk factor for a posttransplant wound infection. Obesity can cause prothrombotic and proinflammatory effects and may increase the risk for postoperative complications in surgery. Specifically, in the setting of kidney transplant, an association has been reported between obesity and the risk for surgical complications, including surgical site infections and lymphatic complications.[27] In obese (body mass index ≥ 30 kg/m^2) recipients, incidence of surgical site infection was higher than in nonobese patients (17.5% vs 6.3%).[8] Treatment depends on whether the wound infection is superficial or deep. Deep infections are treated with drainage either by surgery or by percutaneous drainage and usually antibiotics. Superficial infections are usually treated by opening the surgical wound and allowing it to heal by secondary intention; antibiotics are usually not necessary unless the recipient has significant cellulitis or systemic symptoms.[8]

POSTOPERATIVE HERNIA

Hernia after kidney transplant increases patient morbidity and impacts quality of life. Postoperative hernias are not uncommon to kidney allograft recipients. The most common type of this kind of hernia seems to be the incisional hernias due to prolonged dialysis, immunosuppressive drugs, especially corticosteroids, and prevalence of diabetes. Transplant recipients may have an increased risk to develop incisional hernias because of the use of postoperative immunosuppressive

therapy, which affects wound healing. The incidence of incisional hernia after renal transplant is between 1.6% and 18% in kidney transplant recipients.[28] Renal peritransplant hernia is an uncommon variant of internal hernias caused by entrapment of a bowel loop through a defect in the peritoneum covering the transplanted kidney. This type of hernia was first described as a potentially life-threatening complication in renal transplant recipients. Postoperative hernia should be considered as an iatrogenic surgical complication with an incidence of around 0.45%.[28] In almost all the cases, a defect of the peritoneum is found intraoperatively as a result of improper maneuvers and excessive dissection in the extraperitoneal space during the transplant. This defect can eventually cause an entrapment of the small bowel. Another potential cause of peritoneal defect could be the closing technique, if one or more stitches were to tear the peritoneum.

Incisional hernia may develop after transplant as a result of mycophenolate mofetil use and surgical site infection. Other predisposing risk factors are the following: female sex, duration of the transplant procedure, obesity, other abdominal wall hernias, multiple operations into the ipsilateral iliac fossa, and smoking. These preoperative and perioperative risk factors should be taken into account by surgeons when closing the fascia.

Preoperative weight reduction in obese patients should not only be advised to benefit graft survival, prevent diabetes, and decrease hospital stay but might also prevent postoperative complications, such as wound infection and incisional hernia. Rate of emergency operative repair for an incarcerated incisional hernia is 35%.[28] Recurrences occur in 23% of cases.[28]

Synthetic polypropylene is the mesh used most frequently in our center; this matches use mentioned in the literature for repair of incisional hernias after kidney transplant. Nevertheless, it is conceivable that biologic prosthesis (porcine dermis collagen) could be useful in patients who are prone to development of wound infections.[29]

The first parameter considered in the decision regarding how to repair a patient's abdominal wall defect is the location of the defect. In general, tensor fascia latae is used when the defect is located in the lower quadrants of the abdomen. The component separation method is used as the procedure of first choice when defects are in the midline region.[30]

The second parameter considered is the presence of infection. Evidence of a serious wound infection can delay a definitive repair of the defect. Serious wound infections would include those wounds with a significant amount of necrosis or purulence. In these cases, temporary fascial repair with a prosthetic mesh is performed, leaving the skin incision open. Patients are given antibiotics as appropriate and undergo dressing changes to clear the infection and debride the wound, with definitive repair then conducted when the wound is clinically ready. Wounds that are simply opened and therefore contaminated, but not grossly infected, are irrigated with a pulse lavage, debrided, undergo reexcision of wound edges, and then undergo definitive repair.

In contrast, synthetic materials are associated with increased complications rates, particularly in contaminated wounds. Polypropylene mesh has an increased rate of infection, fistula formation, and extrusion after skin grafting. Incidence of fistula formation after repair with polypropylene mesh approaches 40% after healing by secondary intention.[31]

GASTROINTESTINAL BLEEDING AND PERFORATION

The incidence of gastrointestinal (GI) complications in renal transplant recipients is relatively high compared with that of the normal population. These complications may be severe in about 10% of patients and may lead to graft loss and even patient death.[32]

The most frequent GI complications in renal transplant recipients include oral lesions, esophagitis, peptic ulcer, diarrhea, colon hemorrhage, or colon

perforation. These disorders may be related to drugs, infections, or exacerbation of preexisting GI pathology. Although most of these problems may be managed with appropriate medical treatment, some require surgery.

