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Recovery of Myocardial Functions After Kidney Transplantation in Patients with Heart Failure Due to Uremic Cardiomyopathy

Üremik Kardiyomiyopati ile İlişkili Kalp Yetersizliğinde Böbrek Transplantasyonu Sonrası Miyokart İşlevlerinde İyileşme

ABSTRACT

Objective: Although left ventricular hypertrophy frequently accompanies end-stage renal disease, heart failure (HF) with reduced ejection fraction (EF) is also observed in a subset of patients. In those patients kidney transplantation (KT) is generally avoided due to an increased risk of mortality in addition to the risks associated with HF. This prospective study was designed to follow patients with HF who were being prepared for KT.

Methods: Twenty-five patients with HF due to uremic cardiomyopathy (UC) who had suitable donors (Group 1), 22 patients with HF who could not undergo KT due to a lack of kidney donors (Group 3), and 25 KT candidates with normal ventricular function (Group 2) were included in the study. Left ventricular ejection fraction (LVEF), left atrial diameter (LAD), mitral annular systolic velocity (Sm), left ventricular global longitudinal strain (GLS), and left ventricular mass index (LVMI) values were recorded across four sessions, from pre-transplant to six months post-transplantation. Endomyocardial biopsy was performed for detailed examination of the myocardium in patients in Group 1 and Group 3, and cardiac magnetic resonance imaging (MRI) was performed in all three groups before transplantation.

Results: In Group 1, LVEF, Sm, and left ventricular global longitudinal strain (LV-GLS) increased significantly, while LAD and LVMI decreased, all reaching normal levels. In contrast, no changes were observed in Group 3 and Group 2 ($P < 0.01$ for LVEF, $P < 0.01$ for GLS, $P < 0.01$ for LAD, and $P < 0.01$ for LVMI measurements). No differences in cardiac MRI and biopsy findings were observed between Group 1 and Group 3.

Conclusion: Since myocardial function improved significantly and normalized in all patients with HF, it has been demonstrated that UC can be substantially reversible when treated with KT.

Keywords: Heart failure, kidney transplantation, reversible cardiomyopathies, uremic cardiomyopathy

ÖZET

Amaç: Sol ventrikül hipertrofisi sıklıkla son dönem böbrek hastalığına eşlik etse de bir grup hastada azalmış ejeksiyon fraksiyonu (EF) ile birlikte kalp yetersizliği (KY) görülmektedir. Bu hastalarda KY'ye bağlı risklere ek olarak mortalite riskinde artma nedeniyle böbrek naklinden (BN) genellikle kaçınılmaktadır. Bu prospektif çalışma BN'ye hazırlanan KY'li hastaların takibi amacıyla planlandı.

Yöntem: Üremik kardiyomiyopati (ÜK) nedeniyle uygun donörü olan 25 KY hastası (grup 1), KY olan ancak böbrek donörü olmadığı için BN yapılamayan 22 hasta (grup 3) ve sol ventriküler fonksiyonu normal olan 25 BN adayı (grup 2) çalışmaya alındı. Nakil öncesinden nakil sonrası 6 ayın sonuna kadar dört seansta sol ventrikül EF, sol atriyum çapı (LAD), mitral anüler sistolik hız (Sm), sol ventriküler global uzunlamasına gerilim (GLS), sol ventriküler kitle indeksi (LVMI) değerleri kaydedildi. Grup 1 ve grup 3'teki hastalara miyokardın detaylı incelenmesi amacıyla endomiyokard biyopsi yapıldı; her üç gruba nakil öncesi kardiyak manyetik rezonans görüntüleme (MRG) yapıldı.

Bulgular: LVEF, Sm; ve LV-GLS Grup 1'de grup 3'e göre anlamlı derecede artarken, LAD, LVID ve LVMI azaldı ve hepsi normal seviyelere ulaştı. Buna karşılık, grup 3 ve grup 2'de herhangi bir değişiklik olmadı (LV-EF için $P < 0,01$; GLS için $P < 0,01$; LAD için $P < 0,01$, LVID için $P < 0,01$ ve LVMI için $P < 0,01$). Grup 1 ile grup 3 arasında kardiyak MR ve biyopsi bulguları açısından farklılık yoktu.

Sonuç: Kalp yetersizliği olan tüm hastalarda miyokard fonksiyonlarının anlamlı düzeyde düzelip normale dönmesi nedeniyle; BN ile tedavi edildiğinde ÜK'nin büyük ölçüde geri dönüşümlü olabileceği gösterilmiştir.

Anahtar Kelimeler: Kalp yetersizliği, böbrek nakli, geri dönüşümlü kardiyomiyopatiler, üremik kardiyomiyopati

ORIGINAL ARTICLE
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With its increasing prevalence, chronic kidney disease (CKD) reduces lifespan, particularly by escalating cardiovascular morbidity and mortality, along with a higher incidence of sudden death and heart failure.[1-3] This outcome might be linked to a condition known as uremic cardiomyopathy (UC), characterized by myocardial fibrosis and capillary rarefaction at the cellular level.[4] While left ventricular hypertrophy is the most common phenotype in these patients, heart failure with reduced ejection fraction (HFrEF) and a dilated left ventricle is rarely seen. However, when present, it is often associated with increased mortality and morbidity.[5-9]

Kidney transplantation (KT) is the only treatment that can mitigate myocardial damage associated with the pathogenesis of CKD. Despite the clear improvement in survival and quality of life resulting from successful transplantation compared to hemodialysis, accompanying heart failure (HF) is the primary cause of mortality and graft loss. HF also accounts for the majority of morbidity and healthcare costs within a transplantation program.[10,11] However, cardiovascular issues can induce reluctance among clinicians to perform KT procedures.[2]

For this reason, we designed a prospective study (from June 2019 to December 2022) to follow kidney transplant recipients with HF due to UC who are being evaluated for KT with end-stage renal disease (ESRD). The purpose of our study was to determine whether uremic cardiomyopathy with reduced EF would improve following KT. We also aimed to identify indicators that could predict improvements in myocardial function post-transplantation.

Materials and Methods

To achieve this objective, we evaluated 988 KT candidates between June 2019 and December 2022. Our study plan received approval from Clinical Research Ethics Committee of Yeni Yüzyıl University (Approval Number: 18.06.2019/012, Date: 11.06.2019), and was conducted with each patient's written informed consent (protocol number 18.06.2019/012). We excluded 614 patients with a history of cardiovascular surgery, coronary intervention, structural heart disease, or other cardiovascular issues, including arrhythmias. From the remaining 374 patients, we identified 324 candidates with a normal echocardiogram and 50 patients with HFrEF.

ABBREVIATIONS

CKD	Chronic kidney disease
ECG	Electrocardiography
EF	Ejection fraction
ESRD	End-stage renal disease
GLS	Global longitudinal strain of the left ventricle
HF	Heart failure
KT	Kidney transplantation
LAD	Left atrial diameter
LVEF	Left ventricular ejection fraction
LVIDD	Left ventricular internal diastolic diameter
LVMI	Left ventricular mass index
MRI	Magnetic resonance imaging
Sm	Systolic velocity of the lateral mitral annulus
STE	Speckle tracking echocardiography
UC	Uremic cardiomyopathy

After a detailed cardiological examination and electrocardiography (ECG), transthoracic echocardiography was performed, including conventional measurements and myocardial deformation parameters. Following echocardiography, a detailed structural and pathological investigation of the heart was conducted before transplantation in Groups 1 and 3, using cardiac magnetic resonance imaging (cardiac MRI), coronary angiography with right heart catheterization, and endomyocardial biopsy via the right external jugular vein. This comprehensive investigation was typically conducted for kidney recipients with marked systolic dysfunction to rule out primary myocardial diseases.

Of the patients with reduced ejection fraction (EF), three were excluded due to cardiac amyloidosis. In patients exhibiting normal left ventricular function, coronary ischemia was investigated using exercise or pharmacological stress tests. If signs of coronary ischemia were detected, coronary anatomy was visualized via coronary angiography. Among these patients, those without coronary artery disease or coronary anomalies and with normally functioning left ventricles were classified as Group 2. An endomyocardial biopsy was unnecessary for Group 2.

Ultimately, our selected study groups comprised 25 ESRD patients with reduced EF who had an appropriate kidney donor (Group 1), 22 ESRD patients with HF who were ineligible for KT due to the absence of a donor (Group 3), and 25 KT candidates with normal myocardial systolic function (Group 2) (Figure 1). This study was conducted in accordance with the Declaration of Helsinki. It is important to note that at no stage of this study were artificial intelligence (AI)-enabled technologies, such as large language models (LLMs), chatbots, or image generators, utilized.

