

Original Article

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Evaluation of left ventricular systolic functions in two-dimensional speckle-tracking echocardiography in children with chronic renal failure

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Abstract

Background and aim: Chronic kidney disease may lead to left ventricular dysfunction. Early detection of cardiovascular disease in children with chronic kidney disease is essential to prevent cardiovascular morbidity and mortality in early adulthood. This study aimed to document the dysfunction using methods such as two-dimensional speckle-tracking echocardiography in the early stage. **Methods:** A total of 34 patients diagnosed with chronic kidney disease (mean age \pm standard deviation, 10.5 ± 4.1 years) and 37 sex- and age-matched (mean age 9.8 ± 4.2 years) healthy controls were studied. The results of the two groups were compared along with those of the published studies. **Results:** The echocardiography measurements had no significant difference in the end-diastolic and end-systolic diameter values of left ventricular, ejection fraction, shortening fraction, mitral E value, mitral A value, and E/A ratio between the groups. Pulmonary artery systolic and diastolic pressure and left ventricular mass index were significantly higher in the patient group ($p < 0.01$). The longitudinal global strain values in the apical four-chamber, three-chamber, and two-chamber views and the total global strain values were significantly lower in the patients ($p < 0.01$). The circumferential global strain values in the apical, mid, basal, and total global strain were lower in the patient group, but this difference was statistically significant in the apical global and total global strain values ($p < 0.05$). **Conclusions:** Speckle-tracking echocardiography might help identify subclinical left ventricular dysfunction in patients with chronic kidney disease with unremarkable conventional echocardiography.

Cardiovascular disease is the main reason of mortality and morbidity in patients with chronic kidney disease.^{1,2} Left ventricular hypertrophy and left ventricular systolic and diastolic dysfunction are the most common cardiovascular abnormalities, which are important causes of morbidity and mortality in chronic kidney disease.^{3,4} These cardiac abnormalities might result from a variety of mechanisms, including uremia, sodium and fluid retention, hypertension, anemia, hyperparathyroidism, and abnormalities in the calcium–phosphate homeostasis.^{4,5} Early detection of cardiovascular disease in children with chronic kidney disease would provide an opportunity for targeted intervention in patients to prevent cardiovascular morbidity and mortality.⁶

In patients with chronic kidney disease, conventional transthoracic echocardiography is unable to detect early deterioration of cardiac function.^{7,8} Tissue Doppler imaging is a convenient method to detect early cardiac dysfunction. However, the most important disadvantage of this method is the angle dependency of the Doppler technique. Therefore, this study aimed to document the subclinical cardiac dysfunction in the early stages of chronic kidney disease using novel echocardiography techniques, such as two-dimensional speckle-tracking echocardiography.^{9,10} The advantages of this method are that it is angle independent, less load-dependent, easier to analyse and interpret compared with tissue Doppler imaging, and has less variability between different echocardiographers or the same echocardiographer at different times.¹⁰

Methods

Participants

This prospective study was conducted at the outpatient pediatric nephrology and cardiology departments of the Dokuz Eylul University. The local ethics committee approved this prospective study (registration number: 2014/13-08). The study population included 34 paediatric patients with chronic kidney disease (19 females and 15 males, mean age 10.5 ± 4.1 years, range 2–18 years) with the glomerular filtration rate less than $90 \text{ ml/minute/1.73 m}^2$. Stages of patients were determined according to the kidney disease: improving global outcomes (KDIGO)

classification.¹¹ The glomerular filtration rate of children with chronic kidney disease was calculated by the Schwartz formula. The exclusion criteria were as follows: acute renal failure, congenital or acquired heart disease, low ejection fraction (EF < 60%), arrhythmia, other systemic diseases, and suboptimal image quality. Transthoracic echocardiographic evaluations were performed, 2 hours before haemodialysis. Anthropometric measurements, arterial blood pressure, and 12-lead electrocardiography of the patients were recorded. The selected control group consisted of 37 sex- and age-matched healthy participants with normal physical, laboratory, electrocardiography, and transthoracic echocardiographic results.

Echocardiographic studies

Echocardiographic examinations were performed using an ultrasound device (model iE33, Philips Medical Systems, Netherlands) with an S5–1-MHz transducer by the same observer, blinded to the clinical condition of the patients. Two researchers who were similarly blinded to the clinical condition and grouping of the patients performed the data analysis offline.

The transthoracic echocardiography images were obtained in standard parasternal, apical, and subcostal views. The interventricular septal diastolic and systolic thicknesses, left ventricular end-diastolic and end-systolic diameters, and left ventricular posterior wall diastolic and systolic thickness were measured in the parasternal long-axis M-mode echocardiographic evaluation. The systolic function was assessed from apical four-chamber and two-chamber views by measuring the left ventricular ejection fraction and shortening fraction using the modified biplane Simpson's method. The mitral valve inflow Doppler flow was measured in an apical four-chamber image. Mitral early filling (E), late filling (A), and the E/A ratio were derived to evaluate the left ventricular diastolic function. The pulmonary artery systolic pressure was determined using the Bernoulli equation for the Doppler continuous wave measurement of tricuspid valve insufficiency flow. The right atrial pressure was evaluated using the inferior caval vein inspiratory collapsibility. Using these measurements, the left ventricular mass was computed according to the Devereux formula. The left ventricular mass index was calculated as the ratio between left ventricular mass and body surface area. The left atrial end-diastolic volume was calculated using the prolate ellipsoid method. The left atrial volume index was measured by dividing the left atrial end-diastolic volume by the body surface area calculated using the Mosteller formula.

