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Lung ultrasound for volume status assessment in chronic hemodialysis patients

Ultrasonografija pluća u proceni hipervolemije kod bolesnika na hemodijalizi

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Abstract

Background/Aim. Assessing volume status in chronic hemodialysis (HD) patients is difficult despite several techniques have been developed. The aim of this study was to demonstrate the adequacy and efficacy of lung ultrasound (LUS) and B line score (BLS) in the assessment of volume status in patients on HD in comparison to other techniques: ultrasonographic determination of inferior vena cava diameter (IVCD), echocardiography (ECHO) and B-type natriuretic peptide (BNP) determination. **Methods.** LUS, ECHO, ultrasonography of inferior vena cava in inspiration (IVCDi) and expiration (IVCDe), and BNP sampling were performed before and after HD in 83 patients. **Results.** A significant reduction of BLS, IVCDi, IVCDe, BNP and several ECHO parameters such as left atrium diameter (LA), left ventricular internal dimension in diastole and systole (LVIDd and LVIDs, respectively), and left atrial volume in systole (LAVs), was registered ($p < 0.001$). There was a significant correlation between BLS and BNP before ($p = 0.01$) and after HD ($p = 0.05$), and a weaker but significant correlation between BLS and IVCDi and IVCDe before HD ($p = 0.05$). **Conclusion.** All techniques assessed hypervolemia before and after HD successfully. BNP correlated with LUS before and after HD, and IVCDi and IVCDe correlated with LUS only before HD. LUS is cheap and simple to perform, can be performed bedside and can be reliably used for assessing volume status in HD patients.

Key words:
renal hemodialysis; lung; ultrasonography; natriuretic peptide, brain; vena cava, inferior; echocardiography; water-electrolyte imbalance.

Apstrakt

Uvod/Cilj. Procena stanja volemije bolesnika na hroničnom programu hemodijalize (HD) je teška uprkos postojećim razvijenim tehnikama. Cilj ove studije je bio da pokaže adekvatnost i efikastnost ultrazvuka pluća (UZP) i B linijskog skora (BLS) u proceni stanja volemije kod bolesnika na HD u poređenju sa drugim tehnikama: određivanjem dijametra donje šuplje vene (DŠVD) ultrazvukom, ehokardiografijom (ECHO) i određivanjem nivoa B tipa natriuretskog peptida (BNP) u krvi. **Metode.** UZP, ehokardiografija sa ultrasonografijom donje šuplje vene u inspirijumu (DŠVDi) i ekspirijumu (DŠVDe) i uzorkovanje krvi za određivanje BNP su učinjeni pre i posle HD kod 83 bolesnika. **Rezultati.** Registrovano je značajno smanjenje BLS, DŠVDi i DŠVDe, nivoa BNP i nekoliko ehokardiografskih (EHO) parametara (dimenzije leve pretkomore, komore u sistoli i dijastoli i zapremina leve pretkomore) ($p < 0.001$). Postojala je značajna korelacija između BLS i BNP pre i posle HD ($p = 0.01$), između BLS i EHO parametara ($p = 0.01$), i slabija, ali ipak značajna korelacija između BLS i DŠVDi i DŠVDe pre HD ($p = 0.01$). **Zaključak.** Svim tehnikama je uspešno procenjena hipervolemija pre i posle HD. Vrednosti BNP su korelisale sa nalizom UZP pre i posle HD, a vrednosti DŠVDi i DŠVDe su korelisale sa UZP, uglavnom, pre HD. UZP je jeftina i jednostavna tehnika, može se izvoditi pored postelje i pouzdano koristiti za procenu stanja volemije kod bolesnika na HD.

Ključne reči:
hemodijaliza; pluća; ultrasonografija; natriuretski peptid, moždani; v. cava inferior; ehokardiografija; voda-elektroliti, disbalans.

