Received: 01 Nov 2022 | **Accepted:** 28 Nov 2022
DOI: 10.54005/geneltip.1198059

ORIGINAL ARTICLE

The Evaluation of Cardiovascular System Before and After Renal Transplantation and Its Relationship Between Brain Natriuretic Peptide

Renal Transplantasyon Hastalarında Transplantasyon Öncesi ve Sonrası Kardiyovasküler Sistemin Değerlendirilmesi ve Beyin Natriüretik Peptit İle İlişkisi

[1]Banu Kadıoğlu Yılmaz, [2]Enver Hasanoğlu, [2]Sevcan Azime Bakkaloğlu Ezgü, [2]Ayşe Deniz Oğuz, [3]Hatice Paşaoğlu, [3]Ayşe Fıtnat Tuncel Bahar

[1]Health Sciences University Konya City Hospital, Department of Pediatrics, Konya,Turkey
[2]Gazi University, Department of Pediatrics , Ankara, Turkey
[3]Gazi University, Department of Medical Biochemistry, Ankara, Turkey

Correspondence

Banu Kadıoğlu Yılmaz, Health Sciences University Konya City Hospital, Department of Pediatrics, Konya,Turkey

E-Mail: banukadioglu@yahoo.com.tr

How to cite ?

Kadıoğlu Yılmaz B. , Hasanoğlu E. , Bakkaloğlu S. , Oğuz A. D. , Paşaoğlu H. , Tuncel Bahar A. F. The Evaluation of Cardiovascular System Before and After Renal Transplantation and Its Relationship Between Brain Natriuretic Peptide. Genel Tıp Dergisi. 2022; 32(6): 708-713.

ABSTRACT

Objective: Chronic renal failure(CRF) shortens life due to increased cardiovascular risk despite transplantation in children.We planned to compare the pre and post-transplant cardiovascular system functions biochemically and echocardiographically,and to investigate its relationship with brain-natriuretic-peptide(BNP) in this study.
Materials and Methods: CRF-patients who underwent renal transplantation before the age of 18 and the same number of age-sex-matched healthy controls were included in the study.Pre-post-transplantation body-mass-index(BMI), biochemical values, echocardiographic findings, carotid-intima-media-thickness(CIMT) measurements were compared.Tissue-Doppler-imaging and BNP values of the patients after transplantation were compared with control group.
Results: Total of 64 cases,including 32-patient and 32-control, were evaluated. The values of patients before and after transplantation(7-109 months after transplantation) were compared. After transplantation;BMI values increased significantly (p<0.001),CIMT values decreased significantly(from 0.737±0.087mm to 0.555±0.098mm p<0.001),left-ventricular-mass(LVM) and mass-index(LVMI) were significantly decreased(LVM;156.12±111.17g to 151.13±55.57gr and LVMI;62.33±36.07gr/m2.7 to 45.92±14.30 gr/m2,7, p<0.001),mitral E/A ratio decreased(1.68±0.65 to 1.45±0.29 p<0.001).It was found that LVMI, myocardial-performance-index(MPI), CIMT and BNP values were still significantly higher than healthy controls(p<0.05).It was found that BNP was significantly negatively correlated with BMI and not-correlated with MPI.
Conclusion: Although the cardiac risk factors of renal transplantation patients decrease after transplantation, they still have higher risk than healthy controls.Measurement of MPI and LVMI is important in predicting cardiovascular risk status after renal transplantation.

Keywords: Chronic renal failure, renal transplantation, brain natriuretic peptide, left ventricular mass index, myocardial performance index

