Effects of Renal Transplantation on Cardiac Function and Morphology in the Late Posttransplant Period

Böbrek Naklinin Geç Dönemde Kalp İşlevleri ve Yapısına Etkisi

İsmail KOÇYİĞİT[1]
Aydın ÜNAL[1]
Ahmet ÇELİK[2]
Baki EKER[3]
İdris ARDIÇ[2]
Bülent TOKGÖZ[1]
Oktay OYMAK[1]
Cengiz UTAŞ[1]

1 Erciyes University Faculty of Medicine, Department of Nephrology, Kayseri, Turkey
2 Erciyes University Faculty of Medicine, Department of Cardiology, Kayseri, Turkey
3 Erciyes University Faculty of Medicine, Department of Internal Medicine, Kayseri, Turkey

ABSTRACT

OBJECTIVE: To investigate the effects of renal transplantation on left ventricular (LV) function and morphology in patients with end-stage renal disease (ESRD) in the late posttransplant period.

MATERIAL and METHODS: The prospective study included 40 patients (mean age 33.2 ± 7.7 years;25 female /15 male) with ESRD. In all of these patients, renal transplantation was performed successfully; and the serum creatinine levels were less than 2 mg/dL. The echocardiographic evaluations were performed before renal transplantation and 12. month after renal transplantation. Left ventricular diastolic diameter (LVDD), left ventricular systolic diameter (LVESD), left ventricular mass (LV Mass), left ventricular mass index (LVMI), LV ejection fraction (LVEF), Doppler and tissue Doppler parameters were obtained in all patients.

RESULTS: At the twelfth month, LVDD (48 ± 5 vs 45 ± 6, p: 0.01), LVSD (33 ± 4 vs 29 ± 4, p< 0.001) LVMI (114 ± 31 vs 98 ± 13, p: 0.007) decreased significantly compared to the pretransplant period. There was a significant increase in the LVEF in at the twelfth month (59 ± 5 vs 67 ± 6, p< 0.001). There was a significant improvement between pretransplant period and late posttransplant period with regard to diastolic cardiac function.

CONCLUSION: Renal transplantation had beneficial effects on diastolic and systolic functions and cardiac morphology in the late posttransplant period.

KEY WORDS: Cardiac morphology, Diastolic function, Renal transplantation, Systolic function

ÖZ

AMAÇ: Son dönem böbrek yetmezliği ile izlenen hastalarda nakil sonrası geç dönemde naklin sol ventrikül işlev ve yapısı üzerine etkisini araştırmayı planladık.

GEREÇ ve YÖNTEMLER: 25 kadın /15 erkek olmak üzere 40 son dönem böbrek yetmezliği hastası ile yapılan bu ileri dönük çalışmada tüm hastalara başarılı bir şekilde böbrek nakli yapılmıştır (Tüm hastaların kreatin değerleri (<2mg/dl). Tüm hastalara nakil öncesi ve sonrası 12.ayda ekokardiyografik değerlendirme yapıldı. Bu ekokardiyografik incelemelerde tüm hastalarda sol ventriküler diastolik çap, sol ventriküler sistolik çap, sol ventrikül kitlesi, sol ventrikül kitle indeksi, sol ventriküler ejeksiyon fraksiyonu ayrıca doppler inceleme ve doku dopleri yapıldı.

BULGULAR: On ikinci ayda, sol ventriküler diastolik çap (48 ± 5 vs 45 ± 6, p: 0.01), sol ventriküler sistolik çap (33 ± 4 vs 29 ± 4, p< 0.001) sol ventriküler kitle indeksi (114 ± 31 vs 98 ± 13, p: 0.007) nakil öncesi döneme göre anlamlı şekilde azalmıştır. Sol ventrikül ejeksiyon fraksiyonu on ikinci ayda anlamlı olarak artmıştır (59 ± 5 vs 67 ± 6, p< 0.001). Nakil öncesi döneme göre geç nakil sonrası dönemde diyastolik kardiyak işlevlerde anlamlı bir düzelme görülmektedir.

