



Effect of Hemodialysis on Cardiac Structures and Functions in Chronic Renal Disease Patients

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ABSTRACT

Objective: Although dialysis is a revolutionary treatment for chronic kidney disease, cardiac pathologies continue to be a major cause of morbidity and mortality. Early diagnosis of dialysis related cardiac changes prolongs survival. The aim of our study was to assess the cardiac differences between hemodialysis patients and patients not receiving dialysis with estimated glomerular filtration rate (eGFR) <30 ml/dk. **Materials and Methods:** A total of 50 hemodialysis patients and 50 patients not receiving dialysis with eGFR<30 ml/dk were included in this study. Baseline characteristics, echocardiographic findings, hematological and biochemical parameters were compared between groups. **Results:** Age and gender were similar between groups. Dialysis patients were 69.3±10.5 years of age and 50% were male, patients not receiving dialysis with eGFR<30 ml/dk were 72±10 years of age and 40 % were male. (p=0.150, p=0.211, respectively). Also, hypertension [36(72%) vs 33(66%), p=0.333], diabetes mellitus [23(46%) vs 22(44%), p=0.500] and coronary artery disease [26(52%) vs 23(46%), p=0.345] were similar between groups. Left ventricular hypertrophy [43(86%) vs 33(66%), p=0.035] and tricuspid regurgitation [43(86%) vs 32(64%), p=0.010] were more common in dialysis patients. Pulmonary artery systolic pressure (mmHg) was higher in dialysis patients [33(25-40) vs 25(20-35), p=0.018]. Also, hemoglobin (g/dl) [10.8±1.5 vs 11.6±1.7, p=0.020], hematocrit (%) [33.2±4.6 vs 35.6±5.9, p=0.032] levels were lower and anemia [45(90%) vs 37 (74%), p=0.033] was more frequent in hemodialysis patients. **Conclusion:** Left ventricular hypertrophy, tricuspid regurgitation were more common and pulmonary artery systolic pressure levels were higher in dialysis patients compared to the patients not receiving dialysis with eGFR<30 ml/dk. Also, hemoglobin levels were lower in dialysis patients. This study emphasizes the importance of regular echocardiographic assessment for early diagnosis and management cardiac pathologies in dialysis patients. **Keywords:** Chronic Kidney Disease, Echocardiography, Hemodialysis.

Kronik Böbrek Hastalarında Hemodiyalizin Kalp Fonksiyonları Üzerine Etkisi

ÖZ

Amaç: Diyaliz, kronik böbrek hastalarında çığır açan bir tedavi yöntemidir. Kronik böbrek hastalarında kardiyak patolojilere bağlı morbidite ve mortalite yaygındır. Diyalize bağlı gelişen kardiyak değişikliklerinin erken tanı ve tedavisi sürveyi uzatır. Bu çalışmanın amacı hemodiyaliz hastaları ile glomerüler Filtrasyon Hızı (eGFR) <30 ml/dk olan ve diyaliz almayan hastalar arasındaki kardiyak farklılıkları saptamaktır. **Gereç ve Yöntem:** Bu çalışmaya 50 hemodiyaliz hastası ve 50 eGFR<30 ml/dk olan ve diyaliz almayan hasta dahil edildi. Gruplar arasında demografik özellikler, ekokardiyografik bulgular, hematolojik ve biyokimyasal parametreler karşılaştırıldı. **Bulgular:** Gruplar arasında cinsiyet ve yaş yönünden fark yoktu. Diyaliz hastaları 69,3±10,5 yaşında ve %50'si erkek, eGFR<30 ml/dk olan ve diyaliz almayan hastalar ise 72±10 yaşında ve %40'ı erkekti. (sırasıyla p=0.150, p=0.211). Hipertansiyon [36(%72) karşı 33(%66), p=0.333], diyabet [23(%46) karşı 22(%44), p=0.500] ve koroner arter hastalığı [26(%52) karşı 23(%46), p=0.345] gruplar arasında benzerdi. Sol ventrikül hipertrofisi [43(%86) karşı 33(%66), p=0.035] ve triküspit yetersizliği [43(%86) karşı 32(%64), p=0.010] diyaliz hastalarında daha sıkı. Pulmoner arter sistolik basıncı (mmHg) diyaliz hastalarında daha yüksekti [33(25-40) karşı 25(20-35), p=0.018]. Ayrıca hemoglobin (g/dl) [10.8±1.5 karşı 11.6±1.7, p=0.020], hematokrit (%) [33.2±4.6 karşı 35.6±5.9, p=0.032] düzeyleri daha düşük ve anemi [45(90%) karşı 37(%74), p=0.033] hemodiyaliz hastalarında daha sık saptandı. **Sonuç:** Hemodiyaliz hastalarının, eGFR<30 ml/dk olan ve diyaliz almayan hastalar ile karşılaştırıldığında, sol ventrikül hipertrofisi, triküspit yetersizliği daha sık ve pulmoner arter sistolik basınçları daha yüksekti. Ayrıca diyaliz hastalarında hemoglobin seviyeleri daha düşüktü. Bu çalışma, hemodiyaliz hastalarında kardiyak patolojilerin erken tanısı ve tedavisi için düzenli ekokardiyografik değerlendirmenin önemini vurgulamaktadır.