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Introduction

Hemodialysis (HD) has two important goals in restoring homeostasis in patients with end stage renal disease (ESRD). One is the removal of metabolic waste products from the circulation. The other is removal of excess fluid, which is removed by ultrafiltration (the amount of fluid removed based on the patient's "dry weight"). Dry weight represents a "clinically determined lowest body weight that the patient can tolerate without symptoms of hypovolemia during HD, in absence of clear signs of hypervolemia" [1]. Adequate fluid balance in HD patients is very difficult to achieve without an accurate dry weight. Under- and overestimating dry weight leads to hypo- and hypervolemia, respectively. Both hypo- and hypervolemia cause numerous serious complications and increase morbidity and mortality in HD patients [2]. Hypovolemia manifests as intradialytic hypotension, while hypervolemia presents most commonly as high interdialytic gain, arterial hypertension (HTA), peripheral edema and bibasilar crackles on lung auscultation. Complications include left ventricular myocardial hypertrophy (LVMH), heart failure (HF), pulmonary hypertension and pulmonary edema [3].

Treatment of HTA in patients on HD begins with dry weight reduction. This measure is not without risk, as complications of overshooting the target dry weight include intradialytic hypotension, vascular access thrombosis and accelerated decline of residual renal function. All of these are related to low quality of life and worse prognosis [4].

Studies have shown that clinical assessment of fluid status has low specificity and sensitivity in detecting both under- and overhydration [5]. Patients on HD have 10 to 20 times greater cardiovascular mortality in comparison to the general population [4]. Both hypovolemic hypotensive episodes and chronic hypervolemia greatly contribute to it. A new, more specific and sensitive method for volume status assessment is needed in HD setting.

An ideal volume status assessment method would have to be reliable, simple, fast, non-invasive and inexpensive [6]. No currently available method has all of these characteristics, but all perform better than clinical assessment alone [5]. Some of these methods are bioimpedance, continuous volume monitoring, ultrasonographic measurement of inferior vena cava diameter (IVCD), echocardiography (ECHO), B type natriuretic peptide (BNP) and its N terminal prohormone (NT- proBNP) blood levels [7]. IVCD correlates with volume status in patients on HD. Wider IVCD are registered before HD. Respiratory variations in IVCD, or their absence are also noted before HD, while after HD a decrease in these diameters is noted, as well as an increase of the index of collapsibility [5]. The use of ECHO is not as clearly defined as ultrasonographic measurement of IVCD, but some ECHO parameters show a significant reduction after HD (diameter and volume of the left atrium, end-diastolic and end-systolic left ventricular volume) [8]. BNP, a polypeptide secreted by cardiomyocytes in response to their stretching, can be used as a marker for hypervolemia in patients on HD. Elevated BNP levels are registered in 100% of patients on chronic HD, and these levels decline after dialysis [9]. This reduction can be explained by increased dialytic clearance of BNP or by better volume control leading to a reduction in left ventricle wall stretching and reduced BNP secretion [10].

Some of the flaws of these methods are high price of equipment, high price of supplies and laboratory reagents, longer duration of the examination and the need for specially trained medical staff to perform these ultrasonographic examinations [7]. A new method for assessing volume status in this patient group is needed.

Lung ultrasound (LUS) has emerged as a new method for volume status assessment in patients on HD. LUS works by detecting extravascular lung water (EVLW). EVLW represents the amount of water present in lungs outside of the pulmonary vasculature. It shows the amount of lung congestion, and is elevated in states of hypervolemia, low oncotic pressure and/or increased lung capillary permeability [10]. LUS detects EVLW by registering it as sonographic artifacts called B lines [5]. A B line represents an acoustic shadow that forms when an ultrasonic wave meets edematous interlobulus septa in the lungs [9]. The exam is performed by placing the probe on 28 predetermined points on the chest and then adding the number of registered B lines, thus getting the B line score (BLS) [7].

LUS is a method that has numerous benefits: it is fast, simple, low-cost and readily accessible to secondary health centers, requiring only an ultrasound machine with a convex, linear or sector probe [5].

