Use of Lung Ultrasound with Tissue Doppler Echocardiography to Follow up Cardiovascular State of Haemodialysis Patient

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Abstract

Background: Chronic hypervolemia is the main cause of cardiovascular complications in haemodialysis patients.

Objectives: We aimed to study the effect of lung ultrasound-guided dry weight reduction strategy on the cardiovascular state of hypertensive haemodialysis patients.

Patients and Methods: We carried out a single-blind two-arm randomized trial on 50 hypertensive haemodialysis patients in Qena University Hospital dialysis centre over 8 weeks from 1/11/2020 to 1/1/2021. Patients were divided into usual care group (control arm) and active group(study arm). In study group, dry weight reduction was assessed weekly by lung ultrasonography guided by the total number of B-lines, before the midweek session of haemodialysis. In the control group, dry weight probing was done according to clinical criteria. To assess outcomes, we compared the clinical and echocardiographic improvement in both groups including full clinical assessment, etc at baseline and at the study end.

Results: In study group, dry weight was significantly reduced in comparison with the control group (−0.41 ± 0.32 vs. 0.04 ± 0.09 kg; $P < 0.001$), resulting in a statistically significant reduction in systolic and diastolic blood pressures ($P < 0.001$). Furthermore, a statistically significant reduction in echocardiographic indices of cardiac chambers dimensions occurred in study group, in addition to improvement of the diastolic function of both ventricles.

Conclusion: Ultrafiltration based on assessment of fluid status using lung ultrasound dry weight reduction is better than that based on conventional method regarding both clinical and echocardiographic parameters.

Keywords: echocardiography, dry weight reduction, haemodialysis, hypertension, lung ultrasound.

Introduction

Fluid balance is a cornerstone component in the management of haemodialysis patients.**(Paniagua et al., 2010)** Chronic hypervolemia results in hypertension, increased arterial stiffness, chronic heart failure, left ventricular hypertrophy, and increased mortality **(Voroneanu et al., 2010)** On the other hand, dehydration is complicated by hypotension, cramps, dizziness, etc,so achieving good volume control, results in blood pressure reduction, regression of left ventricular hypertrophy, and increased survival **(Charra et al., 2003)** Ideal dry weight achievement is the most challenging issue in the daily clinical practice in haemodialysis, and it is defined as "the lowest tolerated post-dialysis weight, achieved by gradual reduction in postdialysis weight, at which there are no or minimal signs of volume overload or dehydration**". (Sinha et al., 2009)**There is no simple unique method for achieving optimum dry weight in haemodialysis patients. **(Jaeger et al., 1999)** In most dialysis centres, dry weight reduction is being achieved via the ordinary clinical methods that don't achieve optimum control of blood pressure and hydration status of haemodialysis patients and cause some complications during dialysis,**(Codognotto et al., 2007**)so, other methods have been proposed to control volume status of these patients. Echocardiography is one of these methods, which is used to assess the volume status through inferior vena cava diameter and other echocardiographic indices. **(Civilibal et al., 2009)** Tissue doppler imaging is a new technique that can assess cardiac function independent of volume status and may be useful in early diagnosis. Tissue doppler imaging can efficiently measure relaxation and contraction velocities from the myocardium and is a quantitative method that do not depend on volume overload.**(Drighil et al., 2008)** Lung ultrasound is a non-invasive, radiation-free emerging method that estimate and quantify extravascular lung water. **(Picano et al., 2018)** Its key advantage is the ability to detect pulmonary congestion before being clinically evident. **(Panuccio et al., 2012)** Lung ultrasonography is well validated in haemodialysis patients, it shows strong correlations with left ventricular mass index and left ventricle function, **(Mallamaci et al., 2010)** and anticipate mortality and impending cardiovascular events. **(Zoccali et al., 2018)** A recent study, **Loutradis et al. (2019)**, showed that the use of lung US strategy for volume status assessment and dry weight probing is associated with a significant reduction in ambulatory blood pressure in hypertensive haemodialysis patients. Here, we aimed to study the benefit of dry weight reduction using lung ultrasonography to achieve the optimum blood pressure control (as a primary outcome), and its effect on the echocardiographic parameters of cardiac chambers dimensions in addition to systolic and diastolic functions of both sides (as a secondary outcomes) in hypertensive haemodialysis patients.

Patients and Methods:

Single-blind randomized clinical trial was carried out on 50 hypertensive haemodialysis patients in Qena University Hospital dialysis centre. We included adult patients, aged 18 years or more, on maintenance haemodialysis for 3 months or more, treated with three sessions of haemodialysis per week. Exclusion criteria consisted of: (1) significant valvular heart diseases, (2) impaired LV systolic function (EF<50%), (3) moderate & severe pericardial effusion, (4) congenital heart disease, (5) atrial fibrillation, (6) advanced chest diseases, (7) morbid obesity, (8) haemodynamic instability during dialysis, (9) active malignant diseases or advanced other chronic diseases, (10) pregnancy at start or during study period, (11) change of antihypertensive drug one month before start of the study, (12) modification of dry weight one month before start of the study. The study was approved by the scientific and ethical committees at Qena Faculty of Medicine-South Valley, Qena, Egypt.

Study Protocol:

A written consent was obtained and then baseline evaluation was done which included demographic data, medical history, drug history, family history, surgical history and full clinical examination. Height, weight, body mass index were evaluated, and body surface area (BSA) was calculated using Du Bois formula. Evaluation of blood pressure was done twice, at baseline and study end. Each time, blood pressure is averaged from its measurements twice daily for three consecutive non-dialytic days using Riester mercury sphygmomanometer (desk model).Regarding echocardiographic studies, patients were evaluated twice, at baseline and study end (after 8 weeks), in an interdialytic day. The echocardiographers were not aware with patients grouping and interventions performed during the study. Also, Lung ultrasonography was done twice in addition to weekly follow-up, at baseline and study end (after 8 weeks), in an interdialytic day. After baseline evaluation, patients were randomly divided into two group, usual care and active groups, by a 1:1 ratio. In the group of usual care, dry weight probing was done according to conventional clinical practice. In the active group, reduction of dry weight was guided by the total number of B-lines (US B-lines score) calculated by lung ultrasonography, which was done weekly, just before the midweek session of dialysis as shown in **Figure 1**.B-lines,also known as comet-tails, are defined as hyperechoic reflections which originate fromthepleural line of both lungs, travel perpendicular tothat pleural line and move synchronously with lung respiration. They can quantify extravascular lung water, as shown in **Figure 2**. **(Saad etal.,2018)**

