

# Comparing right ventricular function and pulmonary artery pressure before and shortly after hemodialysis in patients with end-stage renal disease

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## Abstract

**Background:** Early screening and diagnosis of right ventricular (RV) dysfunction and pulmonary artery hypertension is vital in patients with end-stage renal disease (ESRD) because of its relation to patients' survival. The present study is aimed to address and compare RV function parameters and pulmonary artery pressure (PAP) before and shortly after hemodialysis in patients with ESRD.

**Materials and Methods:** This quasi-experimental study performed at Alzahra Hospital in Isfahan in 2014, 40 consecutive patients with ESRD that referred to hemodialysis ward were assessed by M-mode echocardiography and tissue Doppler imaging before and 30 min after completing hemodialysis to assess RV function parameters and PAP.

**Results:** Following hemodialysis, mean body weight, both systolic, and diastolic blood pressures (BPs) and also mean systolic PAP significantly decreased, while tricuspid annulus plane systolic excursion (TAPSE), RV fractional area change (RVFAC) significantly increased 30 min after hemodialysis compared with before this procedure. However, systolic myocardial remained unchanged. Changes in body weight after dialysis was adversely associated with patients' age and duration of dialysis. Moreover, change in PAP was positively associated with the level of serum creatinine.

**Conclusion:** Early reduction in body weight and BP, as well as improvement in RV function, and PAP is predictable shortly after starting hemodialysis in patients with ESRD. We found that RVFAC and TAPSE values were dependent on preload, but RV S' velocity was load independent. Change in body weight is predicted more in older patients and those who undergoing prolonged hemodialysis. Change in PAP is strongly affected by the severity of renal failure, but RV function may not be influenced by age or duration of dialysis.

**Key Words:** End-stage renal disease, hemodialysis, pulmonary artery pressure, right ventricular function

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## INTRODUCTION

Cardiovascular disorders are a major cause for

death and disability in patients with end-stage renal disease (ESRD) that about 40% of recorded cases

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of death in this patients subgroup has been related to the cardiovascular disease worldwide.<sup>[1,2]</sup> These patients frequently suffer hypertension, left ventricular hypertrophy, coronary atherosclerosis, as well as both systolic and diastolic dysfunction.<sup>[3]</sup> It has been well shown that subclinical right ventricular (RV) systolic dysfunction is also prevalent in the patients with ESRD even within the predialysis period.<sup>[4]</sup> Thus, it seems that the initial cardiovascular functional manifestations may be even processed in dependent to dialysis. Along with myocardial dysfunction in ESRD patients, pulmonary artery hypertension (PAH), a severe progressive cardiovascular event, can be frequently occurred in those patients who undergoing prolonged hemodialysis<sup>[3-5]</sup> with an overall wide prevalence rate 19–70%.<sup>[6-8]</sup> It has been now suggested that metabolic and hormonal changes may lead to pulmonary artery stenosis and also pulmonary vascular resistance leading PAH. Furthermore, hemodialysis-related arteriovenous shunts result in increasing cardiac output that may be deteriorated by anemia and fluid overload in these patients. Also, the increase in carbon monoxide can cause increasing pulmonary artery resistance rate leading PAH. Thus, PAH in ESRD patients undergoing prolonged hemodialysis may occur based on multifactorial reasons.<sup>[3,5,9,10]</sup> Echocardiography is a stabilized approach for assessing cardiac ventricular function.<sup>[11]</sup> Screening by Doppler echocardiography in ESRD patients who are a candidate for dialysis has been recommended as a gold procedure for assessing PAH.<sup>[12]</sup> Also, tissue Doppler imaging (TDI) can diagnose early changes in RV function in hemodialysis patients. In this regard, early diagnosis enables the timely interventions that are, now limited to changes in dialysis modality or referring patients for kidney transplantation.<sup>[12-14]</sup>