ÖZ

Amaç: Çocuklarda kronik böbrek yetmezliği(KBY) transplantasyona rağmen artmış kardiyovasküler risk nedeniyle yaşamı kısaltan bir durumdur.Çalışmamızda renal transplantasyon hastalarında transplantasyon öncesi-sonrası kardiyovasküler sistem fonksiyonlarını biyokimyasal ve ekokardiyografik açıdan karşılaştırmayı ve beyin natriüretik peptid(BNP) ile ilişkisini araştırmayı planladık.
Gereç ve Yöntem: KBY tanısı alıp 18 yaşından önce renal transplantasyon yapılan hastalar ve yaş-cinsiyet olarak uyumlu aynı sayıda sağlıklı-kontroller çalışmaya dahil edildi.Bu hastaların transplantasyon öncesi-sonrası vücut kitle indeksleri(VKİ),biyokimyasal değerleri,ekokardiyografik bulguları, karotis-intima-media-kalınlık(CIMT) ölçümleri karşılaştırıldı.Hastalara transplantasyon sonrası bakılan doku-Doppler-görüntüleme(DDG) ile BNP değerleri kontrol grubu ile karşılaştırıldı.
Bulgular: 32-hasta ve 32-kontrol grubu olmak üzere toplamda 64 vaka değerlendirildi. Hastaların transplantasyon öncesi-sonrası(transplantasyondan 7-109 ay sonrası) değerleri karşılaştırıldı.VKİ değerlerinin nakil sonrasında öncesine göre anlamlı derecede arttığı(p<0,001), CIMT değerlerinin nakil sonrası anlamlı derecede gerilediği (0.737±0.087mm'den 0.555±0.098mm'ye p<0,001), sol-ventrikül-kitlesinin(LVM) ve kitle-indeksinin(LVMI) nakil sonrasında belirgin azaldığı(LVM;156,12±111,17gr'dan 151,13±55,57gr'a ve LVMI;62,33±36,07gr/m2,7'den 45,92±14,30 gr/m2,7'a, p<0.001) ve mitral E/A oranının nakil sonrasında gerilediği tespit edildi(1,68±0,65'den 1,45±0,29'a p<0,001).Nakil sonrası dönemdeki hastaların değerleri sağlıklı kontrollerle karşılaştırıldığında; LVMI, miyokardiyal-performans-indeksi(MPI), CIMT ve BNP değerlerinin sağlıklı kontrollerden hala anlamlı derecede yüksek olduğu (p<0,05)saptandı.BNP'nin VKİ ile anlamlı derecede negatif korele olduğu, MPI ile korelasyonu olmadığı bulundu.
Sonuç: Renal transplantasyon hastalarının transplantasyon sonrası kardiyak risk faktörleri azalsa da hala sağlıklı kontrollerden daha fazla riske sahiptirler.MPI ve LVMI ölçümü renal transplantasyon sonrası kardiyovasküler risk durumunu öngörmede önemlidir.

Anahtar Kelimeler: Kronik böbrek yetmezliği, renal transplantasyon, beyin natriüretik peptit, sol ventrikül kitle indeksi, miyokardiyal performans indeksi

Introduction

The prevalence of chronic renal failure in children is approximately 18/1,000,000 (1). The prognosis of chronic kidney diseases has improved in recent years because of effective supportive treatment, advancement of dialysis techniques, and renal transplantation (1). The life expectancy of children with chronic renal failure is relatively short; compared to the life expectancy of healthy children of similar age and race, this period was 40-60 years shorter in patients undergoing dialysis and 20-25 years in transplant patients (2). The most obvious reason for this is accelerated ischemic heart disease and increased cardiovascular mortality caused by the

development of dilated cardiomyopathy (2).

Significant left ventricular hypertrophy is seen in children with chronic renal failure, especially in patients who followed up with long-term dialysis therapy (3,4). While kidney functions improve with a successful kidney transplant, many atherosclerotic risk factors that develop during dialysis also decrease, but some risk factors persist in transplant patients (2).

This study aimed to compare the cardiovascular system findings of renal transplantation patients before and after transplantation and to compare them with the healthy control group, as well as to investigate the relationship between echocardiographic results and serum Brain Natriuretic Peptide (BNP) level.

Materials and Methods

Study design and setting

This study was conducted at the Gazi University Faculty of Medicine, Department of Pediatric Nephrology, Pediatric Cardiology, and Biochemistry. It is a prospective observational study. In our research, pre-transplant laboratory values, echocardiographic findings, CIMT measurement, if any, and laboratory tests performed after transplantation, echocardiographic findings, and CIMT measurements of patients diagnosed with chronic kidney failure and underwent renal transplantation, followed in Gazi University Faculty of Medicine, Department of Pediatric Nephrology were compared. The serum brain natriuretic peptide level, measured simultaneously with tissue Doppler imaging, was compared with the healthy control group.