Anahtar Kelimeler: Kronik Böbrek Hastalığı, Ekokardiyografi, Hemodiyaliz.

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INTRODUCTION

Chronic kidney disease (CKD) is a health problem associated with morbidity and mortality around the world. The estimated prevalence of CKD is 13.4% and patients needing dialysis treatment are between 4.902 and 7.083 million in the world (Levey et al., 2011; Lv & Zhang, 2019). Kidney and cardiovascular diseases share several risk factors, and cardiovascular diseases are frequently encountered in CKD patients. CKD patients having cardiovascular disease (CVD) had 3 to 30 times higher risk of mortality compared to the normal population (Muntner et al., 2013). It is notable that mortality due to CVD are more common than kidney failure among patients with CKD (Go et al., 2004).

Echocardiography is a fast and reliable method for the assessment of cardiac functional and structural abnormalities. Echocardiographic assessment can help to detect the early diagnosis of the CVD in patients of CKD. In a recent study, Tseng et al investigated the echocardiographic abnormalities and their relationship with adverse outcomes in kidney failure patients. They found that echocardiography can help clinicians optimize patient management and identify high risk patients (Tseng et al., 2024). Our study aimed to investigate the effect of the dialysis treatment on cardiac structures and functions in CKD patients.

MATERIALS AND METHODS

50 dialysis patients and 50 patients not receiving dialysis with the estimated glomerular filtration rate (eGFR) <30 ml/dk, who applied to the cardiology outpatient clinic for any reason were included in the study. Inclusion criteria were age >18 years of age and patients receiving hemodialysis for more than 1 year. Exclusion criteria was advanced disease patients requiring intensive care unit.

Body mass index (BMI) was calculated by dividing weight (kilograms) to height (meters) squared (Go et al., 2015). Anemia criteria was <12g/dL in women and <13g/dL in men according to the World Health Organization (WHO) (Cappellini & Motta, 2015). The eGFR was calculated by Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) (Pugliese et al., 2011).

Previously diagnosed with hypertension, using antihypertensive drug or patients having blood pressure $\geq 140/90$ were defined as hypertensive. Left ventricular hypertrophy (LVH) was defined as intraventricular or LV posterior wall thickness ≥ 12 mm (Jameel et al., 2020; Devereux et al., 1986).

Transthoracic echocardiography was performed using a Philips Affiniti 50 Ultrasound System. Each patient underwent two-dimensional transthoracic echocardiography according to the European Association of Echocardiography recommendations

(Evangelista et al., 2008). Ejection fraction (EF) (%), left ventricular end diastolic diameter (LVEDD) (mm), left ventricular end systolic diameter (LVESD) (mm), pulmonary artery systolic pressure (PASP) (mmHg), right ventricular diameter (mm), ascending aorta diameter (mm), left atrium diameter (mm), left ventricular hypertrophy, valvular regurgitation and stenosis, diastolic functions calculated by early (E) and late (A) transmitral diastolic flow velocity, early diastolic annular velocity (E') and E/E' ratio were evaluated.