This article did not focus on the cause of hypervolemia and did not take the patients' cardiologic status, New York Heart Association (NYHA) class, comorbidities or pharmacotherapy into account. Our focus was volume status determined by BLS as a new method and its correlation to volume status assessed by other methods. This approach is justified by the fact that lung congestion quantified by LUS represents a significant predictor of patient survival, irrespective of heart function [2].

Our goal was to demonstrate the adequacy and efficacy of LUS in the assessment of volume status in patients on HD in comparison to other methods: ultrasonography of IVC, ECHO and BNP levels.

Methods

The study was performed from April 2016 to June 2017 on 84 patients in the Dialysis Unit of the Department of Internal Medicine, General Hospital in Kikinda. Inclusion criteria were: age equal to or greater than 18 years and time on chronic HD program longer than 3 months. Exclusion criteria were: patient declining or unable to sign the informed consent, chronic pleuritis, pulmonary fibrosis and pneumectomy. One patient met the exclusion criteria due to dementia, being unable to sign the informed consent, the other 83 were enrolled in the study.

Every patient was clinically evaluated before, during and after dialysis. Lung and heart auscultation, arterial blood pressure, body weight before (pre HD) and after (post HD) dialysis were recorded.

Measurements were made on the first weekly dialysis. LUS, ECHO, ultrasonography of IVC and collection of blood samples for BNP measurements were made immediately prior to dialysis. All patients then underwent HD according to their usual dialysis protocols. After dialysis all measurements were repeated.

LUS was performed before HD using a Samsung Medison MySono U6 portable ultrasound system, with a 3.5 MHz convex probe. Measurement was done in a semi recumbent position. This was chosen as this is how most of our patients lie down during HD, so that the method could later be used in the bedside setting. The probe was placed longitudinally in the 2nd intercostal space on the left parasternal line, and the "bat sign" was seen on screen (Figure 1). The "bat sign" represents a normal LUS finding where the upper and the lower ribs represent the "wings" and the pleural line represents the "back" of the bat. Placing the probe was continued along the 2nd intercostal space in the medioclavicular, anterior axillar and midaxillary line and then in the same fashion along the 3rd and 4th intercostal spaces on the left and the 2nd, 3rd, 4th and 5th intercostal spaces on the right.

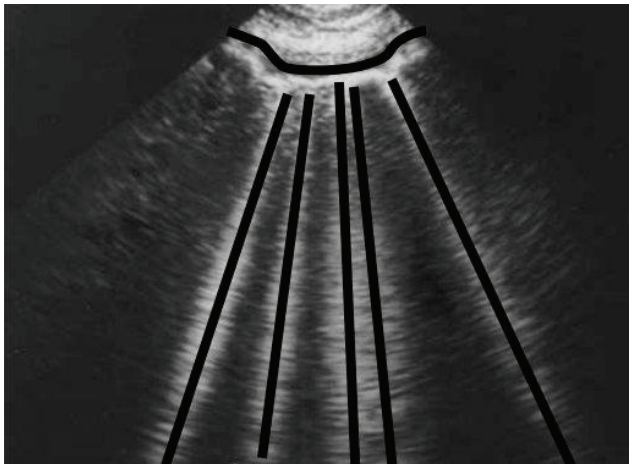

Fig. 1 – Lung ultrasound with visible B lines. Bat sign marked with horizontal curved black line; B lines highlighted with straight vertical lines (Modified image, original image by Lichtenstein et al. [12], Creative Commons License 2.5).

B lines were seen as hyperechogenic dynamic vertical wedge-shaped lines that start at the pleural line and spread to the bottom of the screen without loss of intensity (Figure 1). B lines were counted and noted in a form (Table 1) for each of the 28 positions on the anterolateral chest. The sum of these numbers represents the B line score (BLS). The BLS of less than 8 is considered normal. Lung congestion is estimated as light if the BLS is between 8 and 13, medium if it is between 14 and 30 and severe if the BLS equals more than 30 [7].