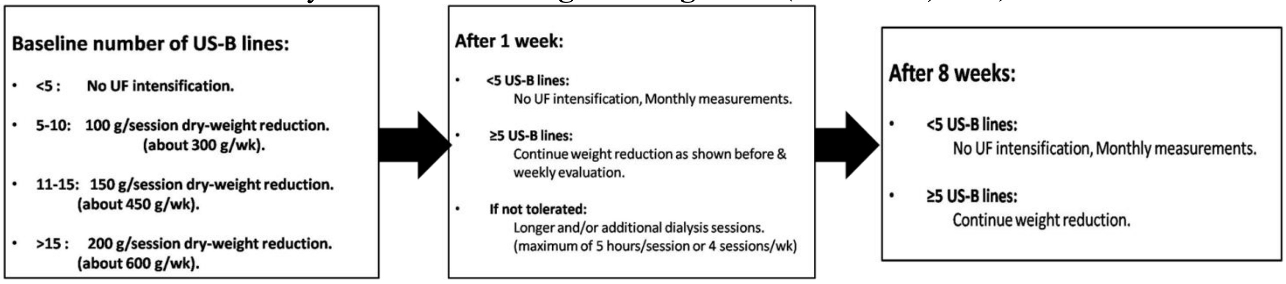


Fig.1. Protocol of reduction of dry weight in the active group. Abbreviation: UF, ultrafiltration.

Lung ultrasonographic studies were done by only one operator in the dialysis unit. Reduction of dry weight started when B-lines were 5 or more. (**Loutradis et al., 2019)**

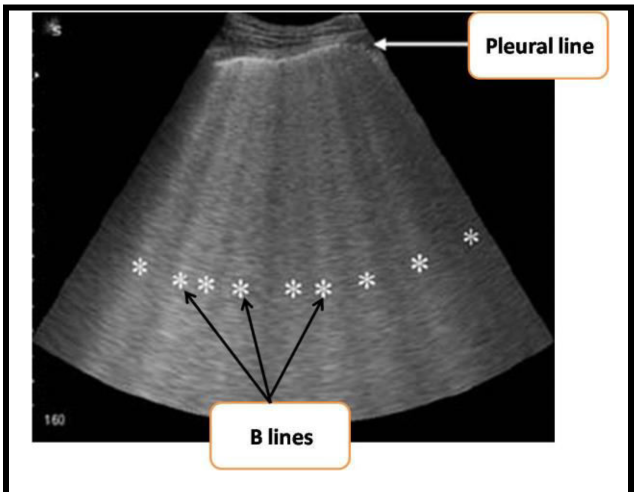


Fig. 2. Lung ultrasound B lines

Lung ultrasonography:

Lung ultrasonography for B-lines measurements was performed in the supine position using Philips ATL HDI ultrasound machine, curvilinear transducer (frequency is 2.5 MHZ - 7.5 MHZ), in both lungs in a quiet room. The transducer will be placed vertically from the2nd to the 5th intercostal space at the right chest side, and from the 2nd to the 4that the left chest side, along the parasternal, mid-clavicular, anterior axiliary, and mid-axillary lines, which is known as 28-zone lung scan protocol.**(Gargani et al., 2016)**

Trans-thoracic echocardiography with tissue doppler imaging for assessment of study outcomes:

Echocardiographic studies were performed in the left lateral position, twice, at baseline and study end (after 8 weeks), in an interdialytic day to assess outcomes, using Philips affinity 70 ultrasound machine, phased array transducer (frequency is 2 MHZ - 7.5 MHZ). **(Lang RM et al., 2015)**. Systolic and diastolic left ventricle dimensions, interventricular septum, and LV posterior wall thickness were evaluated with the parasternal window (long axis view). Left ventricle ejection fraction (LVEF) was evaluated using "bi-plane Simpson method".Left ventricular mass index was evaluated according to "modified cube" formula, then divided by body surface area (BSA). Right and left atrial surface areas and right ventricular diameter were evaluated with apical 4-chamber view. Left atrial and ventricular volumes were evaluated with apical 2 and 4-chamber view and then indexed for body surface area (BSA).IVC diameter was obtained from the subcostal view. **(Lang RM et al., 2015)**

Left ventricular E wave, A wave, deceleration time (DT) of E wave, in addition to E/A ratio were evaluated with pulsed-wave Doppler (PWD) in the apical four chamber view.

We used tissue doppler echocardiography (TDI) to evaluate systolic and diastolic functions (s', e', and a' wave velocities) at mitral and tricuspid annuli, in addition to E/e' and e'/a' ratios. Right ventricle systolic pressure (RVSP) was calculated by Bernoulli equation. **(Nagueh et al., 2016)**

Statistical Analysis:

We expressed continuous variables as mean ± standard deviation, and categorical variables, as absolute and relevant frequencies. Differences in the changes that occurred to our studied parameters between groups during study period were assigned as 1^{ry}and2^{ry} end points. we also reported the values of the baseline and 8-week studies in both groups to produce a comprehensive look of the studied echocardiographic variables. For continuous variables, comparisons inside each group were done with the dependent sample t test, but comparisons between group were done with the independent samples t test. Categorical variables were compared using chi square test or Fisher exact test. Univariate and multivariable logistic regression analysis was done to identify possible factors that resulted in reduction in LV filling pressure (as indicated by decrease of LV E/e' ratio) during the study. We tested variables for interaction, then, variables with P < 0.2 in univariate analysis were selected to be included in the multivariable model. Odds ratios (ORs) were notified with 95% confidence intervals (CIs). We considered P < 0.05 (two tailed) as a statistically significant. We performed Statistical analysis using Statistical Package for Social Sciences 23 (SPSS Inc).

Results

Table 1 shows demographic characteristics of both study groups. We included a total of 50 haemodialysis patients with hypertension, and then they were divided randomly into two groups by assigning 25 patients to each group. There were no statistically significant differences between both groups relating sex, age, body mass index (BMI), residual renal function, presence of chronic diseases, or baseline blood pressure measurements. The percentage of haemodialytic patients that had their dry weight reduced was significantly higher in the active group in comparison with the group of usual care (80% vs. 16%; P < 0.001). So, ultrasound Blines score had significantly decreased in the active group but slightly increased at the group of usual care (−4.48± 1.29 vs. 0.32 ± 0.9; P < 0.001), in the same direction of dry weight changes (−0.41 ± 0.32 vs. 0.04 ± 0.09 kg; P < 0.001).