The ratio of peak E wave to A wave were measured using pulsed wave doppler echocardiography. Early (E') diastolic annular velocity was measured at the septal mitral annulus (Nagueh et al., 2009). Left ventricular diastolic patterns were classified into 4 groups. 1) Normal pattern: $E/A > 0.8$ and with septal $E' \geq 7$ cm/s; 2) Impaired relaxation pattern: $E/A \leq 0.8$ and abnormal E' wave; 3) Pseudonormal pattern: $E/A = 0.8-2.0$ and abnormal E' wave; 4) Restrictive pattern: $E/A > 2.0$ and abnormal E' wave (Matsuo et al., 2018).

Statistical analysis

SPSS 13.0 (SPSS Inc., IBM, Chicago, IL, USA) was used for statistical analyses. Kolmogorov-Smirnov test was used to analyze the distribution of the parameters. Normally distributed variables as mean \pm SD and abnormally distributed parameters are expressed as median and percentiles (25–75). Categorical variables were showed as percentages and frequencies. Categorical variables were tested with the Fisher's exact test or Chi-square. Normally distributed continuous parameters were evaluated with 2 tailed Student's T-test and abnormally distributed parameters with Mann-Whitney U test.

Ethical considerations

The study was conducted in accordance with the declaration of Helsinki and approved by The University's Ethics Committee (Date: 2018, Approval no: KÜ GOKAEK 2018/130).

RESULTS

A total of 50 hemodialysis patients and 50 patients not receiving dialysis with eGFR <30 ml/dk were included in this study. There was not any difference in gender and age between the groups. Dialysis patients were 69.3 ± 10.5 years of age and 50% were male, patients not receiving dialysis with eGFR <30 ml/dk were 72 ± 10 years of age and 40 % were male. ($p=0.150$, $p=0.211$, respectively). BMI (kg/m^2) were similar between groups (26.8 ± 5.4 vs 28.6 ± 5 ; $p=0.178$). Hypertension [36 (72%) vs 33 (66%), $p=0.333$], diabetes mellitus [23(46%) vs 22 (44%), $p=0.500$] and coronary artery disease [26(52%) vs 23(46%), $p=0.345$] were similar between groups. Also, anemia was more common in dialysis patients [45(90%) vs 37 (74%), $p=0.033$] (Table 1).

Table 1. Baseline characteristics of the groups.

| | Hemodialysis patients (n=50) | Patients not receiving dialysis with eGFR<30 ml/dk (n=50) | p |
|--------------------------------------|------------------------------|---|-------|
| Age (years) | 69.3±10.5 | 72±10 | 0.150 |
| Male/female | 25/25 (50%-50%) | 20/30 (40%-60%) | 0.211 |
| Body mass index (kg/m ²) | 26.8±5.4 | 28.6±5 | 0.178 |
| Hypertension | 36 (72%) | 33 (66%) | 0.333 |
| Diabetes mellitus | 23 (46%) | 22 (44%) | 0.500 |
| Coronary artery disease | 26 (52%) | 23(46%) | 0.345 |
| Anemia | 45 (90%) | 37 (74%) | 0.033 |

In echocardiographic parameters; there was no significant difference in EF (%) [55(41-60) vs 55(50-60), p=0.333], LVEDD (mm) [48.8±6.2 vs 48.4±4.6, p=0.766], LVESD (mm) [34±7.7 vs 33.5±5.9, p=0.775], left atrium diameter (mm) [39±7.3 vs 37.5±5.1, p=0.312], ascending aorta (mm) [33 (31-36) vs 35 (32-37), p=0.458] and right ventricular diameter (mm) [25(22-27) vs 23(21-25), p=0.117] were similar between groups. PASP (mmHg) was higher in dialysis patients [33(25-40) vs 25(20-35), p=0.018]. LVH [43(86%) vs 33(66%), p=0.035] and tricuspid regurgitation [43(86%) vs

32(64%), p=0.010] were determined more common in dialysis patients compared to the patients not receiving dialysis with eGFR<30 ml/dk. Mitral regurgitation (p=0.165), aortic regurgitation (p=0.916), aortic stenosis (p=0.469) and pulmonary regurgitation (p=0.339) were similar between groups. E wave [70(60-105) vs 70(60-106), p=0.650], A wave [88±25 vs 93±26, p=0.564], E' wave [6(5-7.5) vs 6.5(5-7), p=0.770] and E wave/E' wave [10.8(10-16) vs 12(10-16), p=0.649] were not statistically different between groups (Table 2 and Table 3).