Colour tissue Doppler echocardiography

The left ventricular myocardial colour tissue Doppler imaging was assessed during both contraction and relaxation. The sample volume was placed at the lateral margin of the mitral annulus on the apical four-chamber view. At least four consecutive cardiac cycles were recorded during the best image quality for evaluation. A Doppler frame scanning rate of 100–140 Hz with 40–80 frames/seconds was used. The systolic velocity (S'), early diastolic myocardial velocity (E'), late diastolic myocardial velocity (A') at the time of atrial contraction, and E'/A' ratio were determined. Late diastole was determined using the index of left ventricular compliance: a ratio of peak trans-mitral early filling (E) velocity to early diastolic mitral annular (E') velocity.

Two-dimensional speckle-tracking echocardiography

For the speckle-tracking echocardiographic evaluation with simultaneous electrocardiography at frame rates of 70–100 frames/

second, apical four-chamber, apical three-chamber, and apical two-chamber images were recorded in the apical view and in the parasternal short-axis view apical, medial, and basal images. At least four consecutive cardiac cycles were recorded during the best image quality for evaluation. The recorded images were transferred onto a DVD and analysed on a computer using the QLAB software (Philips Medical Systems). The mitral annulus lateral and septal and the left ventricular apical endocardial planes were marked for each apical three chambers, providing for automated generation of the left ventricular wall by the programme. The left ventricular endocardial–myocardial border was adjusted manually on the systolic frames. Peak systolic strain, peak systolic strain rate, and global strain values were calculated automatically by the software for the six segments (apical, middle, and basal) based on septum and left ventricular lateral wall motion values. In all the three parasternal views, the endocardial–myocardial border was adjusted manually after the programme automatically generated the ventricular wall.

Speckle-tracking echocardiography is a new technique for evaluating the ventricular function. Regional myocardial functions are evaluated with tissue Doppler echocardiography and speckle-tracking echocardiography. Due to the angle dependence in tissue Doppler echocardiography, the velocity measured with a transducer may differ depending on the variations in tethering and heart motion. On the contrary, in speckle-tracking echocardiography, regional myocardial functions can be evaluated along both the longitudinal and transverse axes regardless of the angle and direction of motion. In speckle-tracking echocardiography, the myocardium is divided into 17 segments, reflecting as much coronary perfusion as possible (Fig 1). And the dimensional deformations, that is, “strain” and deformation velocity in these segments, are evaluated as “strain rate.” Besides segmental functions, global functions were also evaluated. Published reports have shown the superiority of these parameters over transthoracic echocardiography and tissue Doppler imaging in identifying ventricular dysfunction.

Study power

In this sample size, the effect size was calculated as 0.67, at 85% power and 0.05 alpha error, using the G*Power 3.1.9.2 software.

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software, version 22.0 (SPSS Inc., Chicago, IL, United States of America). Continuous data were described as mean \pm standard deviation, while categorical data were presented as the number of patients. The chi-square test was used for comparing categorical variables, while parametric continuous variables were compared using the Student's t-test. Data were checked for normal distribution using the Kolmogorov–Smirnov test. The correlation between two variables was calculated using Pearson's correlation coefficient (r) analysis of variance. A value of $p < 0.05$ was considered statistically significant. The evaluations were repeated by a second, independent observer, to assess inter-observer variability. Inter-observer variability was calculated by dividing the absolute difference between observations by the mean of the two observations.

Results

Cohort characteristics

The characteristics of the patients and the control group are shown in Table 1. The mean age of the 34 patients (19 female and 15 male)