SONUÇ: Böbrek naklinin geç dönemde kardiyak yapı ve kalbin sistolik ve diyastolik işlevleri üzerine yararlı etkilerinin olduğu gösterilmiştir.

ANAHTAR SÖZCÜKLER: Kardiak morfoloji, Diyastolik işlev, Böbrek nakli, Sistolik işlev

Received : 06.01.2011
Accepted : 18.07.2011

Correspondence Address:
İsmail KOÇYİĞİT
Erciyes Üniversitesi Tıp Fakültesi,
Nefroloji Bilim Dalı, Kayseri, Turkey
Phone : +90 352 437 49 37
E-mail : iikocyigit@gmail.com

INTRODUCTION

Left ventricular hypertrophy (LVH) is a very common pathological condition in patients with end-stage renal disease (ESRD) and is an independent risk factor for death and cardiovascular disease (1,2).Several risk factors including uremic toxins, fluid retention and chronic volume overload, renal anemia, hypoalbuminemia, hyperparathyroidism, arteriovenous fistula, and pressure overload have been accused in the pathogenesis of LVH in patients with ESRD (3, 4). Although there are beneficial cardiovascular effects of kidney transplantation, the prevalence of LVH remains high in renal transplant patients, and it may contribute to the high cardiac mortality rate observed in this population (5). Successful renal transplantation improves some risk factors for LVH in chronic uremia, but others including patent arteriovenous fistula, anemia, and hypertension may persist or worsen after transplantation. Furthermore, immunosuppressive drugs such as calcineurin inhibitors, especially cyclosporine, and steroids which have hypertensive adverse effect, play a important role in the development or persistence of LVH after renal transplantation (6). While some prospective studies have demonstrated improvement of LVH after renal transplantation (7, 8), others have not (9, 10). Little is known about the link between causes and consequence of LVH in renal transplant recipients.

The aim of this study was to investigate the effects of renal transplantation on LV function and morphology in patients with ESRD at early and late posttransplant period.

MATERIAL and METHODS

The prospective study was performed in Erciyes University Medical Faculty Hospital between January 2007 and January 2010. The study population consisted of 40 patients with ESRD. The local ethics committee approved the study, and informed consent was obtained for each patient. Twenty one of the 40 patients had undergone hemodialysis and sixteen of the 40 patients had undergone peritoneal dialysis before renal transplantation. Pretransplant dialysis duration was 19 (4-95) months. Preemptive kidney transplantation was performed in only 3 patients. None of the patients had diabetes mellitus. As the immunosuppressive protocol, 27 of patients received prednisolone + tacrolimus + mycophenolic acid and the rest of them receive prednisolone + tacrolimus + mycophenolate mofetil.

Before kidney transplantation, the patients were evaluated by transthoracic echocardiography. In the hemodialysis patients, who were dialyzed three times a week for four hours, the first evaluations were performed within 6 hours after the hemodialysis session to avoid from volume loading. Living donors were the major source of the allograft. Only one patient received an allograft from a cadaveric donor. In all of these patients, renal transplantation was performed successfully; and the serum creatinine levels were less than 2 mg/dL. None of the patients developed acute allograft rejection. The second and third echocardiographic evaluation as performed at 12.month after transplantation.

Patients who had sinus rhythm, LV ejection fraction (EF) above 50%, no history of myocardial infarction, and no evidence of valvular disease were included in this study. Patients with cerebral vascular disease, clinical and electrocardiographic evidence of myocardial ischemia, history of coronary artery disease, pericardial disease, heart failure, valvular heart disease and chronic pulmonary disease were excluded from the study.

Clinical and biochemical data were obtained from each patient on the day of echocardiographic evaluations before and after transplantation.

Echocardiographic Evaluations

The echocardiographies were performed by two cardiology specialists with Vivid 7 instruments (GE Medical Systems, Milwaukee, WI, USA), with a 2.5-MHz transducer and harmonic imaging in the Cardiology Department's Echocardiography Laboratory. All echocardiography results were obtained before and 12 months after renal transplantation. According to the recommendations of the American Society of Echocardiography (11), all echocardiographic examinations were performed with the patient lying in the left lateral decubitus position, and two-dimensional images were recorded and measured at the apical 4 chambers, 2 chambers, and parasternal long axis views. Left ventricular systolic diameters (LVSD), diastolic diameters (LVDD) and LV wall thickness were measured by M-mode echocardiography. Left ventricular ejection fraction (LVEF) was assessed using the modified biplane Simpson's method. Left ventricular mass (LV mass) was calculated by the Penn convention (12).

