Effect of Post-Transplant Cardiac Angiographic Procedures on Post-Transplant Renal Function

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ABSTRACT

Background. Cardiac interventions often are performed before and after renal transplant for coronary artery disease. The aim of this study was to investigate whether post-transplant cardiac coronary procedures affect post-transplant renal function.

Method. We retrospectively included renal transplant recipients who underwent renal transplant procedures at Baskent University between April 28, 1997 and January 20, 2020. We analyzed the effect of cardiac catheterization in renal transplant recipients between 6 and 12 months post-transplant with post-transplant renal function assessed by glomerular filtration rate (GFR). We compared the effect of the type of coronary intervention on GFR change in group 1, whereby group 1 was divided into 2 subgroups (coronary artery bypass grafting [CABG] and stenting). Group 1 included patients who underwent cardiac intervention, whereas group 2 included those who had not undergone cardiac intervention.

Results. In all, 108 patients underwent coronary angiography; 45 (41.7%) had normal coronaries or minimal coronary artery disease (CAD); 37 (34.3%) underwent stent implantation; 26 (24.1%) underwent CABG. The mean post- transplantation GFR of all patients after cardiac catheterization was 84.26+25.91 (mL/min/1.73 m^2). The final, after 12 months mean GFR of all patients was 69.55+27.05. The final GFR was significantly lower than the initial post-renal GFR value in patients who underwent cardiac intervention but not in non-intervened patients.

Conclusion. Invasive cardiac revascularization procedures showed a negative effect on post-transplant renal function in renal transplant recipients. All renal transplant recipients who underwent cardiac intervention survived the intervention, and there was no mortality. The reason for this outcome was assumed to be because of the short follow-up period.

A kidney transplant is the treatment of choice for the management of end-stage renal disease. Compared with dialysis, kidney transplant significantly improves physical performance, quality of life, and social integration. Post-transplantation renal function monitoring is performed using serum creatinine and glomerular filtration rate (GFR) measurements, 24-hour urine samples, and transplant Doppler investigations [1,2]. GFR measurements are commonly used for post-transplant renal function assessment [3]. Patients with chronic kidney disease (CKD) and kidney transplant recipients are at increased risk for atherosclerosis, particularly coronary artery disease (CAD) [4]. It is known that low cardiac output associated with decreased cardiac function also negatively affects renal function, both in the general population and in patients with renal failure [5,6]. Hence, cardiac interventions aimed at restoring cardiac output and mitigating ischemia are frequently performed in patients undergoing renal transplantation [2]. Although intravenous contrast administration is shown to impair renal function in people with CKD [4], it is unknown how these procedures affect renal function in renal transplant recipients [7,8]. Hence, in this study, we aimed to investigate whether post-transplant cardiac invasive procedures, aimed at

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improving cardiac functions, namely coronary angiography, percutaneous coronary intervention (PCI), and coronary artery bypass grafting (CABG), negatively or positively affect post-transplant renal function assessed by GFR in renal transplant recipients.

MATERIALS AND METHODS

We retrospectively included renal transplant recipients who underwent renal transplant operation and post-transplant coronary angiography.

We analyzed the effect of cardiac catheterization in renal transplant recipients between 6 and 12 months post-transplant with post-transplant renal function assessed by GFR at Baskent University Faculty of Medicine between April 28, 1997 and January 20, 2020. We examined their demographic, clinical, and biochemical data including their GFR. The standard immunosuppressive treatment in our center consisted of a calcineurin inhibitor or a mammalian target of rapamycin inhibitor, prednisolone, and mycophenolate mofetil.

The GFR was calculated for both sexes using the Chronic Kidney Disease Epidemiology Collaboration formula. We formed 2 groups based on cardiac intervention status. We compared the effect of the type of coronary intervention on GFR change in group 1, whereby group 1 was divided into 2 subgroups (CABG and stenting). Group 1 included patients who underwent cardiac intervention, whereas group 2 included those who had not undergone cardiac intervention. We compared the post-transplantation first GFR (after 1 month) and the final GFR (after 12 months) measurements in both groups. We also compared the effect of the type of coronary intervention on GFR change in group 1.

Before coronary angiography, preventive measures were taken. N-acetyl cysteine and isotonic saline solution were given intravenously.

In our hospital, diagnostic coronary angiography uses an average of 20 to 30 mL iohexol. However, in the case of a coronary stent implantation, only 50 to 80 mL iohexol was used, as the patient had previously undergone a kidney transplant. GFR data was recorded both after the coronary angiography and before the coronary bypass. However, the data were not included in our study. As standard procedure, preventive measures were taken regarding patients with impaired GFR after coronary angiography.

