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Comparison of the Effects of Dialysis Type on Right Heart Functions in Chronic Renal Failure Patients

Kronik Böbrek Yetmezliği Hastalarında Diyaliz Tipinin Sağ Kalp Fonksiyonları Üzerindeki Etkilerinin Karşılaştırılması

Yasemin KAYA[1]
0000-0001-7360-8090
Muhammet ÖZBİLEN[1]
0000-0001-6052-7486
Seçkin DERELİ[2]
0000-0003-0090-3835
Harun DÜĞEROĞLU[1]
0000-0002-0546-175X
Saadet YILMAZ[1]
0000-0003-4847-1613
Mustafa YENERÇAĞ[2]
0000-0002-0933-7852
Yeliz KAŞKO ARICI[3]
0000-0001-6820-0381

[1]Ordu University Faculty of Medicine Department of Internal Medicine, Ordu, Turkey

[2]Ordu University Faculty of Medicine Department of Cardiology, Ordu, Turkey

[3]Ordu University Faculty of Medicine Department of Biostatistics, Ordu, Turkey

Corresponding Author
Sorumlu Yazar
Yasemin KAYA
ysmnkcmz@gmail.com

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ABSTRACT

Aim: The aim of this study was to compare the effects of dialysis type on right heart functions with two-dimensional speckle tracking echocardiography (2D-STE).
Material and Methods: A total of 53 patients who have peritoneal dialysis and hemodialysis, applied to cardiology and nephrology outpatient clinics, were included in the study. Those with left heart failure, coronary artery disease, primary and secondary pulmonary hypertension, pulmonary embolism, deep vein thrombosis, moderate and severe heart valve failure and stenosis were excluded from the study. Sociodemographic characteristics and biochemical parameters of the patients were recorded. Right heart functions of the patients were evaluated using 2D-STE.
Results: There was no difference between groups with respect to age (p=0.496), the rate of male was higher in hemodialysis group (p=0.006). In comparison of 2D-STE measurements; right atrium (RA) maximum volume and RA minimum volume were significantly higher in hemodialysis patients (p=0.006, p=0.007, respectively). There were no difference between the groups in RA maximum volume index, RA minimum volume index and tricuspid annular plane systolic excursion (TAPSE). RAS strain and RAA strain were significantly lower in hemodialysis patients (p=0.001, p=0.012, respectively). A positive correlation was found between TAPSE and RA maximum volume in hemodialysis patients (r=0.484, p=0.036), and between TAPSE and RA minimum volume in peritoneal dialysis patients (r=0.486, p=0.025).
Conclusion: Right ventricular functions were found to be similar in peritoneal dialysis and hemodialysis patients. It was observed that right atrial functions were better protected in peritoneal dialysis patients than hemodialysis patients.
Keywords: Dialysis; right heart functions; speckle tracking echocardiography.