Echocardiography and IVC ultrasound were performed using Esaote MyLab™Six cardiovascular ultrasound system. ECHO diameters were measured in parasternal view using M mode, volumes were measured in four chamber view, using the area length formula. Systolic dysfunction was defined as ejection fraction of les then 55%. Diastolic dysfunction was determined and graded according to recommendations of the American Society of Echocardiography from April 2016 [13]. IVC diameters were measured in subxiphoid view, 2,5 cm from the right chamber, in non-forced expirium and inspirum. Values were indexed by body surface area, calculated using Du Bois formula.

Blood samples for determination of pre HD BNP levels were collected just prior to initiation of HD. Blood samples for post HD BNP levels were collected immediately before the second dialysis of the week (next HD session), in order to avoid the rise of BNP immediately after HD because of hemoconcentration. BNP blood levels were measured by an immunochemical method on a Siemens ADVIA Centaur® CP Immunoassay System.

We expressed continuous variables as mean ± standard deviation, except when otherwise noted. Categorical variables are presented as numbers and percentages. The distribution of obtained data was tested for normality using the Shapiro-Wilk test. Based on the distribution, differences between techniques pre and post HD were determined using either the paired-sample *t*-test or Wilcoxon test. Correlations between continuous variables were assessed either with the Pearson's coefficient of correlation for normally distributed data or with Spearman's coefficient of correlation for non-normally distributed data. Statistical significance was set at $p < 0.05$. Statistical analysis of the data was performed by use of the commercial statistical software IBM SPSS 23.

Table 1

B line score form

Right hemithorax					Left hemithorax			
Midaxilar	Anterior axilar	Midclavicular	Parasternal	Intercostal space	Parasternal	Midclavicular	Anterior axilar	Midaxilar
				II				
				III				
				IV				
				V	/	/	/	/

Results

Totally, 83 patients were enrolled in this study. Their anthropometric and clinical characteristics are shown in Table 2.

Table 2
Anthropometric and clinical characteristics of patients

Patients' characteristics	Values
Number of patients	83
Age (years), mean ± SD	61.02 ± 11.74
Male/female, n/n	58/25
Hi-flux/low-flux filters, n/n	65/18
Kt/V, mean ± SD	1.14 ± 0.22
MAPpre (mmHg), mean ± SD	94.10 ± 13.10
MAP post (mmHg), mean ± SD	90.86 ± 14.00
Ultrafiltration (L), mean ± SD	3.05 ± 1.00
Weight pre HD (kg), mean ± SD	76.68 ± 16.64
Weight post HD (kg), mean ± SD	73.91 ± 16.36
Hgb (g/L), mean ± SD	105.78 ± 17.78
Alb (g/L), mean ± SD	38.03 ± 4.00
Normal systolic function n (%)	41 (49%)
Systolic dysfunction, n (%)	42 (51)
Normal diastolic function, n (%)	27 (33%)
Diastolic dysfunction, n (%)	56 (67%)

MAP – mean arterial pressure; HD – hemodialysis, Hgb – hemoglobin, Alb –albumin; SD – standard deviation.

Effects of dialysis on the BLS, IVC diameters, collapsibility index, ECHO parameters and BNP levels are shown in Table 3.

Table 3
Differences in volume status parameters before hemodialysis (pre HD) and after hemodialysis (post HD)

Method	Reference interval	Pre HD	Post HD	*p*
BLS*	< 8	18.85	7.3	< 0.0001
BNP (pg/mL)*	< 400	914.07	486.57	< 0.0001
MAP (mmHg)†	70–100	94.1	90.86	0.0094
LA (cm)*	2.7–3.8 (f) 3.0–4.0 (m)	3.78	3.53	< 0.0001
LVIDd (cm)*	3.9–5.3 (f) 4.2–5.9 (m)	5.21	4.96	< 0.0001
LVIDs (cm)†	2.0–2.6	3.69	3.43	< 0.0001
LAVs (mL)*	22–52 (f) 18–58 (m)	60.54	52.36	< 0.0001
IVCDe (mm/m^2)†	8–11.5	10.45	7.85	< 0.0001
IVCDi (mm/m^2)†	-	7.19	4.41	< 0.0001
CCI (%)*	> 50	0.32	0.45	< 0.0001

