

## ORIGINAL ARTICLE

# Use of lung ultrasound to assess volume status and its association with physical examination in patients with chronic kidney disease

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## ABSTRACT

**Introduction.** Defining the optimal hydration status in patients with chronic kidney disease (CKD) is challenging, and the quest for an objective accurate method continues. Lung ultrasound (LUS) is a well-validated technique to estimate volume status. Previous studies examining the relationship between LUS and physical examination demonstrated conflicting results. We aimed to evaluate the correlation between LUS results and physical examination for assessing volume status in patients with CKD, and to compare different LUS protocols.

**Methods.** A prospective, single-center trial correlating physical examination findings to LUS results in different CKD groups, including non-dialysis and dialysis patients. Hemodialysis patients were tested twice, before and after dialysis, to compare results with ultrafiltration volume. Different LUS protocols were performed and compared, including 16-, 12-, and 8-zone measurements.

**Results.** We recruited 175 participants. A strong positive correlation was demonstrated between 16- and 12-zone protocols [ $r = .91$  ( $P < .001$ )] and between 12- and 8-zone protocols ( $r = .951$ ,  $P < .001$ ). Correlation was significant in various CKD groups. While blood pressure did not correlate with LUS score, there was a significant correlation between LUS and other components of the physical examination including lung crackles (OR = 1.15 (95%CI 1.096–1.22),  $P < .01$ ), pleural effusion (OR = 1.15 (95%CI 1.09–2.13),  $P < .01$ ) and peripheral edema ( $r = .24$ ,  $P < .001$ ). Ultrafiltration volume did not correlate significantly with change in LUS scores pre- and post-dialysis ( $r = .169$ ,  $P = .065$ ).

**Conclusion.** Most components of physical examination findings correlated with extravascular lung water assessment on LUS in CKD patients. The use of a simplified pragmatic LUS protocol may facilitate LUS use in clinical practice.

**Keywords:** chronic kidney disease, extravascular lung water, lung ultrasound, volume status

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## KEY LEARNING POINTS

### What was known:

- Lung ultrasound is an objective well-validated method to evaluate dry weight in patients with end stage kidney disease by estimating extravascular lung water. Previous studies have demonstrated conflicting results regarding the relationship between physical examination and ultrasound findings in patients with end stage kidney disease.
- In hemodialysis patients, pre-dialysis ultrasound can be used to guide ultrafiltration volume in dialysis sessions, although it did not prove to impact mortality or cardiovascular outcomes. Whether post-dialysis ultrasound can aid in clinical decisions is unknown.
- Different lung ultrasound protocols exist. While the first standardized lung ultrasound examination was based on evaluation of 28 zones, other simpler approaches make it more clinically relevant, however, non is superior to others in the chronic kidney disease population.

### This study adds:

- We found a significant correlation between physical examination components and extravascular lung water according to lung ultrasound score in a cohort of patients with chronic kidney disease, including oxygen saturation, lung crackles, pleural effusion, and leg edema but not blood pressure.
- In a subgroup analysis, we found that none of the components of the physical examination correlated with lung ultrasound score in patients treated with peritoneal dialysis.
- In hemodialysis patients, we failed to demonstrate a significant correlation between ultrafiltration volume during dialysis sessions and the change in lung ultrasound score, indicating that the variations in body fluids composition are apparently delayed and therefore cannot be used to accurately estimate reaching the dry weight immediately post-dialysis.
- We proved a strong linear correlation between different lung ultrasound protocols including 16-, 12-, and 8-zone measurements, implicating the validity of the simplified exams, which makes it more accessible and practical than the cumbersome multiple zones test.

### Potential impact:

- Although subjective, a comprehensive physical examination remains an important component of volume status assessment in chronic kidney disease patients' population.
- Lung ultrasound may not reflect reliably volume status immediately post-dialysis, a finding that warrants more research to assess its accuracy to support clinical decisions.
- The 12-zone approach is easy to perform in hemodialysis patients with a tunneled catheter; it requires only several minutes and is therefore very accessible. Furthermore, the 8-zone protocol allows to perform the exam during dialysis session without disturbing the patient or compromising the vascular access due to patient movements.

