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Original Article

The Effect of Renal Transplantation on Cardiac Functions

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ABSTRACT. Chronic renal failure is a well-known risk factor for cardiovascular poor outcome. Despite advances in dialysis and renal transplantation, these patients still have high cardiovascular morbidity and mortality. The aim of our study was to evaluate the changes in blood parameters and echocardiographic parameters of patients undergoing renal transplantation in our center. One hundred and eighty-three patients who underwent renal transplantation between September 2012 and January 2016 were included in the study. Pre- and postoperative hemoglobin values, lipid profiles, ejection fractions, presence of left ventricular hypertrophy, presence of diastolic dysfunction, and valve pathologies were retrospectively scanned. Data were obtained from all patients in terms of blood parameters, but we compared 92 patients' echocardiographic data because of lack of both pre- and postoperative echocardiography records. In our study, 124 patients (67.8%) were male, and the mean age was 42.6 ± 14.4 years. Hemoglobin levels (11.2 ± 1.98, 12.7 ± 2.2 mg/dL, P <0.001) and high-density lipoprotein (HDL) values (37.6 ± 10.5, 46.6 ± 13.6 mg/dL, P <0.001) were found to be different significantly. In echocardiographic evaluation, there was no difference between pre- and postoperative ejection fractions in 92 patients. However, patients with preoperative ejection fraction <50% had a significant increase in postoperative ejection fraction (40.1 ± 6.2, 48.4% ± 9.4%, P = 0.012). Renal transplantation can improve left ventricle ejection fraction in patients with basal ejection fraction less than 50% and also provide a significant increase in hemoglobin and HDL levels in all patients. This suggests that renal transplantation may reverse the process for dilated cardiomyopathy and may improve cardiac function in patients with low ejection fraction. However, transplantation should be performed as early as possible in these patients.

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Introduction

Chronic renal failure is a well-known risk factor for cardiovascular poor outcome.[1] Despite advances in dialysis and renal transplantation, these patients still have high cardiovascular morbidity and mortality.[2-4] Renal

transplantation provides longer survival and better quality of life in long-term dialysis patients.[2] Despite significant progress in the care of patients with heart failure (HF), individuals with ESRD and concomitant cardiac dysfunction are generally considered less suitable candidates for kidney transplantation due to increased risk of operative morbidity and mortality. Therefore, the coexistence of HF and renal failure becomes important. In fact, some previous studies have shown that kidney transplantation improves cardiac function.[5-7] The aim of our study was to evaluate the changes in blood parameters and echocardiographic parameters of patients undergoing renal transplantation in our center.

Materials and Methods

Two hundred and thirteen patients were included in the study who underwent renal transplantation between September 2012 and January 2016 in our center. Pre- and postoperative hemoglobin values, lipid profiles, ejection fractions, presence of left ventricular hypertrophy, presence of diastolic dysfunction, and mitral and tricuspid valve insufficiencies were retrospectively scanned. Thirty patients who could not reach any of the pre- or postoperative blood or echo parameters were excluded from the study. Thirty patients were excluded from the study who we could not reach one of the pre- and postoperative blood parameters; as a result, we examined 183 patients' laboratory parameters. Likewise, since the pre- and postoperative echocardiography results of 92 of these 183 patients were obtained, the data of these 92 patients were examined. The reference values for echo parameters were defined based on the American Society of Echocardiography guidelines.[8] Laboratory parameters were obtained from the most recent pretransplant and 12-month posttransplant office visits. One exception was echocardiographic data, the timing of which could not be controlled for in this retrospective study. Echocardiograms were obtained during the pretransplant evaluation, with the most recent one taken into account and the time closest to 12–24 months posttransplantation.

Continuous data were compared preoperatively and postoperatively with K-related samples. Data are expressed as the mean ± standard deviation unless otherwise stated. Categorical data were analyzed with Fisher's exact test and the Chi-squared test. A P <0.05 was considered statistically significant. All analyses were undertaken using the IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA).

Protocols approved by the local ethics committee were utilized throughout the study. A standardized questionnaire was used to collect clinical and demographic information, including medication history.

Results

In our study, 124 patients (67.8%) were male, and the mean age was 42.6 ± 14.4 years. The demographic data of the patients in the study are given in Table 1. In terms of blood parameters, preoperative hemoglobin levels were 11.2 ± 1.98 mg/dL, postoperative hemoglobin values were 12.7 ± 2.2 mg/dL, and this difference was statistically significant (P = 0.001). High-density lipoprotein (HDL) values, one of the lipid parameters, were significantly increased postoperatively (37.6 ± 10.5, 46.6 ± 13.6 mg/dL, respectively, P = 0.001). There was no significant change in low-density lipoprotein (LDL) and triglyceride levels.