***Paired sample *t*-est; †Wilcoxon signed-rank test.**
BLS – B line score; BNP – B type natriuretic peptide; MAP – mean arterial pressure; LA – left atrium; LVIDd – left ventricular internal dimension (diastole); LVIDs – left ventricular internal dimension (systole); LAVs – left atrial volume (systole); IVCDe – inferior vena cava diameter (expirium); IVCDi – inferior vena cava diameter (inspirium); CCI – inferior vena cava collapsibility index; m – males; f – females.

Lung ultrasound

We were able to perform LUS in all patients (100% feasibility). Pre HD BLS ranged from 1 to 159 (mean 19). According to LUS 22/83 (27%) of the patients had normal volume status, 30/83 (36%) had mild hypervolemia, 19/83 (23%) had moderate hypervolemia and 12/83 (14%) had severe hypervolemia. Post HD BLS values ranged from 0 to 109 (mean 7). According to LUS, 65/83 (78%) of the patients had normal volume status post HD, 8/83 (10%) had mild, 8/83 (10%) had moderate and 2/83 (2%) still had severe hypervolemia. A significant reduction of the BLS of 64% was achieved post HD ($p < 0.001$).

The distribution of B lines can be seen in Figure 2.

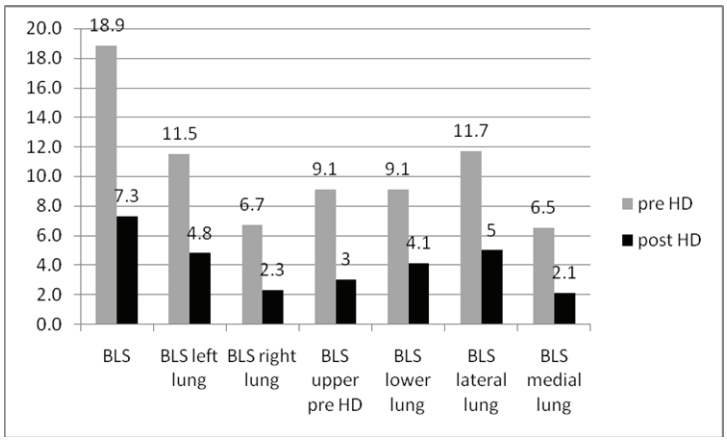

Fig. 2 – Number of B lines detected over each hemithorax, left and right, upper and lower and lateral and medial hemithorax, before and after dialysis.
BLS – B lines score; preHD – pre hemodialysis; postHD – posthemodialysis.

There was a significant difference in the BLS pre HD between the right and left lung (11.46 ± 14.33 vs. 6.75 ± 10.53, respectively; $p < 0.001$) and medial and lateral parts of the chest (6.48 ± 12.08 vs. 11.72 ± 12.88, respectively; $p < 0.001$), while there was no significant difference between upper and lower parts of the chest (9.08 ± 13.66 vs. 9.14 ± 10.54, respectively; $p = 0.9$). Post HD BLS differed significantly between the left and right lung (4.77 ± 6.90 vs. 2.31 ± 6.90, respectively; $p < 0.001$), upper and lower parts of the chest (2.99 ± 7.78 vs. 4.10 ± 6.17, respectively; $p = 0.01$) and medial and lateral parts of chest (2.11 ± 7.13 vs. 4.98 ± 6.95, respectively; $p < 0.001$). There was a significant correlation between the BLS preHD and BNP pre HD ($\rho = 0.49$, $p < 0.001$), as well as between the BLS pre HD and BNP post HD ($\rho = 0.45$, $p < 0.001$). A weaker significant positive correlation was noted between IVCDe pre HD and the BLS both pre HD and post HD, IVCDi pre and post HD and the BLS pre HD, as shown in Table 4.