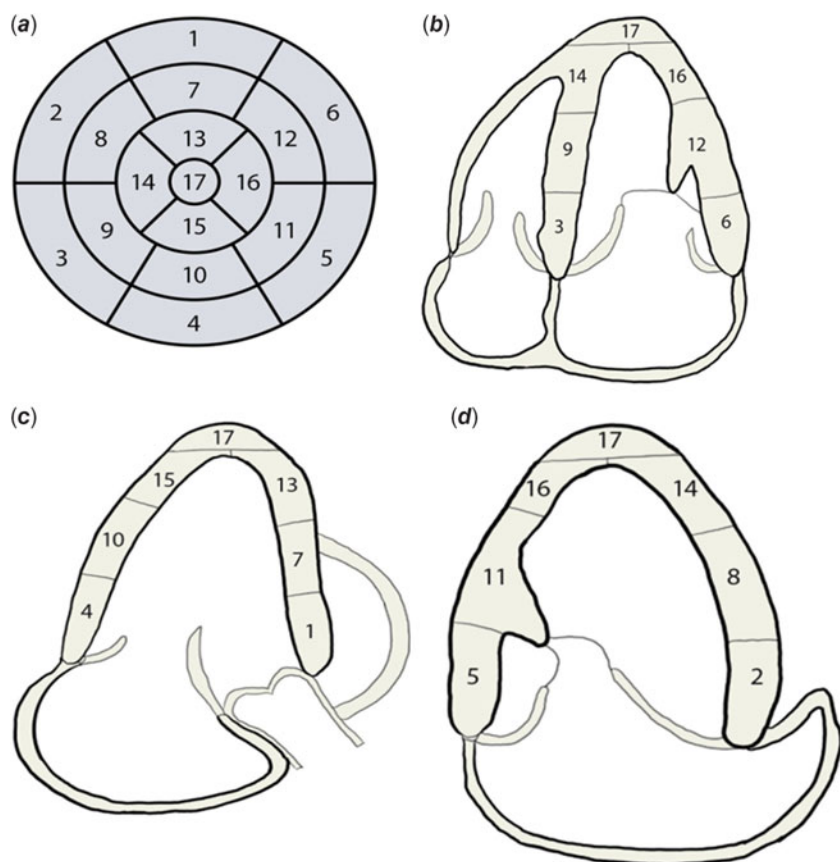


Figure 1. Schematic diagram (a) of the LV segmentation, in apical four-chamber (b), three-chamber (c), and two-chamber views (d).

with chronic kidney disease was 10.5 ± 4.1 years, while that of 37 healthy volunteers (20 female and 17 male) was 9.8 ± 4.2 years. No significant differences were found between the two groups in terms of sex, age, weight, and body mass index ($p > 0.05$). The glomerular filtration rate mean was 37.5 ± 26.2 ml/minute/ 1.73 m² in the patient group. Eight patients were in class II, 10 in class III, 6 in class IV, and 10 in class versus of chronic kidney disease. Among the patients, 10 were on regular haemodialysis treatment. The main causes of chronic kidney disease were congenital renal anomalies (41%), reflux nephropathy (32%), and glomerular disease (26%). The systolic and diastolic blood pressure values of the patients were also significantly higher than those of the controls ($p < 0.05$). A total of 14 patients were treated with antihypertensive medications.

Echocardiographic findings

The transthoracic echocardiography, Doppler, and colour tissue Doppler imaging results are summarised in Table 2. Analysis of transthoracic echocardiographic data of the two groups showed no significant differences in the interventricular septal and left ventricular posterior wall diastolic thicknesses, left ventricular end-diastolic and end-systolic diameters, ejection fraction, shortening fraction, left ventricular mass, and left atrial volume index between the groups. However, pulmonary artery systolic pressure, pulmonary artery diastolic pressure, and left ventricular mass index were significantly higher in the patient group compared with the controls ($p < 0.01$). No significant difference was found in the mitral E value, mitral A value, and E/A ratio between the groups. The colour tissue Doppler imaging showed a significant decrease in the E' value, which resulted in a significant decrease in the E'/A' and

increase in the E/E' ratios between the groups ($p < 0.05$). However, no significant difference was found in the S' and A' values between the groups.

Speckle-tracking echocardiography

The speckle-tracking echocardiographic results of the left ventricular longitudinal peak strain, global strain, and systolic strain rate in the study group are given in Table 3. The apical four-chamber, three-chamber, two-chamber, and total global strain values were significantly lower in the patients group compared with the control group ($p > 0.01$). Moreover, the peak systolic strain values in all segments were lower in the patient group, compared with the control group, but this difference was statistically significant in all 15 segments ($p < 0.05$). The longitudinal systolic strain rate of all 17 segments was lower in the patients. However, this difference was statistically significant only in the measurements of all six segments ($p < 0.05$).

Circumferential peak strain, global strain, and systolic strain rate values of the left ventricular wall results of the study group are given in the Table 4. The apical, mid, basal, and total global circumferential strain values were lower in the patient group, but this difference was statistically significant in the apical global and total global strain values ($p < 0.05$). The circumferential segmental strain values in the all 14 segments were lower in the patients group, compared with the control group. However, this difference was statistically significant only in the measurements of all three segments ($p < 0.05$). Circumferential systolic strain rates of all six segments were lower in the patients. However, this difference was statistically significant only in the measurements of all two segments ($p < 0.05$).

Table 1. Demographic and clinical characteristics of the study population

Parameters	Patients (n = 34)	Controls (n = 37)	p value
Sex (female/male)	19/15	20/17	>0.05
Age (year)	10.5 ± 4.1	9.8 ± 4.2	>0.05
Weight (kg)	33.8 ± 16.7	35.3 ± 15.3	>0.05
Height (cm)	132.0 ± 26.5	136.5 ± 25.6	>0.05
BMI	18.1 ± 4.9	18.0 ± 2.8	>0.05
SBP (mmHg)	114.6 ± 19.7	102.0 ± 7.9	<0.01
DBP (mmHg)	71.8 ± 15.6	59.0 ± 5.9	<0.01
GFR (ml/minute/1.73 m ²)	37.5 ± 26.2		
Haemoglobin (g/dl)	10.6 ± 1.3		
Creatinine (mg/dl)	3.2 ± 2.4		
Calcium (mg/dl)	9.6 ± 0.7		
Phosphorus (mg/dl)	5.1 ± 1.2		
CaxP product	49.8 ± 12.6		
Albumin (g/dl)	4.0 ± 0.6		
PTH (pg/ml)	309.3 ± 333.3		

BMI, Body mass index; Ca, calcium; DBP, diastolic blood pressure; GFR, glomerular filtration rate; P, Phosphorus; PTH, parathyroid hormone; SBP, systolic blood pressure

Table 2. Echocardiographic, Doppler, and tissue Doppler imaging parameters of the study population