Repeated coronary angiography with appropriate interventions were not included in our study.

Statistical analysis

All statistical analyses were performed with SPSS version 21 (IBM, Armonk, NY, USA). Descriptive statistics included mean ± SD, median (min-max), and number (%). The normality of study data was tested using the Kolmogorov−Smirnov test. Normally distributed quantitative variables were compared using paired samples t test and non-normally distributed quantitative variables using the Wilcoxon test. Categoric variables were compared with the χ^2 test or Fisher's exact test. Univariate analysis was used to determine if cardiac intervention or type of cardiac intervention independently affected GFR change. $P < .05$ was considered statistically significant for all comparisons. We performed a univariate logistic regression analysis to determine the individual predictors of GFR, followed by a binary logistic regression analysis to determine the independent predictors of GFR change.

RESULTS

We included 108 patients with a mean age of 52.02 ± 11.5 years. There were 88 men (80%) and 20 women (18.2 %). The demographic and clinical properties of the study population were presented in Table 1. There was no significant difference between patients who underwent coronary intervention and those who did not with respect to demographic and clinical characteristics ($P > .05$ for all comparisons).

All renal transplant recipients who underwent cardiac intervention survived the intervention, and there was no mortality.

The reason for this outcome was assumed to be because of the short follow-up period.

The post-transplant median creatinine of the patients was 1.24 (0.52-6.30). The mean post- transplantation GFR of all patients after cardiac catheterization was 84.26+25.91(mL/min/1.73 m^2).

Of the patients, 108 underwent coronary angiography; 45 (41.7%) had normal coronaries or minimal CAD; 37 (34.3%) underwent stent implantation; 26 (24.1%) underwent CABG. The final, after 12 months mean GFR of all patients was 69.55 +27.05. The median final GFR of patients who underwent cardiac intervention was significantly lower than the initial post-renal GFR value, whereas patients who did not undergo cardiac intervention had similar post-transplantation and final GFR. Furthermore, patients undergoing both PCI and CABG had significantly lower final GFR compared with post-transplantation GFR (Tables 2 and 3).

In the present study, CKD stage worsened the 20 (44.4%) patients in group 1 (intervention) and 18 (28.5%) patients in group 2 (no intervention; Tables 4 and 5).

There was no significant difference between the frequency distributions of the month 1 and 12 CKD grades of the patients according to the groups ($P > .05$).

DISCUSSION

Kidney transplantation is the best available therapy in patients with end-stage renal disease as it can lead to a better quality of life and a higher rate of survival [9,10]. This enables the patient to avoid the complications of dialysis. In many of the kidney transplant registers, cardiovascular diseases (CVDs) are the leading cause of premature death [11]. In hemodialysis patients, mortality due to CVD is about 10 to 20 times higher than in the general population [12,13]. The predictors include the age of the recipient, the transplantation of older donors, and deceased

Table 1. Demographic and Clinical Data of Patients

Characteristic	Result
Female/male patient	20/88
Age at the time of transplant, mean + SD	52.02 + 11.5
HT, n (%)	87 (80.6)
HL, n (%)	58 (53.7)
DM, n (%)	35 (32.4)
Smoker, n (%)	22 (20.4)
Coronary artery disease, n (%)	37 (34.3)
History of coronary artery bypass surgery, n (%)	26 (24.1)
Atrial fibrillation, n (%)	11 (10.2)

Table 2. Comparison of the Status of Cardiac Intervention on GFR Change (Intervention Performed vs No Intervention Performed)

	Post-renal first GFR	Final GFR	*P* value*
Group 1	86.3 (16.8-138.7)	81 (9.6-105)	<.01
Group 2	86.3 (12.3-193.4)	82.7 (6-112.1)	NS

GFR, glomerular filtration rate.
* Paired samples *t* test.

Table 3. Comparison of the Type of Cardiac Intervention on GFR Change

	Post-renal first GFR	Final GFR	*P* value*
CABG (n = 26)	87.9 (16.8-98.3)	81.9 (10.6-92.2)	<.05
Stent implantation (n = 37)	84.4 (36.9-138.7)	80.7 (9.6-105)	<.001

GFR, glomerular filtration rate; CABG, coronary artery bypass grafting.
* Wilcoxon test.

donors, also a delayed transplant function. Additionally, diabetes, peripheral vascular disease, an earlier heart attack, and angina pectoris are the other factors responsible for mortality. Hence, renal transplant recipients are not uncommonly taken to coronary angiography and invasive cardiac procedures, namely PCI and CABG. Because of the progressive and improving diagnostic procedures, stent implantations are preferred to bypass operations. However, patients for whom a bypass operation was recommended continue to be operated on. The SYNTAX score, an angiographic grading tool for determining the complexity of CAD, is very helpful in deciding on the procedure.

