Ultrasonographic Assessment of Extravascular Lung Water in Hospitalized Patients Requiring Hemodialysis: A Prospective Observational Study

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Keywords

Handheld ultrasound machine · Portable ultrasound machine · Lung B-lines · Inferior vena cava · Hemodialysis

Abstract

Introduction: Sonographic technologies can estimate extravascular lung water (EVLW) in hemodialysis (HD) patients. This study investigated the suitability of a handheld scanner in contrast to a portable scanner for quantifying EVLW in hospitalized patients requiring HD. **Methods:** In this prospective study, 54 hospitalized HD patients were enrolled. Bedside lung ultrasound was performed within 30 min before and after dialysis using handheld (phased array transducer, 1.7–3.8 MHz) and portable (curved probe, 5–2 MHz) ultrasound devices. Eight lung zones were scanned for total B-lines number (TBLN). The maximum diameter of inferior vena cava (IVC) was measured. We performed Passing-Bablok regression, Deming regression, Bland-Altman, and logistic regression analysis. **Results:** The 2 devices did not differ in measuring TBLN and IVC ($p > 0.05$), showing a high correlation ($r = 0.92$ and $r = 0.51$, respectively). Passing-Bablok regression had a slope of 1.11 and an intercept of 0 for TBLN, and the slope of Deming regression was 1.02 within the CI bands of 0.94 and 1.11 in the full cohort. TBLN was logarithmically transformed for Bland-Altman analysis,

showing a bias of 0.06 (TBLN = 1.2) between devices. The slope and intercept of the Deming regression in IVC measurements were 0.77 and 0.46, respectively; Bland-Altman plot showed a bias of -0.07 . Compared with predialysis, TBLN significantly ($p < 0.001$) decreased after dialysis, while IVC was unchanged ($p = 0.16$). Univariate analysis showed that cardiovascular disease (odds ratio [OR] 8.94 [2.13–61.96], $p = 0.002$), smoking history (OR 5.75 [1.8–20.46], $p = 0.003$), and right pleural effusion (OR 5.0 [1.2–25.99], $p = 0.03$) were strong predictors of EVLW indicated by TBLN ≥ 4 . **Conclusion:** The lung and IVC findings obtained from handheld and portable ultrasound scanners are comparable and concordant. Cardiovascular disease and smoking history were strong predictors of EVLW. The use of TBLN to assess EVLW in hospitalized HD patients is feasible. Further studies are needed to determine if TBLN can help guide volume removal in HD patients.

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Introduction

Hemodialysis (HD) can efficiently achieve extracorporeal removal of waste products and water from the blood [1]. While achieving optimal volume status is crucial for patients undergoing HD, assessing the dry weight

remains challenging. There is no consensus regarding the optimal method of extracellular volume assessment in HD patients [2, 3]. Volume assessment is usually based on clinical judgment [4], but dry weight estimation is subjective and can often be inaccurate and differ significantly from the actual dry weight.

Lung ultrasound is a novel, reliable, and noninvasive approach to objectively quantify extravascular lung water (EVLW) by detecting B-lines [5]. B-lines are defined as vertical bands of hyperechoic artifacts that originate at the pleural line and traverse the entire ultrasound screen vertically to the bottom of the screen, and multiple B-lines are considered the sonographic sign of interstitial edema [6]. Additionally, ultrasound measurements of the inferior vena cava (IVC) diameter have been used to assess intravascular volume status in HD patients [7]. Portable ultrasound machines on wheels, typically the size of a laptop computer, are commonly used for point-of-care applications in clinical practice [8]. Handheld ultrasound scanners can also be used for the same purposes. Some comparative studies of handheld ultrasound devices with high-end sonographic systems have been reported. The majority of these studies focused on abdominal and pleural applications when evaluating ascites, hydronephrosis, pleural cavities, abdominal aortic aneurysms, and obstetric and gynecological pathologies [9]. A few studies showed good overall agreement for detecting B-lines in patients with heart failure [10] or in pulmonary ICU patients [11, 12]. However, a handheld ultrasound machine's accuracy and performance in evaluating B-lines in HD patients compared to a conventional sonographic machine remains unknown. In this study, we planned to test and validate the clinical applicability of the handheld device in B-lines quantification and IVC measurements in hospitalized patients requiring HD by comparing it with a conventional portable ultrasound machine.

