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ORIGINAL ARTICLE

Impact of lung ultrasound-guided therapeutic approach on haemodialysis treatment in patients with ischemic heart failure

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ABSTRACT

Aim Lung ultrasound (LUS) can be used for an assessment of volume overload in patients with end-stage kidney disease (ESKD) and those undergoing dialysis. The aim of this study was to analyse whether the initial use of LUS in evaluating volume status could benefit patients by optimizing haemodialysis treatment and improving their clinical status.

Methods The study included 50 haemodialysis patients in stage V of ESKD with the diagnosis of ischaemic heart failure with reduced (HFrEF) or midrange ejection fraction (HFmrEF). The assessment of volume status was verified solely by LUS (along with the analysis of B lines as measures of volume status). The specified laboratory parameters were performed initially, after three, and after six months.

Results The number of B-lines on LUS were decreased during the six-month follow-up compared to baseline, indicating a reduction in volume overload due to the LUS-guided protocol. Statistically significant differences were observed in the average creatinine (p=0.001) and parathormone (PTH) (p=0.003) levels over the six-month monitoring period. Significant differences were also noted in triglyceride (p=0.000) and potassium (p=0.02) levels. No significant differences were found in the values of other monitored parameters.

Conclusion In haemodialysis patients diagnosed with heart failure, LUS can aid the achievement of a more efficient volume reduction by decreasing B-lines, which are indicative of congestion. Our study also demonstrated beneficial effects of LUS on potassium and parathormone levels.

Keywords: kidney failure, prognosis, ultrasound

INTRODUCTION

Volume overload is a common issue among patients with end-stage kidney disease (ESKD) and those undergoing dialysis (1). In clinical practice, lung ultrasound (LUS) is increasingly being preferred over chest X-rays (1). The LUS was introduced to intensive care units and emergency departments more than 20 years ago, primarily to assess patients with acute dyspnoea (1,2). Volume overload is a critical and modifiable risk factor associated with a very high mortality risk in ESKD patients undergoing haemodialysis (1,2). Interdialytic fluid accumulation, assessed by total body mass before dialysis or relative volume during dialysis, independently predicts mortality and cardiovascular events in this population (2,3).

Correcting volume overload is a key factor behind the benefits of more frequent haemodialysis (3–5). The LUS allows direct quantification of water accumulated in the lung interstitium, a body fluid compartment strictly dependent on pulmonary pressure and critically influenced by left ventricular filling pressure (1–3). When the air content in the lungs decreases and lung density increases, vertical reverberation artifacts known as B-lines appear. B-lines are observed in patients with heart failure and pulmonary edema, where a higher number of visible B-lines correlates with a lower air-to-water content ratio (3,4). The LUS can detect amounts of free fluid in the lungs that are not verifiable with standard chest X-rays (less than 500 ml of fluid) (3,4). LUS is a valuable tool for stratifying and prognosticating patients with heart failure (HF) and is widely used in stress echocardiography protocol (5–7). The simplified 8-zone LUS protocol is considered effective in assessing real-time fluid volume changes and correlating with haematocrit levels measured during dialysis, providing a valuable method for monitoring fluid status in volume-overloaded patients (6).

In patients undergoing haemodialysis, monitoring conditions such as HF, and optimizing haemodialysis treatment represent a symbiosis of heart failure pharmacological therapy with patient volume management (7). Similar studies have not been conducted in Bosnia and Herzegovina, and generally, this remains a question within the academic community that is still being researched, without a clear conclusion.

The aim of this study was to analyse whether the initial use

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of LUS in evaluating volume status could benefit patients by optimizing haemodialysis treatment and improving their clinical status.

PATIENTS AND METHODS

Patients and study design

The study included 50 haemodialysis patients in stage V of ESKD (eGFR <15 mL/min/72 m²) with a diagnosis of ischaemic heart failure with reduced (HFrEF) or midrange ejection fraction (HFmrEF) treated at the Clinic for Haemodialysis, Clinical Centre of the University of Sarajevo, from January 2023 to December 2023. The assessment of volume status was verified solely by LUS. The inclusion criteria were: age >18 years, on haemodialysis >3 months, and the diagnosis of ischemic heart failure (left ventricular ejection fraction <45%, including patients with HFrEF and HFmrEF). The exclusion criteria were the diagnosis of malignancy or active acute infection.