Echocardiographic Examination

Echocardiograms were performed for all patients in four sequential sessions: before KT, one week or 10 days following KT, at the end of the first month, and finally at the sixth month. These were compared with the initial recordings. Echocardiographic examinations were assessed according to American and European Echocardiography guidelines.[12] Body weight, height, and vital signs were documented at all sessions. Echocardiograms were conducted with the General Electric E9 System (General Electric Vingmed, Milwaukee, Wisconsin) and the Philips Epiq 7 ultrasound system for cardiology, equipped with a 2.5 MHz transducer with a frame rate ranging from 60–92 f/sec. The Modified Simpson's biplane disk summation method was utilized to estimate left ventricular (LV) volumes, ejection fraction, and LV mass. Moreover, tissue Doppler-derived septal and lateral velocities were recorded. The cut-off value for low EF was 35%. All measurements were taken and averaged over three consecutive cardiac cycles. Additionally, an available automated function imaging method was applied for speckle tracking analysis to evaluate global longitudinal strain (GLS) from apical long-axis views (long-axis, 2-chamber, and 4-chamber views) using a previously reported procedure. For the long-axis strain values of the left ventricle, negative values were presented, with a larger negative value indicating greater longitudinal deformation. Examinations adhered to this standard.[12]

Endomyocardial Biopsy

Endomyocardial biopsy, performed through the right external jugular vein, was conducted on patients in Groups 1 and 3

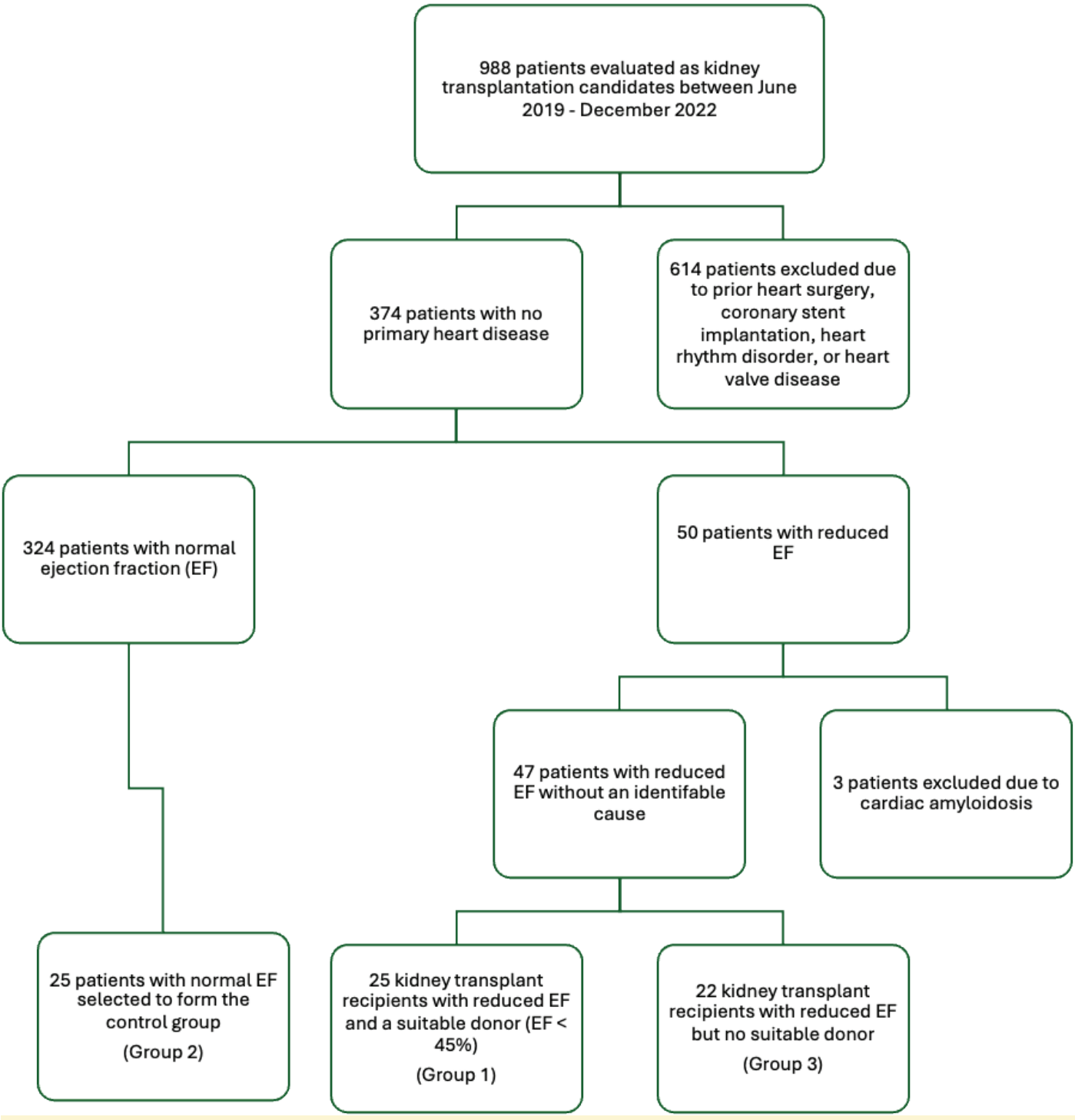

Figure 1. Diagram of patient selection for the study.

before kidney transplantation to demonstrate the presence of uremic cardiomyopathy at the cellular level and eliminate the possibility of other myocardial diseases. We also aimed to capture findings predictive of myocardial recovery or ongoing heart failure in these patients with heart failure. Endomyocardial biopsy was not performed in Group 2 patients who had normal cardiac function, nor was it repeated after transplantation.

Cardiac Magnetic Resonance Imaging

Cardiac MRI was performed to characterize myocardial tissue before kidney transplantation, to confirm that uremic cardiomyopathy was the sole cause of existing heart failure, and to obtain any findings that might predict recovery in patients whose myocardial function would improve. All studies were conducted at 1.5-T (Siemens Avanto, Erlangen, Germany). Standard protocols for LV function and mass used steady-

state free precession imaging. Myocardial characterization assessment was carried out using T1 and T2 mapping. An ECG-gated Modified Look-Locker Inversion recovery sequence with a heartbeat sampling protocol (Siemens WIP 448) was executed to assess native myocardial T1 and extracellular volume (ECV) at basal and mid-short axis levels in diastole. Typical T2 acquisition parameters included three single-shot images acquired at different T2-preparation times (0, 24, and 55 ms, respectively).[13]

Medical Therapy

Group 3 did not receive immunosuppressive therapy due to their inability to undergo transplantation. Groups 1 and 2 both followed the same immunosuppressive regimen, which included cyclosporine, prednisone, and mycophenolate mofetil, along with antihypertensive therapy. The epidemiological features of the individuals enrolled in the study are detailed in Tables 1 and 2.

Statistical Analysis

The Statistical Package for the Social Sciences for Windows, version 27.0 (SPSS Inc., Chicago, IL, USA), was used for data analysis. Descriptive analysis results were presented as mean ± standard deviation for variables with normal distributions, while variables with non-normal distributions were presented as median and interquartile range. Percentages and frequencies were calculated using basic mathematical methods. The Kolmogorov-Smirnov test was applied to evaluate normality. To compare changes in cardiac performance over time between groups, we used the independent t-test for normally distributed variables and the Mann-Whitney U test for non-normally distributed variables. For categorical variables analysis, Chi-square tests were used, while Pearson's or Fisher's exact tests were employed for comparing continuous variables within categorical parameters. A general linear model was used to identify changes over time in left ventricular ejection fraction (LVEF), global left ventricular strain, left atrial diameter (LAD), left ventricular internal diameters, systolic velocity of the lateral mitral annulus, and left ventricular mass index. Statistical significance was set at $P < 0.05$.

Results

This study was conducted with 72 patients, 61.1% ($n = 44$) male and 39.9% ($n = 28$) female, between June 2019 and December 2022. The mean age of all patients was 34.19 ± 12.20, with no significant differences in age, sex, history of hypertension, history of diabetes mellitus, or duration of dialysis among patient groups (Group 1 and Group 3) and patients with normal EF (Group 2) ($P = 0.71$; $P = 0.45$, respectively). Of these patients, 28 were female (Table 1). All patients' ECG recordings were in sinus rhythm at the beginning and during the follow-up period. The epidemiological characteristics of individuals enrolled in the study are presented in Tables 2 and 3. No patient had coronary artery disease, peripheral artery disease, or primary heart valve disease

Table 1. Distribution of Descriptive Characteristics by Groups

		Groups				
		Group 1 (n = 25)	**Group 2 (n = 25)**	**Group 3 (n = 22)**	**Total**	***P***
Age, Years	Mean ± SD	32.68 ± 11.40	34.05 ± 12.46	34.6 ± 9.9	33.92 ± 12.08	***0.71***
	Median (Min-Max)	31.5 (13-48)	33.5 (14-62)	53 (28-61)	33 (13-62)	
Sex	Male	19 (72)	18 (72)	16 (72)	53 (61.1)	***0.063***
	Female	6 (28)	7 (28)	6 (28)	19 (39.9)	

Table 2. Epidemiological Features of the Patients Enrolled in the Study

	Group 1 (n = 25)	**Group 2 (n = 25)**	**Group 3 (n = 22)**	***P***
Hypertension	13	11	15	0.625
Smoking	3	2	3	0.711
Dialysis Duration, months	11 (0-120)	10 (0-170)	10.7 (0-166)	0.45
Heart Rate, beats per minute	72 ± 6.3	77 ± 7.0	69 ± 8.2	0.52
Diabetes Mellitus	4	5	3	0.325
Body Mass Index, kg/m²	27.4 ± 3.6	25.3 ± 4.2	24.3 ± 2.8	0.125
Contributing Factors in Kidney Disease Etiology	Glomerular Diseases: 58 cases Alport Syndrome: 2 cases (both in Group 1) Lupus Nephritis: 1 case (Group 3) Complement-Related Hemolytic Uremic Syndrome (HUS): 1 case (Group 3) Cystinosis: 1 case (Group 1) Other Systemic Vasculitis: 1 case (Group 2) Unknown Cause of Chronic Kidney Disease (CKD): 8 cases			
Primary Glomerulonephritis	21	19	18	0.16
Unknown Cause of Kidney Disease	4	3	5	0.223

at the time of transplantation. The average follow-up duration after KT was 19.0 [13.0–27.0] months. Following KT, creatinine levels and blood pressure measurements significantly decreased (Table 3). At the end of the sixth month, the mean estimated glomerular filtration rate (eGFR) was 79.44 ± 3.53, 7.98 ± 4.8, and 80.14 ± 19.01 ml/min in Groups 1, 3, and 2, respectively. No significant differences were noted between Groups 1 and 2 (P > 0.05). Furthermore, no significant change in glomerular filtration rates was observed among all three groups over 6 months (P > 0.05). No deaths occurred during the follow-up period (Tables 2 and 3).