Two-dimensional, M-mode, and Tissue Doppler echocardiography were performed on an ultrasound machine (Genereal Electric Medical Systems, USA, Vivid 7 Pro Echo machine, Presound alpha 7, IPF 1701 Model, 2009; Hitachi Aloka Medical, Ltd. Tokyo, Japan) with 3,5,7 MHz transducer by a pediatric cardiologist blinded to the study. Standard 2-dimensional measurements (LVEDD;left ventricular end diastolic diameter, LVESD;left ventricular end systolic diameter, IVSD;interventricular septum end diastolic diameter, IVSS; interventricular septum end systolic diameter, LVPWD;left ventricular posterior wall thickness end diastolic, Mitral E (E); peak velocity of early diastolic mitral inflow, Mitral A (A); late diastolic mitral inflow, EF; ejection fraction, SF;shortening fraction) were obtained as recommended by the American Society of Echocardiography and Silverman method (5,6).

Parameters calculated by formula are (7,8);

Relative wall thickness (RWT)= 2xPWD/LVEDD

LVM (gr)=0,8{1,04[([LVEDD+IVSd+PWd]3-LVEDD3)]}+0,6

LVMI (gr/m2,7)=LVM/boy(m2,7)

Left ventricular geometric patern was decribed as below;

Normal (LVMI ≤95p, RWT ≤0,375)

Concentric remodelling (LVMI ≤ 95p, RWT>0,375)

Exantric hypertrophy (LVMI >95p, RWT≤0,375)

Concentric hypertrophy (LVMI >95p, RWT>0,375)

The percentile values of LVM and LVMI were obtained from Khoury's study (9). Mitral annular velocities were measured from septal and lateral mitral annulus and tricuspid annular velocities were measured from right ventricular free wall by tissue Doppler imaging using pulse-wave tissue doppler.

The parameters measured by tissue Doppler echocardiography were; Sm:peak myocardial velocity during systol measured from mitral annulus, St: peak myocardial velocity during systol measured from tricuspid annulus, E':peak myocardial velocity during early diastole, A':peak myocardial velocity during atrial contaction, LVET:left ventricle ejection time, Mc-oT:the time between the closing and openning of mitral valve, RVET:right ventricle ejection time, Tc-oT: the time between the closing and openning of tricuspid valve, LVMPI: left ventricle myocardial performance index, RVMPI:right ventricle myocardial performance index, E'/A' ratio, E/E' ratio. The measurements were done during consecutive 3 cardiac cycle and the mean values calculated.

CIMT measurement were done by radiologist by using ultrasonography machine (EUB 7500, Hitachi) with 13,6 MHz transducer. Measurements were made on patients in supine position from 10 mm proximal of bifurcatio of carotis communis from left and right. Three measurements were made and the mean value calculated.

Serum BUN, creatinine, electrolytes, uric acid, albumin, ferritin, parathormone, lipid profile, complete blood count, C-reactive protein and BNP levels were measured at Gazi University, Department of Biochemistry. Serum BNP levels were measured with specific enzyme-linked immunoassay (ELISA) kits (BIOMEDICA BNP Fragment).

Patient Selection and Ethics

Thirty-two kidney transplant recipients and 32 age and sex-matched healthy subjects were included in the study. The study was approved by Ankara No. 1 Clinical Research Ethics Committee, decision no. 2010/01-160 11.01.2010. All authors participating in the study signed the informed consent form. Patients who were followed up in Gazi University, Department of Pediatric Nephrology between the ages of 5 and 18 and underwent renal transplantation, did not have primary cardiac disease before transplantation, and had at least six months or more past the date of transplantation were included in the study. The healthy

control group was selected from volunteers of similar age, height, weight, and gender, without underlying chronic disease, active infection, and pathological physical examination findings.

Statistical analysis

The data obtained were evaluated in the SPSS (Statistical Package for the Social Sciences Program, for Windows 11.5, Chicago, Illinois, USA) program. The results of all quantitative parameters of the cases were given as +/- standard deviation. The distributions of variables and groups were tested with the Kolmogorov-Smirnov test. ANOVA test was used to compare quantitative data between groups. Pearson test and Spearman correlation test were used to examine the relationships between parameters. The significance level of the results obtained was interpreted with the «p» value in the 95% confidence interval, and P values of <0.05 were considered statistically significant.