An ethical approval was obtained by the Ethics Committee of the Clinical Centre, University of Sarajevo.

Methods

The following laboratory tests were performed for each patient: erythrocyte sedimentation rate (ESR), complete blood count (CBC), serum sodium (Na), potassium (K), calcium (Ca), and phosphate (P) levels, serum creatinine and urea levels, serum albumin levels, values of lipid profile (triglycerides), parathyroid hormone (PTH) and C-reactive protein (CRP).

All patients underwent transthoracic echocardiography, where measurements were taken for ejection fraction of the left ventricle (EFLV) by the Simpson's method (8) left ventricular end-diastolic diameter (LVEDD), left atrial volume index (LAVI), and mid-right-ventricular (RV) diameter.

The patients were followed for six months. Specified laboratory parameters, as well as an analysis of B lines on LUS, were performed initially, after three months, and after six months.

All laboratory tests were conducted at the Institute of Clinical Chemistry and Biochemistry, Clinical Centre of the University of Sarajevo, using standard laboratory procedures (Roche Cobas 4000, Basel, Switzerland). Plasma parathyroid hormone concentration was determined immunoradiometrically using a gamma counter (Roche Cobas E411, Basel, Switzerland) at the Clinic for Nuclear Medicine, Clinical Centre of the University of Sarajevo. At the start of the study, each patient's dry body weight was assessed using the Body Composition Monitor (BCM) (Fresenius Medical Care, Bad Homburg, Germany).

Statistical analysis

The data were processed using standard statistical methods and presented in tables. For categorical variables, results were shown as absolute numbers (N) and frequencies (%) of each category. Kolmogorov-Smirnov or Shapiro-Wilk tests were used, depending on sample size, to assess normality of variable distributions. Results were statistically analysed to determine the mean ±SD (standard deviation) for independent variables with normal distribution, and median and interquartile range (IQR) for independent variables without normal distribution. Spearman's Rho was used to assess the strength of the relationship between two variables. For continuous independent variables with normal distribution, significance of differences was tested using Student's t-test, while for variables without normal distribution, the Mann-Whitney test was used. Differences among multiple groups of variables were assessed using analysis of variance (ANOVA) for normally distributed variables and Kruskal-Wallis test for variables without normal distribution. The $p < 0.05$ (Kruskal-Wallis, Student's t-test) and $p < 0.01$ (Kruskal-Wallis, Student's t-test) were considered statistically significant.

RESULTS

The median age of patients undergoing the haemodialysis treatment was 69.5 (range 56.5-77) years. The median duration of haemodialysis before study inclusion was 22 (20–30.25) months. Out of the total number, 29 (58%) were male.

A statistically significant difference observed in the average values of creatinine ($p=0.001$), eGFR ($p=0.019$), and PTH values over the six-month monitoring period ($p=0.003$) was found (Table 1). Significant differences were also found in triglyceride ($p=0.000$) and potassium values ($p=0.02$). There was no significant difference in the values of other monitored parameters.

A statistically significant negative correlation between the number of B-lines and the value of EFLV (rho=-0.760; $p<0.001$) at the beginning of the study was noticed, indicating that a higher number of B-lines was associated with a lower EFLV. This finding was also confirmed at the end of the study after six months (rho=-0.728; $p<0.001$). A higher number of B-lines was also associated with larger values of LVEDD and LAVI at the beginning of the study, with a significant positive correlation (rho=0.791; $p<0.001$ and rho=0.718; $p<0.001$, respectively) and at the end of the study (rho=0.742; $p<0.001$; rho=0.705; $p<0.001$, respectively).

