Left Ventricular Myocardial Deformations in Hemodialysis Children by Speckle Tracking Echocardiography

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ABSTRACT

BACKGROUND: Cardiac systolic dysfunction was potentially found in adult patients with end-stage renal disease (ESRD) who have preserved left ventricular ejection fraction (EF%). In children with ESRD, little data are available on early changes in myocardial function. This study aimed to detect the early changes in myocardial mechanics in pediatric patients with ESRD using speckle tracking echocardiography (STE).

METHODS: Thirty ESRD children receiving hemodialysis (HD) and 30 age-matched controls were prospectively studied. Patients underwent echocardiographic studies before and after HD. Left ventricular longitudinal strain (LS), circumferential strain (CS), and radial strain (RS) myocardial deformation parameters (strain, strain rate) were evaluated by STE.

RESULTS: The LS was significantly reduced in pre-HD and post-HD patients compared with controls (P<.000). Controls showed the highest global longitudinal strain. The RS measurements did not differ significantly among the studied groups except for the inferior segment that is significantly reduced after HD compared with controls (P<.05). The CS was significantly reduced in pre-HD and post-HD patients compared with controls at the lateral and posterior segments (P=.035 and P=.013, respectively).

CONCLUSION: Speckle-tracking echocardiography might detect early changes in myocardial mechanics in children with ESRD with preserved EF%.

KEYWORDS: End-stage renal disease, children, hemodialysis, speckle tracking echocardiography, strain, strain rate

Introduction

Cardiovascular morbidity and mortality are much prevalent in adults and children with end-stage renal disease (ESRD).1-4 Impaired systolic function and left ventricular hypertrophy (LVH) occurred in young adults with ESRD even at the early stages of chronic kidney disease (CKD).5-9 There is an increased hazard of ischemic heart disease, arrhythmia, stroke, peripheral artery disease, cardiac arrest, and cardiac death in these patients.10 The systolic left ventricular (LV) function generally seems to be well preserved in children with ESRD as reported in previous studies with the use of 2-dimensional (2D) echocardiography and tissue Doppler measurements.6-9,11,12

Speckle tracking echocardiography (STE) permits the evaluation of myocardial mechanics and eventually myocardial deformation.11-15 Speckle tracking echocardiography allows the study of myocardial speed and movement at more than 1 point at the same time.16 By evaluating the myocardial deformation in 3 myocardial layers (longitudinal strain [LS], circumferential strain [CS], and radial strain [RS]), STE was reported to have a part in the early detection of cardiac diseases.17 Speckle tracking echocardiography has been used to detect early changes in myocardial mechanics before the occurrence of the ejection fraction (EF) changes.

A study in children with muscular dystrophy reported that LS changes can be observed before the occurrence of EF changes.18 The same has been described in adults and children exposed to anthracyclines.19-21 A decreased longitudinal strain has been reported to be a significant risk factor for all-cause mortality in adults with ESRD,22 whereas the impairment in renal function as demonstrated by the estimated glomerular filtration rate (eGFR) has been reported to be linked to the decline in strain values,23,24 and our study aimed to detect the early changes in myocardial mechanics and the occurrence of myocardial deformation in pediatric patients with ESRD using the STE as an imaging modality.

Methods

Study population

Thirty Egyptian pediatric patients with advanced CKD (stage 5 based on eGFR) according to the National Kidney

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Foundation classification were included in the study. Children with ESRD were selected from the hemodialysis (HD) unit of the Center of Pediatric Nephrology and Transplantation, Children’s Hospital, Cairo University. Patients were on regular HD for more than 6 months. All patients were in sinus rhythm with the absence of primary myocardial disease. Children with congenital heart disease were excluded. Children were treated with standard bicarbonate-containing bath dialysis, for 3 to 4.5 hours in each session, 3 times per week. The blood flow rate was 5 to 7 mL/kg, and the dialyzer surface area of polysulfone membranes was 1, 7, and 12 m². Informed consent was taken from the parents of all participants, patients, and controls. The study was approved by the Ethics Committees of the National Research Center (NRC) and Faculty of Medicine, Cairo University. The prevalence of hypertension was assessed in patients, by definition of hypertension as a systolic blood pressure (SBP) and/or diastolic blood pressure (DBP) that is >95th percentile on at least 3 occasions for sex, age, and height, irrespective of the use of antihypertensives.