Predisposing factors for the increased risk of GI bleeding in renal transplant recipients are gastric hypersecretion, suppressed platelet count caused by azotemia, immunosuppression-induced thrombocytopenia, antiplatelet effects of immunosuppression, and anticoagulant use. There are many reasons for massive GI bleeding, which include angiomata (30%), diverticulosis (17%), polyps or cancer (11%), focal ulcers (9%), upper GI lesions (11%), and presumed small bowel lesions (9%). No obvious cause or site is identified in about 6% of the cases.[33,34]

Ulcers of the small intestine represent a rare but dreadful complication of renal transplant, development of which may be favored by corticosteroids, intestinal ischemia, and even more often by cytomegalovirus (CMV) infection. The clinical picture consists of periumbilical colicky pain, nausea, and vomiting. Frequently, the patient presents with small bowel obstruction, bleeding, or perforation.

Lower GI bleeding is the second most common major colorectal complication after perforation in renal transplant recipients. Risks of lower GI bleeding in renal transplant recipients exist in the long term, with bleeding episodes occurring within 1 year after transplant. Opportunistic colitis due to CMV infection is the most common cause of lower GI bleeding. Angiodysplasia and diverticular disease are other commonly seen complications after opportunistic colitis in renal transplant recipients.

Primary diagnosis and evaluation of all lesions are done during colonoscopy. When CMV colitis is the cause of bleeding, valganciclovir treatment usually provides a complete cure. There is no need for discontinuation of an immunosuppressive therapy in patients with CMV colitis.

Colon perforation may complicate diverticular disease or be a consequence of intestinal ischemia. The reported incidence of intestinal perforation in renal transplant recipients ranges from 0.6% to 3.4%.[35] Most perforations occur within the first few weeks or months after renal transplant. The pathogenesis is probably related to a high incidence of diverticular disease in patients with polycystic kidneys and chronic renal failure; other risk factors include over-immunosuppression, CMV infection, and the transplant procedure itself. The average mortality rate is 56.5%.[35,36] This high mortality rate may be related to the effects of immunosuppression and the associated poor inflammatory response to the sepsis. Additionally, the immunosuppressive agents might mask the classic clinical findings, such as fever or leukocytosis, in these patients. Pneumoperitoneum on abdominal roentgenogram is not necessarily positive in all patients. Therefore, prompt diagnosis, aggressive surgical care consisting of resectional therapy, use of broad-spectrum antibiotics, and a reduced immunosuppressive protocol are all crucial to positive outcomes.[37]

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Living Kidney Donor Complications

Erdal Karagülle
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A donor candidate is a healthy person whose health and psychosocial examinations have been fully completed. In transplant procedures, the donor operation must be highly safe, and potential complications must be minimized. However, risks associated with living-donor organ donation include both short-term and long-term health risks of the surgical procedure, organ function, and psychological problems. For the recipient, there are a number of possible surgical complications, but all of these are accepted as natural because the operation is a lifesaving procedure. In organ donation procedures, a healthy person is exposed to risk of and recovery from an unnecessary major surgery. Types of risks include immediate and surgery-related risks. Donor-type risks include pain, infection, hernia, bleeding, blood clots, wound complications, and, in rare cases, death. Overall, organ donors fare well over the long term. In addition to physical complications, organ donation may also cause mental health issues, such as symptoms of anxiety and depression. The donated organ may fail in the recipient, causing feelings of regret, anger, or resentment in the donor.

KIDNEY DONATION RISKS

Living-donor kidney transplant is the most widely studied type of living organ donation with more than 50 years of follow-up information. The first living-donor kidney transplant was performed in Boston in 1954. It was made in identical twins by Joseph Murray and his team.[1] The first living-donor kidney transplant in Turkey was performed by Haberal and his team on November 3, 1975.[2] In total, 3102 kidney transplants have been performed at Baskent University, Department of Transplantation between 1975 and 2020. Of these, 2388 (77%) were performed from living donors and 714 (23%) from deceased donors.