Table 2. Echocardiographic parameters of the groups.

| | ESRD patients with undergoing dialysis (n=50) | Patients not receiving dialysis with eGFR<30 ml/dk (n=50) | p |
|---------------------------------|---|---|-------|
| Ejection fraction (%) | 55 (41-60) | 55 (50-60) | 0.333 |
| E wave | 70 (60-105) | 70 (60-106) | 0.650 |
| A wave | 88±25 | 93±26 | 0.564 |
| E' wave | 6 (5-7.5) | 6.5 (5-7) | 0.770 |
| E wave / E' wave | 10.8 (10-16) | 12 (10-16) | 0.649 |
| LVEDD (mm) | 48.8±6.2 | 48.4±4.6 | 0.766 |
| LVESD (mm) | 34±7.7 | 33.5±5.9 | 0.775 |
| Left atrium diameter (mm) | 39±7.3 | 37.5±5.1 | 0.312 |
| PASP (mmHg) | 33 (25-40) | 25 (20-35) | 0.018 |
| Right ventricular diameter (mm) | 25 (22-27) | 23 (21-25) | 0.117 |
| Ascending aorta diameter (mm) | 33 (31-36) | 35 (32-37) | 0.458 |
| Left ventricular hypertrophy | 43 (86%) | 33 (66%) | 0.035 |
| Diastolic dysfunction | 40 (%80) | 38 (%76) | 0.405 |

LVEDD: Left ventricular end diastolic diameter (mm), LVESD: Left ventricular end systolic diameter (mm), PASP: Pulmonary artery systolic pressure (mmHg)

In hematological and biochemical parameters; hemoglobin (g/dl) [10.8±1.5 vs 11.6±1.7, p=0.020], hematocrit (%) [33.2±4.6 vs 35.6±5.9, p=0.032], eGFR (ml/min) [9.9±4 vs 22.3±5, p<0.001] levels were lower and creatinine (mg/dl) [5.5±1.7 vs 2.43±0.6, p<0.001],

urea (mg/dl) [111±40 vs 93±33, p=0.020] levels were higher in dialysis patients compared to the patients not receiving dialysis with eGFR<30 ml/dk. Other Hematological and biochemical parameters were similar between groups (Table 4).

Table 3. Valve stenosis and regurgitations of the groups.

| | ESRD patients with undergoing dialysis (n=50) | Patients not receiving dialysis with eGFR<30 ml/dk (n=50) | p |
|-------------------------|---|---|-------|
| Mitral regurgitation | | | |
| Grade-1 | 20 (40%) | 16 (32%) | 0.165 |
| Grade-2 | 11 (22%) | 10 (20%) | |
| Grade-3 | 3 (6%) | 0 (0%) | |
| Aortic Regurgitation | | | |
| Grade-1 | 12 (24%) | 12 (24%) | 0.916 |
| Grade-2 | 10 (20%) | 9 (18%) | |
| Grade-3 | 0 (0%) | 0 (0%) | |
| Aortic stenosis | | | |
| Grade-1 | 6 (12%) | 3 (6%) | 0.469 |
| Grade-2 | 2 (4%) | 1 (2%) | |
| Grade-3 | 0 (0%) | 0 (%) | |
| Tricuspid regurgitation | | | |
| Grade-1 | 24 (48%) | 18 (36%) | 0.010 |
| Grade-2 | 12 (24%) | 9 (18%) | |
| Grade-3 | 7 (14%) | 5 (10%) | |
| Pulmonary regurgitation | | | |
| Grade-1 | 4 (8%) | 2 (4%) | 0.339 |
| Grade-2 | 0 (0%) | 0 (0%) | |
| Grade-3 | 0 (0%) | 0 (0%) | |