ÖZ

Amaç: Bu çalışmanın amacı diyaliz tipinin sağ kalp fonksiyonlarına etkilerinin iki boyutlu speckle tracking ekokardiyografi (2D-STE) ile karşılaştırılmasıdır.
Gereç ve Yöntemler: Kardiyoloji ve nefroloji polikliniklerine başvuran, periton diyalizi yapan ve hemodiyalize giren toplam 53 hasta çalışmaya dahil edildi. Sol kalp yetmezliği, koroner arter hastalığı, primer ve sekonder pulmoner hipertansiyon, pulmoner emboli, derin ven trombozu, orta ve ileri derecede kalp kapak yetmezliği ve darlığı olanlar çalışma dışı bırakıldı. Hastaların sosyodemografik özellikleri ve biyokimyasal parametreleri kaydedildi. 2D-STE ile hastaların sağ kalp fonksiyonları değerlendirildi.
Bulgular: Yaş açısından gruplar arasında fark yoktu (p=0,496), hemodiyaliz grubunda erkek oranı daha yüksekti (p=0,006). 2D-STE ölçümleri karşılaştırıldığında; sağ atriyum (right atrium, RA) maksimum hacmi ve RA minimum hacmi hemodiyaliz hastalarında anlamlı olarak yüksekti (sırasıyla p=0,006; p=0,007). RA maksimum hacim indeksi, RA minimum hacim indeksi ve triküspit anulusunun sistolde apikale yer değiştirmesi (tricuspid annular plane systolic excursion, TAPSE) açısından gruplar arasında fark yoktu. Hemodiyaliz hastalarında RAS strain ve RAA strain anlamlı olarak daha düşüktü (sırasıyla p=0,001; p=0,012). Hemodiyaliz hastalarında TAPSE ile RA maksimum hacmi arasında (r=0,484; p=0,036) ve periton diyalizi hastalarında TAPSE ile RA minimum hacmi arasında (r=0,486; p=0,025) pozitif korelasyon bulundu.
Sonuç: Sağ ventrikül fonksiyonları periton diyalizi ve hemodiyaliz hastalarında benzer bulundu. Sağ atriyal fonksiyonların periton diyalizi hastalarında hemodiyaliz hastalarına göre daha iyi korunduğu görüldü.
Anahtar kelimeler: Diyaliz; sağ kalp fonksiyonları; speckle tracking ekokardiyografi.

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INTRODUCTION

Renal replacement therapies such as hemodialysis (HD), peritoneal dialysis (PD) and kidney transplantation are required at the last stage of chronic kidney disease (end stage renal disease, ESRD) characterized by progressive and irreversible nephron loss. Cardiovascular diseases are important causes of mortality and morbidity in ESRD (1). In a study, it was found that cardiovascular mortality increased approximately ten times in HD patients compared to those who have not dialysis. Besides, cardiovascular diseases are responsible for approximately half of the deaths of ESRD patients (2,3). 15-28% of the patients who received dialysis indication have a diagnosis of heart failure (4,5). Therefore, early diagnosis of heart failure and taking the necessary precautions to prevent the progression of the disease are important with respect to mortality and morbidity in patients undergoing dialysis.

It is known that conventional echocardiographic methods may be insufficient to show subclinical cardiac dysfunction. Two-dimensional speckle tracking echocardiography (2D-STE), which is different from conventional methods, is a semi-automatic method that can measure cardiac functions (6). It has been shown in previous studies that this method can detect subclinical myocardial dysfunction earlier compared to conventional methods (7).

We aimed to evaluate the effect of dialysis type on right ventricular (RV) functions by 2D-STE in this study.

MATERIAL AND METHODS

Peritoneal dialysis and HD patients who applied to cardiology and nephrology outpatient clinics between January 2017 and August 2017 were screened retrospectively. Twenty-seven HD and twenty-six PD patients were included. These patients were those who had been on dialysis for at least one year. Patients with pulmonary hypertension, pulmonary embolism, deep vein thrombosis, coronary artery disease, moderate and severe heart valve failure and stenosis were excluded. In this study, patients with left ventricular systolic dysfunction (ejection fraction, EF<50%) were excluded then. The age, gender, height, weight (weights measured after dialysis treatment), smoking status and duration of dialysis of the patients were recorded. Whether they had diabetes mellitus, hypertension, hyperlipidemia diagnoses was recorded (all patients had diabetes mellitus). Body mass index (BMI) was calculated using the weight (kg) / height $(m)^2$ formula. Body surface areas were calculated using the Mosteller formula (height (cm) x weight (kg) / $3600)^{½}$. Average of the arterial blood pressure measurements taken on different days were calculated. Patients with blood pressure higher than 140/90 mmHg were considered to be hypertensive. Diabetes mellitus was defined as a fasting blood glucose above 126 mg/dl and HbA1C=6.5.