To evaluate the LV diastolic properties, the mitral inflow velocities were evaluated from the apical four-chamber view with the sample volume placed at the tips of the mitral valve. Pulmonary vein flow velocities were obtained from the right posterior pulmonary vein in the apical view.

LV diastolic filling was analyzed from recordings of mitral inflow Doppler velocities. Diastolic filling was classified on the basis of the peak early diastolic mitral velocity (E), peak late diastolic mitral inflow velocity (A), E/A ratio, E wave deceleration time (DT) and isovolemic relaxation time (IVRT). Also pulmonary vein flow velocities including peak systolic velocity (PVS), peak diastolic velocity (PVd), peak atrial reversal velocity (PVAr), and PVAr duration were recorded. The early diastolic velocities of the mitral annulus (Ea), which have been shown to reflect the rate of myocardial relaxation, were recorded with tissue Doppler imaging (13, 14). The left atrial diameter (LAD), which reflects the LV diastolic filling, was measured in the parasternal long-axis view.

LVH was defined as left ventricular mass index (LVMI), which was calculated with LV Mass in grams divided by body surface area in square meters, higher than 116.0 for men and 104.0 for women (15). Body surface area was calculated by using Mosteller's formula (16).

Statistical Analysis

The SPSS 15.0 statistical software was used for the statistical analysis. The Kolmogorov-Smirnov test was used to determine normality of distributions of variables. Continuous variables with normal distribution were presented as mean ± standard deviation. Median value was used in variables without normal distribution. The categorized variables were given as percentages. To compare variables before renal transplantation and after renal transplantation, the paired t test (for the parametric variables), Wilcoxon test (for the nonparametric variables), and McNemar test (for categorized variables) were used. A p value <0.05 was considered to be significant.

RESULTS

Fifteen of the 40 patients were female and the rest were male in the study. The mean age of the patients was 31 ± 6 years. Among the 40 patients the cause of ESRD was diabetes mellitus in 13, glomerulonephritis in 4, hypertension in 18, and unknown in 5. The patients who had undergone hemodialysis with A-V fistula all had a patent fistula twelve months after transplantation.

Comparison of biochemical and clinical findings between the pretransplant period and posttransplant period is shown in Table I. Levels of serum total cholesterol and high-density lipoprotein, were significantly increased at 12 months after transplantation compared to the pretransplant period. The levels of hemoglobin, albumin and low-density lipoprotein were significantly increased at 12 month after transplantation. However, levels of blood urea nitrogen, serum creatinine, phosphorus, intact parathyroid hormone (iPTH), and calcium x phosphorus product (CaxP) were significantly decreased at the late posttransplant period compared to the pretransplant period. Additionally, levels of corrected calcium had an significant increase at late posttransplant period compared to the pretransplant period.

Table II shows comparison of echocardiographic findings between the pretransplant period and late posttransplant period. LVDD, LVSD, IVSD, LVEF and sPAP showed a significant decrease at the twelfth month after transplantation. Figure 1

Table I: Comparison of laboratory and clinical findings of the patients before and after renal transplantation.

