Common echocardiography findings in pretransplant dialysis patients and their associations

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Available online 23 October 2013

KEYWORDS
Chronic kidney failure; Echocardiography; Kidney transplantation

Summary
Background/Purpose: Abnormality in cardiac structure and function is common in chronic kidney disease (CKD) patients. We aimed to evaluate the prevalence of different abnormal echocardiographic findings in CKD patients and find their associated factors.

Methods: This retrospective cross-sectional study was conducted in the Nephrology and Dialysis Department of the Shiraz University of Medical Sciences. A total number of 1354 kidney transplant candidates between the years 2000 and 2010 were included. Association between variables was assessed by Chi-square test and Student t test. We analyzed our data using multivariate logistic and linear regression when appropriate.

Results: Left ventricular hypertrophy (LVH; 47.5%) was the most common finding in this study, followed by left atrial enlargement (43.7%), diastolic dysfunction (25.4%), left ventricular end diastolic dilation (23.1%), and systolic dysfunction (18.5%), in order of frequency. Older age was associated with abnormality in all echocardiographic indexes. Male gender was associated with LVH and systolic dysfunction. We found an association between a longer duration since CKD diagnosis and LVH. Left ventricular end diastolic dilation, left atrial enlargement, and diastolic dysfunction were associated with a longer duration of dialysis. Anemia was associated with all echocardiographic abnormalities except diastolic dysfunction. Hypoalbuminemia and hypocalcemia were associated with only left atrial enlargement and left ventricular end diastolic dilation, respectively. Patients on peritoneal dialysis had a lower prevalence of left atrial enlargement and left ventricular end diastolic dilation.
**Conclusion:** Different echocardiographic abnormalities, especially LVH, are prevalent among CKD patients. Traditional risk factors, such as age, diabetes mellitus, and hypertension, and uremia-related risk factors, such as anemia and hypoalbuminemia, are associated with an increase in the prevalence of these abnormalities.

**Introduction**

Chronic kidney disease (CKD) patients are at high risk of cardiovascular diseases, which account for about half of the mortalities in this population. Abnormality in cardiac structure and function detected by echocardiography is common in CKD patients. Increasing evidence exists supporting the essential role of this tool in estimating the prevalence of primary heart disease in this population and studying its predisposing factors, prognostic impact, and the effect of therapeutic interventions.

Left ventricular (LV) hypertrophy (LVH) and systolic dysfunction are frequent findings in CKD patients, and represent the strongest risk factors for death and adverse CV outcomes in this population. LV diastolic function is also reduced in this population.

Abnormal filling of the left ventricle and mitral regurgitation also result in an increase in the left atrial size, which also has a prognostic implication.

In this retrospective cross-sectional study, we aimed to evaluate the prevalence of different abnormal echocardiographic findings in 1354 CKD patients undergoing renal replacement therapy and find their clinical associations.

**Methods**

This retrospective cross-sectional study was conducted in the Nephrology and Dialysis Department of Medical University of Shiraz, Iran. Study design was approved by the Research Ethics Committee of Shiraz University of Medical Sciences. Kidney transplant candidates had undergone echocardiographic assessment as a routine pretransplant evaluation in this department between the years 2000 and 2010. The inclusion criterion was patients aged 18–60 years old, on hemodialysis (HD) for at least 3 months, who were candidates for transplant. Patients with congenital and rheumatic heart disease were excluded.

Demographic, clinical (duration of dialysis and the primary cause of CKD), and biochemical (hemoglobin, serum albumin, calcium, and phosphorus) data of these patients in addition to their echocardiographic reports were extracted from their medical records and profiles available in the hospital information support system. The echocardiographic and biochemical data are maximally 3 months apart. All echos were performed within a few hours of HD. Patients underwent two-dimensional, color Doppler, and M-mode echocardiographic evaluation. The following echocardiographic definitions were used. LVH was defined as septal and/or posterior wall thickness ≥ 11 mm in males and ≥ 10 mm in females. LV end diastolic diameter more than 54 mm in females and more than 59 mm in males and left atrial diameter more than 39 mm in females and more than 41 mm in males were considered abnormal. LV ejection fraction less than 55% was indicative of systolic dysfunction. Diastolic dysfunction was defined using transmural inflow pattern.

Data were analyzed by SPSS version 18.0 (SPSS Inc., Chicago, IL, USA). Nominal and categorical variables were described by absolute frequency (%), and scale variables were described as mean ± standard deviation. Association between variables was assessed by Chi-square test and Student t test. Data was analyzed using multivariate logistic and linear regression when appropriate. A p value of <0.05 was considered significant.

