

Effect of Hemodialysis on Global and Regional Cardiac Function in Children With End-stage Renal Disease

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Introduction. Changes in cardiac structure and function are common among patients with end-stage renal disease. The aim of this study was to evaluate the effect of hemodialysis on global and segmental cardiac function in children with end-stage renal disease.

Materials and Methods. Fifty-two children with ESRD who were on long-term hemodialysis at Nemazee Hospital, Shiraz, were enrolled. They underwent echocardiography (M-mode, 2-dimensional, Doppler, and speckle echocardiography) 30 minutes prior to and after hemodialysis, and the values were compared.

Results. The mean age of the patients was 13.00 ± 3.53 years. There was a significant reduction in left ventricular systolic and diastolic dimensions and volume ($P < .001$) and the E:A ratio after dialysis ($P = .03$). Global and longitudinal strain and strain rate showed no significant changes before and after hemodialysis.

Conclusions. Hemodialysis with volume reduction decreases left ventricular volume but not regional strain and strain rate significantly in children. This study showed preload independency of speckle echocardiography in children.

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INTRODUCTION

Changes in cardiac structure and function are common among the patients with chronic kidney disease undergoing hemodialysis. As early as 1827, Richard Bright drew attention to the common presence of left ventricular hypertrophy and thickening of the aortic wall in the patients with end-stage renal disease (ESRD).¹ After that, several studies were done to find the causes and risk factors of these abnormal changes.¹⁻⁵ Most of the literature has used tissue Doppler imaging techniques to assess the long-axis function. One of the disadvantages of this method is the angle dependency of Doppler techniques; therefore, new techniques, such as 2-dimensional (radial and circumferential) strains and strain rates, were introduced. One important advantage of these methods over tissue Doppler imaging techniques is that they are not limited by dependency on the

angle.^{4,6-9} Site specificity and angle independency are also unique characteristics of strain and strain rate data that are presented in some studies.^{10,11}

The individuals undergoing hemodialysis are subject to large body weight alterations caused by alterations in the volume. These sudden changes of volume status during hemodialysis lead to negative alterations on the heart tissue and its function that should be a target of studies for improvement of cardiovascular complication synchronic kidney disease patients.¹³ Conventional echocardiographic parameters of left ventricular and right ventricular systolic and diastolic function have been shown to be load dependent in some studies. Moreover, the impact of preload reduction on tissue Doppler parameters of left ventricular and right ventricular function has been controversial in other studies.¹⁴⁻¹⁶ There are multiple studies in adults with chronic kidney disease that studied

the effect of hemodialysis on heart function by conventional and speckle echocardiography with contradictory results. Few previous studies have investigated the prognostic value of strain or strain rate imaging in cardiac function in children with chronic kidney disease. In this study, effect of hemodialysis on global and segmental cardiac function was assessed in children with end-stage renal disease by using conventional and speckle echocardiography.

MATERIALS AND METHODS

In this pre- and post-interventional study, all children with ESRD who were on hemodialysis for at least 2 months at the hemodialysis center of Nemazee Hospital, Shiraz, Iran, were enrolled. All of the patients were under follow up of a pediatric nephrologist and a cardiologist. The inclusion criteria of the study were age under 18 years, suffering from stage 5 of chronic kidney disease, being on maintenance hemodialysis for at least 2 months, and good-quality echocardiographic images which were acceptable for speckle tracking echocardiography. Net weight reduction postdialysis of more than 500 g was also a rule for being enrolled into the study. On the other hand, the exclusion criteria of the study were malignant hypertension, cardiac arrhythmia, presence of pericardial disease, severe valvular heart disease, history of congenital heart disease, and dilated cardiomyopathy. This study was approved by the Ethics Committee of Shiraz University of Medical Sciences and written informed consent was obtained from all the participants and their parents.

The children underwent echocardiography nearly 30 minutes prior and 30 minutes after a routine hemodialysis session. The echocardiographic studies were performed by one experienced operator using a MyLab 30 echocardiography machine (Esaote SpA, Italy). M-mode, two-dimensional, and Doppler examination in parasternal long and apical 4-chamber views were obtained to evaluate the cardiac function. Left ventricular volume, cardiac output, strain, and strain rate of left ventricle (LV) were measured by speckle tracking. All the echocardiographic measurements were averaged over 3 cardiac cycles during quiet respiration, and cardiac cycle loops with triggered electrocardiogram were stored for offline analysis.

A polysulfone hollow fiber dialysis membrane

was used with variable dialysis solutions. The aim of fluid removal was to achieve a clinically determined 'dry weight' and the minimum weight reduction was 0.5 kg. Hemodialysis was performed 3 times per week for most of the patients and for 3 to 4 hours using acetate-buffered dialysis solution (potassium, 2.0 ± 0.2 mmol/L; sodium, 141.0 ± 1.5 mmol/L; and bicarbonate 26.7 ± 2.4 mmol/L).