Materials and Methods

Patients

The Mayo Clinic IRB approved the study protocol. We conducted this prospective observational single-center study from July 1, 2020, to October 15, 2020, at Mayo Clinic Hospital, Saint Marys Campus in Rochester, Minnesota. Non-ICU patients were enrolled in this study if they were (i) ≥ 18 years old, (ii) currently hospitalized for any reason, (iii) requiring HD during the hospitalization, and (iv) agreeing to provide informed consent for ultrasound scans before and after HD. We excluded patients with (i) known pregnancy at study entry or during the study period, (ii) nonfunctional arteriovenous fistula in the contralateral arm of the

one used as vascular access for the HD session that could interfere with ambulatory blood pressure monitoring, (iii) known severe mental disorder, and (iv) positive coronavirus disease (COVID-19).

The demographic, clinical, and biochemical information was collected from the medical record of each patient. The investigators were not involved in managing these patients, and the information collected on B-lines and IVC dimensions was not provided to the treating physicians. The HD and fluid removal prescription were determined by the nephrologist caring for the patients.

Ultrasound Protocol

We performed lung ultrasound in the supine position at the bedside within 30 min before and after each dialysis session in a quiet room with controlled air temperature ($\sim 22^{\circ}\text{C}$) by 2 independent nephrology fellows who received prior training (J.M. and J.P.T.S.). The examinations were done without prior knowledge of the patient's clinical data. At predialysis, ultrasound imaging was first performed using a handheld ultrasound device equipped with a 1.7- to 2.8-MHz phased array transducer (Vscan Extend; GE Healthcare) by one of the examiners. This was immediately followed with ultrasound imaging using a portable ultrasound machine equipped with a 5- to 2-MHz curved probe (Sonosite M-Turbo; FUJIFILM) by the other examiner. The device was exchanged between the 2 examiners at postdialysis to avoid or decrease interobserver and interdevice variations. The examiners were mutually blinded. Time-gain compensation and the depth were adjusted to obtain B-line and IVC measurements. In general, depth was set up at 18 cm for image captures but adjusted to the patient's body size. When scanning with the portable ultrasound machine, tissue harmonic imaging was on. Tissue harmonic imaging is not supported with the handheld ultrasound device.

TBLN was obtained by scanning 8 lung zones, which consisted of 4 zones in each hemithorax upper and lower anterior chest in the midclavicular and midaxillary lines on either side (Fig. 1a), as in the method previously described [13]. Although detection of B-lines is enhanced by carrying out scans in multiple interspaces [14, 15], scanning 8 lung sites is considered a reasonable approach [2, 13]. This method was used as it would be time-saving and less cumbersome and hence have a greater potential for routine clinical use. B-lines were defined as an echogenic, coherent, dynamic, wedge-shaped signal with a narrow origin in the near field of the image arising from the pleural line and extending to the screen's edge [6]. TBLN ≥ 4 suggests increased EVLW [4]. In this study, we performed the analyses using the full cohort and a subcohort in which participants were found to have ≥ 4 TBLN at predialysis. As previously described [7], the maximum diameter of IVC was measured in the supine position using the M mode at 2 cm below the inferior cavoatrial junction by tracking the distance between anterior and posterior walls of IVC during passive respiration.

Statistical Analysis

Data handling and statistical analysis were performed using JMP Pro software version 14.0 (SAS Institute Inc., Cary, NC, USA). Results are expressed as the mean $\pm$ standard deviation (SD) for normally distributed data and the median (25th, 75th percentiles) for data not showing normal distribution. Statistical significance was determined by the unpaired *t* test (2-tailed) and

Fig. 1. An overview of B-lines and IVC obtained from handheld and portable sonographic machines. **a** The 8 areas of thoracic ultrasonography used for B-line searching in the study. Areas 1 and 3: upper lateral and basal lateral. Areas 2 and 4: upper anterior and lower anterior. Each area was the same on the right and left side. PAL, posterior axillary line; AAL, anterior axillary line; STN, sternum. **b** B-line was searched using both handheld and portable ul-

trasound machines at before and after dialysis. Representative images of B-line showing vertical artifacts fanning out from the lung-wall interface and spreading up to the edge of the screen from a hospitalized patient requiring hemodialysis. **c** The maximum diameter of IVC was measured using ultrasound machines during exhalation in a hospitalized patient requiring hemodialysis. IVC, inferior vena cava.