## INTRODUCTION

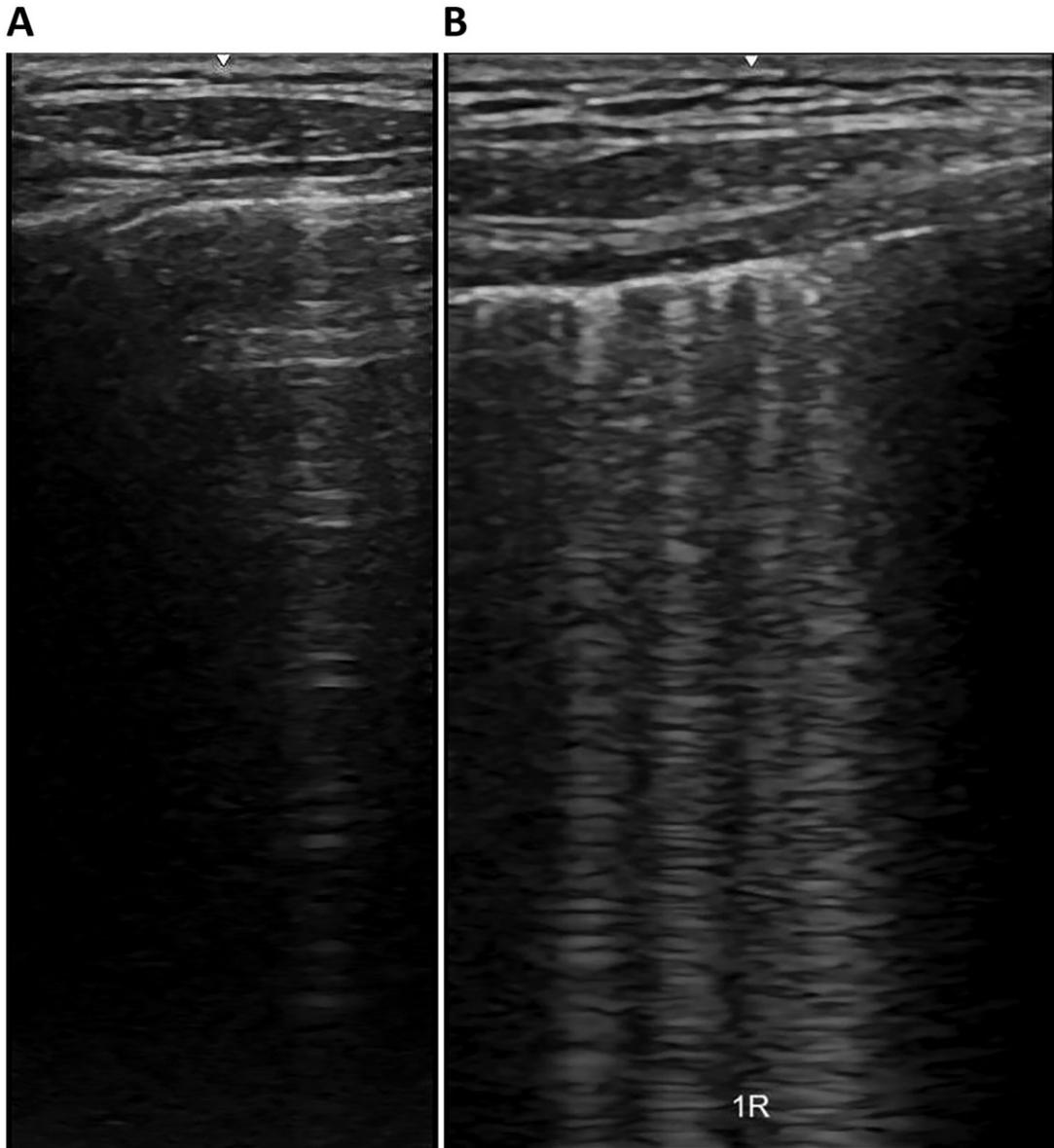
Volume overload is strongly associated with chronic kidney disease (CKD) progression and cardiovascular morbidity or mortality in patients with CKD stage 3–5 [1–4]; however, defining the optimal hydration status in these patients is challenging, in particular in patients with end stage kidney disease (ESKD) [5, 6]. Identifying an accurate and objective method to evaluate volume status and dry weight has been a focus of ESKD research for decades. Most of these methods have not been appropriately tested in clinical trials, and their benefit in clinical practice remains uncertain, except for bioimpedance spectroscopy, which is recommended for body composition assessment in patients treated with hemodialysis (HD), and lung ultrasound (LUS) [1, 7]. LUS is a well-validated technique for estimating extravascular lung water (EVLW). The key parameter to estimate lung water is the counting the so-called ultrasound B-lines, which are equivalent to the Kerley B-lines seen on standard chest X-rays (Fig. 1). As B-lines are likely to present before clinical symptoms of dyspnea appear, they serve as an early marker of EVLW [8]. Employing this technique increases the likelihood of diagnosing volume overload in symptomatic as well as asymptomatic patients with ESKD [9, 10]. The resulting LUS score is a powerful predictor of cardiovascular events and mortality in ESKD patients [11].

A recent systematic review found that blood pressure and peripheral edema poorly correlate with the number of B-lines, but did show a moderate correlation between B-lines and lung aus-

cultation to weight change during HD [12]. This is contrary to the LUST study, in which lung crackles with or without peripheral edema poorly reflected interstitial lung edema as assessed by LUS [13]. Ultrasound findings of EVLW decrease as volume is removed during dialysis, indicating an association between ultrafiltration volume during HD and a subsequent change in B-line number. Therefore, LUS score before and after dialysis could be a direct measure of evaluating real-time changes in EVLW [14]. The correlation between the amount of fluid removed and the reduction in B-line LUS score was confirmed in some trials but not in others [15–18].