Results

Data from 64 subjects, 32 in the patient and 32 in the healthy control groups, were evaluated. The mean age of the patient group was 16.84 ± 3.35 years, and the healthy control group was 16.87 ± 3.38 years. Gender distribution is equal in both groups. Anthropometric measurements of the patient and control groups are given in Table 1.

The mean age at diagnosis was 9.09 ± 3.6 years, and the mean age at transplantation was 13 ± 2.4 years. The mean time after transplantation was 47.90 ± 30.98 months, and the values ranged from 7 months to 109 months. All the patients had only one kidney transplant, 71.87% was from living donors, and 28.13% was from deceased donors. The findings regarding the clinical characteristics of the patients are given in Table 2.

The evaluation of patients' diagnoses with unknown etiology constituted 37.5%, urological causes made up the first rank with 34.37% among those with known etiology, primary glomerulonephritis ranked second at 12.5%, cystic renal diseases ranked third at 6.24%. The classification of the patients according to their etiology is presented in Table 3.

In the comparison of anthropometric measurements of the patients before and after transplantation, there was a statistically significant difference between the mean body mass index before transplantation (17.46 ± 2.21 kg/m2) and post-transplantation (19.86 ± 3.42 kg/m2) (p<0.001).

Table 1. Age, gender, and anthropometric measurements of the patient and healthy control groups

	Patient Group	Control Group	p
Age (years)	16.84 ± 3.35	16.87 ± 3.38	0.971
Height (m)	1.55 ± 0.14	1.56 ± 0.13	0.722
Body Weight (kg)	48.8 ± 14.4	50.5 ± 12.6	0.624
BMI (kg/m^2)	19.86 ± 3.42	20.31 ± 2.72	0.562
Male (%)	20 (62.5)	20 (62.5)	

*BMI: Body mass index

Table 2. Clinical characteristics of the patients

	Patient Group
Age at transplant (years) (mean)	13 ± 2.4
Age at Diagnosis (years) (mean)	9.09 ± 3.68
Time after transplant (months) (mean)	47.90 ± 30.98
Number of transplants	1
Donor feature	
Living donor n(%)	23 (71.87)
Deceased donor n(%)	9 (28.13)
Dialysis type	
Peritoneal dialysis n(%)	15 (46.87)
Hemodialysis n(%)	11 (34.37)
Peritoneal dialysis + Hemodialysis n(%)	3 (9.38)
No dialysis n(%)	3 (9.38)
CKD duration (months) (mean)	54 ± 36.34
Dialysis time (months) (mean)	34.04 ± 25.37

*n: number, %: percent

Table 3. Classification of renal transplantation patients according to their etiology

Diseases	Number of patients	%	Male/ Female
1.Urological Causes			
Vesicoureteral reflux	10	31.25	7/3
Nephrolithiasis	1	3.12	1/0
2.Cystic Renal Diseases			
Multicystic dysplastic kidney	1	3.12	1/0
Nephronophthisis	1	3.12	1/0
3. Renal Agenesis	1	3.12	1/0
4.Primary Glomerulonephritis			
FSGS	2	6.25	0/2
Other (MPGN. Membranous)	2	6.25	2/0
5.Amyloidosis (secondary to FMF)	1	3.12	1/0
6.Vasculitis (microscopic PAN)	1	3.12	0/1
7.Etiology unknown	12	37.5	6/6
Total	32	100	20/12

*FSGS: Focal segmental glomerulosclerosis, MPGN: Membranoproliferative glomerulonephritis, FMF: Familial Mediterranean fever, PAN: Polyarteritis nodosa

CIMT measurement was performed in all patients after transplantation, but only 13 patients' data

of CIMT measurements could be reached before transplantation. When the CIMT measurements of these 13 patients were compared before and after transplantation, it was observed that the mean of their measurements before transplantation decreased from 0.737±0.087 mm to 0.555±0.098 mm after transplantation (p<0.001). Pre-transplantation Hb, Htc, albumin, calcium, and HDL cholesterol values of the patients increased significantly after transplantation (p<0.001), and also significant declines were found in cholesterol, LDL, triglyceride, BUN, creatinine, uric acid, phosphorus, calcium x phosphorus multiplication values (p<0.001).