Fisher or χ^2 (2-sided) test, respectively. Logistic regression model was used when evaluating the probability of detecting TBLN ≥ 4 . The odds ratios (ORs) and 95% confidence interval (CI) were presented. A p value of <0.05 was considered to be statistically significant.

The comparison between devices was made by the Passing-Bablok regression, the orthogonal regression (Deming regression), and the Bland-Altman plot analysis [16–18]. A paired dataset was built by the TBLN or IVC from the portable ultrasound machine as the X-variable and the TBLN or IVC from the handheld ultrasound machine as the Y-variable for the Passing-Bablok regression and the Deming regression analysis. The Bland-Altman Plot was done to check the general agreement instead of the correlation between the 2 devices. The plot was constructed by plotting the difference in the TBLN or IVC diameter between handheld and portable machines as the Y-variable and the average TBLN or IVC diameter of the 2 machines as the X-variable. Of note, one of the critical problems in the Bland-Altman analysis is that the data need to meet the assumption of normal distribution. If the assumption of a normal distribution is not met, data were logarithmically transformed [19].

Data were tested for normal distribution using classical methods such as the Shapiro-Wilk test or Kolmogorov-Smirnov test, and the normality test was passed with the p value >0.05 .

Results

Clinical and Biochemical Characteristics of the Study Population

We included 54 patients with 37 (69%) males and an average age of 61 ± 16 years. The majority of patients had cardiovascular disease (67%) and hypertension (80%). The majority of patients (65%) had known end-stage kidney disease. Approximately three-quarters (74%) underwent HD with a dialysis catheter. Table 1 details the demographic, clinical, and biochemical characteristics of the study population.

Table 1. Patients' demographic, clinical, and laboratory characteristics

Variables	All (n = 54)	TBLN <4 (n = 33)	TBLN ≥4 (n = 21)	p value ^a
Sex, male, n (%)	37 (69)	21 (64)	16 (76)	0.38
Age, years ^b	61.3±15.6	61.8±18.2	61.3±10.9	0.97
BMI, kg/m ²	29.3±8.3	30.5±7.6	27.3±9.1	0.04
History of smoking, n (%)	23 (45)	10 (30)	15 (71)	0.01
Medical history, n (%)				
Diabetes mellitus	21 (39)	13 (39)	8 (38)	>0.99
Cardiovascular disease	36 (67)	17 (52)	19 (91)	<0.001
Dyslipidemia	26 (48)	13 (39)	13 (62)	0.16
Hypertension	43 (80)	26 (79)	17 (81)	>0.99
Indication for hemodialysis, n (%)				
End-stage kidney disease	35 (65)	22 (67)	13 (62)	0.78
Acute kidney injury	19 (35)	11 (33)	8 (38)	
Hemodialysis access, n (%)				
Arteriovenous fistula	14 (26)	8 (24)	6 (29)	0.49
Tunneled	34 (63)	20 (61)	14 (67)	
Temporary	6 (11)	5 (15)	1 (5)	
Ultrafiltration				
Planned ultrafiltration, mL ^b	2,126±1,218	1,982±1,241	2,351±1,175	0.27
Actual ultrafiltration, mL ^b	2,025±1,193	1,946±1,257	2,148±1,102	0.54
Differences, mL ^{c, d}	0 (−3, 141)	0 (−3, 38)	0 (−3, 216)	0.56
24-h urinary volume, mL ^c	100 (0, 355)	0 (0, 400)	100 (0, 342.5)	0.45
≥400 mL, n (%)	12 (22)	8 (24)	4 (19)	0.75
Total output, mL ^{b, e}	2,364±1,203	2,270±1,323	2,512±999.8	0.48
Estimated dry weight, kg ^c	78 (73, 106)	81 (72, 115)	76.3 (72, 96)	0.34
Physical examination, n (%)				
Pedal edema ^f	22 (43)	10 (32)	12 (60)	0.08
Jugular venous pressure ^g	3 (7)	2 (8)	1 (6)	>0.99
Abnormal lung auscultation	16 (29)	8 (24)	8 (38)	0.36
Pleural effusion, n (%)				
Left	10 (19)	4 (12)	6 (29)	0.17
Right	10 (19)	3 (9)	7 (33)	0.04
Laboratory ^b				
BUN, mg/dL	44.2±25.5	42.5±26.1	46.9±24.9	0.40
Creatinine, mg/dL	5.1±2.3	5.3±2.5	4.7±2.0	0.40
Hb, g/dL	8.9±1.1	8.8±1.2	8.9±1.1	0.81
Bicarbonate, mmol/L	24.9±3.2	25.2±3.1	24.6±3.4	0.53
Lactate, mmol/L	1.3±0.6	1.2±0.5	1.4±0.8	0.50
Na ⁺ , mmol/L	136.0±3.7	135.4±4.1	137±2.8	0.09
K ⁺ , mmol/L	4.6±0.5	4.5±0.4	4.7±0.7	0.17
Cl [−] , mmol/L	96.4±3.8	95.7±3.7	97.6±3.6	0.07
Albumin, g/dL	3.5±0.6	3.4±0.6	3.5±0.6	0.56