PAH has no clear manifestation and is also an important cause for mortality and no response to kidney transplantation in ESRD patients.<sup>[14,15]</sup> Thus, early diagnosis of this abnormality in ESRD patients is necessary. Since the early diagnosis of RV dysfunction and PAH can be easily performed by echocardiography, assessing the presence of these two parameters using echocardiography is strongly recommended. Also, the evaluation of the effects of dialysis and reduction of preload on parameters of RV function and pulmonary artery pressure (PAP) can be very helpful to select an appropriate treatment approach to prevent progression of RV dysfunction.<sup>[16,17]</sup> Hence, we aimed to address and compare the frequency of RV dysfunction and PAH before and after hemodialysis in patients with ESRD.

## MATERIALS AND METHODS

This quasi-experimental study performed at Alzahra Hospital in Isfahan in 2014. 40 consecutive patients

with ESRD that referred to hemodialysis ward were included in the study. The main inclusion criteria were age <80 years, the duration of hemodialysis for at least 1-year, hemodialysis for at least 4 h/week; consent to participate in the study, and a good compliance to treatment, according to physician opinions. Those patients with congenital heart disease, pulmonary emboli, chronic obstructive pulmonary disease, unclear echocardiography imaging, history of ischemic heart disease or myocardial infarction, left ventricular dysfunction (left ventricular ejection fraction <50%), interstitial lung disease, valvular heart disease, connective tissue disease or dependent to oxygen therapy were not included. After obtaining informed consent from patients, general questionnaire including baseline characteristics such as gender, age, underlying diseases, age of the onset of renal failure, duration of dialysis, place of shunt (brachial or radial), anthropometric parameters, history of smoking, laboratory parameters, and vital signs were collected by a residents. Then, echocardiography was performed for all patients by a single cardiologist before and 30 min after completing hemodialysis. In this regard, of trans-thoracic echocardiography, M-mode, and TDI was done according to the criteria of American Echocardiography Association.<sup>[15]</sup> The following parameters of RV function were assessed: (1) Tricuspid annulus plane systolic excursion (TAPSE) was assessed with M-mode in an apical four-chamber view, placing the M-mode cursor on the lateral tricuspid annulus. Maximum plane systolic excursion of the lateral annulus was measured (normally, the annular plane is identified on the M-mode recording as the first continuous line immediately below the RV cavity). In this context, TAPSE 1.5–2.0 cm considered as the reference range, 1.3–1.5 cm as mildly abnormal, 1.0–1.2 cm as moderately abnormal, and <1.0 cm as severely abnormal;<sup>[18]</sup> (2) tricuspid lateral annular systolic velocity (Sa) assessed by TDI with a normal range >0.5–1.1; (3) RV fractional area change (RVFAC) was assessed quantitatively based on Simpson method as the percentage of change in cavity area from end diastole to end systole and classified as 32–60% for normal range, 25–31% for mildly abnormal, 18–24% for moderately normal, and ≤17% for severely abnormal; (4) systolic PAP (SPAP) was assessed using the modified Bernoulli formula<sup>[19]</sup> that PAH was defined as at rest SPAP higher than 25 mmHg according to the guidelines of American Heart Association and American College of Cardiology.<sup>[20]</sup>

Results were presented as mean ± standard deviation for quantitative variables and were summarized by frequency (percentage) for categorical variables. Change in RV functional parameters was assessed using paired *t*-test or McNemar test. The Pearson's

correlation test was applied to examine the association between the study measures. For the statistical analysis, the statistical software SPSS version 20.0 for windows (SPSS Inc., Chicago, IL, USA) was used.  $P \leq 0.05$  were considered statistically significant.

## RESULTS

In total, 40 patients were assessed. The mean age was  $60.00 \pm 9.22$  years (ranged 47–78 years) and 57.5% were male. The average pre-dialysis weight was  $69.30 \pm 8.77$  kg that 25.0% had initial body weight higher than 75 kg. The history of hypertension was revealed in 60.0% of subjects. The mean duration of dialysis was also  $2.11 \pm 1.02$  years ranged 1–5 years. The baseline measurements of clinical and laboratory parameters are summarized in Table 1.