Parameters	Patients (n = 34)	Controls (n = 37)	p value
IVSd (cm)	0.68 ± 0.16	0.62 ± 0.10	>0.05
LVDd (cm)	3.88 ± 0.72	3.99 ± 0.60	>0.05
LVDs (cm)	2.46 ± 0.47	2.55 ± 0.43	>0.05
LVPWd (cm)	0.68 ± 0.14	0.63 ± 0.10	>0.05
Ef (%)	66.65 ± 8.09	65.65 ± 7.42	>0.05
Fs (%)	37.03 ± 4.63	36.03 ± 3.71	>0.05
PAPs	33.03 ± 3.89	28.94 ± 2.86	<0.01
PAPd	10.69 ± 2.38	9.00 ± 2.13	<0.01
LVMi	42.33 ± 13.07	36.05 ± 8.30	0.02
LAVI	17.18 ± 5.71	15.46 ± 3.11	>0.05
Mitral E	93.08 ± 16.06	91.71 ± 15.72	>0.05
Mitral A	62.66 ± 12.69	57.86 ± 13.46	>0.05
Mitral E/A	1.51 ± 0.23	1.64 ± 0.35	>0.05
LV S'	9.35 ± 1.98	10.08 ± 1.89	>0.05
LV E'	14.95 ± 3.28	17.14 ± 4.16	0.01
LV A'	8.15 ± 1.73	8.11 ± 1.86	>0.05
LV E'/A'	1.88 ± 0.46	2.17 ± 0.54	0.02
LV E/E'	6.52 ± 1.94	5.44 ± 1.54	0.01

Ef, Ejection fraction; Fs, fractional shortening; IVSd, end-diastolic interventricular septum thickness; LAVI, left atrial volume index; LV A', left ventricular (LV) wall late diastolic velocity; LVDd, end-diastolic LV dimension; LVDs, end-systolic LV dimension; LV E', LV wall early diastolic velocity; LVMi, LV mass index; LVPWd, end-diastolic LV posterior wall thickness; LV S', LV wall systolic velocity; mitral A, late diastolic velocity; mitral E, early diastolic velocity; PAPd, pulmonary artery diastolic pressure; PAPs, pulmonary artery systolic pressure

According to the KDIGO classification, the second and third stages of chronic kidney disease were compared with the fourth and fifth stages of the disease (Table 5), and no significant differences were found among the results of conventional, and Doppler echocardiography, and colour tissue Doppler imaging, and speckle-tracking echocardiography measurements ($p > 0.05$).

A comparison of chronic kidney disease with and without hypertension (Table 5) showed that the left ventricular mass index was significantly higher in the group with hypertension ($p < 0.05$). However, No difference was found in the other values between the hypertensive and non-hypertensive groups, as in the comparison of early-stage and late-stage chronic kidney disease ($p > 0.05$).

The relationship between laboratory findings and speckle-tracking echocardiography results in chronic kidney disease is summarised in Table 6. No correlation was found of longitudinal and circumferential global and total global strain values with haemoglobin, creatinine, albumin, Calcium–phosphorus product and parathyroid hormone levels and glomerular filtration rate ($p > 0.05$).

The inter-observer variability for E'/A' ratio, global longitudinal strain, and global circumferential strain analysis was evaluated in a randomly selected sample of 15 patients. The inter-observer variability for E'/A' ratio, global longitudinal strain, and global circumferential strain was 4.8, 5.8, and 5.6%, respectively.

Discussion

Cardiovascular disease is a major complication in patients with chronic kidney disease and has a major impact on the morbidity and mortality of these patients. Several risk factors, such as hypertension caused by volume overload, anaemia, sodium retention, abnormalities in the calcium–phosphate homeostasis, and arteriovenous fistulas, might contribute to the development of cardiovascular disease. In addition, myocardial fibrosis resulting from chronic inflammation and accumulation of uremic toxins and chronic local ischemia due to insufficient vasodilator response, known as myocardial stunning, contribute to ventricular dysfunction.^{3,4} Transthoracic and Doppler echocardiography evaluation generally show normal results in the early stages of cardiac involvement. Cardiac dysfunction in the subclinical stage may be recognised using methods such as speckle-tracking echocardiography. Early diagnosis of patients with evidence of cardiac dysfunction would be advantageous. Therefore, it might be beneficial for the early start of effective treatment. Four recently published studies evaluated the ventricular function in paediatric patients with chronic kidney disease, using speckle-tracking echocardiography.

Demetgul et al, in their study comparing chronic kidney disease in pediatric patient and healthy control groups, found that the peak systolic strain values were significantly lower in the longitudinal and some circumferential segments in the patient group.¹² In a similar study, Yan et al found that peak systolic velocities decreased in the longitudinal basal and apical segments in the adult patients with chronic kidney disease.¹³ In this study, although left ventricular systolic function as assessed by transthoracic echocardiography appeared to be normal in all cases, the pathological findings of systolic dysfunction were revealed by speckle-tracking echocardiography. All of the global longitudinal strains, some of the global circumferential strains, and most of the segmental strain values were significantly lower in the patient group than the control group.