TBLN, total B-lines number; BUN, blood urea nitrogen; Hb, hemoglobin. ^a p values derived from a 2-sample test either a *t* test or χ^2 /Fisher's exact test for comparison of characteristics in subjects with TBLN <4 versus TBLN ≥ 4. A p value of <0.05 was considered to be statistically significant. ^b Values are expressed as mean ± standard deviation. ^c Values are expressed as median (25th, 75th percentiles). ^d Differences between planned and actual ultrafiltration. ^e Total output was indicated by actual ultrafiltration plus 24-h urinary volume. ^f Unknown in 2 subjects with TBLN <4 and 1 subject with TBLN ≥4. ^g Unknown in 9 subjects with TBLN <4 and 3 subjects with TBLN ≥4.

Comparison between Handheld and Portable Ultrasound Analysis of B-Lines Number

The images obtained from the 2 machines were comparable for both B-lines recognition and IVC measurements (Fig. 1b, c). The statistical comparison of TBLN

and IVC diameters obtained with the handheld ultrasound machine compared to those obtained using the portable ultrasound machine did not show significant differences (Table 2).

Table 2. Comparisons of TBLN and IVC diameters obtained by handheld and portable ultrasound machines

	Handheld	Portable	<i>p</i>
TBLN ^a			
Predialysis	5.5±7.6; 3 (0, 8)	4.8±7.1; 1.5 (0, 6.3)	0.16
Postdialysis	3.8±5.8; 1 (0, 5)	3.1±6.1; 0 (0, 3)	0.47
IVC diameter, cm ^b			
Predialysis	1.8±0.4	2.0±0.5	0.50
Postdialysis	1.8±0.3	1.8±0.5	0.76

TBLN, total B-lines number; IVC, inferior vena cava. ^a Values are expressed as mean ± standard deviation, followed by median (25th, 75th percentiles). ^b Values are expressed as mean±standard deviation.

In the full cohort, regression was performed to compare B-lines measurements between handheld and portable ultrasound analysis. We observed that the values obtained from handheld and portable machines were randomly scattered around the line of equality, and the 2 devices showed a well linear fit with the R^2 of 0.84 (Fig. 2a). The Deming regression slope was 1.02 and that of the Passing-Bablok regression was 1.11, both of which are not confidently different from 1. The intercept of the Deming regression was 0.67 and that of the Passing-Bablok regression was 0, both of which are also not confidently different from 0. The orthogonal fit ratio was found to be 1.04, and the correlation between both machines was 0.92 (Fig. 2a).