The overall life expectancy for those who have donated a kidney is the same for similarly matched nondonor populations.[1] Some studies have suggested that living kidney donors may have a slightly higher risk of kidney failure in the future.[1,3] However, this risk is still lower than the average risk of kidney failure in the general population.[1,3,4] Specific long-term complications associated with living-kidney donation include high blood pressure, elevated protein levels in urine, and reduced kidney function. Therefore, a living kidney donor should be informed in detail about the potential risks of kidney donation to the donor and the benefits of kidney donation to the recipient.[1,3]

The following donor nephrectomy operations can be performed: open nephrectomy, laparoscopic nephrectomy (LDN), hand-assisted laparoscopic nephrectomy (HALDN), robotic nephrectomy (RDN), and hand-assisted robotic nephrectomy.

The first open-donor nephrectomy surgery was performed 66 years ago; this surgery was recognized as the standard operation for many

years. The first LDN operation was performed by Ratner and associates in 1995.[5] The HALDN operation was first performed in 1998.[6] Today, more than 85% of donor nephrectomy operations are performed laparoscopically.[7] The advantages of laparoscopic operations over open surgery include less postoperative pain, lower amount of blood loss, shorter hospital stay, earlier return to daily activities (2 vs 6 weeks), better cosmetic results, and improved patient satisfaction. The conversion rate from LDN to open surgery is between 1.1% and 1.6%. The rate of life-threatening complications is higher.[1,6,8] For LDN procedures, there is learning curve for surgeons and it is an expensive technique. It has been reported that HALDN procedures decrease operative time and have shorter warm ischemia time and lower complication rates than LDN.[6] Technological advances enabled RDN to be first performed in 2002, which was then followed by the hand-assisted RDN operation. The advantages of RDN include lower perioperative complication rates, facilitated tissue dissection, more convenient placement of sutures and knots, and superior graft preservation. Although there is a steeper learning curve, there is markedly improved comfort for surgeons. However, this system requires advanced technology, and it is costly.[9]

Donor nephrectomy is usually performed via open nephrectomy as a standard procedure at the Department of Transplantation of Baskent University. However, donor nephrectomy used to be performed with conventional flank incision until early 2018. For the past 2 years, these operations have been performed with the crescentic incision technique. This technique allows the donor to lie straight on their back, with only a slight turn to one side to allow for the incision. The incision begins 2 cm below the rib, approximately 10 cm from the xiphoid, and forms a 10-cm curve moving out laterally and then returning to the midsection, ending 10 cm from the umbilicus (Figure 1). In a study that compared donor nephrectomy using this incision versus those performed with the conventional flank incision, the new crescentic incision was shown to be both safe and similar to conventional techniques previously described in the literature. In addition, this incision has