Comparing parameters of RV function after and before hemodialysis [Table 2] showed significant changes in all study parameters including TAPSE, RVFAC, and SPAP ( $P < 0.001$ ). In this regard, following hemodialysis, mean body weight, both systolic and diastolic blood pressures (BPs) and also mean SPAP significantly decreased, while TAPSE, RVFAC significantly increased 30 min after hemodialysis compared with before this procedure. However,

systolic myocardial (SM) remained unchanged ( $P = 0.086$ ).

To assess the association between baseline variables and study vital and functional parameters and using the Pearson's correlation test [Table 3], changes in body weight after dialysis was associated with age ( $P = 0.008$ ) and duration of dialysis ( $P = 0.011$ ). Moreover, change in RVFAC and PAP were associated with duration of dialysis and level of serum creatinine ( $P = 0.027$  and  $0.010$ , respectively).

## DISCUSSION

Several recent studies could show paradoxical findings on the changes in RV parameters shortly after hemodialysis. Duran *et al.* showed that acute changes of volume status and electrolytes and autonomic regulation by hemodialysis session did not affect left ventricular diastolic and RV functions.<sup>[21]</sup>

Some studies also showed different acute effects of hemodialysis on systolic and diastolic functional parameters. Akkaya *et al.*<sup>[13]</sup> indicated that the parameters of RV systolic function such as RV S' velocity are independent of preload whereas the conventional parameters of RV diastolic function are preload dependent in patients with end-stage renal failure who undergo regular hemodialysis. McLaughlin *et al.* showed indicators of RV function such as RV S' velocity did not change significantly after hemodialysis. However, the RVFAC, RV myocardial performance index (RVMPI) and TAPSE values were significantly increased. TAPSE was found to be the only parameter that had a positive correlation with the amount of fluid removed.<sup>[20]</sup> Our study could reveal early improvement of RV parameters such as TAPSE, RVFAC, RVMPI, and PAP but not changes in TDI systolic velocity (RV S' velocity) and decrease in RVED area following hemodialysis. However, these changes cannot explain long-term effects of hemodialysis on RV function in these patients. In fact, although most previous studies could indicate decreasing ventricular function a long time after hemodialysis while we investigated the immediate effect of hemodialysis on RV function in this patient.

Our findings may be due to reduced filling pressure shortly after dialysis that result in a reduction of SPAP and RVED area and improvement of RV function parameters. ESRD itself and arteriovenous fistula (AVF) increase in cardiac output both contribute to the development of pulmonary hypertension (PH).

Hemodialysis that carried out through a surgically created native AVF, has been associated with an

**Table 1: Baseline characteristics of study population**

Variables	Mean±SD	Minimum	Maximum
Age, years	60.00±9.22	47.00	78.00
Duration of dialysis, years	2.11±1.02	1.00	5.00
Weight, kg	69.30±8.77	55.00	89.00
Systolic BP, mmHg	133.12±16.78	100.00	170.00
Diastolic BP, mmHg	75.45±6.05	65.00	90.00
Serum BUN	36.18±8.17	22.00	55.00
Serum creatinine	2.93±1.29	2.00	7.00
Serum sodium	138.15±5.22	127.00	148.00
Serum potassium	4.05±0.64	3.00	5.00
Serum calcium	10.33±1.02	8.00	12.00
Serum phosphorus	3.70±0.72	2.00	5.00
Serum hemoglobin	11.55±1.06	10.00	14.00

SD: Standard deviation, BP: Blood pressure, BUN: Blood urea nitrogen

**Table 2: Changes in RV function parameters before and after hemodialysis**

Index	Before dialysis	After dialysis	Mean difference	P
TAPSE	1.47±0.45	1.81±0.43	0.34±0.23	<0.001
RVFAC	32.63±3.11	35.13±3.45	2.50±1.93	<0.001
SM	8.24±1.90	8.50±1.98	0.26±0.66	0.086
PAP	31.48±9.69	29.53±9.56	-1.95±3.17	<0.001
SBP	133.12±16.78	119.23±16.01	-13.90±5.90	<0.001
DBP	75.45±6.05	69.20±4.91	-6.25±4.95	<0.001
Body weight	69.30±8.77	66.95±8.59	-2.35±0.53	<0.001