Endomyocardial Biopsy Findings

Endomyocardial biopsies were initially performed on Group 1 and Group 3 patients to rule out other causes of heart failure (HF) and to confirm a diagnosis based on pathological findings indicative of uremic cardiomyopathy. Group 2 patients did not undergo endomyocardial biopsies, as no HF was detected through echocardiography or cardiac MRI. Notably, both Group 1 and Group 3 exhibited mild myocardial fibrosis, minor myocardial disarray, a slight chronic inflammatory reaction, and moderate cardiomyocyte hypertrophy (P > 0.05) (Table 4, Figures 2 and 3).

Cardiac MRI Findings

The findings for Groups 1 and 3 were similar, showing a slight increase in native T1 values—indicative of interstitial fibrosis—a mild increase in native T2 values, indicating myocardial edema,

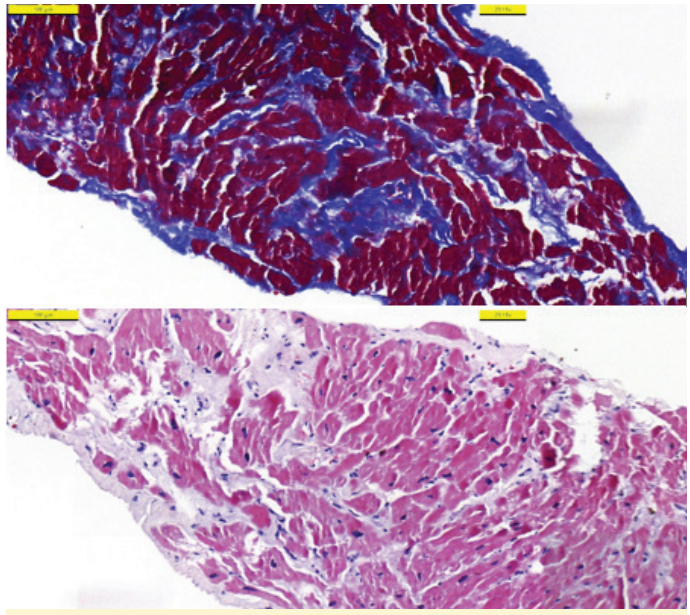

Figure 2. Endomyocardial biopsy specimen of a patient in Group 1 (heart failure with kidney transplantation): The endocardium displays normal histopathology. Moderate myocyte hypertrophy, slight myocardial disarray, mild fibrosis, mild myocardial edema, slight nuclear loss in myocytes, and a chronic inflammatory reaction characterized by perivascular lymphocyte foci were detected in the myocardium.

Table 3. Comparison of Ejection Fraction and Graft Functions After Renal Transplantation (RTx) in Patients with Heart Failure and Normal Ejection Fraction

	KT with HF n = 25	KT with Normal EF n = 25	HF Without KT	*P*
Age, years	32.68 ± 11.40	34.05 ± 12.46	34.6 ± 9.9	P = 0.71
Dialysis Duration, months	11 (0-120)	10 (0-170)	10.7 (0-166)	P = 0.45
GFR before RTx, ml/min GFR 1 week after RTx, ml/min GFR 1 month after RTx, ml/min GFR 6 months after RTx, ml/min	7.96 ± 2.78 80.52 ± 30.78 83.03 ± 31.47 79.44 ± 35.53	8.16 ± 3.39 82.74 ± 33.56 87.15 ± 22.53 80.14 ± 19.01	9.6 ± 4.45 8.9 ± 5.5 8.6 ± 5.7 7.98 ± 4.8	P > 0.05 for all comparisons
EF before RTx, %	31.6 ± 5.31	62.25 ± 2.34	32.22 ± 5.45	P = 0.001
EF 1 week after RTx EF 1 month after RTx EF 6 months after RTx	46.27 ± 3.34 60.91 ± 4.37 64.95 ± 1.84	64.25 ± 1.44 65.50 ± 1.67 65.30 ± 1.86	32.6 ± 1.19 30.63 ± 5.45 32.62 ± 3.36	

Table 4. Pathological Findings Among Groups

	Group 1: KT Recipients with HF	Group 2: KT Recipients with Normal Heart	Group 3: HF due to UC without Kidney Donor	*P*
Myocardial Fibrosis	Mild (+)	Endomyocardial biopsy was not performed in Group 2	Mild (+)	NS
Myocardial Disarray	Slight (+)		Slight (+)	NS
Inflammatory Reaction	Mild chronic (+)		Mild chronic (+)	NS
Cardiomyocyte Hypertrophy	Moderate (++)		Moderate (++)	**NS**
Myocardial Edema	Slight (+)		Slight (+)	**NS**
Nuclear Loss in Myocytes	Mild (+)		Mild (+)	**NS**

Pathological findings among groups: Pathological findings in myocardial samples, including myocardial fibrosis, myocardial disarray, inflammatory reaction within myocardium, cardiomyocyte hypertrophy, myocardial edema, and nuclear loss in myocytes, were classified as mild/slight (+), moderate (++), and severe (+++). (Abbreviations: HF, Heart Failure; KT, Kidney Transplantation; NS, Non-Significant; UC, Uremic Cardiomyopathy.)

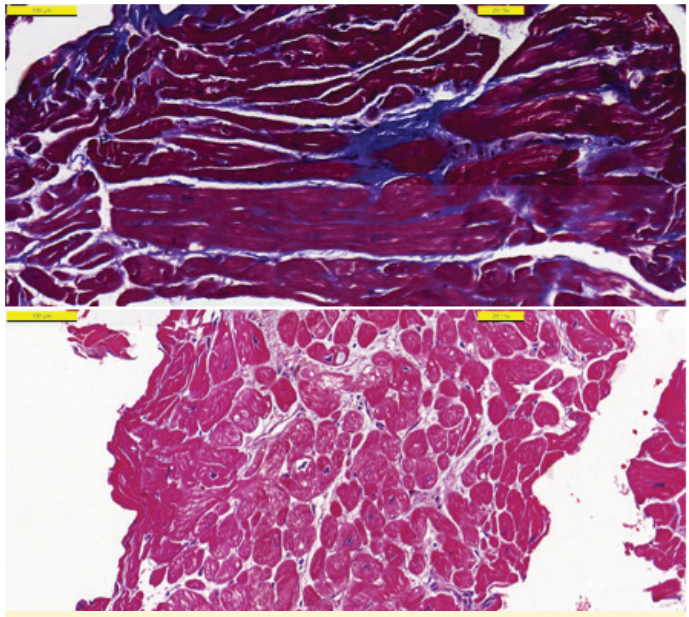

Figure 3. Endomyocardial biopsy specimen from a patient in Group 3 (heart failure without kidney transplantation) 7319B2129: Mild myocardial degeneration characterized by mild nuclear loss in myocytes and slight interstitial edema. Moderate myocyte hypertrophy, slight myocardial disarray, mild chronic inflammatory reaction, and mild subendocardial fibrosis were also observed in the myocardium.

a moderate rise in LV mass, and moderate LV dilation ($P > 0.05$) (Figure 4). In contrast, Group 2 differed from Groups 1 and 3; increases in native T1 and T2 values were less pronounced, and the rise in LV mass was significantly milder. Furthermore, Group 2 showed no signs of LV dilation ($P < 0.05$) (Table 5).

Changes in Echocardiographic Parameters

All echocardiograms were performed by a single observer (YSO). However, all images were re-evaluated, and all measurements were repeated to assess intraobserver variability (Supplementary Table 1). The average absolute differences between left ventricular internal diameter (LVID), LVEF, LAD, left ventricular mass index (LVMI), left ventricular global longitudinal strain (LV-GLS), and mitral annular systolic velocity (Sm) values in the first and second evaluations ranged from 2.3-3.5% for all measurements (Analysis of Variance [ANOVA] $P > 0.05$ for all). The test-retest agreements were satisfactory and showed no significant differences ($P > 0.05$ for all, ANOVA). The average absolute differences between LVID, LAD, LVEF, LVMI, LV-GLS, and Sm values in the first and second evaluations ranged from 2.2-3.3% for all measurements ($P > 0.05$ for all, ANOVA) (Supplementary Table 2).