In the examination of the echocardiographic parameters of the patients before and after transplantation, it was determined that the left ventricular mass (LVM) and mass index (LVMI) decreased significantly in the post-transplant period (from 156,12 ± 111,17 to 151,13 ± 55,57 for LVM and from 62,33 ± 36,07 to 45,92 ± 14,30 for LVMI, both p<0.001). The Mitral E/A ratio reflecting diastolic dysfunction regressed after transplantation (1.68±0.65 vs. 1.45±0.29 p<0.001). While there were 25 patients (78.12%) with left ventricular hypertrophy in the pre-transplant group, this number decreased to 21 (65.62%) patients in the post-transplant period, but the difference was not statistically significant (p=0.667). The echocardiographic data of the patients are summarized in Table 4.

The comparison of echocardiographic, CIMT measurement, and BNP values of the patients after renal transplantation with the healthy control group are summarized in Table 5. Although some parameters measured in echocardiography and CIMT measurement values of the patients after transplantation seem to decrease compared to pre-transplantation, they were still higher than the control group compared to healthy controls. The relevant parameters are shown in Table 5.

The MPI value measured after renal transplantation was correlated with the LVMI value measured after transplantation (p<0.001 and r=0.472). Post-transplant E/A value (p=0.022 , r=-0.286) and post-transplant E'/A' value (p=0.007 , r=-0.332) were negatively correlated with MPI. In addition, post-transplant E/A and post-transplant GFR values were negatively correlated (p=0.026 , r=-0.392). A negative correlation was found between the E/A ratio and E'/A' ratio, and LVMI was evaluated after transplantation (p=0.005 , r=-0.351 and p=0.005 , r=0.350, respectively). A negative correlation was found between the dialysis time of the patients and the post-transplant E/A ratio (p=0.034 , r=-0.375). The findings are summarized in Table 6.

Considering the BNP levels studied in the post-transplant group and healthy controls, the transplant patients' BNP levels were significantly higher than those of the healthy controls (20.62 ± 14.77 vs. 13.28 ± 3.93 fmol/ml). In our study, BNP and LVMI values calculated before and after transplantation were correlated (p=0.026, r=0.392 and p=0.042, r=0.255).

In our study, no correlation was found between MPI and BNP. While there was a significant decrease in the LVMI values of the patients after transplantation, when the difference between LVMI before and after transplantation was evaluated, a correlation was found between this value and BNP and post-transplant proteinuria (shown in Table 7). While there was a correlation between transplantation age and BNP (p=0.045, r=0.357), no correlation was found between dialysis time, CRF duration, and BNP. A negative correlation was found between BMI and BNP after transplantation (p=0.018, r=-0.294). There was a strong correlation between post-transplant proteinuria and BNP (p<0.001, r=0.733).

Table 4. Echocardiographic parameters of renal transplantation patients before and after transplantation

Parameters	Pre-Transplantation	Post-Transplantation	P value
LVEDd (cm)	4.14 ± 0.86	4.38 ± 0.59	**<0.001**
LVEDs (cm)	2.72 ± 0.83	2.53 ± 0.42	**<0.001**
SF (%)	37.15 ± 7.37	38.21 ± 5.65	**<0.001**
EF (%)	66.31 ± 8.46	69.15 ± 5.80	**<0.001**
IVSDd (cm)	1.03 ± 0.23	1.05 ± 0.19	**<0.001**
IVSDs (cm)	1.38 ± 0.35	1.44 ± 0.28	**<0.001**
LVPWd (cm)	1.03 ± 0.45	0.75 ± 0.22	**<0.001**
LVPWs (cm)	1.43 ± 0.36	1.21 ± 0.24	**<0.001**
Mitral E	1.24 ± 0.28	0.94 ± 0.25	**<0.001**
Mitral A	0.78 ± 0.21	0.66 ± 0.18	**<0.001**
Mitral E/A	1.68 ± 0.65	1.46 ± 0.29	**<0.001**
LVM (gr)	156.12 ± 111.17	151.13 ± 55.57	**<0.001**
LVMI (gr/m$^{2.7}$)	62.33 ± 36.07	45.92 ± 14.30	**<0.001**
RWT	0.51 ± 0.21	0.43 ± 0.08	**<0.001**
Left ventricular hypertrophy n (%)	25 (78.12)	21 (65.62)	>0.05
Geometric Pattern			
Concentric hypertrophy n (%)	18 (56.25)	16 (50)	>0.05
eccentric hypertrophy n (%)	6 (18.75)	6 (18.75)	>0.05
Concentric remodelling n (%)	5 (15.6)	7 (21.85)	>0.05
Normal n (%)	3 (9.4)	3 (9.4)	>0.05