While patients in the HD group received dialysis treatment at standard doses with a Kt/V ratio of 1.2 and above in 4-hour sessions 3 times a week, 33% hypertonic glucose dialysate and 95% icodextrin exchanges of all patients in the PD group were performed by continuous ambulatory peritoneal dialysis (CAPD).

The study was approved by the Ethics Committee of Ordu University Faculty of Medicine (18.05.2017, 2017/61).

Blood samples were taken into gel tubes (without anticoagulant) to measure biochemical parameters. After the serum were obtained from the blood samples, they were studied in the Abbott Architect 8000 automatic device. Blood samples were taken into EDTA tubes for hemogram measurement and studied in Abbott Cell-Dyn 3700 device. The glomerular filtration rate (GFR) was calculated with the Modification of Diet in Renal Disease (MDRD) formula as previously defined (8); GFR (mL/min/1.73 m^2) = 186 x serum creatinine$^{-1.154}$ x age$^{-0.203}$ x 0.742 (if female) x 1.212 (if black race).

Speckle Tracking Echocardiography

With a stable ECG recording of the patient holding his breath, RV free wall and right atrial (RA) functions were evaluated by conventional two-dimensional harmonic gray scale echocardiography in apical 4- and 2-chamber images (Philips IE 33 × Matrix, USA). Three cardiac cycles were recorded and averaged, with the frame rate adjusted between 60 and 80 frames per second. The recorded images were saved for later evaluation. Manual monitoring of RV and RA endocardial borders was performed for each view in the final systolic frame. Echocardiographic measurements of the PD patients were made in the morning when the peritoneum was empty before changing the peritoneal fluid. Echocardiographic measurements of HD patients were made in the middle of the week before HD. All echocardiographic measurements were performed according to the guidelines previously published by the American Echocardiographic Association (ASE).

Echocardiographic Measurements

All echocardiographic measurements were made with an echocardiography device (PhilipsIE 33Matrix, USA) equipped with 2.25 to 7.5 MHz imaging transducers. Measurements were made by a cardiologist who have blinded to the study design. Echocardiographic measurements were made the left decubitus position. Simpson's biplane method was used to calculate left ventricular ejection fraction (LVEF) from the apical 4-and 2-chamber views. Pulsed-wave Doppler tricuspid inflow velocities, including early (E) and atrial (A) waves were measured. Tissue Doppler imaging (TDI) measures of myocardial systolic, early diastolic and atrial velocities were assessed at the lateral tricuspid annulus wall. Tricuspid annular plane systolic excursion (TAPSE) was measured in a 4-chamber view by placing the 2D cursor at the tricuspid lateral annulus as previously defined the studies (9). Right atrium maximum volume index was calculated by dividing the RA maximum volume by surface area. RA minimum volume index was calculated by dividing the RA minimum volume by surface area.

Statistical Analysis

The data were examined in terms of normality with Kolmogorov-Smirnov test and variance homogeneity with Levene test. Variables fulfilling the assumptions were compared with Student's t test, while those not fulfilling the assumptions were compared with Welch's t test or Mann-Whitney U test. Categorical data were analyzed using the Pearson chi-square or Fisher's exact test, as appropriate. The numerical variables were summarized as mean±standard deviation and median, interquartile range, minimum-maximum, while the categorical variables were expressed as number and percentage. Pearson correlation coefficient was used for normally distributed variables, while Spearman's rank correlation coefficient was used for non-normally distributed variables. SPSS v.25 (IBM Inc., Chicago, IL, USA) statistical software was used for statistical analyses. Results were evaluated at 95% confidence interval and the significance level was p<0.05.