During follow up, LVEF in Group 1 increased significantly, while there was no change in Group 3 and only a slight increase in Group 2. The change in LVEF for Group 1 cases was found to be significantly higher than that for Group 2 and Group 3 cases

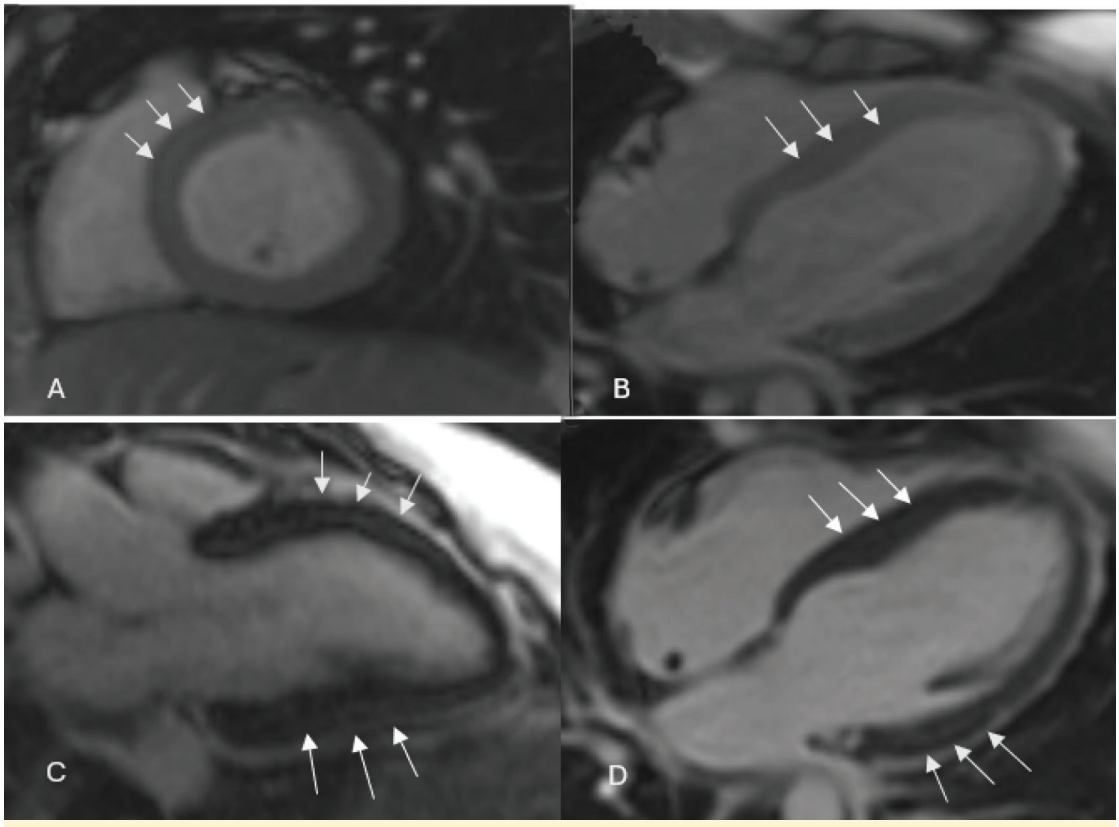

Figure 4. Cardiac magnetic resonance imaging (MRI) images of a patient in Group 1: Images A and B display mid-myocardial fibrosis extending as a thin line along the interventricular septum on T1-weighted imaging. Images C and D show mid-myocardial fibrosis detected by late gadolinium enhancement in the interventricular septum, anterolateral, and inferolateral walls on late-phase contrast imaging.

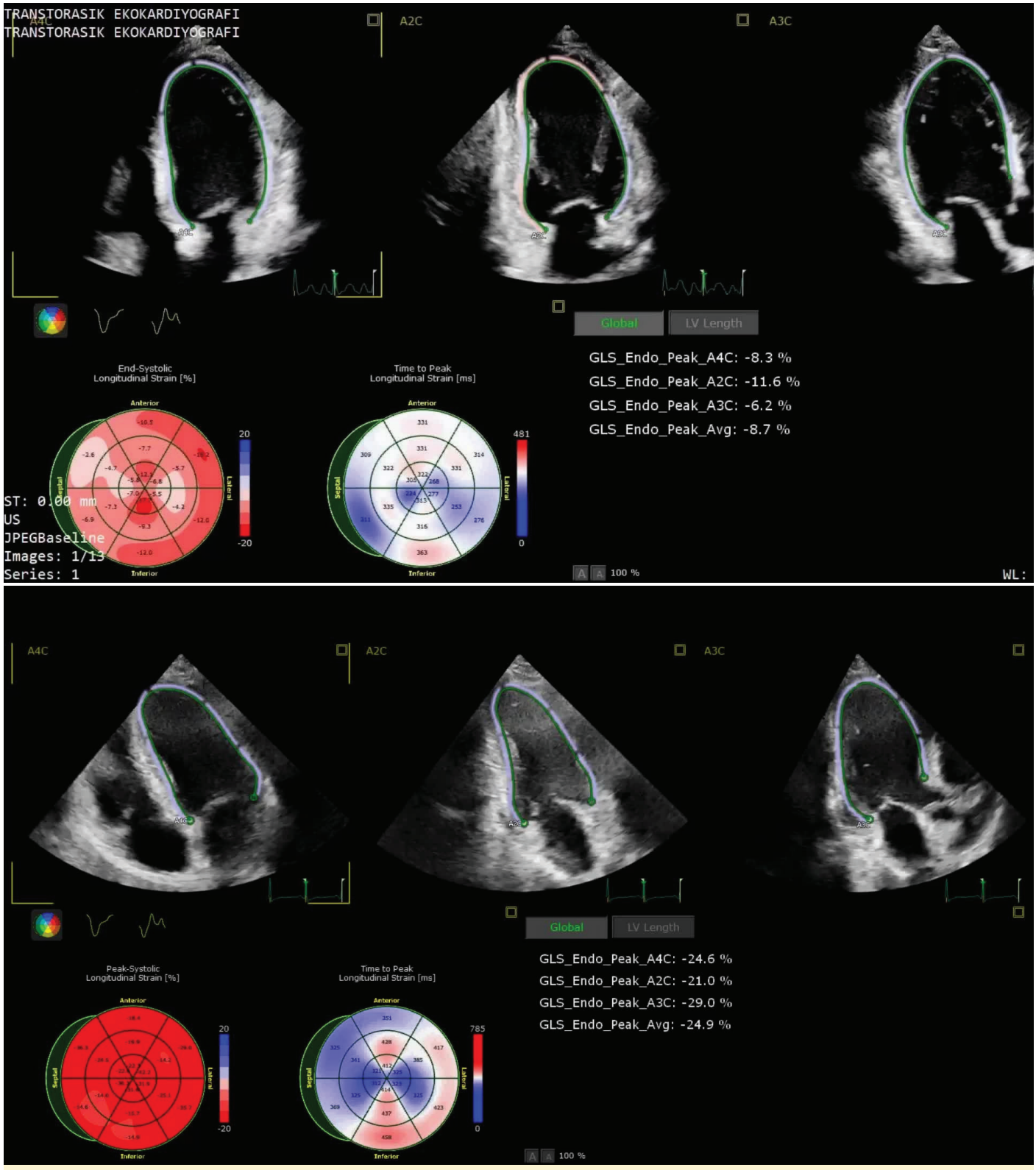

Figure 5. Left ventricular global longitudinal strain (LV-GLS) recordings of a patient before and after kidney transplantation in Group 1.

(*P* = 0.001; *P* = 0.006; P < 0.01 for the first week), (*P* = 0.001; *P* = 0.001; *P* < 0.01 for the first month), and (*P* = 0.001; *P* = 0.001; *P* < 0.01 for the sixth month). LV-GLS values for Group 2 cases were significantly higher than those for Group 1 and Group 3 cases at the beginning (*P* = 0.001; *P* = 0.001; *P* < 0.01). For Group 1 cases, after transplantation, the mean LV-GLS increase was 4.43 ± 2.44% in the first week, 7.07 ± 2.41% at the first month, and 8.51 ± 3.32% at six months compared to the initial examination, all statistically significant (*P* = 0.001; *P* = 0.001; *P* = 0.001; *P* < 0.01). Similarly, the

Table 5. Cardiac Magnetic Resonance Imaging (MRI) Findings

	Group 1: KT Recipients with HF	Group 2: KT Recipients with Normal Heart	Group 3: HF due to UC without Kidney Donor	*P*
Increase in Native T1 Values (Interstitial Fibrosis)	997-1202 ms 1067 ± 34.9 ms	942-979 ms 959 ± 36 ms	996-1196 ms 1066 ± 32 ms	>0.05 between Groups 1 and 3
Increase in Native T2 Values (Myocardial Edema)	52 ± 4 ms	45 ± 2 ms	51 ± 3 ms	<0.05 between Group 2 and Groups 1, 3
Increase in Left Ventricular Mass	Moderate (++)	Mild (+)	Moderate (++)	
Left Ventricular Dilatation	Moderate (++)	-	Moderate (++)	

Cardiac MRI findings among groups: MRI findings, including increase in left ventricular mass and left ventricular dilatation, were classified as mild (+), moderate (++), and severe (+++). (Abbreviations: HF, Heart Failure; KT, Kidney Transplantation; NS, Non-Significant; UC, Uremic Cardiomyopathy.)