Huis et al compared dialysis patients, renal transplant patients, and the healthy control group, and found that dialysis patients and renal transplant patients had statistically significantly lower longitudinal strain values than the control group. However, there was no

Table 3. Comparison of left ventricular longitudinal strain and strain rates between patients and controls

		Longitudinal strain (cm/seconds)			Longitudinal strain rate (per second)		
		Patients (n = 34)	Controls (n = 37)	p value	Patients (n = 34)	Controls (n = 37)	p value
Four chamber (4C)	BIS	-16.7 ± 5.7	-21.2 ± 4.7	<0.01	-1.43 ± 0.45	-1.65 ± 0.63	>0.05
	MIS	-20.3 ± 7.5	-23.4 ± 6.2	>0.05	-1.53 ± 0.45	-1.73 ± 0.63	>0.05
	APS	-18.0 ± 7.6	-23.8 ± 6.3	<0.01	-1.24 ± 0.43	-1.52 ± 0.39	<0.01
	APEX	-17.0 ± 4.9	-22.1 ± 4.2	<0.01	-1.15 ± 0.32	-1.39 ± 0.40	<0.01
	APL	-16.7 ± 5.3	-20.7 ± 5.4	<0.01	-1.34 ± 0.57	-1.48 ± 0.44	>0.05
	MAL	-19.7 ± 6.7	-22.9 ± 6.7	0.04	-1.75 ± 0.50	-2.03 ± 0.57	0.03
	BAL	-17.9 ± 6.2	-21.6 ± 7.8	0.03	-1.80 ± 0.45	-1.91 ± 0.69	>0.05
Three chamber (3C)	BIL	-18.9 ± 7.3	-21.8 ± 5.5	>0.05	-1.83 ± 0.54	-1.95 ± 0.63	>0.05
	MIL	-20.4 ± 6.8	-22.6 ± 5.7	>0.05	-1.89 ± 0.50	-1.84 ± 0.43	>0.05
	APL	-16.7 ± 6.6	-21.2 ± 5.9	<0.01	-1.41 ± 0.49	-1.70 ± 0.41	<0.01
	APEX	-17.1 ± 5.4	-21.5 ± 3.7	<0.01	-1.35 ± 0.50	-1.47 ± 0.39	>0.05
	APA	-18.6 ± 6.3	-22.4 ± 4.2	<0.01	-1.56 ± 0.56	-1.55 ± 0.45	>0.05
	MAS	-21.1 ± 6.6	-25.9 ± 6.2	<0.01	-1.79 ± 0.55	-1.89 ± 0.55	>0.05
	BAS	-15.9 ± 5.1	-21.8 ± 5.5	<0.01	-1.28 ± 0.45	-1.59 ± 0.48	>0.05
Two chamber (2C)	BI	-19.2 ± 5.5	-21.6 ± 7.0	>0.05	-1.92 ± 0.60	-1.84 ± 0.62	>0.05
	MI	-18.7 ± 6.8	-22.2 ± 7.1	0.04	-1.79 ± 0.65	-2.15 ± 0.85	0.04
	API	-17.0 ± 4.2	-19.8 ± 6.5	0.04	-1.45 ± 0.42	-1.55 ± 0.41	>0.05
	APEX	-17.2 ± 4.2	-20.3 ± 4.2	<0.01	-1.29 ± 0.33	-1.30 ± 0.22	>0.05
	APA	-18.3 ± 7.5	-21.8 ± 4.9	0.02	-1.46 ± 0.43	-1.42 ± 0.34	>0.05
	MA	-21.2 ± 5.7	-22.3 ± 6.5	>0.05	-1.68 ± 0.50	-1.73 ± 0.62	>0.05
	BA	-16.5 ± 5.9	-19.1 ± 6.0	>0.05	-1.43 ± 0.45	-1.65 ± 0.49	0.05
4C total strain		-16.6 ± 3.6	-21.0 ± 2.9	<0.01			
3C total strain		-16.6 ± 3.9	-21.0 ± 2.7	<0.01			
2C total strain		-16.7 ± 3.6	-19.7 ± 2.9	<0.01			
Total global strain		-16.6 ± 3.2	-20.6 ± 2.1	<0.01			

APA, Apical anterior; API, apical inferior; APL, apical lateral; APS, apical septal; BA, basal anterior; BAL, basal anterolateral; BAS, basal antero-septal; BI, basal inferior; BIL, basal inferolateral; BIS, basal inferoseptal; MA, mid-anterior; MAL, mid-anterolateral; MAS, mid-anteroseptal; MI, mid-inferior; MIL, mid-inferolateral; MIS, mid-inferoseptal

statistically significant difference between dialysis patients and renal transplant patients.¹⁴ Especially the absence of any difference between the two patient groups suggested that irreversible cardiac impairment started early and cardiac functions did not improve after transplantation. A study conducted on patients with non-uremic hypertension showed that systolic dysfunction occurred in the late stages, although ventricular hypertrophy was detected in the early stages. On the contrary, systolic dysfunction has been shown to start early due to myocardial fibrosis with the effect of chronic inflammation and uremic toxins on patients with chronic kidney disease.^{15,16} In line with the previous studies, this study compared the early-stage (stage 2–3) and late-stage (stage 3–4) chronic kidney disease groups with the control group and found that both early-stage and late-stage longitudinal global and circumferential global strain values were statistically significant compared with those of the control group. However, no statistically significant difference was found between the early-stage and late-stage chronic kidney disease. Huis et al evaluated the left ventricular systolic function of the control group with dialysis and transplant with tissue Doppler imaging; they did not detect any statistically

significant difference in the S' wave velocities, as in this study.¹⁴ This suggested that tissue Doppler imaging changes occurred late in the left ventricular systolic dysfunction and speckle-tracking echocardiography was superior to tissue Doppler imaging in detecting systolic dysfunction.