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, PAP: Pulmonary artery pressure, RVFAC: Right ventricular fractional area change, RV: Right ventricular, TAPSE: Tricuspid annular plane systolic excursion, SM: Systolic myocardial

**Table 3: Association between baseline characteristics and study functional parameters**

Variables	Weight change	SBP change	DBP change	TAPSE change	RVFAC change	SM change	PAP change
Age							
<i>R*</i>	0.412**	0.109	0.265	0.143	0.139	-0.253	0.097
<i>P</i>	0.008	0.502	0.098	0.380	0.391	0.116	0.550
Duration of dialysis							
<i>R*</i>	0.396*	0.198	0.122	0.045	0.204	0.349*	0.160
<i>P</i>	0.011	0.221	0.452	0.783	0.206	0.027	0.323
BUN							
<i>R*</i>	-0.086	0.060	0.163	0.086	0.212	0.072	0.246
<i>P</i>	0.600	0.714	0.316	0.598	0.190	0.659	0.126
Creatinine							
<i>R*</i>	-0.300	0.156	-0.031	0.053	0.129	0.190	0.403*
<i>P</i>	0.060	0.336	0.849	0.747	0.429	0.242	0.010
Sodium							
<i>R*</i>	0.010	0.131	-0.295	-0.087	0.271	-0.157	-0.134
<i>P</i>	0.951	0.421	0.065	0.594	0.090	0.334	0.411
Potassium							
<i>R*</i>	-0.023	0.019	0.020	0.003	0.125	-0.093	0.151
<i>P</i>	0.890	0.907	0.901	0.983	0.444	0.569	0.353
Calcium							
<i>R*</i>	-0.021	-0.061	0.133	-0.099	0.253	-0.035	-0.211
<i>P</i>	0.897	0.709	0.413	0.545	0.116	0.832	0.192
Phosphorus							
<i>R*</i>	0.053	-0.011	0.251	-0.003	0.001	-0.126	-0.161
<i>P</i>	0.745	0.947	0.119	0.985	1.000	0.438	0.321
Hemoglobin							
<i>R*</i>	0.168	-0.120	0.247	-0.060	-0.175	0.118	-0.146
<i>P</i>	0.301	0.462	0.125	0.714	0.280	0.468	0.370

\*Pearson correlation. BUN: Blood urea nitrogen, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, PAP: Pulmonary artery pressure, RVFAC: Right ventricular fractional area change, TAPSE: Tricuspid annular plane systolic excursion, SM: Systolic myocardial, \*: Correlation is significant at the 0.05 level (2-tailed), \*\*: Correlation is significant at the 0.01 level (2-tailed)

increased risk of PH. AVF causes a left-to-right shunt, leading to chronic volume overload, independent of the increase in total body water, thus worsening RV overload and result in RV failure.

It seems that increased PAP in ESRD patients needs to long-term dialysis, while PAP may be unchanged or even transiently improved as shown in the present study. Moreover, different physiological mechanisms more than volume overload have shown to affect change in PAP in ESRD patients, hormonal and metabolic derangement associated with end-stage renal failure might lead to increased pulmonary arterial vasoconstrictor because of endothelial dysfunction and thus increase the pulmonary vascular resistance.<sup>[22]</sup> It should be also noted that in less than half of the patients on long-term hemodialysis, PAH can be occurred, and thus majority of the patients may not experience changes in PAP even in long-term period.<sup>[23]</sup> So that decreased volume overload and adverse cytokines shortly after dialysis may lead to improvement of PAP and RV function.