The Bland-Altman Plot was further done to check the bias and general agreement instead of the correlation between the 2 machines. Because the TBLN was not normally distributed, it was logarithmically transformed for the analysis. The Bland-Altman plot displayed an acceptable agreement between the handheld and portable machines (95% CI: -0.35 to 0.48), although there was a significant bias of 0.06 (integer value or actual TBLN = 1.2, $p = 0.04$) with an SD of 0.21 (integer value or actual SD = 1.6; Fig. 2b).

Comparison between Handheld and Portable Ultrasound Analysis of IVC Measurements

IVC maximum diameters were measured both before and after dialysis in 15 participants. Both Shapiro-Wilk and Kolmogorov-Smirnov tests showed a normal distribution of IVC measurements. The Passing-Bablok regression analysis was not performed as the sample size was small [19]. The 2 devices showed a linear regression

with an R^2 of 0.33. The slope and intercept of the Deming regression were 0.77 and 0.46, respectively. The orthogonal fit ratio was found to be 0.50, with a moderate correlation of 0.57 between both machines. In the Bland-Altman plot, the bias was found to be -0.07 (95% CI: -0.26 to 0.06, $p = 0.21$) with an SD of 0.43, displaying an acceptable agreement between handheld and portable machines (95% CI: -0.94 to 0.74).

Change of TBLN and IVC Diameters after Dialysis

Since TBLN and IVC obtained from handheld and portable ultrasound machines were comparable and concordant, the average TBLN and IVC diameters from both devices were calculated and compared before and after dialysis, respectively. Compared with predialysis, the value of TBLN, not IVC diameters, was significantly ($p < 0.001$) decreased at postdialysis both in the full cohort and in the subcohort (Table 3).

Clinical Predictors for Detection of EVLW

A comparison of patients' baseline characteristics in those with TBLN <4 ($n = 33$) and those with TBLN ≥4 ($n = 21$) is shown in Table 1. In univariate analysis (Table 4), the strongest predictor of EVLW indicated by TBLN ≥4 was the presence of cardiovascular disease (OR, 8.94; 95% CI: 2.13–61.96; $p = 0.002$), followed by the presence of smoking history (OR, 5.75; 95% CI: 1.8–20.46; $p = 0.003$) and right-sided pleural effusion (OR, 5.0; 95% CI: 1.2–25.99; $p = 0.03$). Higher systolic blood pressure level predicted lower likelihood of EVLW (OR, 0.98; 95% CI: 0.95–1.0; $p = 0.04$). Diastolic blood pressure, history of hypertension, BMI, diabetes mellitus, and physical examination findings, such as pedal edema, jugular venous pressure, and abnormal lung auscultation, were not predictors of EVLW (Table 4). Systolic and diastolic blood pressure decreased during dialysis (Fig. 3).

Discussion

We demonstrated that the TBLN and IVC diameters obtained from handheld and portable ultrasound machines are comparable and concordant. We also showed that removal of fluid was correlated with decrease in TBLN. Therefore, a handheld ultrasound device can be used to assess EVLW in hospitalized HD patients by assessing the TBLN in a limited 8-zone lung field.

Fluid removal by dialysis attempts to normalize extracellular fluid volume [1]. Removal of excessive fluid can cause volume depletion (hypovolemia), leading to intra-

Fig. 2. Method comparison between handheld and portable ultrasound analysis of TBLN. **a** Passing-Bablok and orthogonal (Deming) regression analysis of TBLN between handheld and portable ultrasound machines in the full cohort. **b** Bland-Altman plot of the differences in TBLN between handheld and portable ultrasound machines versus the mean value of both measurements in the full

cohort study. Dashed gray lines indicate the limit of agreement (mean $\pm$ 1.96 SD), the solid gray line is the line of equality, the solid red line shows the mean difference (bias), and the dashed red lines show the 95% CI around the mean difference. TBLN, total B-lines number.