**Results**

**Demographic and clinical data**

In this retrospective cross-sectional study, 1354 patients were included. The mean age of the patients was 38.5 ± 13.7 years, with a male:female ratio of 64.6:35.4. Of these patients, 11.6% had hypertension, 11.2% were diabetic, and 5.9% had ischemic heart disease. Patients were on dialysis for a mean duration of 23.9 ± 22.1 months. They underwent dialysis from one to three times a week. Vascular access was performed with arteriovenous fistula in 83% of cases and double lumen in 17% of cases. Among the 1280 patients whose dialysis data were available, 1236 (96.6%) underwent HD and 44 (3.4%) underwent peritoneal dialysis (PD). CKD was
We performed multivariate logistic regression (Table 3), which showed that the presence of LVH was associated with age [odds ratio (OR) = 1.02, 95% confidence interval (CI) = 1.00, 1.04, p = 0.003], dialysis duration (OR = 1.4, 95% CI = 1.2, 1.6, p < 0.001), hemoglobin (OR = 0.9, 95% CI = 0.8, 1.0, p = 0.044), and albumin (OR = 0.8, 95% CI = 0.7, 0.9, p = 0.002). Diastolic dysfunction was associated with age (OR = 1.1, 95% CI = 1.0, 1.2, p = 0.007) and duration of dialysis (OR = 1.3, 95% CI = 1.2, 1.5, p = 0.044).

In addition, multivariate linear regression (Table 4) showed that the LV end diastolic diameter was associated with age (β = 0.05, 95% CI = 0.04, 0.07, p < 0.001, which means that the LV end diastolic diameter increases by 0.05 for each year increase in age), gender (β = -0.4, 95% CI = -0.5, -0.3, p < 0.001), duration since CKD diagnosis (β = 1.4, 95% CI = 1.3, 1.5, p < 0.001), hemoglobin (β = -0.3, 95% CI = -0.4, -0.2, p = 0.003), and calcium (β = -0.4, 95% CI = -0.5, -0.3, p = 0.044).

Left atrial diameter was associated with age (β = 0.07, 95% CI = 0.06, 0.08, p < 0.001), gender (β = -0.2, 95% CI = -0.3, -0.1, p = 0.001), duration since CKD diagnosis (β = 0.03, 95% CI = -0.01, 0.07, p < 0.05), dialysis duration (β = 1.4, 95% CI = 1.3, 1.5, p < 0.001), hemoglobin (β = -0.2, 95% CI = -0.3, -0.1, p = 0.021), and albumin (β = -0.8, 95% CI = -0.9, -0.7, p = 0.049). In addition, systolic dysfunction was associated with only dialysis duration (β = -1.4, 95% CI = -1.5, -1.3, p < 0.001), calcium (β = -0.4, 95% CI = -0.5, -0.3, p = 0.04).

Finally, our results show that patients on PD had a lower prevalence of left atrial enlargement and LV end diastolic dilation. We could not find any similar association in previous studies.

### Discussion

In this retrospective cross-sectional study, we evaluated the prevalence of different echocardiographic abnormalities. We performed multivariate logistic regression (Table 3), which showed that the presence of LVH was associated with age (OR = 1.02, 95% CI = 1.00, 1.04, p = 0.003), dialysis duration (OR = 1.4, 95% CI = 1.2, 1.6, p < 0.001), hemoglobin (OR = 0.9, 95% CI = 0.8, 1.0, p = 0.044), and albumin (OR = 0.8, 95% CI = 0.7, 0.9, p = 0.002). Diastolic dysfunction was associated with age (OR = 1.1, 95% CI = 1.0, 1.2, p = 0.007) and duration of dialysis (OR = 1.3, 95% CI = 1.2, 1.5, p = 0.044).

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Finally, our results show that patients on PD had a lower prevalence of left atrial enlargement and LV end diastolic dilation. We could not find any similar association in previous studies.
abnormalities in 1354 CKD patients. LVH (47.5%) was the most common finding in this study, followed by left atrial enlargement (43.7%), diastolic dysfunction (25.4%), LV end diastolic dilatation (23.1%), and systolic dysfunction (18.5%), in order of frequency. In a study by Foley et al in 1995, the prevalence of echocardiographic abnormalities was evaluated in 433 CKD patients prior to the initiation of dialysis. On echocardiography, 74% had LVH, 32% had LV dilation, and 15% had systolic dysfunction. In another study by Hayashi et al in 2006, conventional echocardiography and tissue Doppler velocity imaging were used to estimate the prevalence of different echocardiographic abnormalities in 40 CKD patients. LVH and diastolic dysfunction were the most common findings in this study. Left atrial enlargement and systolic dysfunction had lower prevalence. To our knowledge, this study is one of the largest studies that evaluate simultaneously the prevalence of these five echocardiographic changes in CKD patients.