The control group included 30 healthy children matched for age and sex with the patients from the same geographic region, socioeconomic conditions, and ethnic background. They were collected from the outpatient pediatric clinic of Medical Research Centre of Excellence (MRCE) at the NRC, Egypt, for routine health examination and periodic checkup. The health status of all children was assessed by medical history and physical examination.

Echocardiographic protocol

All images were obtained using a commercially available cardiac ultrasound machine Vivid 5 Dimension (General Electric Healthcare Company, Milwaukee, WI, USA) using Doppler transducers and 3 and 5 MHz combined imaging. All echocardiographic studies were done 30 minutes pre-HD and 30 minutes post-HD. All images were taken after 20 minutes of rest during quiet respiration, in the left lateral decubitus position. In healthy controls, preload was not manipulated. Cardiac ultrasound machine Vivid 5 Dimension was between 0.61 and 0.79; “moderate,” if the ICC was between 0.41 and 0.60; and “poor,” if the ICC was 0.4 or less. Values of $P<.05$ were considered as statistically significant.

Biochemical tests

Two milliliters of the venous blood sample was collected in EDTA for complete blood count, and 2 mL was collected for obtaining serum. Hemoglobin and creatinine were measured for all patients by automatic biochemistry analyzer.

Statistical Analysis

Statistical analysis was performed using SPSS 16 for Windows (SPSS 16, Inc., Chicago, IL, USA). All group data were reported as mean ± SD. To detect the normality of variables, the Kolmogorov-Smirnov test was used. Means ± SDs were used for the normally distributed data. The unpaired Student $t$ test and Mann-Whitney $U$ test were used to assess differences between 2 groups, whereas the Kruskal-Wallis $H$ test was used to assess differences among different groups. Categorical values were compared using the $\chi^2$ test or Fisher exact test, where indicated. A sample was sized using Power and sample calculation to give us approximately 80% power ($\alpha=0.05, 2$-tailed) to reject the null hypothesis of zero correlation. It was based on the results of the previous study. The intraclass correlation coefficient (ICC) method was used to assess the intraobserver reproducibility and interobserver reliability for the values of 2D LS, RS, and CS. The clinical significance was categorized as follows: “excellent,” if the ICC was 0.80 or greater; “good,” if the ICC was between 0.61 and 0.79; “moderate,” if the ICC was between 0.41 and 0.60; and “poor,” if the ICC was 0.4 or less. Values of $P<.05$ were considered as statistically significant.

Results

Study population

The clinical and the conventional echocardiographic findings are summarized in Tables 1 and 2.
There were significant differences between pre-HD group and controls regarding hemoglobin ($P = .000$), serum creatinine ($P = .000$), and systemic blood pressure for both systolic and diastolic values (SBP: $129 \pm 14$ vs $100 \pm 7$, $P = .001$; DBP: $86 \pm 12$ vs $61 \pm 6$, $P = .001$). Heart rate and interventricular septum were significantly increased in both pre-HD and post-HD groups than in controls ($P = .000$ and $P = .000$, respectively). The early diastolic velocity E of mitral inflow was significantly higher in the pre-HD group and significantly improved after HD compared with controls ($P = .000$). The E/A ratio of mitral inflow is significantly decreased in the post-HD group compared with controls ($P = .004$).

**Myocardial Deformation Parameters**

**Longitudinal strain assessment**

There were statistically significant differences among the 3 groups regarding longitudinal strain at 4-, 2-, and 3-chamber
views. The LS was significantly reduced in pre-HD and post-HD patients compared with controls ($P=.000$). The highest global longitudinal strain was shown in control groups. The global longitudinal strain was significantly reduced in patients before HD compared with controls and further decreased after HD ($P=.000$).

Regarding segmental analysis, significantly reduced values of the LS of anterior, posterior, and inferior segments ($P<.05$) were found in the pre-HD patient group and further decreased after HD ($P<.01$). Also, the segmental anteroseptal and lateral longitudinal strain values were significantly reduced by HD (lateral more affected than septal) (Table 3).