RESULTS

The mean age of PD patients was 45.40±7.21 years and 8 (30.8%) of the patients were male. The mean age of HD patients was 43.22±11.89 years and 18 (69.2%) of the patients were male. There was no difference between groups with respect to age (p=0.496), and the rate of male was higher in the HD group (p=0.006). No difference was found between the groups in terms of hypertension, hyperlipidemia and smoking (Table 1). The duration of dialysis for PD patients was 3 years, the duration of dialysis of HD patients was 5 years, and there was a significant difference between the groups in terms of dialysis durations (p<0.001). BMI and heart rate were higher in PD patients (p=0.075, p=0.052, respectively). There was no difference between the groups in terms of surface areas (Table 1). Ejection fraction of both groups was normal, but significantly higher in PD patients (61.15±5.16 vs. 54.26±10.44, p=0.004). In comparison of 2D-STE measurements between PD and HD patients; RA maximum volume and RA minimum volume were significantly higher in HD patients (p=0.006, p=0.007, respectively). There were no difference between the groups in RA maximum volume index, RA minimum volume index and TAPSE. Also, there was no difference between the groups in terms of RV strain. RAS strain and RAA strain were significantly smaller in HD patients (p=0.001, p=0.012, respectively). There was no statistically significant difference in terms of RV isovolumic contraction time (IVCT-RV), RV isovolumic relaxation time (IVRT-RV), and RV e-time (ET-RV) between the groups (Table 2). A positive correlation was found between TAPSE and RA maximum volume (r=0.484; p=0.036) in HD patients and between TAPSE and RA minimum volume (r=0.486; p=0.025) in PD patients (Table 3).

Table 1. Comparison of demographic, clinic and body characteristics, and biochemical parameters of groups

	n	Peritoneal Dialysis	n	Hemodialysis	p
Gender (male)	26	8 (30.8)	26	18 (69.2)	**0.006**[a]
Age (years)	25	45.40±7.21	18	43.22±11.89	0.496[b]
Body Mass Index (kg/m^2)	25	27.50±6.84	16	23.40±7.61	0.075[c]
Surface area (m^2)	25	1.79±0.23	16	1.75±0.36	0.672[c]
Hypertension	26	19 (76.0)	16	14 (87.5)	0.448[d]
Hyperlipidemia	25	8 (32.0)	16	2 (12.5)	0.265[d]
Smoking	25	6 (24.0)	14	4 (28.6)	0.999[d]
Dialysis year (years)	25	3 (1) [1-5]	18	5 (4) [2-12]	**<0.001**[e]
Hemoglobin (g/dl)	25	12.18±2.01	14	11.59±1.80	0.361[c]
GFR (mL/minute/1.73 m^2)	19	9.89±5.51	7	6.00±1.73	0.082[c]
Creatinine (mg/dl)	25	6.14±2.34	14	9.97±2.68	**<0.001**[c]
Heart rate (beats/min)	26	90.62±9.43	27	85.59±8.97	0.052[c]

GFR: glomerular filtration rate, [a]: Pearson's chi-square test, [b]: Welch's t test, [c]: Student's t test, [d]: Fisher's exact test, [e]: Mann-Whitney U test, descriptive statistics were given as n (%) for categorical variables, and mean±standard deviation or median (interquartile range) [minimum-maximum] values were used for numerical variables, as appropriate

Table 2. Comparison of two-dimensional speckle tracking echocardiography parameters of groups

	n	Peritoneal Dialysis	n	Hemodialysis	p
Ejection fraction (%)	26	61.15±5.16	27	54.26±10.44	**0.004**[a]
RA maximum volume (mL)	26	26.96±9.00	27	42.70±26.04	**0.006**[a]
RA minimum volume (mL)	26	15.85±4.06	27	27.19±19.63	**0.007**[a]
RA maximum volume index (mL/m^2)	19	14.67±4.90	8	25.81±20.10	0.163[a]
RA minimum volume index (mL/m^2)	19	8.82±2.71	8	16.38±15.95	0.223[a]
TAPSE (mm)	26	1.94±0.37	27	2.06±0.51	0.328[a]
RV strain (%)	26	-15.81±4.23	27	-14.86±5.64	0.494[b]
RAS strain (%)	26	30.34±8.24	27	23.65±5.98	**0.001**[b]
RAA strain (%)	26	21.93±7.75	27	17.17±5.16	**0.012**[a]
IVCT-RV (ms)	25	79.60±11.94	27	70.11±22.80	0.246[b]
IVRT-RV (ms)	24	84.75±20.22	27	90.78±24.48	0.171[b]
ET-RV (ms)	25	148.72±47.25	27	162.96±38.09	0.236[b]
Tricuspid E wave (m/s)	12	62 (19.5) [51-100]	9	68 (32) [56-100]	0.422[c]
Tricuspid A wave (m/s)	12	67 (34.5) [48-94]	9	64 (24) [42-90]	0.808[c]
Tricuspid E/A ratio	12	1.1 (0.5) [0.7-1.29]	9	1.2 (0.6) [0.8-1.47]	0.219[c]
Tricuspid deceleration time (m/s)	12	195.0 (39.3) [162-250]	9	190.0 (37.5) [166-216]	0.169[c]