Different methods of LUS exist. The first standardized LUS examination was based on evaluation of 28 zones [19], thereafter other simpler approaches were assessed in order to shorten the test and make it more clinically relevant, including 8- and 4-zone protocols, mostly validated in cardiac patients [20–22]. LUS can be performed in different positions and is most commonly conducted while the patient is supine or sitting. While EVLW distribution may have minor variations between different postures, the changes evolve slowly and the overall degree of congestion remains the same [23, 24].

In this study, we aimed to evaluate the correlation between LUS results and physical examination for assessing volume status in patients with CKD. Additionally, we aimed to compare different LUS methods and evaluate the correlation between LUS score change and ultrafiltration rate in patients undergoing HD.



**Figure 1:** Illustration of sonographic evaluation of lung fluids. (A) Normal lung ultrasound demonstrating A-lines, horizontal echogenic lines that run parallel to the pleural line. (B) Presence of extravascular lung water. B-lines are vertical hyperechoic artifacts that arise from the pleural line, extend to the end of the image without fading, and move synchronously with lung sliding. They result from a decrease in the air content in the lungs due to fluid accumulation.

## MATERIALS AND METHODS

This is a prospective, single-center trial, conducted at the nephrology department in a tertiary hospital. The study protocol was approved by the local ethics committee and was conducted according to GCP requirements, approval number TLV-21-0622. All patients gave informed consent before participation.

### Study population

Ambulatory HD and peritoneal dialysis patients (PD), as well as CKD stages 1–5 non-dialysis (CKD 1–5ND) patients from the outpatient clinic, were screened for eligibility. Patients were considered suitable if they were above 18 years old, had a diagnosis of CKD, were clinically stable as assessed by the investigator, and were willing and able to sign informed consent. Exclusion criteria

included pregnancy, inability to comply with study protocol, or parallel participation in another clinical trial. Patients with respiratory symptoms suggesting of acute pulmonary infection did not participate in the study.

### Study procedure

After informed consent, demographic information and medical history pertaining to each participant were recorded. A standard physical examination was performed by an authorized physician. To minimize interobserver variations, only two physicians were involved in the physical assessment. Initial cases were conducted by both to standardize patients' assessment and definitions, thereafter each participant was inspected by one of the two investigators. Collected indices included height and

weight measurement, documentation of vital signs and evaluation of volume status using lung auscultation and assessment of edema. Peripheral edema was graded 0–4 [25]. Thereafter, LUS was performed to determine congestion level.

PD and CKD1-5ND patients were tested once during a clinic visit. In HD patients, physical examination and LUS were performed both pre- and post-dialysis session. Pre- and post-dialysis weight, as well as total ultrafiltration, were recorded and compared to dry weight. The information derived from the pre-dialysis analysis was not used for clinical decisions to target ultrafiltration. Ultrafiltration was determined by dialysis staff blinded to the pre-dialysis assessment results.

### Lung ultrasound protocol

LUS was performed by an authorized and certified physician or ultrasound technician, using a Philips Lumify Ultrasound System, C5-2 curved array transducer. To reduce the likelihood of interobserver variations, LUS was performed by one of two investigators, after an appropriate pre-training according to the study protocol. Initial exams were performed simultaneously by both investigators to confirm similar definitions. In the sporadic cases of disagreement, it was subjected to the principal investigator's decision. Patients were evaluated in a sitting position. We initially examined 16 zones of the thorax, using longitudinal and transverse planes, through the intercostal space [26]. Eight points were visualized on each hemithorax: superior medial, superior lateral, superior axillary, inferior medial, inferior lateral, diaphragmatic, upper back, and lower back. The 16-zone approach was time consuming and complicated, especially in patients with tunneled dialysis catheters in the Jugular veins. Therefore, during the study, we performed protocol amendment, and substituted to a simplified 12-zone exam, where the superior and inferior lateral zones were abandoned bilaterally [24]. The 16- and 12-zone protocols were compared to assess whether the LUS can be simplified without sacrificing its accuracy. Each zone was assigned 0 points if no evidence of B-lines or had fewer than two separated B-lines, 1 point if more than three B-lines were observed, 2 points when multiple B-lines with coalescing lines were documented, and 3 points in cases of pulmonary consolidation [27]. Subsequently, 12-zone exam scores could range from 0, indicating a normal exam, to 36, indicating worst congestion possible [24, 28, 29]. Measurements were further divided into two groups: The 'low group' had no evidence of congestion or mild congestion (LUS score 0–12) vs the 'high group' that had moderate to severe congestion (LUS score >13).

### Study events

The primary event was to evaluate the correlation between 12-zone LUS results to physical examination in volume status assessment of patients with CKD.