Tables 2, 3 and 4 show the following:

A statistically significant reduction in systolic and diastolic blood pressures in the active group (P < 0.001) with a statistically significant differences between two groups relating systolic and diastolic blood pressures (P =0.005 and P < 0.001 respectively). With statistically significant difference, IVC diameter was reduced in the active group and increased in the usual-care group (−0.23 ± 0.14 vs. 0.08 ± 0.21 cm; P < 0.001) as shown in **Figure 3A**. Also, left atrial surface area, left atrial volume index (LAVi),left ventricular end-diastolic diameter(LVEDD),left ventricular end-diastolic volume index (LVEDVi),right atrial surface area, and right ventricular base diameter were reduced in the active group, but in the group of usual care, there was an increment, with a statistically significant differences between both groups, as follows, (−1.4 ± 1.79 vs. 0.29 ± 1.54 cm^2; P = 0.001), (−4.68 ± 4.69 vs. 0.18 ± 0.87 ml/m^2; P < 0.001), (−1.44 ± 2.1 vs. 0.96 ± 2.13 mm; P < 0.001),(−3.22 ± 2.44 vs. 0.27 ± 3.36 ml/m^2; P < 0.001), (−2.26 ± 0.84 vs. 0.10 ± 0.80 cm^2; P < 0.001),(−0.19 ± 0.22 vs. 0.05 ± 0.14 cm; P < 0.001) respectively, as shown if **Figures 3 C, D, E and F**.

Relating left ventricle mass index (LVMi), the active group had a statistically non-significant decrease, but the group of usual care had an increase(P = 0.151), resulting in a statistically significant change between groups (−3.08 ± 7.49 vs. 1.8 ±6.08 g/m^2; P = 0.015) as shown in **Figure 3B**.

In relation to systolic function of left ventricle (LVEF), there was a statistically significant increase in active group (P = 0.003), and non-significant increase in the usual care group (P = 0.651), with a statistically non-significant change between groups (1.24 ± 1.88 vs. 0.28 ± 6.51 %; P = 0.485). No significant changes observed relating right ventricle systolic function or right ventricle systolic Pressure (RVSP).

Regarding left ventricle diastolic function, there was a statistically significant decrease in E and A waves velocities in the active group (P = 0.001 and P=0.018 respectively) as shown in **Figure 4A**. Also, E wave deceleration time (DT) changed between the two groups with a statistically significant difference (11.48± 31.91vs. -3.76 ± 18.43 ms; P =0.044) as shown in **Figure 4D**.

Concerning diastolic velocities evaluated by tissue doppler echocardiography (TDI), there was a statistically significant increase in left ventricle e' wave velocity at the active group resulted in a statistically significant difference in net changes between the two groups (0.43±0.57 vs.-0.17±1.1 cm/s; P = 0.022) as shown in **Figure 4B**. As a result, left ventricular E/e' ratio decreased significantly in the active group with a significant difference between groups (-1.37±1.07 vs. 0.90±1.45 cm/s; P < 0.001) as shown in **Figure 4C**, and that indicates left side diastolic function improvement in the active group. Regarding right ventricle diastolic function evaluated by tissue Doppler echocardiography (TDI), there was a statistically significant decrease of right ventricle (a') wave

Table 1. Baseline Characteristics of Study Participants

Characteristic		Usual-Care Group (n = 25)	Active Group (n = 25)	P
Age (year)		59.36 ± 6.64	57.16 ± 8.44	0.311
Sex (male)		12 (48%)	15 (60%)	0.395
BMI (kg/m^2)		24.18±1.2	24.24±2.11	0.902
D.M		10 (40%)	8 (32%)	0.556
History of smoking	Ex smoker	8 (32%)	9 (36%)	0.21
	Non smoker	17 (68%)	14 (56%)	
	Smoker	0 (0%)	2 (8%)	
IHD		6 (24%)	4 (16%)	0.725
Residual Urine Output (ml/24h)	Less than 100 ml/24h (anuria)	9 (36%)	11 (44%)	0.619
	From 100 to 250 ml/24h (oliguria)	10 (40%)	8 (32%)	
	From 250 to 400 ml/24h(oliguria)	2 (8%)	4 (16%)	
	From 400 to 2000 ml/24h (normal output)	4 (16%)	2 (8%)	
Vascular Access	AV fistula	23 (92%)	22 (88%)	0.636
	CVC	2 (8%)	3 (12%)	
Baseline SBP		160.00±9.46	161.00±10.3	0.722
Baseline DBP		92.80±5.02	93.20±7.2	0.821

Abbreviations: BMI, body mass index; **D.M**, diabetes mellitus; **IHD**, ischemic heart disease; **AV fistula**, arterio-venous fistula; **CVC**, central venous catheter; **SBP**, systolic blood pressure; **DBP**, diastolic blood pressure.
* Statistically significant.