Parameters	Before RTx 0 month	After RTx 12 months	*P* value 0 vs. 12 Months
Hemoglobin (g/dL)	10.9 ± 1.5	13.0 ± 2.0	<0.001
Total cholesterol (mg/dL)	162 ± 39	189 ± 44	0.001
High density lipoprotein (mg/dL)	33 ± 9	43 ± 14	<0.001
Low density lipoprotein, (mg/dL)	96 ± 33	114 ± 29	0.002
Triglyceride (mg/dL)	141 (57-478)	146 (69-403)	0.5
Blood urea nitrogen (mg/dL)	60 ± 20	16 ± 4	<0.001
Creatinine (mg/dL)	10.9 ± 3.3	1.2 ± 0.3	<0.001
Uric acid (mg/dL)	5.7 ± 1.6	5.9 ± 1.3	0.6
Albumin (g/dL)	3.6 ± 0.5	4.2 ± 0.4	<0.001
Corrected calcium (mg/dL)	8.8 ± 1.0	9.6 ± 0.6	<0.001
Phosphorus (mg/dL)	5.1 ± 1.4	2.6 ± 0.8	<0.001
Calcium × phosphorus (mg^2/dL^2)	46 ± 13	24 ± 7	<0.001
Glucose (mg/dL)	93 ± 21	95 ± 10.4	0.5
Alkaline phosphatase (IU/L)	108 ± 65	89 ± 41	0.1
Parathyroid hormone (pg/mL)	284 (29-2216)	84 (22-215)	<0.001
High sensitive C-reactive protein (mg/dL)	17.1	3.7	0.007
Diastolic blood pressure (mmHg)	82 ± 13	77 ± 9	0.09
Systolic blood pressure (mmHg)	129 ± 15	127 ± 8	0.4

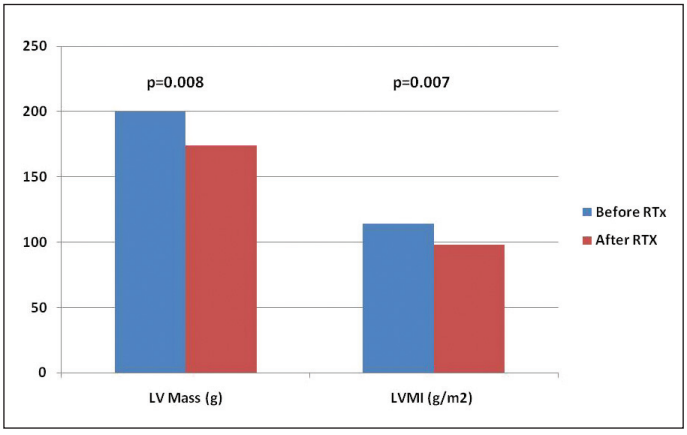

Figure 1: *The comparision of LV mass and LVMI values before and 12 month after renal transplantation (LV= left ventricle, LVMI= levt ventricular mass index, RTx= renal transplantation).*

Table II: Comparison of echocardiographic findings of the patients before and after renal transplantation.

Variables	Before RTx 0 month	After RTx 12 months	P value 0 vs. 12 months
LVDD (mm)	48± 5	45 ± 6	0.01
LVSD (mm)	33 ± 4	29 ± 4	<0.001
IVSD (mm)	12.5±2.2	11.5±1.3	0.001
PWD (mm)	11.1±1.8	10.8±1.2	0.2
Systolic PAP (mmHg)	31 ± 7	26 ± 4	0.001
LVEF (%)	59 ± 5	67 ± 6	<0.001
LVH	25 (62.5%)	10 (25%)	<0.001

Data expressed as mean± SD, or percentage. P<0.05 was accepted as a statistically significant **RTx:** renal transplantation, **LVDD:** left ventricular diastolic diameter, **LVSD:** left ventricular systolic diameter, PAP: pulmonary arterial pressure, **LVEF:** left ventricular ejection fraction

shows the change of LV Mass and LVMI at 12. month after transplantation compared with the values before transplantation. The number of patients with LVH were significantly decreased at the late posttransplant period compared to the pretransplant period (Table II).

The decerelation time of mitral inflow E velocity and IVRT were significantly increased at the twelfth month after transplantation (Table III). Table III also shows the

Table III: The tissue Doppler echocardiography parameters in patients with ESRD before and after renal transplantation.