Secondary events were correlation between LUS score change compared to ultrafiltration rate in HD patients and to compare different LUS methods.

### Statistical analysis

Continuous variables were first tested for normal distribution using the Kolmogorov–Smirnov test and Q–Q plots, and were summarized and displayed as a mean (standard deviation, SD) for normally distributed variables, and as median (IQR, interquartile range) for non-normally distributed variables.

Categorical variables were displayed as number of patients and the percentage in each group. For all categorical variables, the chi-square statistic was used to assess the statistical significance between groups. Continuous variables were compared by using a t-test if normally distributed or by Kruskal–Wallis/Mann–Whitney test if non-normally distributed.

Correlation between continuous parameters was calculated by Pearson's correlation coefficient.

Regression analysis with relevant parameters was performed to identify the significance of total scores on potential parameters.

LUS results using 16-zone were compared to the 12-zone approach using Pearson correlation. We also compared LUS scores with and without the posterior fields. Thereafter, all results were assessed using the 12-zone protocol.

$P < .05$  was considered statistically significant for all analyses. IBM SPSS Statistics for Windows, version 22 (IBM Corp., Armonk, NY, USA) was used for all statistical analyses.

## RESULTS

Among 175 participants, 119 were HD patients, 19 PD and 37 CKD 1–5ND patients (classification according to CKD stages was 4, 12, 7, and 17 patients defined as CKD 1–2, 3, 4, and 5ND, respectively). Every HD patient had two measurements, pre- and post-dialysis. Patients' baseline characteristics according to CKD groups are described in Table 1. Mean age was  $69.8 \pm 13$  years, 35.4% were females. Median 12-zones LUS score was 7 (IQR 4–11).

### Comparison of LUS score and physical examination in the whole cohort

Blood pressure did not correlate significantly with LUS score;  $r = -.041$ ,  $P = .48$  for systolic blood pressure and  $r = -.061$ ,  $P = .30$  for diastolic blood pressure. In HD patients, only pre-dialysis measurements were considered to avoid bias of post-dialysis hypotension.

There was an inverse correlation between participants oxygen saturation on room air and LUS score ( $r = -.24$ ,  $P < .01$ ).

Presence of lung crackles correlated significantly with LUS scores (OR = 1.15 (95%CI 1.096–1.22),  $P < .01$ ) (Fig. 2a). The correlation remained significant after adjustment to possible confounders such as age and gender [OR = 1.13 (95%CI 1.06–1.19),  $P < .01$ ]. Lung wheezes, however, did not correlate with LUS score [OR = 0.93 (0.81–1.057),  $P = .22$ ].

There was a significant correlation between the presence of pleural effusion on physical examination and LUS score before and after adjustment for confounding factors [OR = 1.15 (95%CI 1.09–2.13),  $P < .01$  and OR = 1.11 (95%CI 1.06–1.18),  $P < .01$ , respectively].

Peripheral edema, scored 0–4, had a linear correlation to LUS score ( $r = .24$ ,  $P < .001$ ), even after adjustment for confounding factors ( $r = .125$ ,  $P = .037$ ) (Fig. 2b).

### Comparison of LUS score and physical examination in different CKD groups

In patients treated with HD, while systolic blood pressure did not correlate with LUS score (correlation coefficient of  $-.03$ ,  $P = .63$ ), all other variables measured correlated significantly: lung crackles [OR = 1.13 (95%CI 1.06–1.2),  $P < .001$ ], presence of pleural effusion [OR = 1.18 (95%CI 1.11–1.3),  $P < .01$ ] and peripheral edema, scored 0–4 (correlation coefficient  $.24$ ,  $P = .002$ ).

Table 1: Patients' baseline characteristics according to kidney disease groups.

Parameter	Total N = 175	HD N = 119 <sup>a</sup>	PD N = 19	CKD 1-5ND N = 37	P value
Age (years)	69.8 ± 13	69.5 ± 12.8	73.2 ± 12.4	69.2 ± 13.9	.48
Sex, female (%)	62 (35.4)	44 (37)	6 (32)	12 (32.4)	.8
Comorbidities					
Smoker (active) (%)	46 (26.3)	30 (25.2)	6 (32)	10 (27)	.77
Diabetes mellitus (%)	82 (46.9)	58 (48.7)	8 (42.1)	16 (43.2)	.74
Hypertension (%)	153 (87.4)	105 (88.2)	18 (94.7)	30 (81.1)	.29
Systolic HF (%)	42 (24)	34 (28.6)	3 (15.8)	5 (13.5)	.09
Diastolic HF (%)	90 (51.4)	66 (55.5)	12 (63.2)	12 (32.4)	.023
Diuretic use (%)	109 (62.3)	81 (68.1)	15 (78.9)	13 (35.1)	<.001
GFR (ml/min/1.73 m <sup>2</sup> )	NA	NA	NA	32.7 ± 27	
Study measurements					
SBP (mmHg)	141.6 ± 21.2	141.6 ± 22.4	137.2 ± 13.9	139.8 ± 18.3	.65
DBP (mmHg)	70.1 ± 13.9	69.8 ± 13.9	64.1 ± 16.3	71.8 ± 11.5	.14
O <sub>2</sub> saturation (%)	97.9 ± 2	97.7 ± 1.9	97.1 ± 1.9	98 ± 1.3	.18
12-zone LUS	7.8 ± 5.4	7.8 ± 5.4 <sup>b</sup>	8.7 ± 5.8	6.5 ± 5.1	.26

<sup>a</sup>Number of patients, every patient had two examinations.