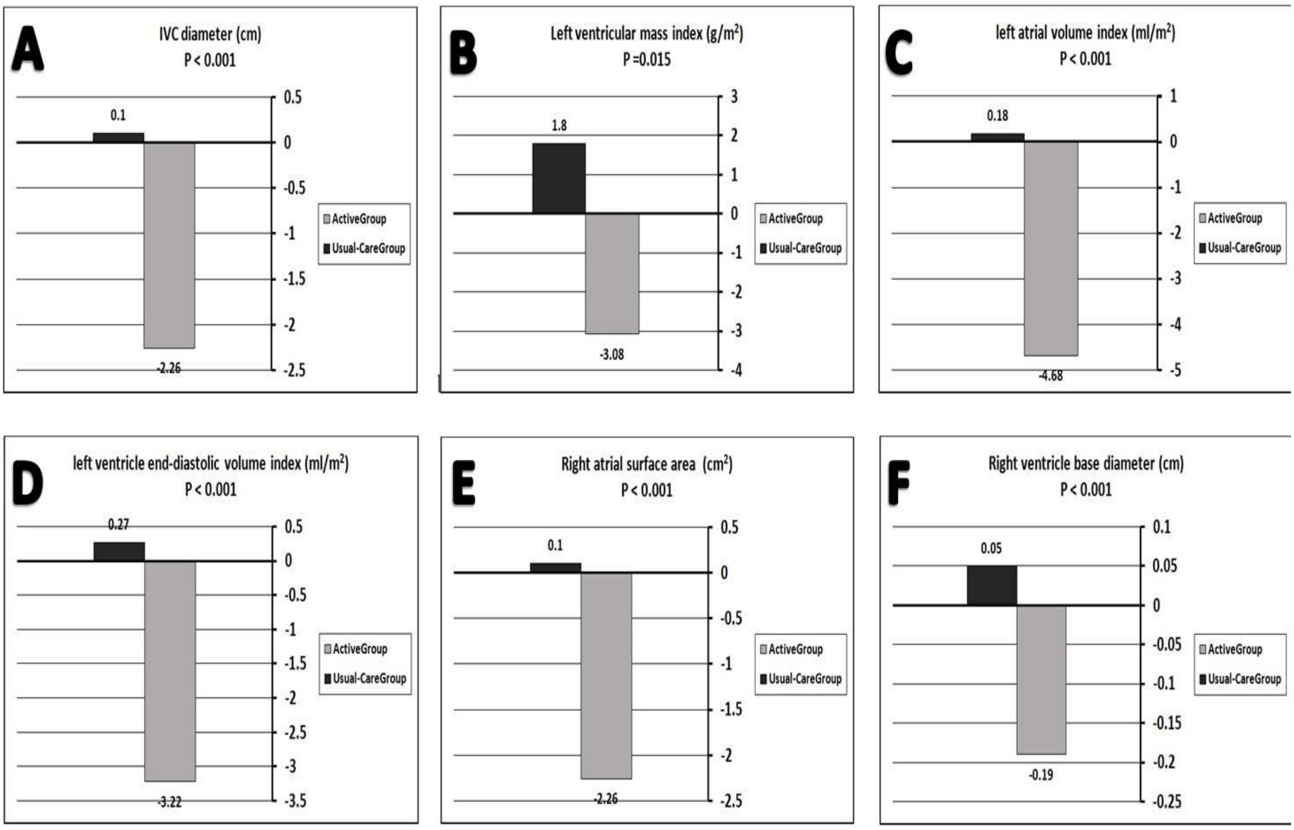


Fig.3. Comparisons for changes betweengroups during the follow-up in (A) Inferior vena cava (IVC) diameter, (B) left ventricular mass index (LVMi), (C) left atrial volume index (LAVi), (D) left ventricularenddiastolic volume index (LVEDVi), (E) right atrial surface area, (F) right ventricle base diameter.

Table 2. showsbaseline and 8-weeks values of echocardiographic parameters, blood pressure, dry-weight and lung U/S B lines score in usual care group patients.

Characteristic	Usual-care group (n = 25)		P
	Baseline	8 Weeks	
Dry Weight (Kg)	72.36 ± 8.51	72.40 ± 8.57	0.425
US B-lines score	7.88 ± 1.59	8.20±0.95	0.088
Average SBP	160 ± 9.46	159 ± 13.23	0.346
Average DBP	92.8 ± 5.02	92.4 ± 5.8	0.647
IVC diameter (cm)	2.01 ± 0.29	2.09 ± 0.305	0.066
LA Surface area(cm2)	20.55 ± 2.25	20.84 ± 2.41	0.358
LAVi (ml/m2)	42.81 ± 6.33	42.99 ± 6.57	0.299
LVEDD (mm)	54.48 ± 4.86	55.44 ± 4.73	0.034*
LVEDVi (ml/m2)	61.68 ± 11.06	61.96 ± 11.21	0.689
RA Surface area(cm2)	20 ± 1.81	20.10 ± 1.64	0.539
RV base diameter(cm)	3.14 ± 0.25	3.19 ± 0.26	0.102
LVMi (g/m2)	139.9 ± 41.96	141.7 ± 42.58	0.151
LV EF (%)	65.44 ± 6.62	66.04 ± 6.75	0.651
RV s′ wave (cm/s)	13.56 ± 2.58	13.74 ± 2.83	0.580
RVSP (mm Hg)	42.32 ± 11.66	42.96 ± 12.73	0.309
LV E wave (cm/s)	87.96 ± 38.74	91.76 ± 42.36	0.004*
LV A wave (cm/s)	76.44 ± 19.28	76.56 ± 19.79	0.944
LV e′ wave (cm/s)	8.16 ± 3.7	7.99 ± 3.98	0.449
LV E wave DT (ms)	212.48±62.49	208.72±77.54	0.318
LV E / e′ ratio	11.05 ± 1.73	11.95 ± 2.04	0.005*
RV e′ wave (cm/s)	11.20 ± 1	11.16 ± 1	0.862

Table 3.showsbaseline and 8-weeks values of echocardiographic parameters, blood pressure, dry-weight and lung U/S B lines score in active group patients.

Characteristic	Active group (n = 25)		P
	Baseline	8 Weeks	
Dry Weight (Kg)	68.92±8.17	68.51±8.23	<0.001*
US B-lines score	7.80±1.38	3.32±1.24	<0.001*
Average SBP	161±10.31	154±8.66	<0.001*
Average DBP	93.2±7.2	86.4±5.87	<0.001*
IVC diameter (cm)	2.067± 0.24	1.84± 0.24	<0.001*
LA Surface area(cm2)	21.26±2.71	19.86±1.96	0.001*
LAVi (ml/m2)	43.4±6.76	38.72±5.59	<0.001*
LVEDD (mm)	56.68±6.12	55.24±6.93	0.002*
LVEDVi (ml/m2)	62±10.1	58.78±8.9	<0.001*
RA Surface area(cm2)	19.1±2.46	16.84±2.66	<0.001*
RV base diameter(cm)	3.32± 0.26	3.14± 0.24	<0.001*
LVMi (g/m2)	139.8±42.53	136.72±44.41	0.051
LV EF (%)	65.44±6.62	66.68±6.84	0.003*
RV s′ wave (cm/s)	14.02±3.42	14.34±2.7	0.197
RVSP (mm Hg)	40.84±12.76	40.6±13.03	0.783
LV E wave (cm/s)	95.24±42.3	90.2±38.35	0.001*
LV A wave (cm/s)	92.2±11.42	90.24±9.75	0.018*
LV e′ wave (cm/s)	7.00±2.80	7.43±3.03	0.001*
LV E wave DT (ms)	214.64±44.39	226.12±27.19	0.085
LV E / e′ ratio	13.46±1.94	12.09±1.24	<0.001*
RV e′ wave (cm/s)	11.04±1.1	11.16±1.31	0.543

Table 4. Net changes occurred between the two groups during follow.