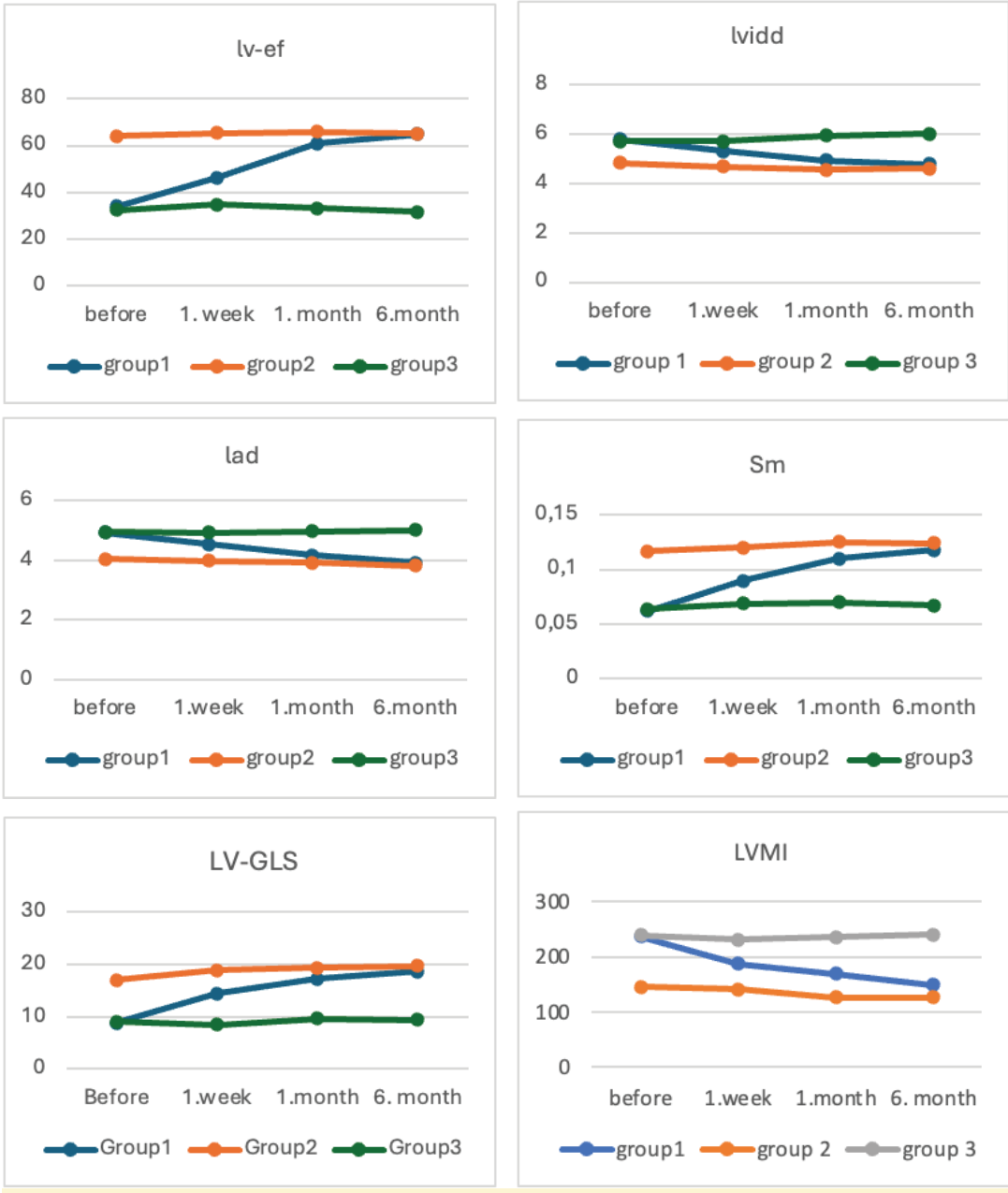

Figure 6. Changes in ejection fraction (EF), left ventricular internal diastolic diameter (LVIDD), left atrial diameter (LAD), systolic velocity of the lateral mitral annulus (Sm), global longitudinal strain (GLS), and left ventricular mass index (LVMI) between groups during follow-up.

Table 6. Results of the Multiple Linear Regression Analysis

Dependent Variable	Independent Variable	B	95% CI Lower	95% CI Upper	Beta	*P*	R^2	ANOVA *P*
LV-GLS	Age, years	0.009	-0.140	0.159	0.021	0.899	0.013	0.989
	Sex	-0.703	-3.409	2.004	-0.064	0.606		
	HT	0.984	-2.102	4.070	0.099	0.527		
	DM	0.044	-3.190	3.279	0.004	0.978		
	Dialysis Duration	-0.028	-0.208	0.152	-0.039	0.757		
	Aortic Distensibility	0.614	-7.288	8.515	0.020	0.877		
LAD	Age, years	0.004	-0.009	0.017	0.095	0.550	0.078	0.489
	Sex	-0.147	-0.379	0.085	-0.152	0.210		
	HT	-0.049	-0.314	0.215	-0.056	0.711		
	DM	-0.096	-0.373	0.182	-0.088	0.494		
	Dialysis Duration	0.006	-0.009	0.022	0.098	0.422		
	Aortic Distensibility	-0.224	-0.901	0.453	-0.081	0.511		
LVEF	Age, years	0.047	-0.409	0.504	0.034	0.836	0.012	0.993
	Sex	2.805	-5.482	11.092	0.084	0.501		
	HT	1.566	-7.883	11.014	0.051	0.742		
	DM	1.101	-8.801	11.003	0.029	0.825		
	Dialysis Duration	-0.060	-0.612	0.491	-0.027	0.828		
	Aortic Distensibility	-3.248	-27.441	20.945	-0.034	0.789		
Sm	Age, years	0.032	-0.076	0.097	0.097	0.556	0.029	0.587
	Sex	-0.156	-0.423	0.092	-0.174	0.310		
	HT	-0.053	-0.317	0.225	-0.062	0.723		
	DM	-0.089	-0.363	0.152	-0.089	0.464		
	Dialysis Duration	0.003	0.009	0.026	0.099	0.432		
	Aortic Distensibility	-0.234	-0.915	0.468	-0.088	0.531		
LVMI	Age, years	0.077	-0.309	-0.909	0.097	0.650	0.011	0.986
	Sex	0.765	-2.482	-3.487	-0.162	0.510		
	HT	0.987	-2.883	-7.365	-0.061	0.523		
	DM	0.652	-3.621	-8.569	-0.079	0.369		
	Dialysis Duration	0.569	-0.216	-0.687	0.089	0.258		
	Aortic Distensibility	-5.235	-9.632	-17.458	-0.086	0.509		

Linear regression analysis was performed to assess the effect of potential confounders. DM, Diabetes Mellitus; HT, Hypertension; LAD, Left Atrial Diameter; LVEF, Left Ventricular Ejection Fraction; LV-GLS, Global Longitudinal Strain of the Left Ventricle; LVMI, Left Ventricular Mass Index; Sm, Systolic Velocity of the Lateral Mitral Annulus (Tissue Doppler).

change in GLS for Group 1 was found to be significantly higher than for Group 2 and Group 3 ($P = 0.001$; $P = 0.011$; $P < 0.05$ for the first week), ($P = 0.001$; $P = 0.009$; $P < 0.01$ for the first month), ($P = 0.001$; $P = 0.008$; $P < 0.01$ for the sixth month) (Figure 5, Supplementary Tables 3 and 4). Consistent with the LVEF and LV-GLS results, the change in Sm value in Group 1 was significantly higher than in Group 2 and Group 3 ($P = 0.001$; $P = 0.049$; $P < 0.05$ for the first week), ($P = 0.001$; $P = 0.001$; $P < 0.01$ for the first month), and ($P = 0.001$; $P = 0.001$; $P < 0.01$ for the sixth month) (Supplementary Tables 3 and 4).

LV internal diastolic and systolic diameters (left ventricular internal diastolic diameter [LVIDD]- left ventricular internal systolic diameter [LVIDS]), LAD, LV mass, and LV mass index decreased significantly, while the mitral annular systolic wave with tissue Doppler echocardiography (Sm), LVEF, and global longitudinal strain of the left ventricle (LV-GLS) showed an increase (Supplementary Tables 3 and 4, Figure 6, Supplementary

Videos 1-4). There were no significant changes in right ventricular parameters after transplantation. Similarly, LV diastolic function parameters showed no substantial changes after kidney transplantation, although there was a trend (P = 0.064) toward a lower E/E' ratio after KT. Aortic elastic properties, including aortic strain, aortic distensibility, beta index, and elastic modulus, also showed no significant improvements at the one-year follow-up (P-values of 0.54, 0.075, 0.065, and 0.069, respectively).

According to the correlation analysis, there were no statistically significant relationships between age, gender, hypertension (HT), diabetes (DM), dialysis duration, and GLS, LAD, and EF measurements (P > 0.05). However, there was a statistically significant positive relationship between distensibility and GLS (r = 0.487) and EF (r = 0.337), as well as a statistically significant negative relationship between distensibility and LAD (r = -0.492, P < 0.05). However, because at least two variables must be present for multiple linear regression analysis, it could not be performed with aortic distensibility (Supplementary Table 5).

The evaluation of the effects of independent variables on dependent variables using multiple linear regression analysis revealed that the effects of age, gender, hypertension, DM, dialysis duration, and aortic distensibility on LV-GLS, LAD, LVEF, Sm, and LVMI were not statistically significant. In the analyses conducted for LV-GLS and LVEF, the explanation ratio (R^2) for dependent variables in the model was substantially low, at 0.013 and 0.078, respectively, while ANOVA P-values were 0.989 and 0.489, indicating the model's lack of significance. Similarly, R^2 values for LAD, Sm, and LVMI were 0.078, 0.029, and 0.011, respectively, with ANOVA P-values of 0.489, 0.587, and 0.986, indicating a lack of statistical significance for the model (Table 6).

Discussion

While low EF is observed in 30–35% of patients undergoing hemodialysis, the actual prevalence of HF with reduced EF among ESRD patients, excluding those with primary structural heart disease, is approximately 8%.[14] Typically, left ventricular hypertrophy and preserved EF are common phenotypes in chronic renal failure; however, UC with systolic dysfunction presents a most severe scenario due to the significant hesitation surrounding transplantation decisions in these cases.[14,15] Our study demonstrated that LVEF, LV-GLS, LAD, Sm, LVMI, and LVIDD improved following KT, particularly in patients with uremic cardiomyopathy presenting with HFrEF. The clinical signs of HF had fully regressed by the six-month follow-up.

Although it is generally accepted that successful KT can reverse left myocardial hypertrophy and systolic dysfunction, a recent meta-analysis reported that this outcome could not be statistically proven due to methodological limitations in previous studies.[16] The primary distinction in our study is that we specifically focused on patients with HF due to UC, excluding any cases of HF potentially caused by primary heart diseases. That being said, several historically significant studies have investigated the impact of KT on cardiac function.

One such study, conducted by Parfrey et al.,[17] followed 102 ESRD patients who received successful renal transplants. They found that fractional shortening of the left ventricle improved after transplantation in patients who had experienced HF, concluding that the correction of the uremic condition via KT led to normalization of LV contractility, regression of hypertrophy, and improvement cavity volume.

Research by Melchor et al.[18] was among the early studies documenting the benefits of kidney transplantation on LV dysfunction. They demonstrated an improvement in LV systolic functions and observed normal echocardiograms in 69% of patients after one year.