<sup>b</sup>LUS score in hemodialysis patients is according to 238 examinations.

Abbreviations: HF, heart failure; SPB, systolic blood pressure; DBP, diastolic blood pressure.

In the 19 participants treated with PD, none of the components of the physical examination correlated with LUS score, including systolic blood pressure (correlation coefficient .19,  $P = .46$ ), lung crackles [OR = 1.13 (95%CI 0.94–1.36),  $P = .18$ ], pleural effusion [OR = 1.01 (95%CI 0.83–1.23),  $P = 0.99$ ], and peripheral edema (correlation coefficient .30,  $P = .22$ ).

In 37 patients with CKD1-5ND, lung crackles and peripheral edema correlated with LUS score [OR = 1.25 (95%CI 1.05–1.5),  $P = .01$  and correlation coefficient .34,  $P = .013$ , respectively], however, systolic blood pressure and pleural effusion failed to show a significant correlation (correlation coefficient .20,  $P = .14$  and OR = 1.12 (95%CI 0.97–1.13),  $P = .11$ , respectively).

### Comparison of different congestion groups according to LUS score and physical examination

Patients' characteristics according to congestion group are presented in Table 2. No congestion or mild congestion (LUS score 0–12, 'low group') was measured in 246 measurements, compared to moderate to severe congestion (LUS score >13, 'high group') in 49 measurements. Patients in the low group were younger (mean age 68.5 ± 13.5 in the low group vs 75.6 ± 6.8 in the high group,  $P < .01$ ).

There was no correlation between groups and mean systolic blood pressure (low group 141.1 ± 21.3 mmHg, high group 141.1 ± 22.7 mmHg,  $P = .996$ ). Room air saturation correlated significantly between groups (low group 97.8% ± 1.5%, high group 96.6% ± 2.9%,  $P = .004$ ).

Dividing the results into low and high groups demonstrated a significant correlation with physical examination findings including lung crackles ( $r = .31$ ,  $P = .001$ ), presence of pleural effusion ( $r = .29$ ,  $P = .001$ ), and leg edema ( $r = .16$ ,  $P = .006$ ).

### Correlation between LUS and ultrafiltration in HD patients

There was an insignificant correlation (but a trend) between ultrafiltration volume, expressed by the change in pre- and post-dialysis weight, and change in LUS scores pre- and post-dialysis ( $r = .169$ ,  $P = .065$ ) (Fig. 3).

We further calculated the percentage of weight reduction as delta weight (pre-dialysis weight minus post-dialysis weight) divided by pre-dialysis weight. We could not find a statistical correlation between percentage of weight reduction and LUS ( $r = -.35$ ,  $P = .7$ ).