### Radial strain assessment

The RS measurements did not differ significantly among the studied groups except for the inferior segment that is insignificantly reduced after HD when compared with controls ($P=.09$) (Table 3).

### Circumferential strain assessment

The posterior segment was significantly reduced in pre-HD and post-HD patients compared with the control group ($P=.035$). Also, the lateral segment was significantly lowered in pre-HD and post-HD patients compared with the control group.

| Table 3. Peak systolic longitudinal, radial, and circumferential strains (%) according to segments in the studied groups. |
|---------------------------------------------------------------|
| **Longitudinal strain, %**                                    |
|                                                               |
| PRE-HD (N=30)                                                 |
| POST-HD (N=30)                                                |
| HEALTHY CONTROLS (N=30)                                       |
| **P VALUE**                                                  |
| **P VALUE**                                                  |
| **P VALUE**                                                  |
| **P VALUE**                                                  |
| PRE-HD VS CONTROL                                            |
| POST-HD VS CONTROL                                           |
| PRE-HD VS POST-HD                                            |
|                                                               |
| Average                                                      |
| $-16.00 \pm 3.50$                                            |
| $-12.06 \pm 10.01$                                           |
| $-18.85 \pm 1.18$                                           |
| .000*                                                       |
| .004*                                                       |
| .000*                                                       |
| .043*                                                       |
| Anteroseptal                                                 |
| $-15.43 \pm 5.99$                                            |
| $-15.17 \pm 5.59$                                           |
| $-20.40 \pm 2.32$                                           |
| .004*                                                       |
| .002*                                                       |
| .003*                                                       |
| .806                                                       |
| Anterior                                                     |
| $-17.80 \pm 7.15$                                            |
| $-16.70 \pm 6.74$                                           |
| $-26.40 \pm 5.10$                                           |
| .003*                                                       |
| .002*                                                       |
| .01*                                                        |
| .728                                                       |
| Lateral                                                      |
| $-16.17 \pm 7.08$                                            |
| $-14.27 \pm 7.14$                                           |
| $-22.20 \pm 8.85$                                           |
| .020*                                                       |
| .020*                                                       |
| .010*                                                       |
| .313                                                       |
| Posterior                                                    |
| $-16.20 \pm 5.45$                                            |
| $-14.70 \pm 5.44$                                           |
| $-20.50 \pm 4.17$                                           |
| .007*                                                       |
| .013*                                                       |
| .002*                                                       |
| .272                                                       |
| Inferior                                                     |
| $-16.38 \pm 5.57$                                            |
| $-14.83 \pm 5.31$                                           |
| $-20.20 \pm 2.94$                                           |
| .023*                                                       |
| .057*                                                       |
| .005*                                                       |
| .290                                                       |
| Septum                                                       |
| $-14.30 \pm 4.24$                                            |
| $-14.90 \pm 5.13$                                           |
| $-17.70 \pm 2.00$                                           |
| .093                                                        |
| .018*                                                       |
| .148                                                        |
| .499                                                       |
|                                                               |
| **Radial strain, %**                                          |
|                                                               |
| Anteroseptal                                                  |
| $13.43 \pm 10.06$                                             |
| $12.83 \pm 7.73$                                             |
| $17.80 \pm 8.40$                                             |
| .322                                                        |
| .163                                                        |
| .159                                                        |
| .994                                                       |
| Anterior                                                     |
| $11.85 \pm 9.90$                                             |
| $12.73 \pm 9.28$                                             |
| $14.10 \pm 8.79$                                             |
| .510                                                        |
| .257                                                        |
| .406                                                        |
| .614                                                       |
| Lateral                                                      |
| $13.17 \pm 10.24$                                            |
| $14.50 \pm 11.03$                                            |
| $10.00 \pm 2.94$                                             |
| .793                                                        |
| .730                                                        |
| .531                                                        |
| .657                                                       |
| Posterior                                                    |
| $19.70 \pm 16.49$                                            |
| $15.77 \pm 12.96$                                            |
| $15.20 \pm 8.78$                                             |
| .715                                                        |
| .696                                                        |
| .696                                                        |
| .441                                                       |
| Inferior                                                     |
| $13.13 \pm 8.38$                                             |
| $12.37 \pm 7.39$                                             |
| $20.00 \pm 10.17$                                            |
| .090                                                        |
| .050                                                        |
| .035*                                                       |
| .894                                                       |
| Septum                                                       |
| $14.13 \pm 11.08$                                            |
| $14.60 \pm 23.68$                                            |
| $13.50 \pm 6.36$                                             |
| .430                                                        |
| .573                                                        |
| .199                                                        |
| .419                                                       |
|                                                               |
| **Circumferential strain, %**                                 |
|                                                               |
| Anteroseptal                                                  |
| $-21.03 \pm 14.04$                                           |
| $-21.33 \pm 12.99$                                           |
| $-30.40 \pm 11.95$                                           |
| .070                                                        |
| .026*                                                       |
| .039*                                                       |
| .894                                                       |
| Anterior                                                     |
| $-14.18 \pm 7.73$                                            |
| $-14.17 \pm 9.72$                                           |
| $-18.50 \pm 6.57$                                           |
| .149                                                        |
| .089                                                        |
| .064                                                        |
| .673                                                       |
| Lateral                                                      |
| $-15.00 \pm 1.50$                                            |
| $-16.17 \pm 7.26$                                           |
| $-20.80 \pm 3.71$                                           |
| .013*                                                       |
| .002*                                                       |
| .028*                                                       |
| .504                                                       |
| Posterior                                                    |
| $-13.50 \pm 5.93$                                            |
| $-14.10 \pm 7.92$                                           |
| $-20.00 \pm 5.08$                                           |
| .035*                                                       |
| .007*                                                       |
| .034*                                                       |
| .935                                                       |
| Inferior                                                     |
| $-11.85 \pm 9.88$                                            |
| $-16.27 \pm 9.01$                                           |
| $-13.90 \pm 6.54$                                           |
| .077                                                        |
| .246                                                        |
| .583                                                        |
| .027*                                                       |
| Septum                                                       |
| $-15.83 \pm 6.71$                                            |
| $-18.67 \pm 9.31$                                           |
| $-21.10 \pm 5.11$                                           |
| .124                                                        |
| .034*                                                       |
| .210                                                        |
| .366                                                       |