In a study by Wali et al.,[19] 138 patients with CKD and HF (LVEF < 40%) were followed, though the study did not exclude patients with atherosclerotic heart disease. All patients were assessed for coronary artery disease, and those who were able underwent revascularization (via angioplasty or bypass surgery). The left ventricular ejection fraction increased significantly at both the six- and 12-month follow-ups.

Abbot et al.[20] demonstrated a significant reduction in congestive heart failure (CHF) prevalence from 4.9% to 1.4% at one year in a retrospective study of 29,597 KT patients.

In this study, we also monitored global longitudinal strain of the left ventricle (LV-GLS) and tissue Doppler parameters, revealing that the existing left ventricular dysfunction is primarily attributable to a loss of contractile reserve. Our goal was to identify even subclinical LV dysfunction that may persist following successful KT. While previous studies have documented improvements in subclinical LV systolic dysfunction following KT,[21-26] our study is the first to specifically exclude patients with HF associated with primary heart disease.

Decreased GLS is observed across renal diseases and in KT recipients.[22,26] Rakhit et al.[21] were the first to demonstrate that this reduction could be improved by KT, while it tends to worsen in patients who remain on dialysis. Hewing et al.[23] showed a significant reversal of LV hypertrophy and substantial recovery in LV function, assessed through speckle tracking echocardiography (STE). Hamidi et al.[25] reported earlier improvements in myocardial function just one month post-KT, although they did not categorize patients by primary heart diseases, as we did not either.

Our study differed by excluding cases of low EF due to primary heart diseases. Our cohort was composed of a relatively younger population without histories of diabetic nephropathy or hypertension as causes of ESRD. Additionally, dialysis duration was also short across all patient groups. Thus, we can confidently state that our cohort included only patients with HF due to ESRD. This likely explains why LV systolic function fully recovered in all patients and remained stable over nearly two years of follow-up. Notably, none of the patients developed rejection or graft failure. Consequently, we were unable to observe whether a decline in GFR or new kidney damage might cause a regression in LV function.

Endomyocardial biopsy and cardiac MRI were performed on patients with heart failure before kidney transplantation at the beginning of the study. The primary purpose of conducting biopsy and cardiac MRI was both to rule out other pathologies that

could cause heart failure and to confirm the presence of uremic cardiomyopathy. Additionally, at the beginning of the study, we aimed to determine whether systolic or diastolic dysfunction would improve in patients with uremic cardiomyopathy and whether biopsy or MRI findings could provide clues to predict outcomes in the improved group. Among our patients, there were three candidates for kidney retransplantation and one patient who was successfully resuscitated after cardiac arrest. For these patients, it was necessary to make important decisions, including accepting a certain preoperative risk and approving the use of a healthy donor kidney.

Sudden death is the most common mode of death in CKD.[27] Studies have shown that the likelihood of survival in CKD decreases by nearly 50% following a diagnosis of HF.[14,27,28] Enhancing renal function through KT in patients with CHF not only disrupts this cycle[19] but may also reverse cardiac dysfunction, reduce the risk of sudden death, and improve quality of life.[19] Therefore, patients with ESRD should be advised to consider KT as soon as HF is diagnosed.

Limitations

The number of patients in our study may initially seem low. However, uremic cardiomyopathy with systolic dysfunction—unrelated to primary structural heart disease—is a rare condition, limiting the number of eligible patients for our study.

The absence of repeated cardiac MRI scans after kidney transplantation may be considered a limitation in proving myocardial recovery. However, in this study, which presents results from a relatively short-term follow-up, post-echocardiographic recovery cardiac MRI was not included in the planning phase due to constraints in our country regarding hospital appointment availability and funding. We hope that future studies will incorporate repeat cardiac MRI investigations to further support our findings.

Conclusion

Heart failure patients with reduced ejection fraction due to uremic cardiomyopathy have the worst prognosis among those with end-stage renal failure, accounting for around 8% in various studies. Given the increased propensity for cardiac arrhythmias and heightened mortality in this group, it is rare for these patients to reach cardiological evaluation as kidney transplant candidates. However, in a surprising finding, clinical and echocardiographic signs of heart failure completely regressed after successful kidney transplantation in 25 patients with uremic cardiomyopathy and heart failure with reduced ejection fraction. Since a significant improvement was observed in myocardial systolic function and myocardial deformation parameters at the six-month follow-up of all 25 high-risk HF patients, we conclude that uremic cardiomyopathy can be reversible when treated with KT. Although its occurrence in renal failure cannot be prevented, HF due to uremic cardiomyopathy can be reversed with KT. Furthermore, patients with end-stage renal failure accompanied by HF should be prioritized for KT as soon as HF is diagnosed. It is important to recognize that uremic cardiomyopathy, which results in reduced EF HF, may have a distinctly better prognosis after KT compared to other types of HF.

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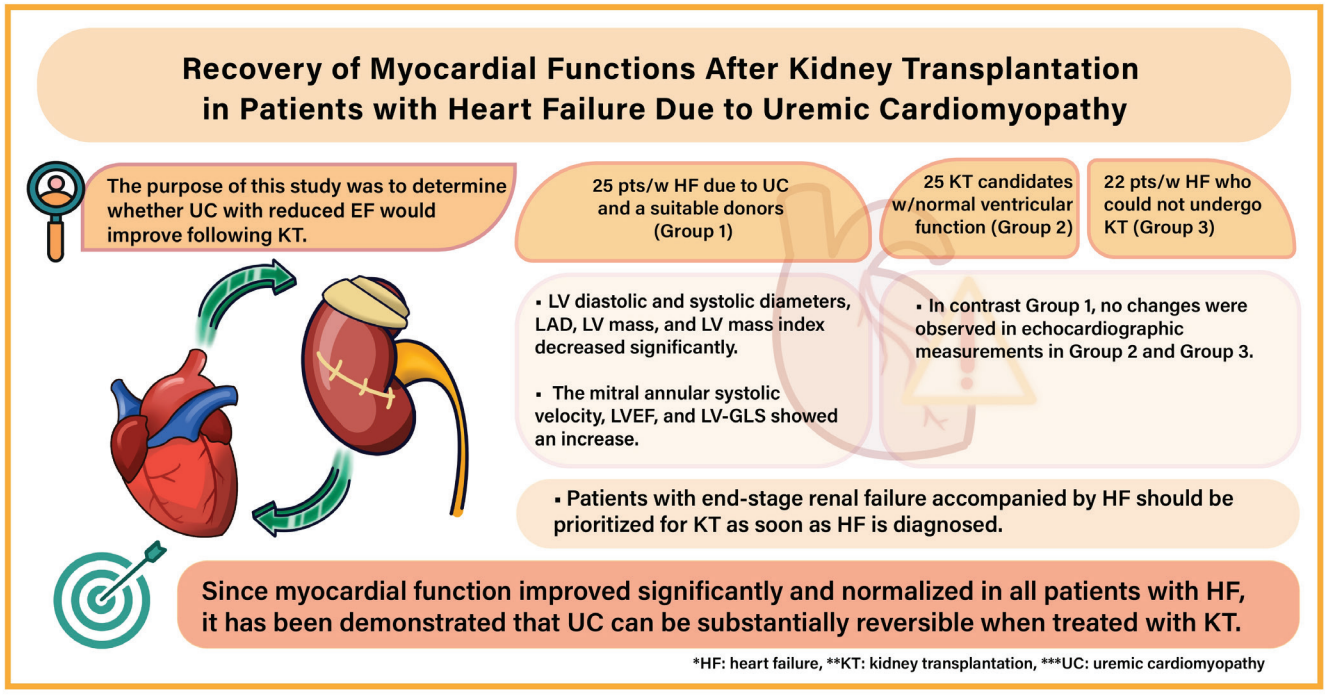

Supplementary Table 1. Intraobserver Correlation Coefficients (IOCC) of LVEF, LV-GLS, LAD, Sm, LVMI, and LVID Measurements Across Echocardiography Sessions

	IOCC1 (95% CI)	IOCC2 (95% CI)	IOCC3 (95% CI)	IOCC4 (95% CI)
LVIDD	0.79 (0.77-0.80)	0.81 (0.79-0.82)	0.78 (0.77-0.81)	0.77 (0.76-0.79)
LAD	0.90 (0.89-0.91)	0.90 (0.83-0.91)	0.88 (0.86-0.89)	0.89 (0.87-0.90)
Sm	0.88 (0.87-0.89)	0.86 (0.85-0.88)	0.88 (0.87-0.89)	0.89 (0.86-0.91)
LVEF	0.86 (0.84-0.87)	0.87 (0.86-0.89)	0.85 (0.84-0.89)	0.87 (0.86-0.89
LV-GLS	0.88 (0.86-0.89)	0.87 (0.85-0.88)	0.88 (0.86-0.89)	0.89 (0.87-0.90
LVMI	0.78 (0.75-0.82)	0.79 (0.76-0.81)	0.78 (0.76-0.81)	0.77 (0.76-0.78)

CI, Confidence Interval; IOC, Intraobserver Correlation Coefficient; LAD, Left Atrial Diameter; LVEF, Left Ventricular Ejection Fraction; LV-GLS, Left Ventricular Global Longitudinal Strain; LVIDD, Left Ventricular Internal Diastolic Diameter; Sm, Systolic Myocardial Velocity of the Lateral Mitral Annulus.