For echo parameters, there was no significant difference between the values of 92 patients whose ejection fractions were screened preoperatively and postoperatively, whereas 21 patients with a preoperative ejection fraction below 50% had a significant increase after transplantation (40.1% ± 6.2%, 48.4% ± 9.4%, P = 0.012) (Table 2).

Patients' immunosuppressive treatment and other medical treatments are given in Table 3. All of the patients were given deltacortril. The most preferred immunosuppressive agents were mycophenolate mofetil (MMF) and tacrolimus.

Therefore, to investigate the effect of other drugs that affect HDL increase, we compared the drugs for two groups of patients whose

Table 1. Demographic and laboratory parameters of all patients.

Patient characteristics	Patients (*n*=183)
Male sex (%)	124 (67.8)
Age (years)	42.6±14.4
Hypertension (%)	116 (63.4)
Diabetes mellitus (%)	29 (15.8)
Hyperlipidemia (%)	24 (13.1)
Smoking history (%)	37 (20.2)
CAD family history (%)	13 (7.1)
CAD history (%)	16 (8.7)
Hemoglobin (mg/dL)	11.2±1.98
Preop LDL (mg/dL)	106.9±36.5
Preop HDL (mg/dl)	37.6±10.5
Preop triglyceride (mg/dL)	168.9±98.1
Postop Hb (mg/dL)	12.7±2.2
Postop LDL (mg/dL)	108.8±36.6
Postop HDL (mg/dL)	46.6±13.6
Postop TG (mg/dL)	169.2±90.9
Preop EF (%)	56.7±7.19
Postop EF (%)	56.1±7.71

CAD: Coronary artery disease, Preop: Preoperative, Postop: Postoperative, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, TG: Triglyceride, Hb: Hemoglobin, EF: Ejection fraction.

Table 2. Comparison of laboratory parameters and ejection fraction in pre- and postoperative patients.

	Preoperative values	Postoperative values	*P*
Hemoglobin (mg/dL)	11.2±1.98	12.7±2.2	0.001
HDL (mg/dL)	37.6±10.5	46.6±13.6	0.001
LDL (mg/dL)	106.9±36.5	108.8±36.6	0.428
Triglyceride (mg/dL)	168.8±98.1	169.1±90.6	0.919
EF (%) (*n*=92)	56.7±7.19	56.1±7.71	0.509
EF preoperative %50< (%) (*n*=21)	40.1 ± 6.2	48.4±9.4	0.012

LDL: Low-density lipoprotein, HDL: High-density lipoprotein, EF: Ejection fraction, Preop: Preoperative.

Table 3. Drug usage of all patients.

	Patients (*n*=183)
ASA (%)	107 (57.8)
ACEI/ARB (%)	40 (21.6)
Beta-blockers (%)	58 (31.4)
Calcium channel blockers (%)	71 (38.4)
Statins (%)	10 (5.4)
Fibrates (%)	8 (4.3)
Tacrolimus (%)	132 (72.1)
Mycophenolate mofetil (%)	173 (94.5)
Cyclosporine (%)	41 (22.2)
Azathioprine (%)	7 (3.8)

ASA: Acetylsalicylic acid, ACEI/ARB: Angiotensin-converting enzyme inhibitor/angiotensinogen receptor blocker.

Table 4. Comparison of drug usage between high-density lipoprotein increased and decreased patients.

	HDL increased (*n*=136)	**HDL decreased (*n*=47)**	***P***
ASA	77	30	0.492
ACEI/ARB	27	13	0.307
Beta-blockers	41	17	0.470
Calcium channel blockers	52	19	0.863
Statins	8	2	0.959
Fibrates	5	3	0.425
Tacrolimus	98	34	0.970
Mycophenolate mofetil	130	43	0.283
Cyclosporine	32	9	0.683
Azathioprine	4	3	0.375

ASA: Acetylsalicylic acid, ACEI/ARB: Angiotensin-converting enzyme inhibitor/angiotensinogen receptor blocker.

HDL levels raised and decreased after transplantation, as shown in Table 4. There was no difference between the groups in terms of the drugs.

According to the other echocardiographic parameters such as left ventricular hypertrophy, valve insufficiencies, and diastolic dysfunction, there were no significant differences between the two groups (Table 5).