All the data were reported as a mean \pm standard deviation for continuous variables. Normality of data distributions were evaluated using the Kolmogorov-Smirnov test, and the paired *t* test was used for comparison of the echocardiography models with normal distribution. The SPSS software (Statistical Package for the Social Sciences, version 22.0, SPSS Inc, Chicago, IL, USA) was used for the analysis. A difference was considered significant if the *P* value was $< .05$.

RESULTS

A total of 52 echocardiography images were recorded in the children with ESRD (mean age, 13.00 ± 3.53 years; 62.5% boys) who were on routine hemodialysis between December 2013 and November 2016. The mean weight of the patients was 41.15 ± 15.75 kg before hemodialysis and 39.00 ± 15.71 after hemodialysis. The mean reduction of body weight was 1.76 ± 0.80 kg ($3.10 \pm 1.72\%$ decrease in the body weight).

M-mode echocardiography showed significant decreases in systolic dimension (3.13 ± 0.70 cm to 3.02 ± 0.89 cm, $P < .001$) and diastolic LV dimension (4.87 ± 0.83 cm to 4.69 ± 1.17 cm, $P < .001$). Other M-mode echocardiography parameters are shown in Table 1. Pulse Doppler echocardiography of the mitral valve showed a significant decrease of the E:A ratio (1.73 ± 0.31 to 1.61 ± 0.21 , $P = .03$). Measurement of volume

Table 1. M-Mode Parameters Before and After Hemodialysis

| M-Mode Parameters | Before Hemodialysis | After Hemodialysis | <i>P</i> |
|--|---------------------|--------------------|----------|
| Ejection fraction, % | 64.60 ± 8.17 | 64.64 ± 7.25 | .13 |
| Shortening fraction | 35.76 ± 6.61 | 35.64 ± 5.32 | .21 |
| Cardiac output | 52.96 ± 3.12 | 62.37 ± 2.98 | .12 |
| Left ventricular systolic dimension, cm | 3.13 ± 0.70 | 3.02 ± 0.89 | $< .001$ |
| Left ventricular diastolic dimension, cm | 4.87 ± 0.83 | 4.69 ± 1.17 | $< .001$ |

of left ventricle in 4-chamber view by speckled tracking echocardiography showed significant changes in the diastolic volume (111.5 ± 34.85 mL to 98.32 ± 27.89 mL, $P = .001$) and in the systolic volume (57.56 ± 18.95 mL to 59.02 ± 17.03 mL, $P = .001$). Cardiac output did not change significantly after hemodialysis (4.34 ± 1.52 L/min to 3.29 ± 1.17 L/min, $P = .14$). Diastolic sphericity index decreased (0.52 ± 0.15 to 0.51 ± 0.13 , $P = .006$), but there was no change in systolic sphericity index (0.45 ± 0.15 to 0.49 ± 0.18 , $P = .07$) after hemodialysis. Longitudinal strain and strain rate measurement showed no significant changes in different parts of the cardiac walls before and after the hemodialysis sessions (Tables 2 and 3).

DISCUSSION

The present study aimed to investigate the effects of hemodialysis-mediated preload reduction on some new echocardiographic indexes in children with ESRD. Several studies have been conducted on the hemodialysis-induced changes of cardiac function. However, contradictory results have been obtained regarding the hemodialysis-induced changes of cardiac function and cardiac indexes,^{17-19,28-30} and most of these studies were done in adult population.^{12,28,29} In this study, M-mode echocardiography and speckle echocardiography showed significant changes in the ventricular volume in both systole and diastole after hemodialysis therapy. Ejection fraction and cardiac

output were not changed significantly.

Burton and colleagues studied 70 ESRD adult patients with echocardiography before, during, and after dialysis and reported that more than half of these patients developed significant LV regional wall motion abnormalities.²⁹ Another study by this group in pediatric patients aged 2 to 17 years was about LV systolic function and regional wall motion abnormalities that showed LV ejection fraction was unchanged but regional wall motion abnormalities changed significantly. This discrepancy was justified with varying degrees of compensatory hyperkinesis in segments that were not affected.²⁴ These two studies suggested that hemodialysis-induced LV dysfunction occurred in a large proportion of ESRD patients. Nonetheless, these findings cannot be extrapolated to other ESRD populations because of differences in patient characteristics and treatment options. In our study, there are no significant changes in ejection fraction and shortening fraction before and after hemodialysis.