Characteristic	Changes during follow-up		P
	Usual-care group	Active group	
Dry Weight (Kg)	0.04± 0.09	-0.41±0.32	<0.001*
US B-lines score	0.32±0.9	-4.48±1.29	<0.001*
Average SBP	-1±5.2	-7±8.54	0.005*
Average DBP	-0.4±4.31	-6.8±4.97	<0.001*
IVC diameter (cm)	0.08±0.21	-0.23±0.14	<0.001*
LA Surface area(cm2)	0.29±1.54	-1.4±1.79	0.001*
LAVi (ml/m2)	0.18±0.87	-4.68±4.69	<0.001*
LVEDD (mm)	0.96±2.13	-1.44±2.1	<0.001*
LVEDVi (ml/m2)	0.27±3.36	-3.22±2.44	<0.001*
RA Surface area(cm2)	0.10±0.80	-2.26±0.84	<0.001*
RV base diameter(cm)	0.05±0.14	-0.19±0.22	<0.001*
LVMi (g/m2)	1.8±6.08	-3.08±7.49	0.015*
LV EF (%)	0.28±6.51	1.24±1.88	0.485
RV s′ wave (cm/s)	0.17±1.53	0.32±1.19	0.713
RVSP (mm Hg)	0.64±3.08	-0.24±4.31	0.411
LV E wave (cm/s)	3.8±6.01	-5.04±6.57	<0.001*
LV A wave (cm/s)	0.12±8.49	-1.96±3.86	0.273
LV e′ wave (cm/s)	-0.17±1.1	0.43±0.57	0.022*
LV E wave DT (ms)	-3.76±18.43	11.48±31.91	0.044*
LV E / e′ ratio	0.90±1.45	-1.37±1.07	<0.001*
RV e′ wave (cm/s)	-0.04±1.13	0.12±0.97	0.595

RV a′ wave (cm/s)	**9.88 ± 1.7**	**10.40 ± 1.68**	**0.079**	**10.04±1.61**	**9.16±1.40**	**0.004***	**0.52±1.42**	**-0.88±1.36**	**0.001***
RV e′ /a′ ratio	**1.156 ± 0.16**	**1.1 ± 0.16**	**0.067**	**1.12± 0.18**	**1.23± 0.21**	**0.002***	**-0.06±0.16**	**0.12±0.17**	**<0.001***

Abbreviations:LA, left atrium**; RA**, right atrial;**LVEDD**, left ventricular end-diastolic diameter**; IVC**, inferior vena cava**;RV**, right ventricular**;LVMi**, left ventricular mass index**;LV EF**,left ventricular ejection fraction**;LAVi**, left atrial volume index;**RVSP**, right ventricular systolic pressure**;E**, early peak diastolic velocity**;A**, late peak diastolic velocity**;LVEDVi**, left ventricular end-diastolic volume index**DT**, E wave deceleration time**;e′**, tissue-doppler early diastolic velocity**;s′** , tissue-doppler systolic velocity**;SBP**, systolic blood pressure**;DBP**, diastolic blood pressure.*Statistically significant

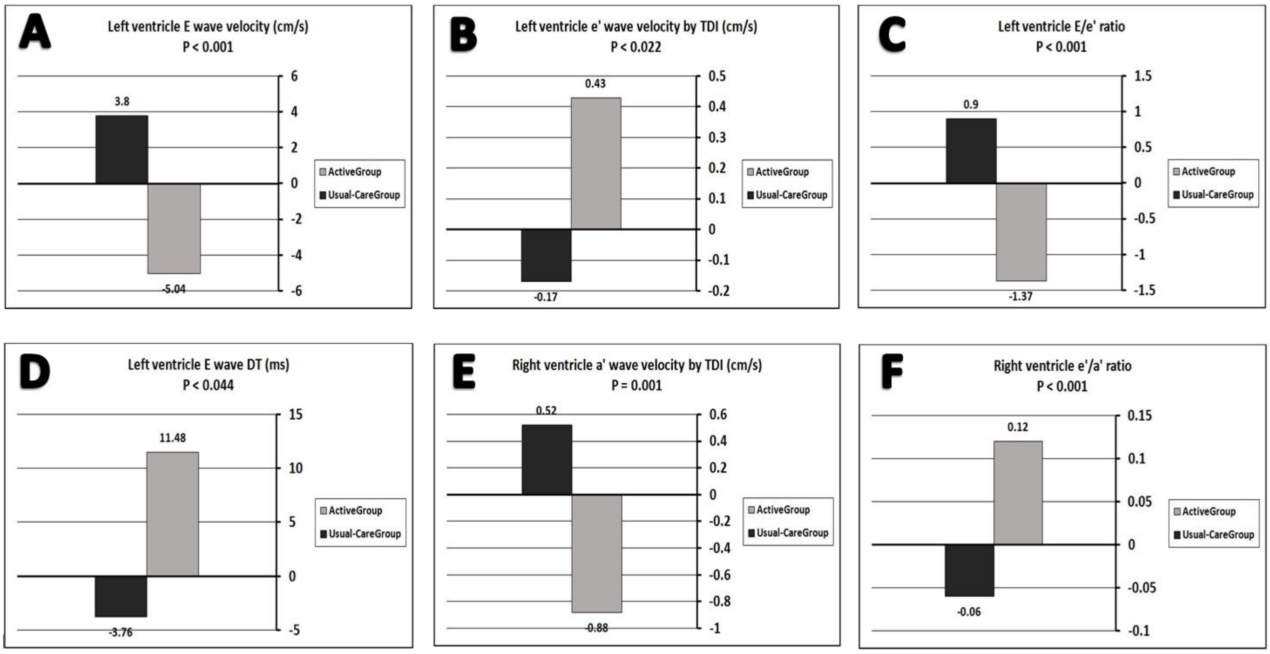


Fig.4. Comparisons among changes betweenboth groups during follow-up:**(A)**left ventricle E wave velocity,**(B)** left ventricle e' wave velocity by TDI, **(C)**left ventricle E/e' ratio, **(D)** left ventricle E wave deceleration time, **(E)** right ventricle a' wave velocity by TDI,**(F)** right ventricle e'/a' ratio.

velocity in the active group with a significant difference between the two groups (-0.88±1.36 vs. 0.52±1.42 cm/s; P = 0.001) as shown in **Figure 4E**. As a result, right ventricle e'/a' ratio had a statistically significant difference between groups (0.12±0.17 vs. -0.06±0.16; P < 0.001) as shown in **Figure 4F**, and that indicates right side diastolic function improvement in the active (study) group.

Neither hospitalizations nor vascular access complications occurred in both groups. Also, there were no deaths in both groups during study period.

We performed regression analysis (univariate & multivariable) to demonstrate the possible causes of LV filling pressure reduction (LV E/e' ratio reduction) during the study. The dependent variable was "LV E/e' ratio reduction", and the independent variables were many factors that may interfere with preload reduction as an. In multivariable analysis, as shown in **Table 5**, dry weight reduction during follow-up (OR, 7.025; 95% CI, 1.03-47.914; P = 0.047) was the only parameter independently associated with LV E/e' ratio reduction, among the examined factors.