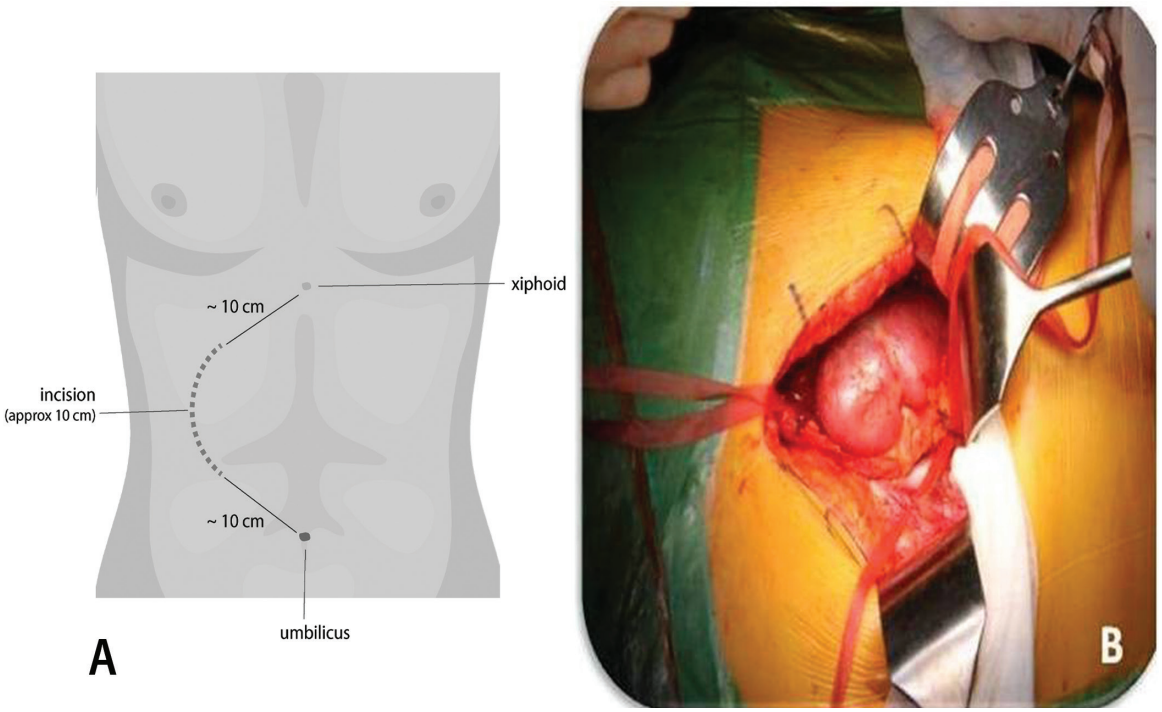

Figure 1. Schematic **(A)** and Intraoperative View **(B)** of the Crescentic Incision Technique in Kidney Donor Nephrectomy

increased comfort for the patient, the surgeon, and the anesthesiologist during surgery and results in a shorter surgery time.[10]

Determining the technique for donor nephrectomy must be always based on the principle of exposing the donor to the lowest possible risk while providing optimal graft survival and function. None of the above-mentioned techniques are much more ideal than another. Special emphasis must be based on characteristics of factors and preferences of patients in the preoperative period.[8]

IMMEDIATE AND SURGICAL RISKS

Complications related to kidney donation surgeries include the following: conversion to open nephrectomy (incidence rate of 1.1%-1.6%),[1] hematoma (incidence rate of 0.1%-05%),[1] infections (such as urinary tract infection or wound infection; incidence rate of 0.6%-7.8%),[11] intestinal injury (incidence rate of 0.1%-0.4%),[1] intestinal obstruction (incidence rate of 1%),[7] need for reoperation (such as for bleeding; incidence rate of 0.1-0.5%),[1] pulmonary complications (incidence rate of 0.2%),[3] readmission to hospital (incidence rate of 2.1%),[1] hernia (incidence rate of 0.1%-0.7%),[1] and death (worldwide mortality rate for living kidney donors of 0.03%-0.06%).[1,3,4]

According to data from the United States, major complications reported from 2008 included bleeding (2.2%), hernia (0.8%), and bowel obstruction (1%). Three donation-related deaths were reported between 2005 and 2009. Further analysis of over 80 000 US donors between 1994 and 2009 revealed a surgical mortality rate of 0.03%.[12] Mortality rates reported in 2008 and those reported in 2010 and 2015 were similar. However, a marked reduction has been observed in rates of bleeding (0.3%), intestinal injury (0.25%), and hernia (0.4%).[1]

At the Department of Transplantation of Baskent University, perioperative major complications, such as Clavien grade 3 events, were observed in 2 patients (0.3%). These complications were in the form of bleeding from the renal vein stump in a patient and small intestinal injury in another. Postoperative complications, such as Clavien grade 1-2 events, were observed in 23 patients (3.55%) and included intestinal obstruction in 5 patients (0.77%), wound site infection in 7 patients (1.08%), hematoma at operation site in 4 patients (0.61%), and hernia in 7 patients (1.08%). No donor mortalities were seen.

A joint Canadian and Australian study published in 2019 reported 142 (13.6%) perioperative (55 intraoperative and 87 postoperative) complications among 1042 kidney donors who had received laparoscopic or open donor procedures. The most common intraoperative complication was organ injury, and the most common postoperative complication was intestinal obstruction. Most complications were minor (90%); however, 12 donors (1%) experienced a major complication but no donor deaths were reported.[7] Complication rates at the Department of Transplantation of Baskent University are lower than those rates. This result can be explained by our experience of over 25 years and use of open nephrectomy as the standard procedure.