Table 4. Hematological and biochemical parameters of the groups.

| | ESRD patients with undergoing dialysis (n=50) | Patients not receiving dialysis with eGFR<30 ml/dk (n=50) | P |
|------------------------------|---|---|--------|
| Glucose (mg/dl) | 134 (97-192) | 117 (96-163) | 0.250 |
| HbA1c | 6.1 (5.4-8.1) | 6.3 (5.8-7.5) | 0.510 |
| Hemoglobin (g/dl) | 10.8±1.5 | 11.6±1.7 | 0.020 |
| Hematocrit (%) | 33.2±4.6 | 35.6±5.9 | 0.032 |
| Platelet (x1000/uL) | 235±71 | 210±70 | 0.093 |
| WBC (x1000/mm ³) | 7.7 (6.2-9.5) | 7 (5.7-8.7) | 0.079 |
| eGFR (ml/min) | 9.9±4 | 22.3±5 | <0.001 |
| Creatinine (mg/dl) | 5.5±1.7 | 2.43±0.6 | <0.001 |
| Urea (mg/dl) | 111±40 | 93±33 | 0.020 |
| AST (U/L) | 16 (13-21) | 18 (16-21) | 0.075 |
| ALT (U/L) | 13 (10-15) | 14 (11-17) | 0.095 |
| Total Cholesterol (mg/dL) | 213±58 | 190±47 | 0.084 |
| Triglyceride (mg/dL) | 169 (110-224) | 123 (86-228) | 0.122 |
| LDL (mg/dL) | 120±44 | 113±36 | 0.474 |
| HDL (mg/dL) | 45±14 | 44±13 | 0.927 |
| TSH (mIU/L) | 1.2 (0.6-2.7) | 1.5 (1.2-2.6) | 0.150 |

WBC: White blood cell count, eGFR: Estimated glomerular filtration rate, AST: Aspartate transaminase, ALT: Alanine transaminase, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, TSH: Thyroid Stimulating Hormone.

DISCUSSION

Dialysis treatment has revolutionized kidney failure patients and extended their lives. However, the most common cause of death is still cardiac causes in CKD patients. Early diagnosis and treatment of cardiac diseases can make a positive contribution to mortality and morbidity in dialysis patients. In this study, we have aimed to the functional and structural changes on echocardiography and blood parameters differences in dialysis patients compared to the

patients not receiving dialysis with eGFR<30 ml/dk. Left ventricular hypertrophy, tricuspid regurgitation were more common and pulmonary artery systolic pressure levels were higher in dialysis patients. LVH is a frequent structural cardiac abnormality in CKD patients. Also, LVH is a predictor for mortality, especially in dialysis patients (Parfrey et al., 1996). Ahmed HA et al. detected LVH in 80% of dialysis patients (Al Qersh et al., 2016). In a Zoccali et al.'s study, LVH was found in 77% of dialysis patients

(Zoccali et al., 2004). LVH is reported in 16–50% of stages 1–3 CKD patients, 50–70% of stages 4 and 5 CKD patients, and in 70–90% of dialysis patients (Liu et al., 2015). In our study, LVH was more common in dialysis patients. 86% of dialysis patients had LVH and 66% of patients not receiving dialysis with eGFR<30 ml/dk had LVH. Chronic hypervolemia triggers the LVH and arterial stiffness in dialysis patients (Abdelazim et al., 2022). The volume accumulated in the body between dialysis sessions increases preload and causes the LVH. Also, electrolyte imbalance, uremic toxins, metabolic and hematological changes especially anemia are other risk factors for LVH in dialysis patients.

Bhandari R. et al. (Bhandari et al., 2023) found that the most common echocardiographic finding was valvular heart disease which was detected in 78.5% of dialysis patients. Saxena et al.'s study, the major echocardiographic abnormality was tricuspid regurgitation in 66% of dialysis patients (Saxena et al., 2017). In our study, tricuspid regurgitation was more common in dialysis patients (86%). Grade 1 tricuspid regurgitation was 48%, Grade 2 tricuspid regurgitation was 24% and Grade 3 tricuspid regurgitation was 14% of the patients. Fluid balance is a critical component of the dialysis patients. The occurrence of chronic hypervolemia in these patients can lead to right ventricular overload resulting in tricuspid regurgitation and pulmonary hypertension. Also, due to the intermittent nature of dialysis therapy, in interdialytic periods, increases and decreases in volume may explain the frequent tricuspid regurgitation in dialysis patients.