Discussion

Renal transplantation decreases mortality in end-stage renal disease patients. Previously, there are several studies investigating the effects of renal transplantation on cardiac functions. In a study performed with SPECT imaging,[9] renal transplant patients were compared with nontransplant patients, and a significant change was observed in the ejection fractions of transplanted patients (72 ± 10% vs. 67% ± 10%, P =0.001). Although the improvement in ejection fraction was thought to be due to volume management, no significant changes were found in the left ventricular end-diastolic volumes between the two groups. This was thought to be due to the effective removal of toxins and the prevention of uremic cardiomyopathy rather than the effect of transplantation on volume. In the same study, electrocardiographic parameters were also screened, but no significant difference was found. In our study, there were no significant differences in ejection fractions when 92 patients were considered. However, in patients with ejection fraction of 50% and less, ejection fraction was significantly improved after transplantation (40.1 ± 6.2 vs. 48.4 ± 9.4, P = 0.012). One reason of this situation may be due to the high mean ejection fraction in pretransplant echocardiographies. In our study, the number of patients who compared their echoes was 92 and higher like the previous study. On the other hand, it can be predicted

Table 5. Comparison of pre- and postoperative echocardiography parameters.

	Preoperative echo parameters	**Postoperative echo parameters**	***P***
Left ventricular hypertrophy	74	65	0.05
Left ventricle diastolic dysfunction			
Stage 1	46	31	0.135
Stage 2	8	7	0.272
Stage 3	1	2	0.898
Mitral regurgitation mild	43	38	0.535
Mitral regurgitation moderate	4	7	0.612
Tricuspid regurgitation mild	35	33	0.879
Tricuspid regurgitation moderate	8	6	0.424

that patients with low ejection fraction may benefit more than patients with normal ejection fraction.

In another study,[10] patients with ejection fraction below 50% before renal transplantation were examined, and it was found that EF was significantly improved in patients with both mild and moderate HFs after transplantation. In 66 patients with mild left ventricular systolic dysfunction, EF before transplantation was 41% ± 10% and 50% ± 12% after transplantation (P <0.0001). In patients with moderate dysfunction (n = 28), EF was 32% ± 7% before transplantation and 47% ± 14% after transplantation (P <0.001). This suggests that the ejection fraction is not the most important value for determining the preoperative cardiac risk. In the same study, they found that the best survival was determined in patients with normal ejection fraction. Survival of patients with more than 10% improvement in ejection fraction after transplantation was significantly better than patients with <10% improvement in ejection fraction. In our study, mortality was observed in only six patients during follow-up, so no data were compared for survival.

Omrani et al[11] studied 181 patients with ejection fraction below 50% and performed echocardiography at six and 12 months. Echocardiography showed a significant improvement in ejection fractions compared to basal echoes both six and 12 months. In the same study, they found that left ventricular hypertrophy also regressed and mitral and tricuspid valve insufficiencies decreased after transplantation. In another study examining left ventricular hypertrophy (LVH)[12] post transplantation, 63% of renal transplant recipients showed normal echocardiographic finding of LV, while 37% of patients remained with LVH after first post-transplant year. These findings were similar to our study. In our study, left ventricular hypertrophy regressed after transplantation (P = 0.05). Unlike, there was no significant difference in valve insufficiencies before and after transplantation (Table 5). This may be due to the small number of patients with severe valve insufficiency in our study cohort. There was no significant difference between the two groups in terms of diastolic functions although they were reduced numerically.

Dyslipidemia is often seen with renal disease and is associated with increased cardiovascular mortality and morbidity.[13] Immunosuppressants and steroids used after transplantation have important effects on lipid metabolism. In a comprehensive study in which these effects were investigated by drug classes,[14] the highest change in total cholesterol and triglyceride was shown to be associated with cyclosporine/sirolimus or cyclosporine/everolimus use. Moreover, it was shown that average HDL cholesterol decreased by 14% in men and 22% in women. However, in subgroup analyses, in patients who were receiving tacrolimus and mycophenolate mofetil, HDL cholesterol increased in men from 41 ± 10 mg/dL to 47 ± 12 mg/dL, in women HDL cholesterol increased from 47 ± 12 mg/dL to 56 ± 11 mg/dL. In our patient population, MMF (94.5%) and tacrolimus (72.1%) were the most commonly used drugs, and it may be the reason of increased HDL cholesterol. While LDL and triglyceride increased slightly, HDL cholesterol increased significantly after trans-plantation (37.6 ± 10.5 vs. 46.6 ± 13.6, P = 0.001). This emphasizes the importance of drug selection after transplantation. No significant difference was seen with the use of other drugs on HDL levels. In another study, serum total cholesterol and triglyceride levels tended to increase during CyA and steroid therapy among patients undergoing renal transplantation Independent of hyperlipidemia risk factors.[15] Following the transplantation, the lipid profiles of the patients should be followed up during the controls and medical treatment should be kept in mind if LDL cholesterol is persistently higher which is a cardiovascular risk factor.

As a result, renal transplantation can improve left ventricle ejection fraction in patients with basal ejection fraction <50%. This suggests that the risk assessment of patients with low ejection fraction should be made carefully before transplantation because there will be improvement after transplantation in cardiac

functions. At the same time, lipid side effects of some immunosuppressive agents were observed less than others, so it could be a guide for treatment selection.

Conflict of interest: None declared.

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