Table 4
Spearman's correlation between lung ultrasound and other volume status assessment techniques

Parameter	BLS pre HD	BLS post HD
BLS pre HD	-	$\rho = 0.81^{\dagger}$
BLS post HD	$\rho = 0.81^{\dagger}$	-
BNP pre HD	$\rho = 0.49^{\dagger}$	$\rho = 0.45^{\dagger}$
BNP post HD	$\rho = 0.44^{\dagger}$	$\rho = 0.42^{\dagger}$
IVCDe pre HD	$\rho = 0.29^{\dagger}$	$\rho = 0.22$*
IVCDe post HD	$\rho = 0.27^{ns}$	$\rho = 0.29^{ns}$
IVCDi pre HD	$\rho = 0.26^{*}$	$\rho = 0.21^{ns}$
IVCDi post HD	$\rho = 0.23^{*}$	$\rho = 0.23^{*}$
CCI pre HD	$\rho = -0.20^{ns}$	$\rho = -0.23^{*}$
CCI post HD	$\rho = -0.16^{ns}$	$\rho = -0.13^{ns}$

BLS – B line score, BNP – B type natriuretic peptide; IVCDe – inferior vena cava diameter (expirium); IVCDi – inferior vena cava diameter (inspirium); CCI – inferior vena cava collapsibility index; HD – hemodialysis. Statistically significant difference: $^{*}p < 0.05$, $^{\dagger}p < 0.01$, ns – no significance.

Echocardiography and inferior vena cava ultrasonography

Left ventricular ejection fraction (LVEF) ranged from 29% to 70% (mean 54 ± 8%). Systolic dysfunction was present in 42/83 (51%) of the patients, while 41/83 (49%) of the patients had normal systolic function. Normal diastolic function was present in 27/83 (33%), while diastolic dysfunction was present in 56/83 (67%) of the patients. Grade I diastolic dysfunction was present in 36/83 (43%) of the patients, grade II diastolic dysfunction in 9/83 (11%) and grade III in 11/83 (13%) of the patients.

IVC dimensions in expirium pre HD ranged from 5.74 mm to 16.14 mm (mean 10.45 ± 2.28 mm) and from 3.57 mm to 13.69 mm (mean 7.85 ± 2.18 mm) post HD. Inferior vena cava dimension in inspirium pre HD ranged from 0.96 mm to 15.12 mm (mean 7.19 ± 2.70 mm) and from 0.65 mm to 15.12 mm (mean 4.41 ± 2.19 mm) post HD. The inferior vena cava collapsibility index (CCI) was calculated according to the formula:

$$CCI = \frac{IVCDe - IVCDi}{IVCDe} \times 100\%$$

and ranged from 6% to 91% (mean 32±15%) pre HD and from 11% to 92% (mean 45 ± 17%) post HD. A significant reduction of both IVCDe (25%) and IVCDi (38%) was registered post HD ($p < 0.0001$), as well as significant increase in the CCI of 58% ($p < 0.0001$).

According to IVCDe dimensions (cutoff value of 11.5 mm/m^2) 24/83 (29%) of the patients were hypervolemic pre HD, while 59/83 (71%) had normal volume status. After dialysis only 5/83 (6%) were hypervolemic, while 78/83 (94%) had normal hydration status.

A significant positive correlation detected between IVCe pre HD and IVCe post HD (r = 0.77, $p < 0.001$), IVCi pre HD and IVCi post HD (r = 0.77, $p < 0.001$), IVCe pre HD and IVCi pre HD (r = 0.62, $p < 0.001$), IVCi pre HD and IVCe pre HD (r = 0.81, $p < 0.001$), IVCi pre HD and IVCe post HD ($p = 0.67$, $p < 0.001$), IVCe post and IVCi post HD (r = 0.77, $p < 0.001$) was noted.

A significant positive correlation was found between the BLS pre HD and post HD and several ECHO parameters (Table 5).