*LVEDd: Left Ventricular end-diastolic diameter, LVEDs: Left ventricular end-systolic diameter, SF: shortening fraction, EF: Ejection fraction, IVSDd: Diastolic wall thickness of the interventricular septum, IVSDs: Systolic wall thickness of the interventricular septum, LVPWd: Left ventricular posterior diastolic wall thickness, LVPWs: Left ventricular systolic posterior wall thickness, RWT: Relative wall thickness, E: early diastolic flow, A: atrial systolic flow velocity, LVM: Left ventricular mass, LVMI: Left ventricular mass index

Table 5. Echocardiographic parameters of CIMT and BNP values of post-renal transplantation patients and healthy controls

Parameters	Post-Transplantation	Healthy Control	P value
LVEDd (cm)	4.38 ± 0.59	3.63 ± 0.13	**<0.001**
LVEDs (cm)	2.53 ± 0.42	2.29 ± 0.16	<0.01
SF (%)	38.21 ± 5.65	35.46 ± 5.23	**<0.001**
EF (%)	69.15 ± 5.80	67.46 ± 5.84	<0.05
IVSDd (cm)	1.05 ± 1.19	0.93 ± 0.09	<0.01
IVSDs (cm)	1.44 ± 0.28	1.02 ± 0.27	**<0.001**
LVPWd (cm)	0.75 ± 0.22	0.56 ± 0.03	**<0.001**
LVPWs (cm)	1.21 ± 0.24	1.03 ± 0.10	**<0.001**
Mitral E	0.97 ± 0.19	1.12 ± 0.09	**<0.001**
Mitral A	0.68 ± 0.14	0.70 ± 0.13	<0.05
Mitral E/A	1.46 ± 0.29	1.64 ± 0.34	<0.05
Mitral E/E'	7.07 ± 1.53	6.59 ± 0.92	<0.05
LVM (gr)	151.13 ± 55.57	73.59 ± 10.83	**<0.001**
LVMI (gr/m$^{2.7}$)	45.92 ± 14.30	22.66 ± 6.09	**<0.001**
RWT	0.43 ± 0.08	0.31 ± 0.02	**<0.001**
Geometric Pattern			
Concentric hypertrophy n (%)	16 (50)	0	
eccentric hypertrophy n (%)	6 (18.75)	0	
Concentric remodelling n (%)	7 (21.85)	0	
Normal n(%)	3 (9.4)	32 (100)	
Left Ventricle MPI	0.42 ± 0.11	0.37 ± 0.04	<0.05
CIMT left (mm)	0.583 ± 0.109	0.465 ± 0.078	**<0.001**
CIMT right (mm)	0.538 ± 0.094	0.472 ± 0.102	<0.01
CIMT mean (mm)	0.560 ± 0.091	0.468 ± 0.084	**<0.001**
BNP (fmol/ml)	20.62 ± 14.77	13.28 ± 3.93	<0.01

*RWT: Relative wall thickness, MPI: Myocardial performance index, CIMT: Carotid intima-media thickness, BNP: Brain natriuretic peptide

Table 6. Correlations between MPI and LVMI

Variable	MPI		LVMI	
	r	P	r	p
E/A ratio	**-0.286***	0.022	**-0.351***	**0.005**
E/E' ratio	0.142	0.263	**0.261***	0.037
MPI	-	-	-	-
LVMI (gr/m$^{2.7}$)	**0.472***	**<0.001**	-	-
eGFR(mL/min/1.73 m^2)	-0.001	0.997	-0.205	0.261
Dialysis duration	-0.071	0.7	0.118	0.521