Rakha et al found that global and segmental longitudinal and circumferential strain values were lower than those before dialysis in patients with end-stage chronic kidney disease. They explained that blood volume, arterial pressure, electrolytes, and deterioration in neuronal response triggered acute cardiac stress as a result of haemodialysis.¹⁰ Similar studies reported on the activation of different ways of injury in the chronic period of haemodynamic and metabolic changes triggered by haemodialysis. As a result of such endothelial dysfunction, inflammatory activation, high-energy phosphate depletion, and impaired neuronal response, a pathology called “myocardial stunning” due to ischemia and fibrosis was developed. Furthermore, the aforementioned explained the ejection fraction invariance caused by the development of the active compensatory hyperkinesia of unaffected segments during myocardial stunning.^{17,18} However, Burton et al in their study on adult

Table 4. Comparison of left ventricular circumferential strain and strain rates between patients and controls

		Circumferential strain (cm/seconds)			Circumferential strain rate (per second)		
		Patients (n = 34)	Controls (n = 37)	p value	Patients (n = 34)	Controls (n = 37)	p value
Basal	BAS	-27.4 ± 7.3	-30.9 ± 7.9	>0.05	-2.04 ± 0.44	-2.11 ± 0.50	>0.05
	BA	-19.3 ± 8.3	-23.0 ± 6.8	0.04	-1.79 ± 0.64	-1.75 ± 0.44	>0.05
	BAL	-23.1 ± 6.9	-21.3 ± 6.4	>0.05	-1.71 ± 0.40	-2.09 ± 0.69	<0.01
	BIL	-20.0 ± 5.9	-22.1 ± 6.5	>0.05	-1.93 ± 0.51	-1.96 ± 0.68	>0.05
	BI	-20.1 ± 6.4	-21.0 ± 6.2	>0.05	-1.80 ± 0.41	-1.73 ± 0.41	>0.05
	BIS	-23.8 ± 8.2	-24.4 ± 6.8	>0.05	-1.98 ± 0.59	-1.83 ± 0.43	>0.05
Mid	MAS	-26.2 ± 8.4	-28.1 ± 9.1	>0.05	-2.09 ± 0.60	-2.09 ± 0.59	>0.05
	MA	-22.2 ± 8.1	-24.7 ± 7.5	>0.05	-2.05 ± 0.57	-1.98 ± 0.51	>0.05
	MAL	-21.7 ± 8.8	-24.5 ± 6.7	>0.05	-2.02 ± 0.62	-1.96 ± 0.59	>0.05
	MIL	-21.2 ± 6.1	-19.7 ± 6.3	>0.05	-1.99 ± 0.67	-1.77 ± 0.43	>0.05
	MI	-21.6 ± 7.3	-23.7 ± 6.5	>0.05	-1.94 ± 0.50	-1.87 ± 0.42	>0.05
	MIS	-22.9 ± 8.8	-25.3 ± 5.7	>0.05	-1.91 ± 0.61	-1.71 ± 0.43	>0.05
Apical	APS	-23.9 ± 8.2	-25.5 ± 7.4	>0.05	-1.92 ± 0.51	-1.88 ± 0.47	>0.05
	APA	-20.5 ± 6.7	-28.0 ± 5.3	<0.01	-1.63 ± 0.38	-1.92 ± 0.43	<0.01
	APL	-21.9 ± 6.3	-23.8 ± 6.0	>0.05	-1.83 ± 0.51	-1.77 ± 0.42	>0.05
	API	-20.9 ± 7.3	-24.5 ± 5.8	0.02	-1.75 ± 0.54	-1.83 ± 0.48	>0.05
Basal total strain		-20.9 ± 5.4	-22.8 ± 3.4	>0.05			
Mid total strain		-21.5 ± 5.7	-23.3 ± 3.7	>0.05			
Apical total strain		-21.3 ± 6.0	-25.1 ± 4.6	<0.01			
Total global strain		-21.1 ± 5.0	-23.7 ± 3.3	0.015			

APA, Apical anterior; API, apical inferior; APL, apical lateral; APS, apical septal; BA, basal anterior; BAL, basal anterolateral; BAS, basal aneroseptal; BI, basal inferior; BIL, basal inferolateral; BIS, basal inferoseptal; MA, mid-anterior; MAL, mid-anterolateral; MAS, mid-anteroseptal; MI, mid-inferior; MIL, mid-inferolateral; MIS, mid-inferoseptal

Table 5. Comparison of echocardiographic parameters between early-stage with late-stage chronic kidney disease and normotensive with hypertensive chronic kidney disease