Variables	Before RTx 0 month	After RTx 12 months	P value 0 vs. 12 Months
E/A	0.80± 0.17	0.97± 0.22	0.003
E/Ea	9,6± 3.4	6.5± 1.4	<0.001
E dec t	134± 42	174± 43	0.002
IVRT	87± 19	97± 23	0.007
PVS/PVd	0.85± 0.21	1.2 ± 0.4	0.001

Data expressed as mean± SD, P<0.05 was accepted as a statistically significant **RTx:** Renal transplantation, **E:** peak early diastolic mitral inflow velocity, **A:** peak late diastolic mitral inflow velocity, **Ea:** early diastolic myocardial velocity, **DT:** E wave deceleration time, **IVRT:** isovolemic relaxation time, PVS: pulmonary vein peak systolic velocity, **PVd:** pulmonary vein peak diastolic velocity.

improvement of cardiac diastolic functions with E/A ratio, E/Ea ratio, Pulmonary vein S/D ratio at the late period after renal transplantation.

On the other hand, there was no significant difference between the pretransplant period and posttransplant period with regard to other parameters including PWD and LAD.

DISCUSSION

In the present study, there were three main findings. Firstly, LV Mass, LVMI, and prevalence of LVH decreased after kidney transplantation and there was statistical significance in these parameters. Secondly, there was significant improvement in diastolic function parameters between the pretransplant period and posttransplant period. Finally, there were significant improvements in cardiac morphologic parameters including LVDD, LVSD, IVSD and in LVEF.

Cardiovascular complications are the major cause of morbidity and mortality in ESRD patients. LVMI is one of the most important prognostic factors for cardiovascular events (17). Prevalence of LVH in patients with ESRD is very high even after successful renal transplantation. Ferraira et al. found that presence of LVH was 75% and 59% before renal transplantation and after 3 months of follow-up in 24 patients aged mean 33 ± 10 years (8). In another study, the presence of LVH decreased from 70% to 40% at mean 3.2 months of posttransplant period (18). Similarly, in the study we observed a high prevalence of LVH and a significant decrease in this prevalence at twelfth month after transplantation.

In many studies it was found that LVMI was significantly decreased after kidney transplantation (18, 19), whereas some studies did not observe this improvement (9, 10). In the development of LVH in patients with ESRD, there are several risk factors including uremic toxins, older age, anemia, hypoalbuminemia, hyperparathyroidism, arteriovenous fistula, hypertension, diabetes, and volume overload (3, 4, 20). Arce Salinas et al. also showed the increase of LV mass and LVMI after renal transplantation with 13 ESRD patients (21). Similarly, we showed the decrease of LV mass and LVMI in the 40 patients with ESRD, but we also showed an improvement in diastolic functions after late renal transplantation.

In the present study, we observed that hyperparathyroidism parameters including iPTH and CaxP were meaningfully decreased after renal transplantation. On the other hand, there was no significant difference between the two periods in terms of the level of hemoglobin and albumin and diastolic and systolic blood pressure values. Our patients were relatively younger and none of them were diabetic. It has been observed that the use of cyclosporine associates with hypertension and LVH both in renal transplant recipients and in patients with bone marrow transplantation compared to use of tacrolimus (22, 23). However, all of our patients were treated with tacrolimus.

Another important finding in the present study was a significant increase in LV systolic functions after kidney transplantation. This might be the result of an improvement in the overvolemic state during the dialysis period after transplantation. Similar findings were observed by Bialostozky and colleagues. They found that the percentage of patients with low LVEF decreased from 53% to 20% and mean LVEF increased from 48% to 58% after renal transplantation in 30 patients with ESRD (24).

Similar to LVEF, the diastolic function parameters including mitral inflow Doppler velocities, pulmonary vein flow velocities, and tissue Doppler imaging findings indicated an improvement in diastolic function. LV diameters including LVDD and LVSD were also significantly lower in the posttransplant period compared to the pretransplant period. These findings possibly resulted from an improvement in volume overload after transplantation. Iqbal et al similarly found a significant decrease in LAD, LVDD, and LV end diastolic volume index after kidney transplantation(19).

Sahagún-Sánchez G. et al. showed that renal transplantation diminishes hypertrophy and improves left ventricular systolic and diastolic function (25). The present study also showed that LV diastolic and systolic functions significantly improved after renal transplantation in patients with ESRD. Improvements in diastolic function parameters will be more significant with longer follow-up periods.

In conclusion, renal transplantation had beneficial effects not only on diastolic functions but also on systolic functions and cardiac morphology in the late posttransplant period.

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