There was a statistically significant (P < 0.001), positively related moderate correlation between left ventricle E/e' ratio and US B lines change, as shown in **Figure5**.

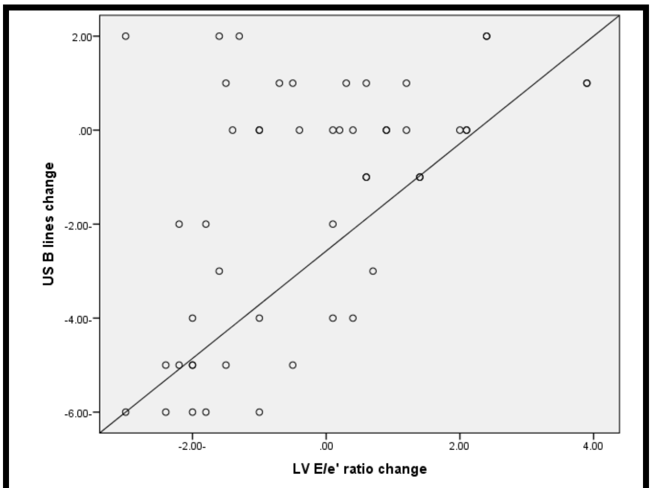


Figure 5. Correlation between left ventricle E/e' ratio & US B lines change.

Figure 6 shows left ventricular E/e' ratio reduction (LV filling pressure reduction) during follow up in a one of the active group patients.

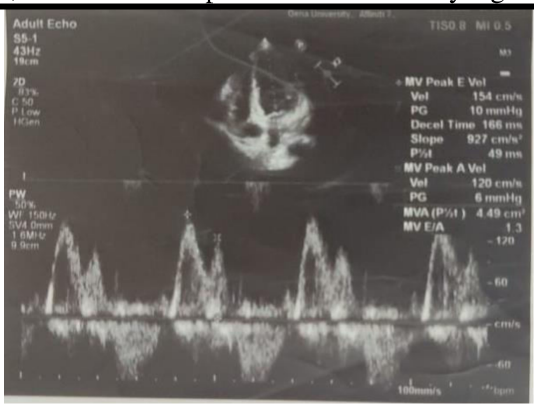
Discussion

Cardiovascular complications are the main cause of death in haemodialysis patients; so, achieving good volume control results in blood pressure reduction, regression of left ventricular hypertrophy, and increased survival. We aimed in this work to study the benefit of using lung ultrasonography in guiding the process of

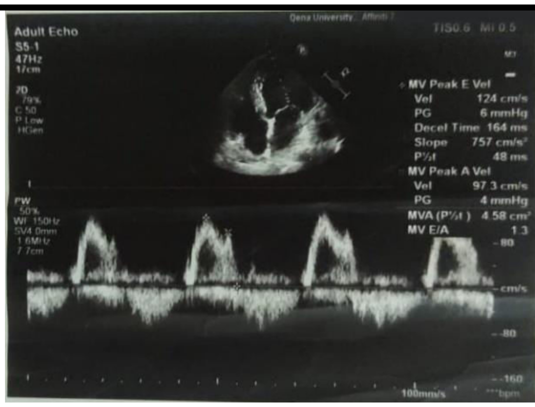
Table 5. Regression analysis (univariate & multivariable)ofparameters thatmightcauseLV E / e′ ratio reduction during follow up.

Predictors	Univariate		Multivariate	
	Odds ratio (95% C.I)	P	Odds ratio (95% C.I)	P
Age, per one yearabove	0.963 (0.885-1.049)	0.388		
Sex (male)	1.612(0.527-4.93)	0.403		
Body mass index, per one kg/m^{2}above	1.289(0.905-1.835)	0.159	1.457 (0.96-2.211)	0.077
Diabetes mellitus	0.622 (0.195-1.99)	0.424		
Ischemic heart disease	0.545(0.133-2.235)	0.4		
Baseline LV mass index, per one g/m^{2}above	1.002(0.989-1.016)	0.733		
Baseline LV ejection fraction, per 1% above	0.98(0.9-1.068)	0.649		
Reduction of dry weight during study	8.167(1.945-34.282)	0.004	7.025 (1.03-47.914)	0.047*
Reduction of ultrasound Blines during study	3.2(1.004-10.203)	0.049	2.755 (0.664-11.435)	0.163
SBP reduction during follow-up	1.379(.453-4.197)	0.572		
DBP reduction during follow-up	3.2(1.004-10.203)	0.049	0.938 (0.162-5.418)	0.943

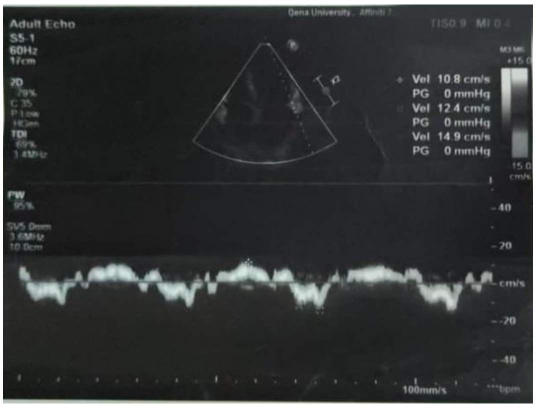
Abbreviations: **CI**, confidence interval; **LV**, left ventricular; **OR**, odds ratio; **SBP**, systolic blood pressure; **DBP**, diastolic blood pressure.*Statistically significant.



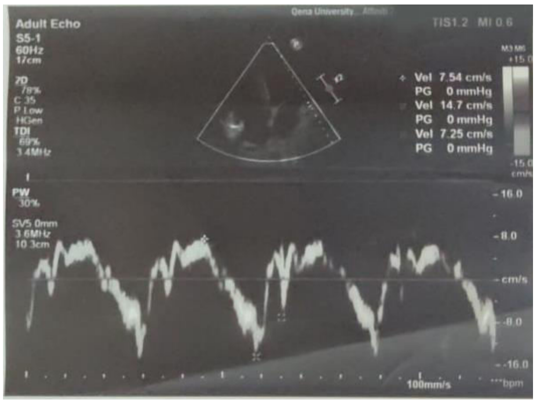
Baseline left ventricle E wave velocity (PWD) = 154 cm/s



Study end left ventricle E wave velocity = 124 cm/s



Baseline left ventricle e' wave velocity (TDI) = 12.4 cm/s
Baseline left ventricular E/e' ratio = 12.4



Study end left ventricle e' wave velocity (TDI) = 14.7 cm/s
Study end left ventricular E/e' ratio =8.4

Fig. 6. left ventricular E/e' ratio reduction during follow up in one active group patient

reduction of dry weight to achieve the optimum blood pressure control (as a primary outcome) and its effect on the echocardiographic parameters of cardiac chambers dimensions in addition to LV and RV systolic and diastolic functions (as a secondary outcomes) in hypertensive haemodialysis patients.