	Stage 2-3 (n = 18)	Stage 4-5 (n = 16)	p value	Normotensive (n = 20)	Hypertensive (n = 14)	p value
LVDd	3.89 ± 0.60	3.85 ± 0.84	>0.05	3.84 ± 0.62	4.04 ± 0.78	>0.05
LVDs	2.47 ± 0.40	2.43 ± 0.53	>0.05	2.45 ± 0.41	2.50 ± 0.53	>0.05
PAPs	32.50 ± 3.05	33.59 ± 4.68	>0.05	32.00 ± 3.79	34.00 ± 4.00	>0.05
LVMI	40.75 ± 10.12	44.10 ± 15.91	>0.05	38.46 ± 8.28	48.20 ± 15.83	0.03
Mitral E/A	1.54 ± 0.24	1.47 ± 0.20	>0.05	1.57 ± 0.24	1.42 ± 0.17	>0.05
LV S'	9.15 ± 1.74	9.60 ± 2.26	>0.05	9.55 ± 2.05	9.28 ± 1.94	>0.05
LV E'/A'	1.91 ± 0.48	1.83 ± 0.45	>0.05	2.07 ± 0.49	1.66 ± 0.35	>0.05
4-Chamber TS	16.42 ± 3.79	16.93 ± 3.51	>0.05	17.86 ± 3.97	15.79 ± 2.99	>0.05
3-Chamber TS	16.32 ± 4.08	17.06 ± 3.95	>0.05	17.11 ± 2.85	16.93 ± 5.14	>0.05
2-Chamber TS	16.77 ± 3.28	16.81 ± 4.11	>0.05	17.41 ± 3.15	16.50 ± 4.27	>0.05
Global longitudinal TS	16.52 ± 3.20	16.75 ± 3.37	>0.05	17.38 ± 2.68	16.36 ± 3.75	>0.05
Basal TS	20.29 ± 6.48	21.66 ± 4.16	>0.05	20.74 ± 6.10	21.07 ± 5.53	>0.05
Mid TS	20.56 ± 6.91	22.60 ± 4.27	>0.05	21.94 ± 5.85	20.46 ± 6.08	>0.05
Apical TS	20.80 ± 6.81	21.93 ± 5.33	>0.05	22.33 ± 5.42	21.15 ± 7.08	>0.05
Global circumferential TS	20.34 ± 6.04	21.93 ± 3.69	>0.05	21.50 ± 5.34	20.62 ± 5.24	>0.05

LV A', Left ventricular (LV) wall late diastolic velocity; LVDd, end-diastolic LV dimension; LVDs, end-systolic LV dimension; LV E', LV wall early diastolic velocity; LVMI, LV mass index; LV S', LV wall systolic velocity; mitral A, late diastolic velocity; mitral E, early diastolic velocity; PAPs, pulmonary artery systolic pressure; TS, total strain

Table 6. Correlation between speckle tracking echocardiography and laboratory findings

	Hemoglobin		Creatinine		Albumin		CaxP		PTH		GFR	
	R	p	R	p	R	p	R	p	R	p	R	p
4-Chamber TS	0.19	0.30	0.10	0.59	-0.16	0.38	0.18	0.30	-0.05	0.76	0.01	0.91
3-Chamber TS	0.11	0.55	-0.02	0.89	-0.11	0.54	0.19	0.29	0.18	0.31	-0.14	0.42
2-Chamber TS	0.09	0.62	-0.19	0.30	0.01	0.95	0.20	0.26	0.01	0.94	-0.15	0.38
Global Longitudinal TS	0.16	0.38	-0.07	0.70	-0.07	0.69	0.21	0.25	0.05	0.77	-0.09	0.59
Basal TS	0.04	0.81	-0.11	0.55	-0.25	0.18	0.07	0.71	0.11	0.53	-0.07	0.69
Mid TS	0.08	0.67	0.03	0.85	-0.22	0.25	0.29	0.12	0.15	0.43	-0.20	0.26
Apical TS	0.29	0.14	0.06	0.75	-0.13	0.50	0.33	0.07	0.26	0.16	-0.26	0.14
Global Circumferential TS	0.13	0.50	0.02	0.90	-0.26	0.17	0.29	0.12	0.20	0.29	-0.24	0.17

Ca, calcium; GFR, glomerular filtration rate; P, Phosphorus; PTH, parathyroid hormone; TS, total strain
 p < 0.05 significant

patients, showed that reversible segmental left ventricular dysfunction progressed and became irreversible within 1 year in patients undergoing haemodialysis.¹⁹ As a result, it was assumed that all segments were affected by myocardial stunning during the period when ejection fraction started to decrease. On the contrary, several other studies on paediatric and adult patients showed that the global longitudinal strain value did not change after haemodialysis.^{20,21–24} In this study, while the segmental longitudinal strain rate and the circumferential strain rate were lower in 23 segments compared with the control group, only 8 segments were statistically significant. Similarly, Demetgul et al found a statistically significant decrease in the longitudinal and circumferential strain rate values in the patient group.¹² In addition, despite no difference in the mitral E/A ratios between the patient and control groups, they showed that the diastolic strain rate was statistically significantly lower in the patient group compared with the control group, and early diastolic dysfunction could be detected in addition to the left ventricular systolic dysfunction.

On the contrary, the longitudinal global strain and circumferential global strain values were statistically significantly lower in both early- and late-stage chronic kidney disease groups compared with the control group.

In summary, the present study showed that speckle-tracking echocardiography might be useful in the early detection of left ventricular systolic dysfunction in children with chronic renal failure. The ease of use of these techniques and the availability of reference values might suggest their possible use in the follow-up of patients with chronic kidney disease. Demonstration of early cardiac effects in these patients might help minimise cardiac impairment by taking precautions. Further studies are needed to determine the clinical significance of these findings.

Study limitations

This study had several limitations. The first was that the study population was relatively small. The second was that the after-dialysis parameters were not evaluated in the patient group. The third was that laboratory markers were not used that might have shown cardiac involvement.

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Conflict of interests. None.