Data presented as mean ± SD or percentage. Abbreviation: HD, hemodialysis.

* $P < .05$ was considered statistically significant.
group (P=.013). The anteroseptal segment was also insignificantly affected by HD (P=.07) (Table 3).

**SR Assessment**

**Four-chamber view**

The SR values of the patients’ groups and controls at the 4-chamber view are shown in Table 4. The control group had statistically significantly lower global peak A (peak late diastolic strain) SRs at the septal and lateral segments, and the pre-HD and post-HD groups had statistically significantly lower peak E (peak early diastolic strain) at septal and lateral segments compared with controls (P<.01). Regarding segmental analysis, statistically significant reduced values of peak systolic SR (peak S) of the lateral and septal segments (P<.05) were found in the patient groups. The most negative peak S value was −1.30 ± 0.44 in the lateral segment of the post-HD patient group and 1.28 ± 0.48 in the lateral segment of the control group (P=.039).

**Two-chamber view**

The control group had statistically significantly lower global peak A SRs at the anterior segment, and the pre-HD and post-HD patients had statistically significantly lower peak E at the inferior and anterior segments (P<.05). Regarding segmental analysis, statistically significant reduced values of peak S of the anterior segment (P<.05) were found in the patient groups. The most negative peak LS value was −1.58 ± 0.53 in the anterior segment of the pre-HD patient group and −2.13 ± 0.39 in the anterior segment of the control group (P=.005) (Table 4).

**Three-chamber view**

The control group had statistically significantly lower global peak A SRs at the anteroseptal segment, and the pre-HD and post-HD patients had statistically significantly lower peak E at the posterior and anteroseptal segments (P<.01). Regarding segmental analysis, statistically significant reduced values of peak S of the posterior segment (P<0.05) were found in the pre-HD and post-HD groups. The most negative peak LS value was −1.34 ± 0.58 in the posterior of the post-HD patient group and −1.57 ± 0.78 in the posterior segment of the control group (P=.022) (Table 4).