Supplementary Table 2. Absolute Average Differences of Repeated Echocardiographic Measurements at Each Session

	Pretransplant	1st Week	1st Month	6th Month
LVIDD	2.2	2.3	2.5	2.3
LAD	2.3	2.5	2.6	2.4
LVEF	2.6	2.8	2.7	2.6
LVMI	2.9	3.0	3.1	3.3
LV-GLS	2.2	2.3	2.4	2.2
Sm	2.9	3.2	3.1	2.8

LAD, Left Atrial Diameter; LVEF, Left Ventricular Ejection Fraction; LV-GLS, Left Ventricular Global Longitudinal Strain; LVIDD, Left Ventricular Internal Diastolic Diameter; Sm, Systolic Myocardial Velocity of the Lateral Mitral Annulus.

Supplementary Table 3. Evaluation of LVEF, LVIDD, and LAD Measurements by Groups

EF		**Groups**				
		Group 1 (n = 25)	**Group 2 (n = 25)**	**Group 3 (n = 22)**	**Total**	***P***
Initial Examination	Mean ± SD	34.14 ± 5.45	63.95 ± 1.79	32.6 ± 5.41	47.37 ± 15.68	[a]***0.001***
	Median (Min-Max)	36 (23-41)	64 (59-67)	34 (27-39)	39 (23-67)	
1 Week	Mean ± SD	46.27 ± 3.34	65.41 ± 1.68	34.8 ± 5.4	53.69 ± 11.57	[a]***0.001***
	Median (Min-Max)	46.5 (41-52)	65.5 (63-69)	33 (29-41)	51 (29-69)	
1 Month	Mean ± SD	60.91 ± 4.37	65.82 ± 1.89	33.2 ± 5.59	60.29 ± 10.16	[a]***0.001***
	Median (Min-Max)	62.5 (54-68)	65.5 (62-69)	32 (27-39)	64 (27-69)	
6 Months	Mean ± SD	64.95 ± 1.84	65.18 ± 1.84	31.6 ± 4.62	61.65 ± 10.47	[a]***0.001***
	Median (Min-Max)	65 (60-68)	65 (62-68)	30 (27-37)	65 (27-68)	
Change from Initial to 1 Week	**Change**	12.14 ± 4.74	1.45 ± 1.10	2.20 ± 2.39		[a]***0.001***
	P	[c]***0.001***	[c]***0.001***	[c]***0.104***		
Change from Initial to 1 Month	**Change**	26.77 ± 5.19	1.86 ± 1.13	0.60 ± 1.95		[a]***0.001***
	P	[c]***0.001***	[c]***0.001***	[c]***0.414***		
Change from Initial to 6 Months	**Change**	30.82 ± 5.65	1.23 ± 1.19	-1.00 ± 2.35		[a]***0.001***
	P	[c]***0.001***	[c]***0.001***	[c]***0.461***		

LVIDD		**Groups**				
		Group 1 (n = 25)	**Group 2 (n = 25)**	**Group 3 (n = 22)**	**Total**	***P***
Initial Examination	Mean ± SD	5.75 ± 0.41	4.84 ± 0.38	6.00 ± 0.33	5.37 ± 0.62	[a]***0.001***
	Median (Min-Max)	5.5 (5.3-6.6)	4.9 (3.8-5.5)	6 (5.5-6.3)	5.4 (3.8-6.6)	
1 Week	Mean ± SD	5.30 ± 0.21	4.68 ± 0.36	6.00 ± 0.29	5.09 ± 0.52	[a]***0.001***
	Median (Min-Max)	5.3 (4.9-5.8)	4.7 (3.7-5.4)	6.1 (5.6-6.3)	5.1 (3.7-6.3)	
1 Month	Mean ± SD	4.94 ± 0.28	4.42 ± 0.37	6.10 ± 0.20	4.82 ± 0.59	[a]***0.001***
	Median (Min-Max)	4.9 (4.1-5.4)	4.6 (3.6-4.9)	6.1 (5.9-6.3)	4.8 (3.6-6.3)	
6 Months	Mean ± SD	4.78 ± 0.22	4.41 ± 0.37	6.12 ± 0.19	4.75 ± 0.58	[a]***0.001***
	Median (Min-Max)	4.8 (4-5.1)	4.6 (3.6-4.9)	6.1 (5.9-6.4)	4.8 (3.6-6.4)	
Change from Initial to 1 Week	**Change**	-0.44 ± 0.26	-0.16 ± 0.90	-0.00 ± 0.10		[a]***0.001***
	P	[c]***0.001***	[c]***0.001***	[c]***1.000***		
Change from Initial to 1 Month	**Change**	-0.80 ± 0.40	-0.42 ± 0.17	0.10 ± 0.25		[a]***0.001***
	P	[c]***0.001***	[c]***0.001***	[c]***0.285***		
Change from Initial to 6 Months	**Change**	-0.96 ± 0.37	-0.43 ± 0.18	0.12 ± 0.28		[a]***0.001***
	P	[c]***0.001***	[c]***0.001***	[c]***0.414***		

LAD		**Groups**				
		Group 1 (n = 22)	**Group 2 (n = 22)**	**Group 3 (n = 5)**	**Total**	***P***
Initial Examination	Mean ± SD	4.86 ± 0.29	4.14 ± 0.3	4.94 ± 0.17	4.54 ± 0.47	[a]***0.001***
	Median (Min-Max)	4.9 (4.5-5.3)	4.2 (3.7-4.8)	4.9 (4.7-5.1)	4.5 (3.7-5.3)	
1 Week	Mean ± SD	4.53 ± 0.22	3.98 ± 0.27	4.94 ± 0.19	4.33 ± 0.41	[a]***0.001***
	Median (Min-Max)	4.5 (4.2-5)	4 (3.6-4.5)	5 (4.6-5.1)	4.3 (3.6-5.1)	
1 Month	Mean ± SD	4.15 ± 0.2	3.76 ± 0.25	4.96 ± 0.31	4.06 ± 0.43	[a]***0.001***
	Median (Min-Max)	4.2 (3.8-4.5)	3.8 (3.2-4.2)	5.1 (4.5-5.3)	4.1 (3.2-5.3)	
6 Months	Mean ± SD	3.92 ± 0.15	3.69 ± 0.23	5.02 ± 0.26	3.93 ± 0.43	[a]***0.001***
	Median (Min-Max)	3.9 (3.6-4.2)	3.7 (3.1-4.1)	5.1 (4.7-5.3)	3.9 (3.1-5.3)	
Change from Initial to 1 Week	**Change**	-0.33 ± 0.19	-0.15 ± 0.1	0.00 ± 0.33		[a]***0.001***
	P	[d]***0.001***	[d]***0.001***	[c]***0.891***		
Change from Initial to 1 Month	**Change**	-0.71 ± 0.2	-0.38 ± 0.20	0.02 ± 0.45		[a]***0.001***
	P	[d]***0.001***	[d]***0.001***	[c]***0.892***		
Change from Initial to 6 Months	**Change**	-0.94 ± 0.23	-0.45 ± 0.22	0.08 ± 0.41		[a]***0.001***
	P	[d]***0.001***	[d]***0.001***	[c]***0.588***		

[a]Kruskal-Wallis Test; [c]Wilcoxon Signed Ranks Test; ***P* < 0.01. Group 1: HF (+) KT (+cc); Group 2: HF (-) KT (+); Group 3: HF (+) KT (-).
HF, Heart Failure; KT, Kidney Transplantation; LAD, Left Atrial Diameter; LVEF, Left Ventricular Ejection Fraction; LVIDD, Left Ventricular Internal Diastolic Diameter.

Supplementary Table 4. Evaluation of LV-GLS, Sm, and LVMI Measurements by Groups

GLS		Groups				
		Group 1 (n = 25)	Group 2 (n = 25)	Group 3 (n = 22)	Total	*P*
Initial Examination	Mean ± SD	10.11 ± 2.99	17.66 ± 3.72	7.8 ± 2.45	13.26 ± 5.19	[a]***0.001***
	Median (Min-Max)	8.9 (6-15.6)	18 (2.1-20.7)	7.6 (5.7-11.8)	13.6 (2.1-20.7)	
1 Week	Mean ± SD	14.54 ± 1.44	18.89 ± 1.47	8.42 ± 2.51	15.87 ± 3.62	[a]***0.001***
	Median (Min-Max)	14.6 (11.6-17.2)	18.6 (17.2-21.4)	8.1 (6-11.7)	16.5 (6-21.4)	
1 Month	Mean ± SD	17.18 ± 0.8	19.62 ± 1.48	9.74 ± 2.22	17.51 ± 3.17	[a]***0.001***
	Median (Min-Max)	17 (15.9-18.9)	19.6 (17.7-22.8)	10.2 (5.9-11.5)	17.8 (5.9-22.8)	
6 Months	Mean ± SD	18.62 ± 0.89	19.66 ± 1.51	9.5 ± 1.93	18.16 ± 3.25	[a]***0.001***
	Median (Min-Max)	18.6 (17.5-21)	19.5 (17.8-23)	10.3 (6.1-10.8)	18.6 (6.1-23)	
Change from Initial to 1 Week	**Change**	4.43 ± 2.44	1.23 ± 3.94	0.62 ± 1.12		[a]***0.001***
	P	[c]***0.001***	[c]***0.001***	[c]***0.131***		
Change from Initial to 1 Month	**Change**	7.07 ± 2.41	1.96 ± 4	1.94 ± 1.96		[a]***0.001***
	P	[c]***0.001***	[c]***0.001***	[c]***0.138***		
Change from Initial to 6 Months	**Change**	8.51 ± 3.32	2 ± 4.01	1.7 ± 2.19		[a]***0.001***
	P	[c]***0.001***	[c]***0.001***	[c]***0.138***		