### Assessment of different lung scanning protocols

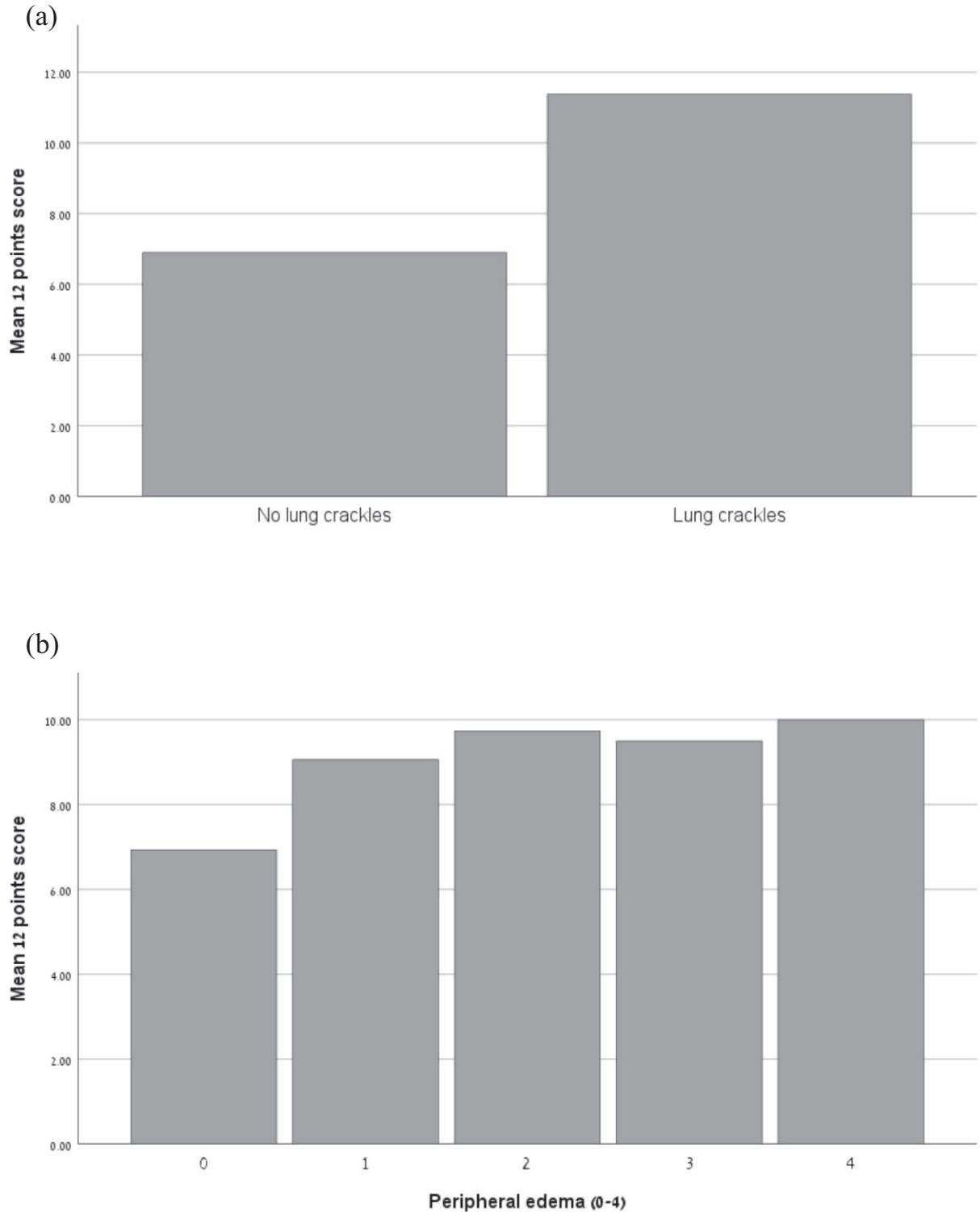
We compared between the 16- and 12-zone protocols (superior and inferior lateral points were spared). A Pearson correlation coefficient of .91 ( $P < .001$ ) indicated a strong positive correlation between the two variables (Fig. 4). When evaluating the different patient groups—HD, PD, and CKD1-5ND—all had a strong correlation between both protocols [a Pearson correlation coefficient of .907 ( $P < .001$ ) for HD, Pearson correlation coefficient of 1.0 ( $P < .001$ ) for PD and a Pearson correlation coefficient of 1.0 ( $P < .001$ ) for CKD1-5ND].

A comparison of LUS scores with (12 zones) and without posterior thorax fields (8 zones) identified a strong linear correlation ( $r = .951$ ,  $P < .001$ ).

## DISCUSSION

In the current study, performed in patients with variable stages of CKD, we demonstrated a good correlation between signs of fluid overload on physical examination and EVLW as evidenced by LUS score, but found no correlation to blood pressure. We also confirmed that a simplified, more pragmatic LUS protocol can be used to assess volume status in patients with CKD.

The prevalence of volume overload increases as kidney function declines, and is highest in dialysis patients. Volume overload is sometimes difficult to assess in daily practice as the clinical signs are often not specific nor sensitive [30]. Uncontrolled hypertension and blood pressure variability are considered an early sign of volume overload, both in CKD non-dialysis and in dialysis patients, frequently preceding other clinical signs of fluid excess [31–33]. Contrary to this concept, in our study blood pressure did not correlate with evidence of volume overload as measured by LUS score. The pathophysiology of hypertension in CKD is multifactorial and complex, especially in dialysis patients. Although volume overload is an important factor, other



**Figure 2:** Mean 12-zone LUS score according to physical examination findings. (a) Mean 12-zone LUS score in participants with and without lung crackles ( $r = .31$ ,  $P = .001$ ). (b) Mean 12-zone LUS score according to peripheral edema scored 0-4 ( $r = .16$ ,  $P = .006$ ).

contributors to elevated blood pressure include arterial stiffness, sympathetic hyperactivity, enhanced renin-angiotensin-aldosterone activity, and endothelial dysfunction [34]. These can act as possible confounders and reduce blood pressure sensitivity and specificity in volume assessment.

In contrast to blood pressure, other components of the physical examination had a positive correlation to LUS score, including oxygen saturation, lung crackles, pleural effusion, and leg edema, both in the whole cohort and in the group of patients treated with HD, who constituted most of the cohort. This is in

Table 2: Patients' characteristics according to congestion group.