RA: right atrium, TAPSE: tricuspid annular plane systolic excursion, RV: right ventricle, IVCT-RV: isovolumic contraction time-right ventricle, IVRT-RV: isovolumic relaxation time-right ventricle, ET-RV: ejection time-right ventricle, E: early, A: atrial, [a]: Welch's t test, [b]: Student's t test, [c]: Mann-Whitney U test, descriptive statistics were given as mean±standard deviation or median (interquartile range) [minimum-maximum], as appropriate

Table 3. Correlation coefficients between the variables

	TAPSE			
	PD		HD	
	r	p	r	p
RA maximum volume	0.292	0.199	0.484	**0.036**
RA minimum volume	0.486	**0.025**	0.345	0.148
RA maximum volume index	0.307	0.201	0.565	0.145
RA minimum volume index	0.386	0.103	0.626	0.097
RV strain	0.307	0.176	-0.052	0.832
RAS strain	-0.081	0.727	-0.072	0.770
RAA strain	-0.118	0.611	0.516	**0.024**

TAPSE: tricuspid annular plane systolic excursion, PD: peritoneal dialysis, HD: hemodialysis, RA: right atrium, RV: right ventricle

DISCUSSION

In this study, in which the effects of PD and HD on right heart functions were compared with 2D-STE, RV functions were similar. But, it was observed that RA functions were significantly better preserved in patients who had PD compared to HD.

Peritoneal dialysis and HD are well-known treatment methods for patients with ESRD. Despite advances in dialysis therapies, cardiovascular mortality in patients with ESRD is still very high. Especially, deterioration in cardiac functions is observed more frequently in dialysis patients than in the healthy population, and is the leading cause of death in this patient group (4). Besides traditional risk factors such as coronary artery disease, diabetes mellitus, and hypertension are more common in ESRD patients compared to the healthy population, these causes such as volume load, uremic cardiomyopathy, hypotension attacks, anemia, oxidative stress, arteriovenous (AV) fistula, left ventricular hypertrophy can cause deterioration in cardiac functions (9,10).

Over hydration is one of the major problems in the development of cardiovascular problems in patients who had HD and PD. (11-13). Even though the RV works against low pressure under normal conditions, it can adapt to changes in volume load. Right heart dysfunction may develop in patients whose volume load might increase too much, such as ESRD. Such situations may impair the quality of life by causing the already increased peripheral ponding to become more prominent in right heart failure. However, it has not been clearly elucidated which HD or PD provides better volume control even if recent studies PD is thought to provide better fluid control than HD (15). In studies in the literature, it was thought that while RV functions were relatively protected in PD, the adverse effects of RV functions in HD patients may be due to the presence of AV fistula that causes high output in this group (16,11).