Table 5
Spearman's correlation between lung ultrasound and echocardiographic parameters

Parameter	BLS pre HD	BLS post HD
LA pre HD	$\rho = 0.31^{\dagger}$	$\rho = 0.31^{\dagger}$
LA post HD	$\rho = 0.30^{\dagger}$	$\rho = 0.28^{*}$
LVIDdpre HD	$\rho = 0.28^{\dagger}$	$\rho = 0.23^{*}$
LVIDd post HD	$\rho = 0.27^{*}$	$\rho = 0.17^{ns}$
LVIDs pre HD	$\rho = 0.31^{\dagger}$	$\rho = 0.23^{*}$
LVIDs post HD	$\rho = 0.32^{\dagger}$	$\rho = 0.21^{ns}$
LAVS pre HD	$\rho = 0.32^{\dagger}$	$\rho = 0.28^{*}$
LAVS post HD	$\rho = 0.33^{\dagger}$	$\rho = 0.29^{\dagger}$

BLS – B line score; LA – left atrium diameter; LVIDd – left ventricular internal dimension in diastole; LVIDs – left ventricular internal dimension in systole; LAVS – left atrial volume in systole.
Statistically significant difference: $*p < 0.05$, $\dagger p < 0.01$, ns = no significance.

BNP

Pre HD BNP ranged from 59.3 pg/mL to 5,000 pg/mL [median 484,5, interquartile range (IQR) 954,7]. Post HD BNP ranged from 16.4 to 4,253.2 (median 197.9, IQR 473.3). We considered BNP levels above 400 pg/mL elevated. There were normal BNP levels before HD in 36/83 (43%) of the patients and 47/83 (57%) of the patients had elevated BNP levels. Post HD, 54/83 (65%) of the patients had normal BNP levels and 29/83 (35%) of the patients had elevated BNP levels.

Discussion

The aim of our study was to validate LUS for assessment of volume status in patients on chronic hemodialysis by performing it pre and post HD and by comparing it to other

methods of volume status assessment - ECHO, BNP, IVCD in inspirium and expirium including the CCI [5]. Their flaw is the requirement of specially trained staff (cardiologist), and an adequate echocardiographic window, which not all patients have. This goes even more for other ECHO parameters, such as diameters of LA, LV, volume of LA, LV, which require the use of echocardiographic cabinet, a cardiologist, an adequate chest anatomy and more time for the exam.

Our sample population showed a male predominance. Half of our patients had systolic and two thirds had diastolic dysfunction. Other authors had similar samples [2, 11, 14–20], while others had samples with low number of cardiac patients [7, 16]. Since 80% of all hemodialysis patients have some cardiac disease [ischemic heart disease (39%), congestive heart failure (40%), arrhythmia (31%) and other heart conditions (63%)] this sample is acceptable [17].

What we found is that all techniques for volume assessment showed its significant reduction post HD. This shows that the techniques in question can detect hypervolemia and can detect changes in volume status. This conclusion is supported by a number of studies [6, 7, 11, 14–16, 18–22]. What was also established was that a significant correlation exists between these methods, albeit of varying degree. This is also supported by studies by Vitturi et al. [22], Alexiadis et al. [23], Basso et al. [7] and Donadio et al. [6]. What was interesting was that no method in our study showed a correlation with reduction of weight during HD. Similar results were reported by several studies [2, 14]. Others found this not to be the case [16, 22]. This could be explained by the notion that IVC diameters are representative of intravascular filling grade, and LUS via BLS quantifies the level of extravascular imbibition of the lung interstitium. IVC diameters are not sensitive to detect volume change in a short amount of time, as in HD. An equilibrium between compartments takes time to be established after dialysis [22]. On the other hand, LUS measures changes in real time, therefore being more practical, as it can be performed immediately after dialysis, or even during dialysis [22].

LUS also takes less time to perform and is not as dependent on patients' anatomy. The staff can be educated in this method in a relatively short time [5]. It can be performed at patient bedside. The flaw of this method is that it detects extravascular lung water index (EVLW) in the same manner as fibrosis of the lung interstitium so it cannot be used for volume assessment in patients with interstitial lung disease [5].