In the present study, we investigated short-term RV involvement in hemodialysis patients, in an attempt to determine the prevalence of RV functional improvement in these patients. We emphasized the parameters of TAPSE, RVFAC, and SM as reliable and sensitive indicators for evaluating the RV function. The TAPSE is a good parameter to evaluate the RV function and it correlates closely with SM and RVFAC in a variety of patient populations.<sup>[24]</sup> In our study, TAPSE was increased in 85% of the patients seems to be considerable. This may be due to the effects of changes in preload on RV function.<sup>[25]</sup> It can be demonstrated that preload reduction during hemodialysis causes change in cardiac filling and contractility so that early preload reduction can result in increased contractile function despite reduced filling pressure.<sup>[25]</sup> RVFAC is another measure of RV systolic function that has been shown to correlate well with RV ejection fraction by MRI.<sup>[26]</sup> In the present study, RVFAC was increased in 87.5% of the hemodialysis group. A statistically significant increase was found in RVFAC in the patients when compared with before dialysis.

Improvement of RV function after HD may be due to the Frank–Starling-mechanism, with increase of RV contractility following acute afterload reduction.<sup>[27]</sup>

Similarly Christophe Nasri showed amelioration of RV functional parameters only in patients with SPAP-reduction of more than 14.5 mmHg. This may be due to that RV function was afterload dependent so when PAP was reduced, the RV function become better and in patients without significant SPAP, irreversible adverse RV remodeling was occur so not respond to preload reduction.<sup>[22]</sup>

We expected decrease in SM velocities following preload reduction by dialysis on the basis of the Frank–Starling mechanism but reduction in afterload and wall stress due to dialysis lead to improvement of TDI systolic velocity so that we see no significant changes in these parameters in our study similar to Pabst *et al.* and López-Candales *et al.* findings. Another reason for no changes in RV S' velocity in these studies may be due to less volume of ultrafiltration compared with below studies that showed a decrease in TDI systolic velocity.<sup>[23,24]</sup> Before dialysis, the patient has high preload that result in mask impairment of early diastolic filling.

Preload reduction with dialysis resulting in decreased peak early filling velocities that may unmask delayed relaxation not apparent prior to dialysis.

Other findings of the current study were significant correlation of RV function parameters and two important baseline indices of age and duration of dialysis. In this regard, change in SM parameter after hemodialysis was inversely correlated to duration of dialysis. Moreover, change in PAP was positively associated with the level of the serum creatinine level before dialysis. However, two parameters of advanced age and dialysis duration were not correlated with none of other study indices including TAPSE and RVFAC. Here are two important points. First, it seems that the changes in PAP can be independent of RV functioning status that the severity of PAH can be affected by severity of renal failure assessed by serum creatinine level, but TAPSE and RVFAC are independent to renal dysfunction. As shown by Said *et al.*,<sup>[4]</sup> PAH may not significantly be associated with RV dysfunction in these patients. The second point is that the changes in RV function that may be certainly referred to the period before starting dialysis. On the other hand, RV dysfunction may be affected by characteristics and parameters related to own renal failure than to dialysis. Said *et al.*,<sup>[4]</sup> also indicated that RV dysfunction is highly prevalent among ESRD patients even before starting dialysis

therapy. Thus, the severity of RV dysfunction may be affected by other important parameters mostly related to the stages of renal function, not to dialysis characteristics.

## CONCLUSION

Shortly after hemodialysis in patients with ESRD, considerable changes in body weight, BP, RV function parameters such as TAPSE, RVFAC and PAP but no changes in RV tissue Doppler S' (RV S') velocity was seen so that these parameters independent of preload, but RVFAC and TAPSE values were dependent on preload.

In this regard, the change in body weight is positively associated with age and duration of dialysis, while changes in SPAP are mainly associated with the severity of renal failure assessed by serum creatinine level. Also, we could show early reduction in weight, BP, as well as improvement in RV function parameters and also PAP shortly after starting hemodialysis in these patients.

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## Conflicts of interest

There are no conflicts of interest.

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