Hypertrophy is the common reaction of the heart to volume and pressure overload in CKD patients similar to other causes of overload. The left atrium enlarges passively due to increased LV end diastolic pressure because it tries to fill the left ventricle despite high impedance. LV dilatation needs more time and severity of volume and pressure overload, and accordingly has a lower frequency. In the beginning, LVH is adaptive; however, it ultimately becomes maladaptive following myocyte death when systolic dysfunction occurs. Thus, systolic dysfunction can be a terminal event in a hypertrophied heart. Other pathophysiologic processes such as coronary artery disease, malnutrition, and hyperparathyroidism can also cause systolic dysfunction in end stage renal disease (ESRD). Diastolic dysfunction in CKD is a result of many pathophysiologic processes such as hypertension, coronary artery disease, and chronic uremia.

In the second part of this study, we evaluated the association between echocardiographic abnormalities and different clinical factors. Some of the evaluated factors were traditional risk factors for cardiovascular disease. Older age was found to be associated with abnormality in most of the echocardiographic indexes assessed in this study. This association has consistently been present in previous study. Tripepi et al showed that the association between age and some of these abnormalities is largely dependent on age-related risk factors such as inflammation, mainutrition, and arterial rigidty. Male gender was associated with LVH, LV end diastolic dilatation, and left atrial dilatation in our study. Gender difference in echocardiographic abnormalities among CKD patients has not been a consistent finding.

We also evaluated whether the underlying etiology of CKD has any effect on the prevalence of assessed echocardiographic indexes. Diabetes mellitus and hypertension, as two well-known traditional cardiovascular risk factors, were associated with LVH, systolic, and diastolic dysfunctions in univariate analysis. In a previous study, diabetes mellitus and hypertension have also been shown to correlate with these echocardiographic abnormalities; however, in multivariate analysis this association was not confirmed, which is consistent with the results of Grossman et al's study.

We found an association between a longer duration of dialysis and LVH. Although many studies have shown an increase in the prevalence of LVH in CKD patients over time, studies showing that regression of this echocardiographic abnormality in CKD patients is possible also exist. This can be explained by the different types of interventions used in this population and different strategies adopted in managing the risk factors affecting the progression of this condition.

LV end diastolic dilatation, left atrial enlargement, and diastolic dysfunction were associated with a longer duration of dialysis in this study. This can be explained by the fact that many cardiac structural and functional abnormalities progress over time in this population even after initiation of renal replacement therapy, as shown in previous studies.

In this study, we also evaluated the association between some uremia-related cardiovascular risk factors, such as serum albumin, anemia, total serum calcium and

<table>
<thead>
<tr>
<th>Variables</th>
<th>Left ventricular hypertrophy</th>
<th>Diastolic dysfunction</th>
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<tbody>
<tr>
<td></td>
<td>OR</td>
<td>p</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
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<td></td>
</tr>
<tr>
<td>Female</td>
<td>0.03</td>
<td>0.17</td>
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<tr>
<td>Type of dialysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peritoneal dialysis</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>0.01</td>
<td>0.999</td>
</tr>
<tr>
<td>Age</td>
<td>1.02</td>
<td>0.001</td>
</tr>
<tr>
<td>Duration of CKD diagnosis (mo)</td>
<td>1.0</td>
<td>0.923</td>
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<tr>
<td>Duration of dialysis (mo)</td>
<td>1.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>0.9</td>
<td>0.044</td>
</tr>
<tr>
<td>Albumin</td>
<td>0.8</td>
<td>0.020</td>
</tr>
<tr>
<td>Calcium</td>
<td>0.9</td>
<td>0.302</td>
</tr>
<tr>
<td>Phosphate</td>
<td>1.1</td>
<td>0.084</td>
</tr>
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</table>

LVH = left ventricular hypertrophy; OR = adjusted odds ratio.

Echocardiography findings in dialysis patients
phosphate, and echocardiographic abnormalities. The hemoglobin level was associated with LVH, LV end diastolic diameter, and left atria dimension. This association is in agreement with the results of many previous studies, which has introduced anemia as one of the correctable factors in the development and progression of different echocardiographic abnormalities. Anemia induces LV dilation and compensatory LV hypertrophy, and is a risk factor for de novo heart failure and earlier death. Each g/dL fall in hemoglobin from the reference value was associated with a 10 g/m² rise in the LV mass index. Our finding showed that each 1 mg/dL decrease in hemoglobin level was associated with increases in LV end diastolic dimension by 0.3 mm and left atrial dimension by 0.2 mm. Another study revealed significant independent associations between the degree of LV dilation and anemia. Some studies reported that correction of anemia with erythropoietin failed to induce regression of concentric LV hypertrophy or LV dilation, but it could prevent LV dilation in patients with normal LV volumes.