	Low group (score 0–12) N = 246 <sup>a</sup>	High group (score >13) N = 49 <sup>a</sup>	P value
Age	68.5 ± 13.5	75.6 ± 6.8	<.01
Gender female (%)	92 (37)	14 (28)	.26
Diabetes mellitus (%)	115(47)	25(51)	.34
Hypertension (%)	216 (88)	43 (87)	.99
Heart failure (%)	137 (56)	42 (86)	<.01
CKD group (%)			.54
Hemodialysis (%)	198 (80)	41 (84)	
PD (%)	15 (6)	4 (8)	
CKD 1–5 non-dialysis (%)	33 (13)	4 (8)	
eGFR (ml/min/1.73 m <sup>2</sup> ) (only for CKD 1–5 non-dialysis)	34.6 ± 28.8	16.4 ± 8.9	.02
LUS score (12 points)	6 ± 3.5	17 ± 3.6	<.01

<sup>a</sup>According to number of LUS examinations.

contradiction to the findings of the LUST Trial, in which physical examination findings of lung crackles and leg edema did not reflect LUS results in patients undergoing HD [13]. Further studies performed in patients treated with HD demonstrated limited accuracy of the physical examination in fluid overload detection when compared to more validated methods such as bioimpedance, especially in asymptomatic patients [5, 6]. However, while LUS is a validated, well-studied technique for lung water estimation [35], physical examination remains a highly important and feasible tool to assess fluid status in clinical practice for decisions on ultrafiltration volume in hemodialysis sessions and when targeting dry weight. Therefore, its importance cannot be underestimated. Our findings of a significant correlation between physical examination and volume status according to LUS score indicate that a comprehensive physical examination remains an important component of volume status assessment in this patient population.

Contrary to the findings in the entire cohort and in HD, we were unable to demonstrate a correlation between components of the physical examination and LUS score in patients treated with PD. While this may be due to a small sample size, previous trials in patients treated with PD also did not find an association between pedal edema and evidence of lung water on LUS [10, 36], which raises a question regarding LUS validity in this subgroup of patients.

Previous studies estimated the effectiveness of LUS use to guide ultrafiltration volume in HD sessions. Zoccali *et al.* demonstrated a reduction in lung congestion with ultrasound-guided treatment that was performed pre-dialysis, compared to conventional treatment; however, there was no difference in mortality or cardiovascular outcomes between groups [37]. In the current study, LUS was performed before and after dialysis, however, the study was observational, and according to study protocol LUS results did not influence clinical decisions. We failed to establish a significant correlation between ultrafiltration volume during dialysis sessions and the change in LUS score (although there was a trend), suggesting that the variations in body fluids composition are possibly delayed. This important finding should be taken into consideration when LUS is used post-dialysis to support clinical decisions.

Different LUS scanning protocols are described in the literature. Some count every lung comet/B-line [9] while others use a more comprehensible scoring system [28]. Protocols also vary by the number of scanned zones [19–22]. In the current study, we initially used a 16-zone approach. It was time consuming since the left lateral zones are more challenging to inspect due to interference by the heart, and in patients with a tunneled catheter the superior lateral point location may not be accurate. Therefore, we shifted to the 12-zone approach with a significant positive correlation between the protocols, proving its accuracy. Furthermore, even when the posterior thorax zones were discarded, the correlation to the 12-zone protocol was significant. This finding is consistent with previous finding of Torino *et al.* who found that the eight and the 28-zone protocols were highly interrelated in a cohort of HD patients [22]. Transition to the 12-zone approach, especially if performed by an experienced