As part of these procedures, a contrast agent is administered, which may unfavorably affect kidney function.

In the literature, there are various results and opinions about the effect of contrast agents on kidney function. Zhang et al. showed that percutaneous cardiological intervention has been effectively performed in patients after kidney transplantation. There were no serious complications after the intervention and the kidney function recovered well after treatment [14]. In contrast Agrawal et al showed that contrast-induced acute kidney injury often occurs in renal transplant recipients after cardiac catheterization [15]. Furthermore, they showed that the use of iso-osmolar contrast compared to low-osmolar contrast was

Table 4. CKD Stages of the Intervention Group

			CKD stages at month 12					
Group: intervention			I >90	II 60-89	IIIB 30-44	IV 15-29	V <15	Total
CKD stages at month 1	I >90	n	3	7	2	1	2	15
		%	20%	46.7%	13.3%	6.7%	13.3%	100%
	II 60-89	n	2	33	2	1	2	40
		%	5.0%	82.5%	5%	2.5%	5%	100%
	IIIB 30-44	N	0	2	1	1	0	4
		%	0%	50%	25%	25%	0%	100%
	IV 15-29	N	0	1	0	0	0	1
		%	0%	100%	0%	0%	0%	100%
Total	n		5	43	5	3	4	60
	%		8.3%	71.7%	8.3%	5%	6.7%	100%

Likelihood ratio = 11.785 *P* = .463

CKD, chronic kidney disease.

Table 5. CKD Stages of No Intervention Group

			CKD stages at month 12						
Group: no intervention			I >90	II 60-89	IIIA 45-59	IIIB 30-44	IV 15-29	V <15	Total
CKD stages at month 1	I>90	N	6	6	0	0	1	2	15
		%	40%	40%	0%	0%	6.7%	13.3%	100%
	II 60-89	N	1	13	2	2	3	2	23
		%	4.3%	56.5%	8.7%	8.7%	13.0%	8.7%	100.0%
	IIIB 30-44	N	1	1	0	0	0	0	2
		%	50%	50%	0%	0%	0%	0%	100%
	IV 15-29	N	1	3	0	0	0	0	4
		%	2%	75%	0%	0%	0%	0%	100%
	V <15	N	0	1	0	0	0	0	1
		%	0.0%	100.0%	0.0%	0.0%	0.0%	0.0%	100.0%
Total	n		9	24	2	2	4	4	45
	%		20%	53.3%	4.4%	4.4%	8.9%	8.9%	100%

Likelihood ratio = 17.405 *P* = .627

CKD, chronic kidney disease.

associated with a lower risk for contrast-induced acute renal insufficiency.

Rajan et al. showed that the development in diagnostic and device technology enabled improved diagnosis and percutaneous treatment of transplant renal artery stenosis. The use of alternative contrast media and complementary medication reduced the likelihood of contrast media nephropathy [16]. According to our results, the post-transplant intervention reduced final GFR significantly compared with the first final GFRs. GFR drops significantly in both types of intervention, therefore, no interventional difference can be mentioned. Additionally, estimated GFR values are excellent, and differences are <10%. Because there is no difference between the 2 interventions, we must pay attention to the kidney function and the GFR in both cardiac procedures. It is unclear why diagnostic angiography did not adversely affect post-transplant renal function as did the cardiac invasive procedures. The reason for this occurrence may have multiple explanations. First, both procedures are substantially longer than coronary angiography and may thus increase renal injury [17]. In PCI, a higher volume of contrast material is administered, and peripheral embolism is more common. In CABG, the cardiopulmonary pump may increase renal ischemia and renal arterial embolism [18,19]. Second, patients who underwent cardiac invasive procedures may have a more severe form of coronary disease and thus more severely affected myocardial pump function, affecting renal function negatively [20]. Thus, contrast material administration may not be the sole culprit in the deterioration of renal function in transplant recipients.

Despite these differences, we should continue the invasive procedures and pay the price otherwise these patients are not transplantable and have to lead a limited life.

Study limitations

The limitations of the present study were its retrospective design and relatively low number of patients.

CONCLUSIONS

The results of this study demonstrated that there was a significant effect of invasive cardiac revascularization procedures but not diagnostic coronary angiography on post-transplant renal function assessed by GFR in renal transplant recipients. For this reason, clinicians should pay attention to the need for cardiac revascularization of each patient individually to protect the kidneys as much as possible.

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