Pulmonary hypertension has been frequently described in dialysis patients (Havlucu et al., 2007). Pulmonary hypertension is a progressive disorder with increased mortality and morbidity. Yigle et al. showed significantly lower survival rate in dialysis patients with pulmonary hypertension (Yigle et al., 2009). In our study, PASP was significantly elevated in dialysis patients compared to the patients not receiving dialysis with eGFR<30 ml/dk. Chronic volume overload, calcium and phosphate metabolism irregularities causing pulmonary artery calcification and increased blood flow from arteriovenous fistula may induce the higher pulmonary artery pressures (Mukhtar et al., 2014). Diastolic dysfunction is the extensive functional cardiac abnormality in echocardiography examination of dialysis patients. and Dialysis patients have a high incidence of diastolic dysfunction. LV diastolic dysfunction was 72.30% of the dialysis patients in Bhandari R et al.'s study (Bhandari et al., 2023). Farshid et al. demonstrated that the diastolic dysfunction was 86% of dialysis patients and diastolic dysfunction was a strong predictor for mortality (Farshid et al., 2013). In our study, LV diastolic dysfunction was 88% of the dialysis patients. However, there was no statistically significant difference between the groups.

Patients with chronic kidney disease had lower EF values compared to the normal individuals (Arshi et al., 2016). As expected, EF were lower in our study population. But we did not find significant differences between groups. Although it is not the subject of this study, the effect of dialysis on systolic functions is more evident in speckle tracking studies [Yip et al., 2018; Terhuerne et al., 2021] and may be useful in evaluating the effect of dialysis on systolic functions compared to the ejection fraction.

In blood parameters; anemia is significantly related with mortality in dialysis patients (Shivendra et al., 2014). Adera et al. demonstrates that the prevalence of anemia rises with worsening renal function: Stage 1-2, stage 3A, stage 3B, stage 4 and stage 5 CKD were 20%, 44.8%, 46.4%, 81.1%, and 93.8%, respectively (Adera et al., 2019). Several studies show the prevalence of anemia in CKD patients not receiving dialysis up to 60%. Also, at least 90% of dialysis patients will develop anemia (Shaikh et al., 2024). In our study, anemia was more frequent in dialysis patients. Anemia was 80% of dialysis patients and 62% of patients not receiving dialysis with eGFR<30 ml/dk. Cardiac abnormalities are common in dialysis patients like in our study. Regular echocardiographic assessment can help the early diagnosis of cardiac abnormalities and reduce cardiac morbidity and mortality.

Limitations and Strengths

There were some limitations in our study. First, the presented study was conducted on a small number of patients. Second, echocardiographic evaluations have been done as a routine with no relation to timing after hemodialysis session. Repeating echocardiography before and after dialysis may be useful in detecting acute dialysis related changes. Third, different types of echocardiographic methods such as speckle tracking imaging may be beneficial for detecting dialysis related changes (Adera et al., 2024).

CONCLUSION

Echocardiography is the simplest and reliable method for evaluating cardiac structures and functions in CKD patients. Left ventricular hypertrophy, tricuspid regurgitation and higher pulmonary artery systolic pressure levels were more common in dialysis patients compared to the patients not receiving dialysis with eGFR<30 ml/dk. These findings not only take attention to the cardiac impacts of dialysis but also highlight the importance of regular cardiac assessment of these patients for early diagnosis and management.

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Conflict of Interest

No conflict of interest has been declared by the author(s).

Author Contributions

Plan, design: OA; **Material, methods and data collection:** OA; **Data analysis and comments:** OA; **Writing and corrections:** OA.

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Ethical Approval

Institution: Kocaeli University Non-Interventional Clinical Research Ethics Committee

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