**Interobserver and intraobserver reproducibility**

The intraobserver ICCs were above 0.8, that is, they ranged between 0.81 and 0.9 for all the deformation parameters. The intraobserver and interobserver reproducibility were acceptable for the mean measurements of the LS, CS, and RS in all segments of the 3 levels of LV.

**Discussion**

This study gives more understanding of the acute effects of HD on LV myocardial deformation parameters and the LV cardiac function in ESRD pediatric patients with maintained EF. With the use of echocardiographic features of the 3 types of strain (LS, RS, and CS) and the different SRs, myocardial mechanics were demonstrated in a pediatric cohort of patients (before and after HD), encompassing significant impairment in cardiac function and further deterioration following HD. This study displayed that assessment of myocardial deformation using deformation imaging was simple, convenient, and extremely reproducible.

Tissue Doppler echocardiography and speckle echocardiography (strain and SR) are comparatively new echocardiographic techniques and substantial models to evaluate asymptomatic patients. Tissue Doppler imaging permitted an itemized examination of the cardiac function and is greatly used to assess children with several conditions. Our previous study demonstrated that early diastolic dysfunction is detected using tissue Doppler echocardiography in children with ESRD on HD. Despite its accuracy, tissue Doppler echocardiography cannot evaluate the regional deformation or its abnormalities.

Strain and SR echocardiography succeeded in dealing with the hardness of tissue Doppler imaging such as angle dependency, preload effects, and translational motion of the heart, so were adopted as novel tools in the evaluation of myocardial performance and properties of regional deformation. Speckle tracking (strain imaging), mainly, allowed an evaluation of myocardial motion and deformation regardless of the angle and geometry, enabling an improvement in the examination of the myocardial mechanics. Two-dimensional strain and SR echocardiography can also evaluate several clinical morbidities such as Marfan syndrome, obesity, hypertension, post-exercise hypertension, and healthy children and infants.

Our study showed that LS of LV was significantly reduced in pediatric patients with ESRD before HD and further deteriorated following HD compared with normal controls. The global LS was significantly reduced after HD. Controls showed the highest global longitudinal strain. Regarding segmental analysis, statistically significant reduced values of end-systolic LS of most segments were found in the pre-HD group and further decreased after HD. The RS measurements were not significantly different between the patient groups and the controls except for the inferior segment that is significantly reduced after HD. The posterior segment of CS was significantly reduced in pre-HD and post-HD patients. Also, the lateral and the anteroseptal segments of CS were significantly affected by HD. These results propose that STE reveals longitudinal deformation changes and diastolic dysfunction in children with ESRD with preserved LVEF. Our results were in agreement with a recent study by Rakha et al that reported that after HD significant decline in LVEF and global and segmental strains can be diagnosed in ESRD pediatric patients using 2D speckle tracking, despite the nonsignificant changes in systolic functions obtained from the conventional echocardiography. This is considered additional evidence of the deleterious effect of HD on myocardial functions, particularly in the pediatric age. However, Amoozgar et al recently reported that HD with
volume reduction in children with ESRD decreases LV volume, with no significant changes in regional strain or SR.

The sum of all the regional shortening in the LV is reflected by the LVEF, and regional wall motion impairment may lower the LVEF only when several segments are involved. The diastolic dysfunction in these patients groups may be heterogeneous, but the heart could be affected globally in the long term. Early disclosure of longitudinal strain impairment may help the physician to recognize high-risk patients with future unfavorable cardiovascular situations.

### Table 4. Values of strain rate according to segments obtained from the 4-, 2-, and 3-chamber images in the studied groups.