Sm		Groups				
		Group 1 (n = 25)	Group 2 (n = 25)	Group 3 (n = 22)	Total	*p*
Initial Examination	Mean ± SD	0.06 ± 0.01	0.12 ± 0.01	0.06 ± 0.02	0.09 ± 0.03	[a]***0.001***
	Median (Min-Max)	0.06 (0.05-0.09)	0.11 (0.09-0.14)	0.05 (0.04-0.08)	0.08 (0.04-0.14)	
1 Week	Mean ± SD	0.09 ± 0.02	0.12 ± 0.01	0.07 ± 0.01	0.1 ± 0.03	[a]***0.001***
	Median (Min-Max)	0.09 (0.01-0.11)	0.12 (0.11-0.15)	0.06 (0.05-0.08)	0.1 (0.01-0.15)	
1 Month	Mean ± SD	0.12 ± 0.01	0.14 ± 0.01	0.07 ± 0.01	0.12 ± 0.02	[a]***0.001***
	Median (Min-Max)	0.12 (0.1-0.14)	0.14 (0.12-0.16)	0.06 (0.06-0.08)	0.12 (0.06-0.16)	
6 Months	Mean ± SD	0.12 ± 0.03	0.13 ± 0.04	0.07 ± 0.01	0.12 ± 0.04	[a]***0.004***
	Median (Min-Max)	0.13 (0.01-0.15)	0.14 (0.02-0.16)	0.07 (0.06-0.08)	0.13 (0.01-0.16)	
Change from Initial to 1 Week	**Change**	0.02 ± 0.02	0.01 ± 0.01	0.01 ± 0.01		[a]***0.001***
	P	[c]***0.001***	[c]***0.001***	[c]***0.102***		
Change from Initial to 1 Month	**Change**	0.05 ± 0.02	0.02 ± 0.01	0.01 ± 0.01		[a]***0.001***
	P	[c]***0.001***	[c]***0.001***	[c]***0.059***		
Change from Initial to 6 Months	**Change**	0.06 ± 0.03	0.01 ± 0.04	0.01 ± 0.01		[a]***0.001***
	P	[c]***0.001***	[c]***0.008***	[c]***0.059***		

LVMI		Groups				
		Group 1 (n = 25)	Group 2 (n = 25)	Group 3 (n = 22)	Total	*P*
Initial Examination	Mean ± SD	208.77 ± 31.71	119.68 ± 31.17	203.94 ± 36.65	168.28 ± 54.25	[a]***0.001***
	Median (Min-Max)	202.2 (167-277.2)	120.3 (63-176.6)	194.1 (166.1-243.9)	173.2 (63-277.2)	
1 Week	Mean ± SD	170.01 ± 17.63	113.28 ± 29.71	196.23 ± 33.61	147.21 ± 40.41	[a]***0.001***
	Median (Min-Max)	168.7 (147.7-209.2)	112.7 (60.4-166)	199.4 (155.2-237.7)	155 (60.4-237.7)	
1 Month	Mean ± SD	147.36 ± 22.17	100.51 ± 26.56	204.4 ± 30.88	132.14 ± 41.38	[a]***0.001***
	Median (Min-Max)	139.7 (120.9-203.1)	104.5 (57.9-150.6)	217.9 (154-231.6)	130.6 (57.9-231.6)	
6 Months	Mean ± SD	132.65 ± 16.42	100.01 ± 26.53	209.03 ± 31.12	125.79 ± 39.43	[a]***0.001***
	Median (Min-Max)	130.1 (111.4-181)	105.4 (53.6-150.6)	218.9 (155-231.6)	124.1 (53.6-231.6)	
Change from Initial to 1 Week	**Change**	-38.76 ± 26.69	-6.4 ± 3.56	-7.71 ± 13.31		[a]***0.001***
	P	[c]***0.001***	[d]***0.001***	[c]***0.225***		
Change from Initial to 1 Month	**Change**	-61.42 ± 23.32	-19.17 ± 9.26	0.45 ± 26.57		[a]***0.001***
	P	[c]***0.001***	[d]***0.001***	[c]***0.686***		
Change from Initial to 6 Months	**Change**	-76.13 ± 28.3	-19.67 ± 9.47	5.09 ± 35.85		[a]***0.001***
	P	[c]***0.001***	[d]***0.001***	[c]***0.686***		

[a]Kruskal-Wallis Test; [c]Wilcoxon Signed Ranks Test; [d]Paired Samples Test; ***P* < 0.01. Group 1: HF (+) KT (+); Group 2: HF (-) KT (+); Group 3: HF (+) KT (-). HF, Heart Failure; KT, Kidney Transplantation; LV-GLS, Left Ventricular Global Longitudinal Strain; LVMI, Left Ventricular Mass Index; Sm, Systolic Velocity of the Lateral Mitral Annulus.

Supplementary Table 5. Results of Correlation Analysis of Demographic Factors on Cardiac Functions

		GLS	***LAD***	***EF***
Age	rho	*-0.086*	*0.150*	*-0.022*
	p	*0.471*	*0.209*	*0.855*
Sex	rho	*-0.066*	*-0.114*	*0.057*
	p	*0.581*	*0.342*	*0.636*
HT	rho	*0.090*	*-0.094*	*0.047*
	p	*0.453*	*0.431*	*0.695*
Diabetes	rho	*0.002*	*-0.136*	*0.010*
	p	*0.984*	*0.254*	*0.934*
HD Month	rho	*-0.017*	*0.063*	*-0.019*
	p	*0.885*	*0.600*	*0.873*
Distensibility	rho	*0.487***	*-0.492***	*0.337***
	P	***0.000***	***0.000***	***0.004***

***P* < 0.01, **P* < 0.05 statistically significant; *P* > 0.05 not significant. 0 ≤ *r* ≤ 0.25: Very weak correlation; 0.26 ≤ *r* ≤ 0.49: Weak correlation; 0.50 ≤ *r* ≤ 0.69: Moderate correlation; 0.70 ≤ *r* ≤ 0.89: Strong correlation; 0.90 ≤ *r* ≤ 1: Very strong correlation (Source: Akgül vd. 2003); Spearman correlation test. Akgül A, Çevik O. İstatistiksel Analiz Teknikleri. Ankara: Emek Ofset; 2003:358.

Supplementary Annotation:

Ejection Fraction (EF) Measurements by Groups: During follow-up, EF in Group 1 increased significantly, while no change was observed in Group 3 and a slight increase occurred in Group 2. The change in EF for Group 1 was found to be significantly higher than that for Groups 2 and 3 (*P* = 0.001; *P* = 0.006; *P* < 0.01 for the first week; *P* = 0.001; *P* = 0.001; *P* < 0.01 for the first month; *P* = 0.001; *P* = 0.001; *P* < 0.01 for the sixth month) (Supplementary Table 1).

Left Ventricular Internal Diastolic Diameter (LVIDD) Measurements by Groups: The change in LVIDD in Group 1 was found to be significantly higher than in Groups 2 and 3 (*P* = 0.001; P = 0.001; *P* < 0.01 for the first week; *P* = 0.004; *P* = 0.001; *P* < 0.01 for the first month; *P* = 0.001; *P* = 0.001; *P* < 0.01 for the sixth month) (Supplementary Table 1).

Left Atrial Diameter (LAD) Measurements by Groups: The change in LAD in Group 1 was significantly higher than in Groups 2 and 3 (*P* = 0.008; *P* = 0.011; *P* < 0.05 for the first week; *P* = 0.001; *P* = 0.001; *P* < 0.01 for the first month; *P* = 0.001; *P* = 0.001; *P* < 0.01 for the sixth month) (Supplementary Table 1).

Systolic Velocity of Lateral Mitral Annulus (Sm) Measurements by Groups: The change in Sm in Group 1 was significantly higher than in Groups 2 and 3 (*P* = 0.001; *P* = 0.049; *P* < 0.05 for the first week; *P* = 0.001; *P* = 0.001; *P* < 0.01 for the first month; *P* = 0.001; *P* = 0.001; *P* < 0.01 for the sixth month) (Supplementary Table 2).

Global Longitudinal Strain (GLS) Measurements by Groups: Initial GLS values in Group 2 were significantly higher than those on Groups 1 and 3 (*P* = 0.001; *P* = 0.001; *P* < 0.01). For Group 1, following transplantation, the mean GLS increased by 4.43 ± 2.44% at the first week, 7.07 ± 2.41% at the first month, and 8.51 ± 3.32% at six months compared to initial examination, all statistically significant (*P* = 0.001; *P* = 0.001; *P* = 0.001; *P* < 0.01). Pairwise comparisons showed the change in GLS for Group 1 was significantly higher than in Groups 2 and 3 (*P* = 0.001; *P* = 0.011; *P* < 0.05 for the first week; *P* = 0.001; *P* = 0.009; *P* < 0.01 for the first month; *P* = 0.001; *P* = 0.008; *P* < 0.01 for the sixth month) (Supplementary Table 2).

Left Ventricular Mass Index (LVMI) Measurements by Groups: The initial LVMI value in Group 2 was significantly lower than in Groups 1 and 3 (*P* = 0.001; *P* = 0.005; *P* < 0.01) before transplantation. Pairwise comparisons revealed that the change in LVMI for Group 1 was significantly higher than in Groups 2 and 3 (*P* = 0.001; *P* = 0.001; *P* < 0.01 for the first week; *P* = 0.001; *P* = 0.001; *P* < 0.01 for the first month; *P* = 0.001; *P* = 0.001; *P* < 0.01 for the sixth month) (Supplementary Table 1).

Supplementary Videos:

Video 1. Automated left ventricular quantification images of a Group 1 patient before kidney transplantation, showing decreased left ventricular global longitudinal strain values.

Video 2. Automated left ventricular quantification images of the same Group 1 patient after kidney transplantation, showing improved left ventricular global longitudinal strain values.

Video 3. Left ventricular four-chamber view depicting impaired left ventricular systolic function before kidney transplantation.

Video 4. Left ventricular four-chamber view demonstrating recovered left ventricular systolic function after kidney transplantation.