LONG-TERM MEDICAL RISKS

Kidney donors typically experience a 20% to 30% decrease in kidney function (as measured by the glomerular filtration rate) after donation. The remaining kidney compensates for the loss of the kidney through a process called hyperfiltration. In an 8-year follow-up of living kidney donors at the Transplantation Department of Baskent University, the donors' last creatinine level was between 0.62 and 1.84 mg/dL (mean and standard deviation of 1.1 ± 0.2 mg/dL). The final glomerular filtration rate was between 88 and 115 mL/min/1.73 m^2 (mean and standard deviation of 99.4 ± 7.5 mL/min/1.73 m^2). Other complications that may occur in the long-term after the surgery to donate a kidney include the following: hypertension (medication required) (incidence of 8.8%-16% at 10 years),[1,13] development of end-stage renal disease (incidence of 0.3%),[1,3] and increased protein spilled into the urine (incidence of 12.7%-20%).[11,14]

SUMMARY

Although the risks of donor nephrectomy for kidney transplant are low, it is not a smooth surgical procedure for donors. Donor candidates should be well informed about the risks of surgery. Donor selection should be done meticulously. Donor nephrectomy surgery should be done at centers with sufficient experience and equipment. It is necessary to minimize complications with proper donor assessment and the application of rigorous surgical techniques. Long-term follow-up of donors is also required.

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Author Index

A
AĞILDERE MA 25
AKDUR A 211, 235
ANDİÇ Ç 255
AYVAZOĞLU SOY EH 129, 151

B
BOYVAT F 84

C
COŞKUN M 42
ÇALIŞKAN K 274

F
FIRAT A 116

H
HABERAL M 1, 3
HABERAL KM 203
HARMAN A 99

İ
İGÜS B 159, 166

K
KARACA AS 129
KARAGÜLLE E 281
KARAKAYA E 211, 235
KESİM Ç 255, 264
KIRNAP M 151
KURAL RAHATLI F 191
KUŞ M 274

M
MORAY G 68

Ö
ÖZEN Ö 133
ÖZYER UE 242

T
TÜRK E 281

U
USLU N 60

Y
YARBUĞ KARAKAYALI F 129
YILDIRIM E 281
YILDIRIM S 175

Subject Index

A

Abscess
- Liver
  - CT Diagnosis 57
  - MR Diagnosis 57
  - Percutaneous Treatment 168
- Renal
  - CT diagnosis 208
  - Percutaneous Treatment 269
  - US diagnosis 198

Acute Tubular Necrosis
- CT Diagnosis 203-204
- Renal US Diagnosis 192, 198

Arterial Steal Syndrome
- Angiographic Diagnosis 92
- Endovascular Treatment 93
- US Diagnosis 62

Arterioportal Fistula
- CT Diagnosis 47
- Endovascular Treatment 93
- Vascular Complications 68

Arteriovenous Fistula
- CT diagnosis (Renal) 203
- Endovascular Treatment (Renal) 230, 257
- US diagnosis (Renal) 195
- Vascular Complications 70, 205, 222

B

Bile Leaks
- Percutaneous Treatment 142

Bilomas
- Percutaneous Treatment 142

Bile Stones 131

Biliary
- Complications 129
- Leak 130
- Leakage (CT Diagnosis) 53
- Sludge or Stone (CT Diagnosis) 54

Biliary Stricture 131
- CT Diagnosis 53
- Percutaneous Treatment 136

Brain Death 4, 25

C

Central Nervous System Complications 26

Cardiopulmonary Complication Rates After Donor Hepatectomy 179

Choledochocholedochostomy 130

Choledochojejunostomy 130

Color Doppler Ultrasonography
- Liver 45
- Renal 191

COVID-19 Pandemia 1

D

Donor Hepatectomy
- Life-Threatening Complications 180

Donor Nephrectomy 235
- Surgical Risks 281

E

End-Diastolic Velocity (Liver) 60

External Iliac Artery Dissection in Renal Transp. 213

G

Gastrointestinal Bleeding 152, 278

Gastrointestinal Perforation 153, 278

H

Hematoma
- CT Diagnosis (Liver) 57
- CT Diagnosis (Renal) 207
- Percutaneous Treatment (Renal) 269
- Postoperative 167
- US Diagnosis (Renal) 197

Hemobilia
- Causes 131
- Intervention 145

Hemodialysis 1

Hepatic Arterial Complications
- US Diagnosis 61

Hepatic Arterial Reconstruction Technique 71

Hepatic Artery Pseudoaneurysm
- CT Diagnosis 46
- Liver Transplant Complications 68
- US Diagnosis 63