Transthoracic echocardiography is the most common diagnostic method used in clinical practice for evaluation of RV functions. Some studies have evaluated the changes in left ventricular parameters caused by a decrease in preload however the results regarding the RV are not clear (17,18). Therefore, it is important which parameters and echocardiographic examinations to use when evaluating RV functions. Although tissue Doppler parameters can be used in the evaluation of RV, systolic and diastolic functions, it is controversial whether these parameters are independent of preload (19,20). However, some studies have found that sudden decreases in preload cause a decrease in tricuspid lateral annulus systolic velocity in patients with normal RV function (21,22). Functional evaluation of the RV is very difficult due to the complex geometric structure of the RV, which is in the form of a half-moon, and because the RV is load dependent, it can be exposed to pericardial effects and right-sided volume and pressure load. (23-25). Techniques such as magnetic resonance imaging and radionuclide ventriculography used for quantitative calculation of right ventricular ejection fraction (RVEF) are invasive, relatively expensive, time-consuming and affected by the complex geometry of the RV (11,26). These methods cannot be applied very much in clinical practice. There are different echocardiographic parameters to evaluate RV systolic functions. One of the most frequently used methods is TAPSE (15). Many studies have found a very strong correlation between TAPSE and RV systolic functions (27). TAPSE values greater than 20 mm indicate normal functions of the RV, while a value smaller than 20 mm indicates impaired functions in varying degrees. In our study, TAPSE value, which is an indicator of RV systolic functions, was similar in patients who had PD and HD. In a previous study, it has been shown that over hydration caused by AV fistula impairs significantly RV systolic functions in HD patients than PD patients (28). Similarly, in a study comparing PD patients with healthy people, it was observed that RV systolic functions were preserved (29). It was thought that one of the reasons why PD preserves RV functions better than HD may be that sudden decreases in preload are less common in this patient group. However, RV functions were similar in PD and HD patients in our study. Although severe and advanced ventricular dysfunction can be detected in ESRD patients using different echocardiographic parameters, it may be insufficient to detect early ventricular dysfunction (26). STE conventional echocardiography is widely used to detect normal appearing systolic dysfunction (30). Early diagnosis of subclinical myocardial dysfunction has been possible in ESRD patients with the help of new echocardiographic methods such as STE (31). In this study, when PD and HD patients were evaluated with 2D-STE, which showed more sensitive cardiac functions, ventricular functions were found to be similar.

In our study, RA strain values were found to be significantly better in patients who had PD compared to HD while RV strain values were determined similar in PD patients and HD patients. When the studies in the literature and our study results are evaluated together, PD seems to be superior in protecting RA functions. In previous studies, the RA not only acts as a reservoir and channel, but reduces the pressure in the central venous circulation, acts as a buffer while supporting RV filling, and helps prevent acute increases in RV diastolic pressure (32-34). Atrial function impairments are known to be an early indicator of ventricular systolic dysfunction, and atrial strain values have been shown to be associated with RV functions (35). Therefore, monitoring of atrial functions is important for early detection of RV systolic dysfunction in ESRD patients receiving dialysis treatment. In our study, it was found that RA functions were better preserved in PD patients. RA global strain values were better in PD patients compared to HD patients. RA volume values were higher in HD patients than PD patients. Since long-term volume burden will affect the right heart functions in these patients, the follow-up of RA functions will be useful especially in the early prediction of subclinical systolic dysfunctions in this patient group.

Limitations

Our study includes small number of patients, and there was no long-term clinical outcome data such as cardiovascular event rates and survival evaluation. These seems to be the most important study limitation. Another limitation of this study is represented by its retrospective design. Additional limitations include the lack of using cardiac magnetic resonance imaging for RV functional assessment and the 2D-strain method for the determination of right heart function.

CONCLUSION

Most of the previous studies have evaluated the effect of dialysis type on left ventricular functions. A few studies have compared right heart functions in patients who had PD and HD. In this study, it was shown that RV functions were similar protected in patients who underwent PD and HD. But RA functions were better protected in patients who underwent PD than HD. More studies are needed to confirm the clinical implications of our findings.

Ethics Committee Approval: The study was approved by the Ethics Committee of Ordu University Faculty of Medicine (18.05.2017, 2017/61).

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