*MPI: Myocardial performance index, LVMI: Left ventricular mass index, eGFR: Estimated glomerular filtration rate

Tablo 7. Correlations between the difference of LVMI (LVMIpretransplant–LVMIposttransplant), BNP and post-transplant proteinuria

	Difference of LVMI	(LVMIpretransplant–LVMIposttransplant
	r	P
BNP	**0.371**	**0.036**
Proteinuria (post-transplant)	**0.455**	**0.009**

Discussion

The present study assessed and compared the echocardiographic and biochemical parameters, CIMT measurements between renal transplant patients and healthy controls in addition pre- and posttransplant period, as well as the association between BNP and echocardiographic findings in transplanted patients for the first time in pediatric age group.

We found that the LVMI decreases after transplantation; however, it remains still high compared to controls.

In our study, similar to the study of Kim et al., we found that patients' LVMI values were significantly decreased after transplantation but still higher than in the control group (10). In the study of Bullington et al., post-transplant echocardiograms of kidney-transplanted patients were retrospectively analyzed, and echocardiograms of patients 14, 33, and 49 months after transplantation were compared (11). There was no significant difference between the first and third evaluations (11). In the same study, no decrease was found in the prevalence of LVH in the period after transplantation (11). In our study, the prevalence of LVH decreased from 78.12% to 65.62%, but this value was statistically insignificant (p=0.667). Although there is a decrease in the LVMI values of the patients over time after transplantation, the fact that this does not lead to improvement in LVH indicates that the patients who have undergone kidney transplantation are at chronic cardiovascular risk. Similar to the study of Kim et al., a significant negative correlation was found between LVMI measured after transplantation and the ratio of E/A and E'/A' in our study (10). The increase in LVMI seems to be associated with the deterioration of diastolic functions.

In our study, the BNP level was associated with LVMI, but the relationship between MPI and BNP, which was shown in studies conducted in patient groups with other diseases, could not be demonstrated in our study (12,13). Might be caused by the fact that, unlike other patient groups, systolic functions in transplant patients improved compared to pre-transplantation. In our study, it was observed that BNP level and BMI were negatively correlated, similar to those in the literature, and it has been shown that the reason for this was that BNP receptors, which are found in large numbers in adipose tissue, bind circulating BNP and lower the serum level (14). We found a significant correlation between the E/E' ratio measured by tissue Doppler examination, which is one of the diastolic dysfunction parameters, and the E'/A' ratio and BNP, while no similar correlation was found with E/A measured by traditional echocardiography.

In another study that draws attention to the importance of tissue Doppler examination (TDE), although the E/A ratio measured by the traditional method is normal when the TDE and E/E' and E'/A' ratios are examined, it is found that patients have diastolic dysfunction and these values are correlated with LVH (15). Therefore,

we can say that performing TDE, especially in groups at cardiovascular risk, provides additional benefits in determining diastolic dysfunction.

Left ventricular mass index showed sustained improvement up to 12 years in post-transplant patients (16). However, LVM continues to increase in post-transplant patients whose hypertension cannot be controlled (16).

A study including 43 patients observed that the prevalence of LVH decreased from 19 to 9 in the post-transplant period (17). A significant decrease in the mean LVMI and the prevalence of LVH after transplantation was found in this study (17). It was 25 patients with LVH in our research in the pre-transplant period, and it decreased to 21 in the post-transplant period.

While death from cardiac causes is 3% in the general population between the ages of 1-24 years, this rate is 32% in hemodialysis patients aged 0-19 years and 28% in peritoneal dialysis patients (18). Although this rate decreased to 22% after transplantation, it is still seven times more than the cardiac mortality rate of the general population (18). Therefore, further studies are needed to identify cardiac risk factors that may affect mortality after renal transplantation and to find treatments to eliminate these factors.

There are some limitations in our study. The small sample size, being a non-randomized study, and the evaluation time for the post-transplant patients was not the same time were the limitations.