In this work, dry weight reduction in the active group resulted in reduction of systolic and diastolic blood pressures and IVC diameter. Also, there was an improvement in echocardiographic indices of the four cardiac chambers dimensions (left atrial surface area, left atrial volume index, right atrial surface area, left ventricular end diastolic diameter and left ventricular volume index). Also, left and right diastolic function improvement occurred, in addition to LV filling pressure reduction indicated by reduced LV E/e' ratio. In addition, left ventricle ejection fraction (LVEF) increased in active group. These effects occurred possibly due to the greater preload reduction happened in active group during follow-up in comparison with the control group. In this study also, we found that dry weight reduction was the only independent factor associated with the decrease in LV E/e' ratio in the studied population, and this augments the concept of volume overload reduction using lung ultrasound guidance to probe and reduce dry weight.

Loutradis et al. (2020)revealed that dry weight reduction led to a significant reductions in IVC diameter and improvement in echocardiographicindicesof cardiac chambers dimensions in active group, also there was an improvement in late active diastolic function and decrease in LV filling pressure, and this augments our study. Unlike our study results, **Loutradis et al. (2020)** didn't show left ventricle ejection fraction (LVEF) increase, right ventricle diastolic function improvement, or left ventricle mass index (LVMi) reduction in the active group, and this may be due to the hypervolemic state of the majority of our haemodialysis patients in comparison with the study population of **Loutradis et al. (2020),** so a greater volume reduction was performed in the active group of our study population.

Loutradis et al. (2019), showed that lung US strategy use for volume status assessment and dry weight probing is associated with a significant reduction in ambulatory blood pressure in hypertensive haemodialysis patients with a difference in blood pressure reduction of 6/3.3 mm Hg, and that agreed with our study results. Many other studies from the early days of haemodialysis showed that volume reduction is associated with blood pressure reduction in haemodialysis patients**.** In **Cirit et al. (1995)**, a number of 7 hypertensive haemodialysis patients underwent a 6.7 kg reduction in dry weight, and the result was a 46/22 mm Hg decrease in predialysis blood pressure.

In **Agarwal et al. (2011)**, haemodialysis patients were randomly assigned into two groups, the first group received the standard treatment, the second group (ultrafiltration group or the active group) underwent dry weight probing (reduction of 0.9 kg along 4 weeks), the results showed that there was a significantly higher reduction in the left ventricle internal diameter and left ventricle mass index (LVMi) in the active group, agreeing with our study results. In another study**, London et al. (2001)** demonstrated that reduction of volume overload resulted in LVH reduction in haemodialysis patients, and that LVH reduction had a positive effect on survival of haemodialysis patients, supporting our study results.

There was a need for novel treatment strategies such as the measurement of extravascular lung water by lung ultrasonography which has the priority in clinical research in haemodialysis patients **(Zoccali et al., 2018).** In **Torino et al. (2016)** study, the use of the standard clinical criteria to assess volume excess, such as lung crackles and peripheral oedema, had low sensitivity for detecting interstitial pulmonary oedema, and lung ultrasound was more reliable for that role, which boosts our study results.

Mallamaci et al. (2010) showed that the degree of lung congestion - evaluated with lung ultrasound -was strongly associated with left ventricle dysfunction, then **Pardała et al. (2019)** confirmed that by declaring that there was a significant negative relationship between the B-lines number detected by lung US and left ventricle ejection fraction in haemodialysis patients.

Agricola et al. (2005) and other previous studies clarified that the number of B-lines -

assessed by lung ultrasound - reflects LV filling pressure which is considered as an accurate representation to central circulation. Supporting that, our study demonstrated that changes in cardiac chamber dimensions and LV filling pressures are attributed to the reduction in hypervolemia, not to blood pressure decrease per se. In multivariable regression analysis, we demonstrated that dry weight reduction- alone- was associated with LV E/e' ratio reduction independently. Thus, reversal of hypervolemia may cause LV preload reduction, resulting in LV filling pressure reduction consequently, leading to left atrial afterload reduction that may revert cardiac chamber enlargement in the long term**. (Abhayaratna et al., 2006)**

Supporting our results from the opposite direction, **Tsilonis et al. (2016)** showed that continuous volume accumulation over the long interdialytic interval (the second and third interdialytic day) in haemodialysis patients resulted inleft and right atrial enlargement, RVSP elevation and congestion of pulmonary circulation.

About 80% of the active group patients underwent a dry weight with an accurately planned algorithm, so hypotensive episodes were avoided. The small sample size andshort follow-up duration were the main limitation sides in our study, so a larger sample size with longer periods of time are needed and this is a matter for a forthcoming study.

Conclusion

Ultrafiltration based on assessment of fluid status using lung ultrasound dry weight reduction is better than that based on conventional method regarding both clinical and echocardiographic parameters.