DISCUSSION

The results of the study showed that many disorders are observed in laboratory and echographic parameters of patients with ESKD. Anaemia in kidney patients is of multifactorial origin, a consequence of decreased erythropoietin secretion, folic acid and vitamin B12 deficiencies, iron homeostasis disorders, shortened erythrocyte lifespan, and the presence of uremic, toxic inhibitors of erythropoiesis (9). Anaemia in kidney patients has multifactorial origin; it is most often normocytic, normochromic, and hypo proliferative (9). In our study, all haemodialysis patients had some degree of anaemia, which varied during the follow-up. It should be noted at the outset that the red blood cell line in haemodialysis patients had target values for haemoglobin (Hgb) and haematocrit (Hct) that indicate the "stability" of anaemia. Target values for Hgb (100-110 g/L) and Hct (30%) were aimed for and maintained with erythropoiesis-stimulating agents. All patients in our study were on erythropoietin therapy, typically receiving 4000/6000 IU weekly, adjusted based on hemogram results. On average, the patients achieved target hemogram values with adjusted doses. Variations in volume status, monitored by different diagnostic methods, did not significantly affect

Table 1. Monitored laboratory parameters and B lines obtained from lung ultrasound (LUS)

Variable	Basal	After three months	After six months	p
		Median (IQR)		
C-reactive protein (mg/L)	5.4 (2.1–6.65)	4.5 (2.4–6.7)	4.35 (2.8 -7.77)	0.847
Pre-dialysis urea (mmol/L)	15.6 (12–19.8)	15.5 (11.5–19.4)	13.2 (11.2–18.5)	0.27
Pre-dialysis creatinine (µmol/L)	774 (677.8–892.3)	733.5 (639.3–76.2)	688.5 (588.8–90.5)	0.001
Albumins (g/L)	36 (33.5–37)	35 (31–36)	35 (32.75–36)	0.117
Globulins (g/L)	30.5 (30–35)	32 (30–34.25)	32.5 (30–35)	0.818
Parathormone (pmol/L)	362 (310.5–461.75)	354.5 (276.25–16)	408.5 (276.5–46.5)	0.003
Calcium (mmol/L)	2.13 (2.05–2.34)	2.15 (2.11–2.36)	2.31 (2.12–2.43)	0.071
Chloride (mmol/L)	102.5 (99–111)	104 (100–109)	105 (100–112)	0.168
Phosphates (mmol/L)	1.21 (1.06–1.36)	1.2 (1.01–1.43)	1.1 (1.01–1.23)	0.118
B lines	13.5 (4.75–26.25)	10 (1–16.25)	9.5 (1.0–12.75)	0.093
		Mean ±SD		
Serum total protein (g/L)	66.94±5.17	68 (61–70.25)	67 (61.75–71)	0.758
Triglycerides (mmol/L)	3.59±1.15	2.34±08	2.25±0.67	0.000
Sodium (mmol/L)	137.98±3.33	137.32±3.35	137.76±2.92	0.594
Potassium (mmol/L)	5.83 ± 0.71	5.52±0.59	5.44±0.69	0.02

IQR, interquartile range; SD, standard deviation

hemogram values, though some patients with hypervolemia experienced a drop. Timely detection and correction of volume status, combined with erythropoiesis-stimulating agents, helped maintain target hemogram values throughout the study.

In addition to anaemia, our results indicate that in patients with terminal chronic kidney disease (CKD), higher levels of PTH and phosphorus, and lower levels of serum calcium and albumin were found. Hypocalcaemia and elevated PTH levels are disturbances described in the context of secondary hyperparathyroidism, recognized as a risk factor contributing to cardiovascular disease in patients in the terminal stage of CKD. As eGFR decreases, PTH levels increase, accompanied by mineral metabolism disorders. With further progression of CKD, phosphorus levels rise and serum calcium levels decline. Previous studies have confirmed that even a single haemodialysis session can increase markers of inflammation such as pentraxin-3 and high-sensitivity CRP, as well as markers of oxidative stress such as serum malondialdehyde (10). Patients with CKD on chronic haemodialysis often have low albumin levels, possibly due to increased albumin loss (proteinuria) if residual diuresis or dietary factors are maintained, though this was not analysed in our study. We observed lower total protein, albumin, and triglyceride levels, along with higher PTH values. Chronic extracellular volume expansion is common in end-stage CKD and may be unnoticed in mild to moderate cases, but severe fluid overload requires urgent haemodialysis initiation or additional dialysis sessions for those already undergoing chronic treatment. Although weight gain during dialysis is not necessarily synonymous with increased volume (10), this simple parameter is associated with frequent mortality risk (11). The limited correlation between volume overload parameters such as total body water and B-lines on LUS suggests that dysfunction and structural abnormalities of the left ventricle play a major role in pulmonary congestion in haemodialysis patients. This hypothesis is supported by the observation that B-lines are inversely correlated with parameters of systolic and diastolic function.