Ethical standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008, and has been approved by the University of Dokuz Eylul Research Ethics Board.

Data availability statement. The datasets generated during and/or analyzed during the current study are not publicly available but are available from the corresponding author on request.

References

- Jardine AG, McLaughlin K. Cardiovascular complications of renal disease. *Heart* 2001; 86: 459–466.
- Chavers BM, Molony JT, Solid CA, Rheault MN, Collins AJ. One-year mortality rates in US children with end-stage renal disease. *Am J Nephrol* 2015; 41: 121–128.
- Dyadyk OI, Bagriy AE, Yarovaya NF. Disorders of left ventricular structure and function in chronic uremia. *Eur J Heart Fail* 1999; 1: 327–336.
- Rakhit DJ, Zhang XH, Leano R, Armstrong KA, Isbel NM, Marwick TH. Prognostic role of subclinical left ventricular abnormalities and impact of transplantation in chronic kidney disease. *Am Heart J* 2007; 153: 656–664.
- Anna B, Matilda L, Jacek N, et al. Effects of hemodialysis on the cardiovascular system: quantitative analysis using wave intensity wall analysis and tissue velocity imaging. *Heart Vessels* 2011; 26: 289–297.
- Schoenmaker NJ, Kuipers IM, Lee JH, et al. Diastolic dysfunction measured by tissue Doppler imaging in children with end-stage renal disease: a report of the RICH-Q study. *Cardiol Young* 2014; 24: 236–244.
- Edwards NC, Hirth A, Ferro CJ, Townsend JN, Steeds RP. Subclinical abnormalities of left ventricular myocardial deformation in early-stage chronic kidney disease: the precursor of uremic cardiomyopathy. *J Am Soc Echocardiogr* 2008; 21: 1293–1298.
- Shawky AM, Hamdy RM, Elmadboluy AA. Clinical utility of left ventricular strain, wall stress and serum brain natriuretic peptide levels in chronic hemodialysis patients. *Egyptian Heart J* 2018; 70: 329–335.
- Voigt JU, Pedrizzetti G, Lysyansky P, et al. Definitions for a common standard for 2D speckle tracking echocardiography: consensus document of the EACVI/ASE/Industry task force to standardize deformation imaging. *J Am Soc Echocardiogr* 2015; 28: 183–193.
- Rakha S, Hafez M, Bakr A, Hamdy N. Changes of cardiac functions after hemodialysis session in pediatric patients with end-stage renal disease: conventional echocardiography and two-dimensional speckle tracking study. *Pediatr Nephrol* 2020; 35: 861–870.
- KDIGO 2012 Clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl* 2013; 3: 136.
- Demetgul H, Giray D, Delibas A, Hallioglu O. 2D-Speckle tracking echocardiography contributes to early identification of impaired left ventricular

- myocardial function in children with chronic kidney disease. *Cardiol Young* 2018; 28: 1404–1409.
13. Yan P, Li H, Hao C, et al. 2D-speckle tracking echocardiography contributes to early identification of impaired left ventricular myocardial function in patients with chronic kidney disease. *Nephron Clin Pract* 2011; 118: 232–240.
 14. Huis M, Schoenmaker NJ, Groothoff JW, et al. Impaired longitudinal deformation measured by speckle-tracking echocardiography in children with end-stage renal disease. *Pediatr Nephrol* 2016; 31: 1499–1508.
 15. Scharer K, Schmidt KG, Soergel M. Cardiac function and structure in patients with chronic renal failure. *Pediatr Nephrol* 1999; 13: 951–965.
 16. Santos M, Shah AM. Alterations in cardiac structure and function in hypertension. *Curr Hypertens Rep* 2014; 16: 428–435.
 17. Hothi DK, Rees L, Marek J, Burton J, McIntyre CW. Pediatric myocardial stunning underscores the cardiac toxicity of conventional hemodialysis treatments. *Clin J Am Soc Nephrol* 2009; 4: 790–797.
 18. Zuidema MY, Dellsperger KC. Myocardial stunning with hemodialysis: clinical challenges of the cardiorenal patient. *Cardiorenal Med* 2012; 2: 125–133.
 19. Burton JO, Jefferies HJ, Selby NM, McIntyre CW. Hemodialysis-induced cardiac injury: determinants and associated outcomes. *Clin J Am Soc Nephrol* 2009; 4: 914–920.
 20. Mendes L, Ribeiros R, Adragão T, et al. Load-independent parameters of diastolic and systolic function by speckle tracking and tissue Doppler in hemodialysis patients. *Rev Port Cardiol* 2008; 27: 1011–1025.
 21. Murata T, Dohi K, Onishi K, et al. Role of hemodialytic therapy on left ventricular mechanical dyssynchrony in patients with end-stage renal disease quantified by speckle-tracking strain imaging. *Nephrol Dial Transplant* 2011; 26: 1655–1661.
 22. Dandel M, Lehmkühl H, Knosalla C, Suramelashvili N, Hetzer R. Strain and strain rate imaging by echocardiography – basic concepts and clinical applicability. *Curr Cardiol Rev* 2009; 5: 133–148.
 23. Geyer H, Caracciolo G, Abe H et al. Assessment of myocardial mechanics using speckle tracking echocardiography: fundamentals and clinical applications. *J Am Soc Echocardiogr* 2010; 23: 351–369.
 24. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging* 2015; 16: 233–70.