The BLS was the greatest in the more lateral parts of the lung. Left lung had a greater number of B lines detected. This information can be used to streamline the LUS process and make it even simpler by focusing on the regions where B lines are more numerous.

We found that the BLS correlates with ECHO parameters (LA, LAVS, LVIDd and LVIDs,). This is supported by a study of Mallamaci et al. [11] , who found that the BLS correlates with LVMI, LVES, E/e', LAV, EDLVL. On the other hand, other authors like Siriopol et al. [2] and Weitzel et al. [14] found no association between change of the BLS and ECHO measurements, despite similar study population.

High concentrations of BNP were also reported pre and post HD. While other authors did not report post HD increase of BNP we detected it at the start of our study and adjusted the time of blood sampling for determination of post HD BNP. BNP has an advantage in the setting of HD because of its lower molecular weight, meaning it is readily dialyzed, as opposed to NT- proBNP which is not cleared by low flux filters because of higher molecular weight [24]. We know that the number of B lines correlates with natriuretic peptide levels [5].We also know that despite differences in BNP clearance across filter membranes, several studies support direct association between natriuretic peptides and overhydration in dialysis patients [25]. In our study a positive correlation was shown between the BLS and BNP levels, both pre and post HD. Donadio et al. [6] supported this by reporting similar results in their study, where they established a positive correlation only between pre HD BLS and pre HD BNP. Paudel et al. [20] showed similar results on a positive correlation between the BLS and NT-pro BNP in patients on peritoneal dialysis. On the other hand, Basso et al. [7] found no correlation between the BLS and BNP levels.

Some authors argue that increased levels of circulating BNP and NT- proBNP in patients on HD and their reduction after dialysis indicate that both BNP and NT-proBNP act as composite markers of hypervolemia, systolic dysfunction and left ventricular hypertrophy [9]. It is proven that increased levels of BNP and NT-proBNP are reliable predictors of all-cause and cardiovascular mortality [9].

We found a weaker but significant correlation between pre HD and post HD BLS and pre HD IVCDe and between pre HD and post HD BLS and pre HD IVCDi. No correlation was found between the BLS and CCI. These results are supported by Basso et al. [7] who report positive correlation between IVCD in inspiration (pre and post HD) and expiration (only pre HD) and the CCI (only pre HD). Vitturi et al. [22] report a positive relationship between BLS changes and changes in IVCDe and IVCDi, but not the CCI. However, Trezzi et al. [16] did not find these relationships.

Adjusting of dry weight based on IVC measurements resulted in a significant reduction of intradialytic events such as cramps, nausea, hypotension, an improvement in quality of life, and delayed left ventricle hypertrophy and chamber dilatation in hypervolemic patients on HD when compared with clinical assessment of dry weight [26].

LUS has a few limitations. It cannot differentiate edematous (wet) B lines of pulmonary congestion from fibrotic (dry) B lines, which are related to interstitial pulmonary fibrosis. Integration with other methods can help here, as well as a repeat LUS after an intervention which changes the volume state of the patients, because wet B lines change with volume expansion or depletion, while dry B lines are fixed. It is also not possible to distinguish EVLW accumulation due to heart failure and that of acute respiratory distress syndrome, even though the latter has a more irregular fragmented pattern with alternating spaces of highly concentrated B lines and those that are spared. The third limitation is that LUS cannot detect underhydration [5].

Ther are two flaws of this study. First, it was a single center cross-sectional study on a somewhat heterogeneous sample in terms of cardiac function. Another flaw is that

LUS, like other ultrasonographic methods, is observer dependent.

Conclusion

LUS can be used to assess volume status in patients on chronic hemodialysis. Our data show that LUS correlates well with BNP levels and slightly less well with IVCD. Overhydration is associated with both greater IVCD and BNP levels, and thus the BLS can also be considered a marker of volume status. LUS is cheap, simple to perform, can be performed bedside and thus can be a reliable indicator for a patient's volume status and can easily be made part of routine patient care protocol.

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