Previous studies have also declared that hypoalbuminemia, as an index of malnutrition and hypocalemia, and hyperphosphatemia, as a part of hyperparathyroidism-related cardiomyopathy, affect the prevalence of different echocardiographic abnormalities. In this study; hypoalbuminemia was associated with left atrial enlargement and LVH. We could not find any association between hyperphosphatemia and assessed echocardiography indexes.

Calcium level was associated with LV end diastolic and left atrial dimensions. Each 1 mg/dL decrease in calcium level was associated with increases in LV end diastolic dimension and left atrial dimension by 0.4 mm.

Hypoalbuminemia may result from malnutrition and albuminuria in CKD. Data have shown that hypoalbuminemia predicts the incident of heart failure autonomously in patients with end-stage renal disease and elderly patients. It may contribute to the progression of heart failure by favoring volume overload, myocardial edema, exacerbation of oxidative stress and inflammation, and diuretic resistance. Hypoalbuminemia provokes a low plasma oncotic pressure, which facilitates the development of pulmonary edema in patients without a critical increase in pulmonary capillary hydrostatic pressures. Harnett et al. and Gupta et al. showed that in patients with end-stage renal disease, hypoalbuminemia predicted de novo heart failure independently of age, serum hemoglobin, blood pressure, LV systolic function, and hypertrophy.

Hypocalcemic dilated cardiomyopathy is a rare cause of heart failure in adults, and most studies on this topic were conducted in pediatric groups. Hypocalcemia related with cardiomyopathy in renal failure has rarely been reported in the literature. Common reports were in idiopathic hyperparathyroidism or after parathyriodectomy in adults. Hypocalcemia reduces myocardial contractility and plays a central role in muscle contraction. Calcium ion is required for the depolarization/repolarization phases of the cardiac cycle via the slow calcium channels. It is also important for the activation of actin so that myosin can form crossbridges to cause contraction. Hypocalcemia can delay the conduction of cardiac impulse and weaken contractility. In the majority of reports, correction of hypocalcemia was associated with the resolution of congestive heart failure and improvement of LV geometry; systolic function improved completely. Finally, our results show that patients on PD had a lower prevalence of left atrial enlargement and LV end diastolic dilation. We could not find any similar association in previous studies.

One limitation of this study is its retrospective cross-sectional design, and our results should be interpreted in the context of the results of previous and future clinical trials. Factors that had been described to affect the prevalence of echocardiographic abnormalities in CKD patients were unavailable to us. Some important ones are smoking history, results of blood pressure monitoring, inflammatory indices such as reactive protein (CRP) and parathyroid

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**Table 4** Linear regression of the association between quantitative clinical factor and echocardiographic abnormalities in hemodialysis patients.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Left ventricular end diastolic diameter</th>
<th>Left atrial diameter</th>
<th>Systolic dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>Beta</td>
<td>p</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>−4.2</td>
<td>0.277</td>
<td>0.004</td>
</tr>
<tr>
<td>Age</td>
<td>0.05</td>
<td>0.065</td>
<td>0.007</td>
</tr>
<tr>
<td>Duration of CKD diagnosis (mo)</td>
<td>1.4</td>
<td>0.138</td>
<td>0.001</td>
</tr>
<tr>
<td>Duration of dialysis (mo)</td>
<td>0.02</td>
<td>0.057</td>
<td>0.056</td>
</tr>
<tr>
<td><strong>Type of dialysis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peritoneal dialysis</td>
<td>−8.1</td>
<td>0.057</td>
<td>0.087</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>−0.31</td>
<td>−0.097</td>
<td>0.003</td>
</tr>
<tr>
<td>Albumin</td>
<td>0.1</td>
<td>0.009</td>
<td>0.271</td>
</tr>
<tr>
<td>Calcium</td>
<td>−0.4</td>
<td>−0.065</td>
<td>0.046</td>
</tr>
<tr>
<td>Phosphate</td>
<td>0.1</td>
<td>0.037</td>
<td>0.252</td>
</tr>
</tbody>
</table>

CKD = chronic kidney disease.
hormone (PTH) level, which were missing in our database. Introduction of newer techniques in echocardiographic assessment of patients such as three-dimensional echocardiography and tissue Doppler velocity imaging techniques may enrich our results further.

In conclusion, different echocardiographic abnormalities in the left side of the heart are prevalent among CKD patients. The most common finding is LVH. Traditional risk factors, such as age, diabetes mellitus, and hypertension, and uremia-related risk factors, such as anemia and hypalbuminemia, are associated with an increase in the prevalence of these abnormalities.

Acknowledgments

The Nephro-Urology Research Center of Shiraz University of Medical Sciences financially supported this study. This article was derived from a student’s thesis (Dr Zahra Asem).

References