|                          | PRE-HD (N=30) | POST-HD (N=30) | HEALTHY CONTROLS (N=30) | P VALUE | P VALUE PRE-HD VS CONTROL | P VALUE POST-HD VS CONTROL | P VALUE PRE-HD VS POST-HD |
|--------------------------|---------------|----------------|-------------------------|---------|---------------------------|---------------------------|--------------------------|
| **Four-chamber view**    |               |                |                         |         |                           |                           |                          |
| Peak systolic strain rate (Peak S) |               |                |                         |         |                           |                           |                          |
| Septum                   | –1.12 ± 0.24  | –1.15 ± 0.29   | –1.28 ± 0.22             | .037*   | .222                      | .362                      | .904                     |
| Lateral                  | –1.20 ± 0.37  | –1.30 ± 0.44   | –1.28 ± 0.48             | .039*   | .205                      | .020*                     | .092                     |
| Peak early diastolic strain rate (Peak E) |               |                |                         |         |                           |                           |                          |
| Septum                   | 1.51 ± 0.63   | 1.45 ± 0.59    | 2.37 ± 0.62              | .002*   | .001*                     | .001*                     | .959                     |
| Lateral                  | 2.19 ± 1.17   | 2.13 ± 1.13    | 2.24 ± 1.32              | .004*   | .002*                     | .002*                     | .773                     |
| Peak late diastolic strain rate (Peak A) |               |                |                         |         |                           |                           |                          |
| Septum                   | 1.32 ± 0.78   | 1.31 ± 0.73    | 0.72 ± 0.36              | .037*   | .022*                     | .013*                     | .917                     |
| Lateral                  | 1.72 ± 1.21   | 1.61 ± 1.70    | 1.16 ± 0.41              | .028*   | .022*                     | .007*                     | .844                     |
| **Two-chamber view**     |               |                |                         |         |                           |                           |                          |
| Peak systolic strain rate (Peak S) |               |                |                         |         |                           |                           |                          |
| Inferior                 | –1.03 ± 0.39  | –1.09 ± 0.52   | –1.37 ± 0.32             | .060    | .021*                     | .038*                     | .859                     |
| Anterior                 | –1.58 ± 0.53  | –1.57 ± 0.59   | –2.13 ± 0.39             | .005*   | .002*                     | .003*                     | .847                     |
| Peak early diastolic strain rate (Peak E) |               |                |                         |         |                           |                           |                          |
| Inferior                 | 1.32 ± 0.66   | 1.22 ± 0.74    | 2.17 ± 0.60              | .002*   | .001*                     | .002*                     | .464                     |
| Anterior                 | 2.26 ± 1.48   | 5.65 ± 20.69   | 5.07 ± 1.47              | .000*   | .000*                     | .000*                     | .351                     |
| Peak late diastolic strain rate (Peak A) |               |                |                         |         |                           |                           |                          |
| Inferior                 | 1.50 ± 1.8    | 1.19 ± 0.66    | 0.97 ± 0.51              | .639    | .881                      | .501                      | .459                     |
| Anterior                 | 1.09 ± 0.78   | 1.25 ± 0.66    | 0.66 ± 0.39              | .036*   | .104                      | .012*                     | .188                     |
| **Three-chamber view**   |               |                |                         |         |                           |                           |                          |
| Peak systolic strain rate (Peak S) |               |                |                         |         |                           |                           |                          |
| Posterior                | –1.15 ± 0.71  | –1.34 ± 0.58   | –1.57 ± 0.78             | .022*   | .013*                     | .040*                     | .040*                    |
| Anteroseptal             | –1.32 ± 1.19  | –1.32 ± 0.81   | –1.83 ± 0.91             | .064    | .027*                     | .089                      | .395                     |
| Peak early diastolic strain rate (Peak E) |               |                |                         |         |                           |                           |                          |
| Posterior                | 1.53 ± 0.93   | 1.20 ± 0.97    | 2.32 ± 1.05              | .016*   | .035*                     | .011*                     | .113                     |
| Anteroseptal             | 2.33 ± 1.54   | 1.74 ± 1.56    | 4.00 ± 2.20              | .005*   | .017*                     | .007*                     | .046*                    |
| Peak late diastolic strain rate (Peak A) |               |                |                         |         |                           |                           |                          |
| Posterior                | 1.17 ± 0.69   | 1.28 ± 0.70    | 1.03 ± 1.14              | .061    | .082                      | .019*                     | .385                     |
| Anteroseptal             | 1.11 ± 0.64   | 1.20 ± 0.77    | 0.59 ± 0.36              | .057    | .020*                     | .036*                     | .698                     |