References

- **Abhayaratna WP, Seward JB, Appleton CP, Douglas PS, Oh JK, Tajik AJ, Tsang TS. (2006).** Left atrial size: physiologic determinants and clinical applications. Journal of the American College of Cardiology, 47(12):2357-63.
- **Agarwal R, Bouldin JM, Light RP, Garg A. (2011).** Probing dry-weight improves left ventricular mass index. American journal of nephrology, 33(4):373-80.
- **Agricola E, Bove T, Oppizzi M, Marino G, Zangrillo A, Margonato A, Picano E. (2005).** "Ultrasound comet-tail images": a marker of pulmonary edema: a comparative study with wedge pressure and extravascular lung water. Chest, 127(5):1690-5.
- **Charra B, Chazot C. Volume control, blood pressure and cardiovascular function. (2003).** Nephron Physiology, 93(4):p94-101.
- **Cirit M, Akcicek F, Terzioğlu E, Soydaş C, Ok ER, Özbaşli ÇF, Başçi A, Dorhout Mees EJ. (1995).** 'Paradoxical'rise in blood pressure during ultrafiltration in dialysis patients. Nephrology Dialysis Transplantation, 10(8):1417-20.
- **Civilibal M, Caliskan S, Oflaz H, Sever L, Candan C, Canpolat N, Kasapcopur O, Arisoy N. (2009).** Left ventricular function by 'conventional'and 'tissue Doppler'echocardiography in paediatric dialysis patients. Nephrology, 14(7):636-42.
- **Codognotto M, Piccoli A, Zaninotto M, Mion M, Plebani M, Vertolli U, Tona F, Ruzza L, Barchita A, Boffa GM. (2007).** Renal dysfunction is a confounder for plasma natriuretic peptides in detecting heart dysfunction in uremic and idiopathic dilated cardiomyopathies. Clinical chemistry, 53(12):2097-104.
- **Drighil A, Madias JE, Mathewson JW, El Mosalami H, El Badaoui N, Ramdani B, Bennis A. (2008).** Haemodialysis: effects of acute decrease in preload on tissue Doppler imaging indices of systolic and diastolic function of the left and right ventricles. European Journal of Echocardiography, 9(4):530-5.
- **Gargani L, Sicari R, Raciti M, Serasini L, Passera M, Torino C, Letachowicz K, Ekart R, Fliser D, Covic A, Balafa O. (2016).** Efficacy of a remote web-based lung ultrasound training for nephrologists and cardiologists: a LUST trial sub-project. Nephrology Dialysis Transplantation, 31(12):1982-8.
- **Jaeger JQ, Mehta RL. (1999)**. Assessment of dry weight in hemodialysis: an overview. Journal of the American Society of Nephrology, 10(2):392-403.
- **Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P. (2015).** Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. European Heart Journal-Cardiovascular Imaging, 16(3):233-71.
- **London GM, Pannier B, Guerin AP, Blacher J, Marchais SJ, Darne B, Metivier F, Adda H,**

Safar ME. (2001). Alterations of left ventricular hypertrophy in and survival of patients receiving hemodialysis: follow-up of an interventional study. Journal of the American Society of Nephrology, 12(12):2759-67.

- **Loutradis C, Papadopoulos CE, Sachpekidis V, Ekart R, Krunic B, Karpetas A, Bikos A, Tsouchnikas I, Mitsopoulos E, Papagianni A, Zoccali C. (2020).** Lung ultrasound–guided dry weight assessment and echocardiographic measures in hypertensive hemodialysis patients: a randomized controlled study. American Journal of Kidney Diseases, 75(1):11-20.
- **Loutradis C, Sarafidis PA, Ekart R, Papadopoulos C, Sachpekidis V, Alexandrou ME, Papadopoulou D, Efstratiadis G, Papagianni A, London G, Zoccali C. (2019).** The effect of dry-weight reduction guided by lung ultrasound on ambulatory blood pressure in hemodialysis patients: a randomized controlled trial. Kidney international, 95(6):1505-13.
- **Mallamaci F, Benedetto FA, Tripepi R, Rastelli S, Castellino P, Tripepi G, Picano E, Zoccali C. (2010).** Detection of pulmonary congestion by chest ultrasound in dialysis patients. JACC: Cardiovascular Imaging, 3(6):586-94.
- **Nagueh SF, Smiseth OA, Appleton CP, Byrd BF, Dokainish H, Edvardsen T, Flachskampf FA, Gillebert TC, Klein AL, Lancellotti P, Marino P. (2016).** Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. European Journal of Echocardiography, 17(12):1321-60.
- **Paniagua R, Ventura MD, Ávila-Díaz M, Hinojosa-Heredia H, Méndez-Durán A, Cueto-Manzano A, Cisneros A, Ramos A, Madonia-Juseino C, Belio-Caro F, García-Contreras F. (2010).** NT-proBNP, fluid volume overload and dialysis modality are independent predictors of mortality in ESRD patients. Nephrology Dialysis Transplantation, 25(2):551-7.
- **Panuccio V, Enia G, Tripepi R, Torino C, Garozzo M, Battaglia GG, Marcantoni C, Infantone L, Giordano G, De Giorgi ML, Lupia M. (2012).** Chest ultrasound and hidden lung congestion in peritoneal dialysis patients. Nephrology Dialysis Transplantation, 27(9):3601-5.
- **Pardała A, Lupa M, Chudek J, Kolonko A. (2019).** Lung Ultrasound B-lines Occurrence in Relation to Left Ventricular Function and Hydration Status in Hemodialysis Patients. Medicina, 55(2):45.
- **Picano E, Scali MC, Ciampi Q, Lichtenstein D. (2018).** Lung ultrasound for the cardiologist. JACC: Cardiovascular Imaging, 11(11):1692-705.
- **Saad MM, Kamal J, Moussaly E, Karam B, Mansour W, Gobran E, Abbasi SH, MahgoubA, Singh P, Hardy R, Das D. (2018)**. Relevance of B-lines on lung ultrasound in volume overload and pulmonary congestion: clinical correlations and outcomes in patients on hemodialysis. Cardiorenal medicine, 8(2):83-91.
- **Sinha AD, Agarwal R. (2009).** Opinion: can chronic volume overload be recognized and prevented in hemodialysis patients? The pitfalls of the clinical examination in assessing volume status. InSeminars in dialysis, Vol. 22, No. 5, pp. 480-482. Oxford, UK: Blackwell Publishing Ltd.
- **Torino C, Gargani L, Sicari R, Letachowicz K, Ekart R, Fliser D, Covic A, Siamopoulos K, Stavroulopoulos A, Massy ZA, Fiaccadori E. (2016).** The agreement between auscultation and lung ultrasound in hemodialysis patients: the LUST study. Clinical Journal of the American Society of Nephrology, 11(11):2005-11.
- **Tsilonis K, Sarafidis PA, Kamperidis V, Loutradis C, Georgianos PI, Imprialos K, Ziakas A, Sianos G, Nikolaidis P, Lasaridis AN, Karvounis H. (2016).** Echocardiographic parameters during long and short interdialytic intervals in hemodialysis patients. American Journal of Kidney Diseases, 68(5):772-81.
- **Voroneanu L, Cusai C, Hogas S, Ardeleanu S, Onofriescu M, Nistor I, Prisada O, Sascau R, Goldsmith D, Covic A. (2010).** The relationship between chronic volume overload and elevated blood pressure in hemodialysis patients: use of bioimpedance provides a different perspective from echocardiography and biomarker methodologies. International urology and nephrology, 42(3):789-97.
- **Zoccali C, Mallamaci F. (2018)**. Mapping progress in reducing cardiovascular risk with kidney disease: managing volume overload. Clinical Journal of the American Society of Nephrology, 13(9):1432-4.
- **Zoccali C, Tripepi R, Torino C, Bellantoni M, Tripepi G, Mallamaci F. (2013)**. Lung congestion as a risk factor in end-stage renal disease. Blood purification, 36(3-4):184-91.