One of the most widely used methods for assessment of impaired LV relaxation was Doppler measurement of mitral inflow velocity (E:A ratio). However, left atrial pressure and preload significantly affect the E:A ratio. Due to chronic hypervolemia associated with chronic kidney disease, E:A ratio may not be an ideal means of assessing the diastolic function.^{28,30-31} In this study, the E:A ratio decreased significantly after hemodialysis, which shows load dependency of these velocities. Some studies showed that some indexes of Doppler echocardiography were preload dependent.^{23,24} Dincer and colleagues showed that mitral inflow E and A wave velocities and the E:A ratio decreased significantly after hemodialysis,²³ and Agmon and colleagues showed that after hemodialysis, mitral inflow E velocity decreased and deceleration time increased and a smaller decline in mitral inflow A velocity, resulting in a significant decline in the E:A ratio.²⁴

Tissue Doppler imaging was recently introduced as a less load-dependent and more accurate means of evaluating the diastolic function in the patients with chronic kidney disease,^{4,20-22} such as the study of Bauer and coworkers, which reported that tissue Doppler imaging-derived measurements were not significantly affected by hemodialysis.²² Amoozgar and colleagues showed that the Ea velocity of

Table 2. Longitudinal Strain Before and After Hemodialysis

| Strain Parameter, % | Before Hemodialysis | After Hemodialysis | P |
|---------------------|---------------------|--------------------|-----|
| Basal septum | -14.69 ± 4.18 | -12.86 ± 3.22 | .96 |
| Mid septum | -15.44 ± 2.26 | -13.37 ± 4.22 | .54 |
| Apical septum | -18.40 ± 6.51 | -14.16 ± 6.18 | .06 |
| Apical lateral | -14.88 ± 5.44 | -11.53 ± 4.24 | .29 |
| Mid lateral | -13.11 ± 5.16 | -10.74 ± 4.93 | .77 |
| Base lateral | -15.23 ± 6.47 | -11.80 ± 5.93 | .63 |

Table 3. Longitudinal Strain Rate Before and After Hemodialysis

| Strain Rate Parameters, S-1 | Before hemodialysis | After hemodialysis | P |
|-----------------------------|---------------------|--------------------|-----|
| Base septum | -0.90 ± 0.27 | -0.82 ± 0.18 | .85 |
| Mid septum | -0.91 ± 0.15 | -0.84 ± 0.20 | .85 |
| Apical septum | -1.10 ± 0.46 | -0.84 ± 0.31 | .18 |
| Apical lateral | -0.92 ± 0.46 | -0.70 ± 0.23 | .96 |
| Mid lateral | -0.91 ± 0.34 | -0.77 ± 0.24 | .28 |
| Base lateral | -1.07 ± 0.40 | -0.96 ± 0.32 | .06 |

the lateral mitral annulus and the Aa velocity of the tricuspid annulus decreased significantly in the adolescents after hemodialysis.²⁵ They used pulse tissue Doppler imaging for evaluation of the preload status of the hemodialysis patients.²⁵

Furthermore, Hayashi and coworkers⁷ showed an improvement in the cardiac function after hemodialysis by tissue Doppler velocity imaging. They showed that tissue Doppler velocity imaging was more sensitive than conventional echocardiography in detecting diastolic dysfunction and disturbances in contractility and contraction in patients with LV hypertrophy secondary to ESRD. Our results showed significant reduction in the LV systolic and diastolic dimensions after hemodialysis, which is in agreement with the results of some previous studies.^{4,21}

Two-dimensional strain has been applied and validated in the LV and right ventricular function.¹¹ Although initially it was thought that tissue velocities and strain were relatively independent of loading conditions, subsequent research showed contradictory results.^{17,32} Rakhit and coworkers studied the prognostic roles of subclinical LV abnormalities on transplantation in chronic kidney disease. They showed that strain and strain rate, while influenced by loading conditions, were more independent of loading compared to tissue velocities.⁸

Murata and colleagues conducted the first study to quantify the global LV function and elucidate the effects of hemodialysis therapy on echocardiographic parameters by speckle-tracking echocardiography in the patients with ESRD.²⁶ They showed that hemodialysis therapy dramatically improved only the radial LV dyssynchrony, which strongly indicates that radial LV dyssynchrony is sensitive to the alterations in the volume status. The exclusion criteria of that study were the same as ours and the target group included adult patients with ESRD. The results of our study showed no significant changes in the net value of wall velocities and strain and strain rate. The mean changes of mid-walls and basal wall strain rate before and after the hemodialysis were significant in the study by Hayashi and coworkers.⁷ In our study, the changes of strain and strain rate were not significant.

Another study in adult ESRD patients showed systolic myocardial velocity and global and

longitudinal strain were also similar and without significant changes before and after hemodialysis like our study, but they mentioned similar results before and after hemodialysis according to tissue Doppler imaging and color tissue Doppler imaging parameters.³²

One of the limitations of the present study was the impossibility of blinding the study because the echocardiographer acquiring the images was aware of the time of imaging in relation to dialysis session. Nonetheless, all the echocardiographies were done by an assigned pediatric cardiologist. Another study limitation was the personal dependency of the echocardiography procedure that hampered its application substantially.

CONCLUSIONS

Hemodialysis with volume reduction in children with ESRD decreases LV volume, but does not change regional strain and strain rate significantly.

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CONFLICT OF INTEREST

None declared.

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