Data presented as mean ± SD or percentage. Abbreviation: HD, hemodialysis. *P < .05 was considered statistically significant.
Diastolic dysfunction usually occurs before systolic function in hypertensive patients,35 and this has been previously reported in pediatric ESRD.8,35 The diastolic dysfunction could be linked to volume status or declare the lowered LV compliance or may be due to an inflammatory response induced by uremic toxins or be linked to the maladaptive hypertrophic response that happened to these particular patients.35 However, a decrease in preload could also cause a reduction in E wave, independent of diastolic dysfunction. Several factors can affect E/A ratio, including preload and left atrial pressure.38

In this study, interventricular septum in systole and LV posterior wall diameter were significantly increased in both pre-HD and post-HD groups than in controls, with a preserved systolic function detected with conventional echocardiography. Speckle-tracking echocardiography demonstrated a decreased LS in our pediatric patients on HD, proposing that the longitudinal function is lowered in the patient group, whereas the radial and circumferential functions are mildly affected. The possible causes for this result are the augmented LV wall thickness and cross-fiber shortening, which exert their effects as the interaction between a contraction and a systolic increase in the cross-sectional area of all differently aligned myocardial layers, and also, the curvature radius of the circumferentially oriented myocardial fibers is smaller than that of the longitudinal fibers, which may entail lower stress and consequently delay the appearance of functional abnormalities.30 In addition to that, myocardial deformation happens in 3 dimensions and can be detected in the longitudinal direction, as well as in the circumferential and radial directions. Subepicardial fibers are important components in both the RS and the LS, and subendocardial fibers play a major role in CS.34 The subepicardium is more susceptible to myocardial ischemia and stiffness than the subendocardium. So, myocardial stiffness might be a factor that causes changes in the function of LV long axis earlier than in the function of short axis in patients with ESRD.

Left ventricular concentric hypertrophy is mostly developed due to the hypertrophic response in the mid-myocardial layers, which are mostly circumferentially oriented. This can compensate for the longitudinal function reduction and can explain the maintained LVEF. In hypertensive patients, the changes are most evident in the basal parts. An impairment in longitudinal function usually happens before the changes occurred in circumferential and radial function in patients with LVH as a result of pressure overload, whereas in patients with hypertrophic cardiomyopathy or systemic disease, also radial strain can be diminished.39 The impairment in longitudinal function with maintained LVEF has been reported in other diseases, mostly in patients with LVH.39 Hothi et al40 reported a lowered LS in children on HD with preserved global function.

In patients with ESRD, hypertension and uremic toxins are independently connected with the occurrence of LVH and ventricular dysfunction.9,41 In adult patients with ESRD, systolic dysfunction may develop at a relatively early stage, mostly due to direct response to uremic toxins or due to myocardial fibrosis developed by chronic inflammation. Although the nature of these toxins is mostly unknown, some factors in uremic plasma had potentially negative inotropic and chronotropic effects.13 This fibrosis is a substantial stimulus of the myocardial electrical instability and consequently arrhythmia.9 Also, another hallmark of ESRD, endothelial dysfunction, may progress to an insufficient vasodilatory response in the thickened LV and eventually local ischemia, further enhancing the occurrence of fibrosis.1,24,42

### LIMITATIONS

Some limitations of this study should be noted. First, the sample size was small, which limited the statistical power of analysis. Second is the lack of detailed information on measurements of ventricular volumes or LV mass index. Moreover, we did not correlate the results of 2-dimensional STE analysis with dialysis-related variables.

### CONCLUSIONS

Two-dimensional STE analysis offers a useful tool for predicting the myocardial dysfunction of the LV in ESRD children on HD in the absence of systolic dysfunction. We found a significant LS impairment precedes the RS and CS impairments and could be an early predictor of systolic dysfunction in pediatric ESRD patients with preserved EF. The long-term significance of these results and whether the LS reduction can be used as a specific early predictor of cardiovascular morbidity and mortality in children with ESRD need further larger studies. Two-dimensional STE and LS might be sensitive predictors of LV global and regional systolic dysfunction.

### AUTHOR CONTRIBUTIONS

MFE, FAM, IAESS .AMB & YAEMAER carried out all patients work up, IAESS had performed the echocardiographic measurements, MFE had interpreted the data, performed the statistical analysis and had written the manuscript. All authors read and approved the final manuscript.

### ETHICAL APPROVAL

All procedures performed in studies involving human participants were following the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

### INFORMED CONSENT

Informed consent was obtained from all individual participants included in the study.

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