One limitation of the study is the lack of consideration for quantitative parameters of systolic and diastolic heart function, despite patients being diagnosed with heart failure.

Systolic parameters refer to left ventricular ejection fraction or global longitudinal strain of the left ventricle, while diastolic parameters include tissue Doppler parameters at the mitral annulus, pulmonary vein inflow, left atrial volume index, left atrial strain parameters, and left atrial stiffness index (8,12,13). Volume status assessed by LUS based on the number of B-lines, followed a clear pattern of interdialytic loss during haemodialysis. For these patients, achieving dry weight is crucial, though this parameter is variable and often requires adjustment. A normal LUS finding, defined as 15 or fewer B-lines, is associated with optimal volume management. The question arises regarding the utility of LUS in patients with ESRD (14,15). A study involving 367 patients on chronic haemodialysis who had high cardiovascular risk verified that treatment strategy guided by lung ultrasound effectively alleviated lung congestion, but it did not outperform usual care in improving the primary or secondary outcomes of the trial (15). One study did not show any benefit from LUS-guided therapy and haemodialysis (16). On the other hand, it has been reported that LUS is an affordable, user-friendly, and real-time method that allows for accurate dry weight assessment (17). The number of B-lines has been identified as an important indicator to monitor in haemodialysis patients, as it is directly linked to volume overload (18). Performing LUS before haemodialysis is considered valuable, as it helps to determine the most suitable therapeutic approach, potentially reducing cardiovascular risk, irrespective of heart function (19). Other studies also suggest that LUS is beneficial for optimizing treatment in haemodialysis patients (20,21). A meta-analysis concluded that LUS can effectively assess the volume status of haemodialysis patients in real time, with the number of B-lines before dialysis being strongly linked to poorer prognosis. However, when compared to routine care, LUS-guided volume management in haemodialysis patients does not significantly reduce mortality or cardiovascular events (22).

The study's limitation certainly lies in the small sample size, but considering the patient population in our geographical area, this was to be expected. Additionally, a comprehensive assessment of the right ventricle on echocardiography would undoubtedly provide additional data, as would the analysis of strain of all cardiac chambers.

In conclusion, in haemodialysis patients diagnosed with heart failure, LUS can aid the achievement of a more efficient

volume reduction by decreasing B-lines, which are indicative of congestion. The number of B-lines correlates with the systolic function of the left ventricle, as well as with the systolic and diastolic function of the left atrium. Our study also demonstrated beneficial effects of LUS on potassium and parathormone levels.

AUTHOR CONTRIBUTIONS

Conceptualization, N.P., B.P., H.R. and E.B.; Data curation, N.P. and E.B.; Formal Analysis, N.P., H.R. and E.B.; Funding acquisition, N.P., B.P. and E.B.; Investigation, N.P., B.P. and H.R.; Methodology, N.P., B.P. and E.B.; Project administration, N.P., B.P., H.R. and E.B.; Resources, N.P., B.P., H.R. and E.B.; Software, N.P., B.P., H.R. and E.B.; Supervision, N.P., B.P., H.R. and E.B.; Validation, N.P., B.P., H.R. and E.B.; Visualization, N.P., B.P., H.R. and E.B.; Writing – original draft, N.P., B.P., H.R. and E.B.; Writing – review & editing, N.P., B.P., H.R. and E.B. All authors have read and agreed to the published version of the manuscript.

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TRANSPARENCY DECLARATION

Conflict of interests: None to declare.

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