Hepatic Artery Rupture (CT) 47

Hepatic Artery Stenosis
- CT Diagnosis 44
- Endovascular Treatment 85
- Liver Transplant Complications 68
- US Diagnosis 63

Hepatic Artery Thrombosis
- CT Diagnosis 45

Endovascular Treatment 87
Liver Transplant Complications 42
Hepatic Blood Flow 68
Hepatic Infarction (CT) 58
Hepatic Venous Complications
US Diagnosis 66
Vascular 77
Hepatic Venous Outflow Obstruction
Endovascular Treatment 116
Hepatic Venous Stenosis (CT) 47
Hepaticojejunostomy 53
Hepatocellular Carcinoma 57, 84
Hepatopedal Flow Pattern 61
History of Organ Transplantation 3

I
Incisional Hernia 151
Inferior Vena Cava
US Diagnosis 66
Vascular Complications 78
Intraabdominal Hemorrhage 151

K
Kidney Transplant 1, 211
Living-Donor 228
US Diagnosis of Complications 192

L
Large-for-Size Syndrome 151
Liver Transplant 1, 68
Rejection CT Diagnosis 57
Living-Donor
Hepatectomy 175
Living-Liver Donor
Biliary Complications 179
Mortality 186
Postoperative Care 176
Preparation 176
Surgical Complications 177
Treatment of Complications 184
Lymphocele
Percutaneous Treatment 268
Renal CT 207
Renal Transplant Complications 275
Renal US 198

M
MESOT 1
Magnetic Resonance (MR)
Angiography (Liver) 25, 43
Cholangiography 43
Multidetector CT
Angiography (Liver) 42

N
Nephrolithiasis (Renal CT) 206
Nonvascular or Nonbiliary Complications (CT) 57

P
Peak Systolic Velocity
Liver 60
Renal 191
Percutaneous Fluid Drainage 170
Percutaneous Liver Biopsy 159
Perigraft Fluid Collections
Percutaneous Treatment 264
US Diagnosis 267
Portal Vein Complications
CT Diagnosis 48
Thrombosis 75
Portal Vein Stenosis
CT Diagnosis 49
Endovascular Treatment 100
Vascular Complications 76
Portal Vein Thrombosis
CT Diagnosis 49
Endovascular Treatment 108
US Diagnosis 64
Vascular Complications 76
Post Donor Hepatectomy Liver Failure 180
Postoperative Hernia 277
Posttransplant Lymphoproliferative
Renal CT 209
PRES Syndrome 27
Pseudoaneurysm
Endovascular Treatment (Liver) 95, 230
US Diagnosis (Renal) 195

R
Renal Allograft Rejection (Renal US) 199
Renal Artery Anastomosis Technique 212
Renal Artery Stenosis
CT Diagnosis 204
Endovascular Treatment 222
Surgical Management 216

US Diagnosis of Renal Transplant 192
Renal Artery Thrombosis
CT Diagnosis 204
Surgical Management 214
US Diagnosis 194
Renal Biopsy
Percutaneous 255
Transvenous 257
Renal Graft Vascular Thromboses
Endovascular Treatment 227
Renal Obstruction
CT Diagnosis 216
Renal Vein Anastomosis Technique 218
Renal Vein Thrombosis
CT Diagnosis 204
Endovascular Treatment 228
Surgical Management 218
US Diagnosis 194
Renal Vein Stenosis
CT Diagnosis 204
Resistive Index 60

S
Sphincter of Oddi Dysfunction 131, 146
Surgical Site Infections 282

T
TDTD 1
TOND 1
Transjugular Liver Biopsy 161
Transplant Programs 1
Triphasic Waveform 61
TTS 1

U
Ureter Anastomosis Technique 235
Urinary Obstruction
Ureteral Obstruction 238
CT Diagnosis 203
Percutaneous Treatment 242
Renal US 196
Urinary Leaks
Percutaneous Treatment 251
Renal CT 206
Renal US 197
Urine Leakage 237
Urinoma
CT Diagnosis 206
Percutaneous Treatment 271
US Diagnosis 197
Urologic Complications
Percutaneous Treatment 264
Postransplant 235

V
Vascular Reconstruction in Liver Transplant 68