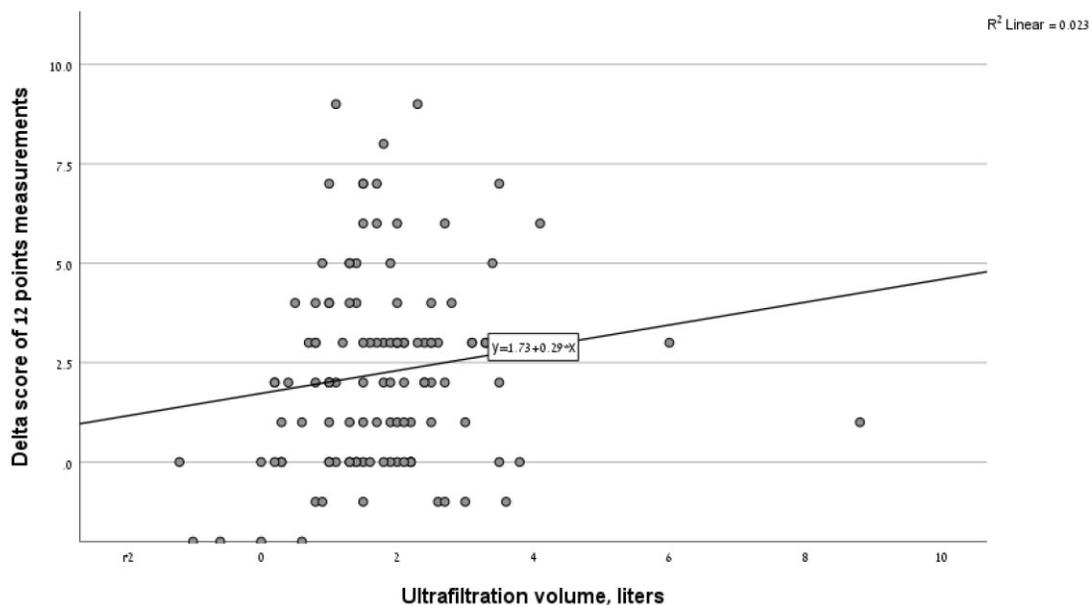


Figure 3: Correlation between ultrafiltration volume during hemodialysis and change in LUS score ( $r = .169$ ,  $P = .065$ ).

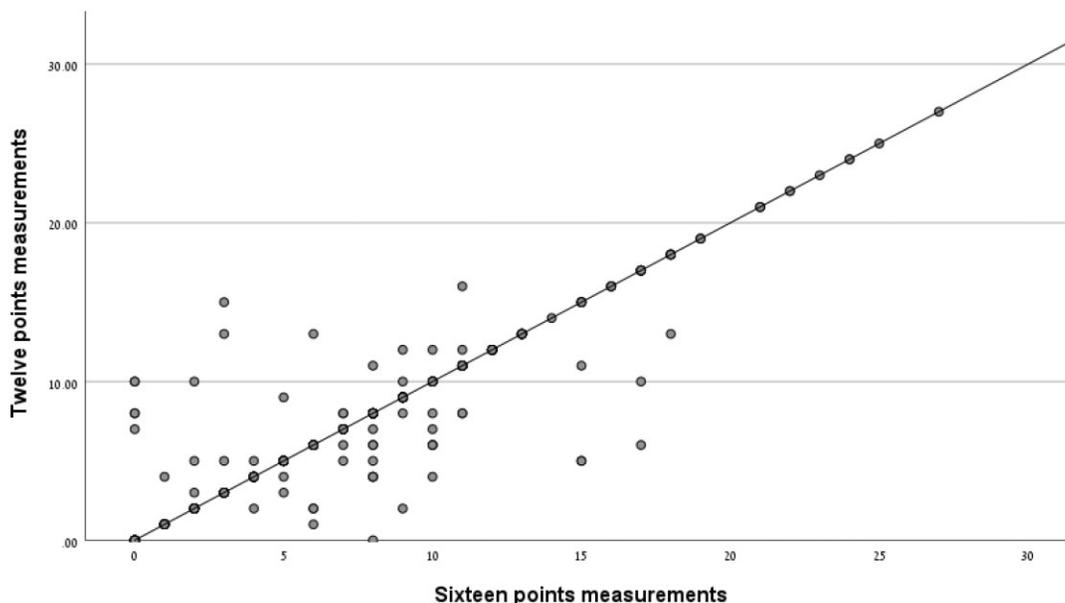


Figure 4: A comparison between the 16- and 12-zone protocols. Pearson correlation coefficient was .91 ( $P < .001$ ).

physician or technician, requires only several minutes per exam, and makes it more accessible than the cumbersome multiple zones test. Further omission of the posterior zones allows to perform LUS even during dialysis session without disturbing the patient or compromising the vascular access.

The study has several limitations. Being a single-center study could lead to bias. Additionally, LUS is operator-dependent and therefore susceptible to bias, however, only two operators performed all the inspections with the principal investigator's supervision. Physical examination is also performer-dependent, therefore to avoid bias, only two authorized physicians examined the patients. LUS and physical examination were performed at a single time point, and may not be reproducible in repeated assessment, which is another limitation. However, the comparison between them was performed in different patient settings and volume status and is therefore valid. One of the strengths of the current study is the diverse cohort, including patients in different CKD stages and dialysis modalities, yet the number of participants treated with PD was low, therefore it is likely that statistical significance could not be reached in this subgroup of patients. Further studies are needed to assess LUS findings in this group of patients.

## CONCLUSION

Physical examination findings including oxygen saturation, lung crackles, pleural effusion, and leg edema (but not blood pressure) correlated with EVLW findings on LUS in a cohort of patients with CKD. The use of a simplified pragmatic LUS protocol may facilitate LUS use in clinical practice.

## ACKNOWLEDGEMENTS

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## DATA AVAILABILITY STATEMENT

The data underlying this article will be shared on reasonable request to the corresponding author.

## CONFLICT OF INTEREST STATEMENT

Orit Kliuk-Ben Bassat declares lecture fees from AstraZeneca. Other authors declare no conflict of interest.

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