Conclusion

Cardiovascular risk factors of renal transplant patients are most severe during end-stage renal disease, and some of these risk factors significantly decrease after transplantation. However, this reduction may not always be as significant as in LVH. It should be kept in mind that these patients are still at significant cardiovascular risk. Therefore they should be followed up regularly even if their renal function tests return to normal after transplantation. Calculating MPI and LVMI in echocardiographic evaluation is essential in predicting patients' immediate and future cardiovascular risk status. Also, tissue Doppler echocardiography is more sensitive than traditional echo, so if available, patients should also be assessed by TDE. The correlation of serum BNP level with LVMI can be used as a marker in these patients, but BMI should be considered.

References

1.Kliegman R Stanton B St Geme JW Schor NF Behrman RE Nelson WE. Nelson Textbook of Pediatrics. 20th ed. Philadelphia Pennsylvania: Elsevier; 2016

2.Mitsnefes MM. Cardiovascular complications of pediatric chronic kidney disease. Pediatr Nephrol. 2008;23(1):27-39.

3.Mitsnefes MM, Daniels SR, Schwartz SM, Meyer RA, Khoury P, Strife CF. Severe left ventricular hypertrophy in pediatric dialysis: prevalence and predictors. Pediatr Nephrol. 2000;14(10-11):898-902.

4.Mitsnefes MM, Barletta GM, Dresner IG, et al. Severe cardiac hypertrophy and long-term dialysis: the Midwest Pediatric Nephrology Consortium study. Pediatr Nephrol. 2006;21(8):1167-1170.

5.Henry WL, DeMaria A, Gramiak R, et al. Report of the American Society of Echocardiography Committee on Nomenclature and Standards in Two-dimensional Echocardiography. Circulation. 1980;62(2):212-217.

6.Silverman N. Quantitative methods to enhance morphological information using M-mode Doppler and cross sectional ultrasound. Pediatric echocardiography. Williams & Wilkins Baltimore, MD; 1993. p. 35-108.

7.Devereux RB, Alonso DR, Lutas EM, et al. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. Am J Cardiol. 1986;57(6):450-458.

8.Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr. 2005;18(12):1440-1463.

9.Khoury PR, Mitsnefes M, Daniels SR, Kimball TR. Age-specific reference intervals for indexed left ventricular mass in children. J Am Soc Echocardiogr. 2009;22(6):709-714.

10.Kim GB, Kwon BS, Kang HG, et al. Cardiac dysfunction after renal transplantation; incomplete resolution in pediatric population. Transplantation. 2009;87(11):1737-1743.

11.Bullington N, Kartel J, Khoury P, Mitsnefes M. Left ventricular hypertrophy in pediatric kidney transplant recipients: long-term follow-up study. Pediatr Transplant. 2006;10(7):811-815.

12.Ono M, Tanabe K, Asanuma T, et al. Doppler echocardiography-derived index of myocardial performance (TEI index): comparison with brain natriuretic peptide levels in various heart disease. Jpn Circ J. 2001;65(7):637-642.

13.Kargin R, Esen O, Akçakoyun M, et al. Relationship between the tissue Doppler-derived Tei index and plasma brain natriuretic peptide levels in patients with mitral regurgitation. J Heart Valve Dis. 2010;19(1):35-42.

14.Wang TJ, Larson MG, Levy D, et al. Impact of obesity on plasma natriuretic peptide levels. Circulation. 2004;109(5):594-600.

15.Hayashi SY, Rohani M, Lindholm B, et al. Left ventricular function in patients with chronic kidney disease evaluated by colour tissue Doppler velocity imaging. Nephrol Dial Transplant. 2006 Jan;21(1):125-32.

16.de Verteuil I, Fitzpatrick J, Alvarez Elias AC, et al. Longitudinal Changes in Cardiac Structure and Function in Pediatric Kidney Transplant Recipients. Hypertension. 2022;79(8):1680-1689.

17.Ramoğlu MG, Uçar T, Yılmaz S, et al. Hypertension and improved left ventricular mass index in children after renal transplantation. Pediatr Transplant. 2017;21(8):10.1111/petr.13066.

18.Weaver DJ, Mitsnefes M. Cardiovascular Disease in Children and Adolescents With Chronic Kidney Disease. Semin Nephrol. 2018;38(6):559-569.