Table 3. Comparisons of TBLN and IVC diameters before and after dialysis

	Full cohort (<i>n</i> = 54)			Subcohort with ≥ 4 TBLN (<i>n</i> = 21)		
	predialysis	postdialysis	<i>p</i> value	predialysis	postdialysis	<i>p</i> value
TBLN ^a	5.2±7.2; 2.3 (0, 7.1)	3.5±5.8; 1.0 (0, 3.4)	<0.001	11.7±7.9; 9 (6, 16.8)	8.0±7.2; 5.8 (3, 11.4)	<0.001
IVC, cm ^b	2.0±0.4	1.8±0.4	0.16	2.0±0.5	1.9±0.6	0.56

TBLN, total B-lines number; IVC, inferior vena cava. ^a Values are expressed as mean ± standard deviation, followed by median (25th, 75th percentiles). ^b Values are expressed as mean±standard deviation.

dialytic hypotension. Inadequate fluid removal leads to volume excess (hypervolemia) and hypertension [1]. The application of lung ultrasound used to detect B-lines has been shown to improve the quality of care and management of patients undergoing HD, as it accurately estimates volume status by measuring EVLW [5].

B-lines perceived by ultrasound are identified as vertical hyperechoic lines. Although no anatomical or histological structures correspond to this artifact, it has been proposed that thickened interlobular septate or reverberations among microbubbles at the alveolar surface may account for the appearance of B-lines [20]. The number of B-lines is believed to reflect the extent of EVLW. Zoccali et al. [21] first showed that B-lines detected on lung ultrasound are an independent risk factor for death and cardiovascular events in patients on HD, which was subsequently confirmed by Saad et al. [22]. B-line number decreases quantitatively during the HD treatment and correlates with the ultrafiltration volume and time on dialysis [2]. In our study, cardiovascular disease and smoking history were the strongest predictors of EVLW. The presence of right-sided pleural effusion was also an indicator of EVLW. Results of physical examinations, such as pedal edema, jugular venous pressure, and abnormal auscultation, were not associated with EVLW. In addition, our data also showed that TBLN and blood pressure were significantly decreased after dialysis in hospitalized patients requiring HD. Lung ultrasound-guided dry weight estimation can effectively and safely reduce ambulatory blood pressure levels, resulting in improved blood pressure control among hypertensive patients on long-term HD [23]. Hence, the dry weight and adequacy of volume removal could be assessed using TBLN on lung ultrasonography. However, it remains unclear how to guide dry weight estimation to avoid or decrease intradialytic complications through the use of lung ultrasound in hospitalized patients who require HD. IVC diameter, to some extent, may correlate with the changes in the volume status [7]. IVC diameter and collapsibility assessment have been

Table 4. Univariate analysis for finding a predictor of TBLN ≥ 4

Variables	Odds ratio (95% CI) ^a	<i>p</i> value
BMI (kg/m ²) ^b	0.95 (0.88, 1.02)	0.15
Systolic BP (mm Hg) ^b	0.98 (0.95, 1)	0.04
Diastolic BP (mm Hg) ^b	1 (0.96, 1.05)	0.94
History of smoking	5.75 (1.80, 20.46)	0.003
Medical history		
Diabetes mellitus	0.95 (0.31, 2.91)	0.92
Cardiovascular disease	8.94 (2.13, 61.96)	0.002
Dyslipidemia	2.50 (0.83, 7.96)	0.11
Hypertension	1.14 (0.29, 4.92)	0.85
Pedal edema	3.15 (0.998, 10.55)	0.05
Jugular venous pressure	0.65 (0.03, 7.31)	0.73
Abnormal lung auscultation	1.92 (0.58, 6.43)	0.28
Left pleural effusion	2.9 (0.72, 12.89)	0.14
Right pleural effusion	5 (1.2, 25.99)	0.03

TBLN, total B-lines number; CI, confidence interval; BP, blood pressure. A *p* value of <0.05 was considered to be statistically significant. ^a Odds ratios with 95% CI and *p* values calculated using the logistic-regression model for evaluating association between the variable and the probability of TBLN ≥ 4 . ^b Odds ratios for continuous variables are per unit change in regression.

described as tools that can assist in the adequate evaluation of venous congestion [7]. In our study, the maximum IVC diameters did not change remarkably after dialysis. In agreement with these results, Trezzi et al. [24] reported no difference in the IVC index between before and after dialysis. Also, Basso et al. [25] demonstrated that IVC maximum diameter correlated with hydration status only at predialysis, not postdialysis, in chronic HD patients. These data suggested that IVC measurements may not be a good estimator of dry weight in patients undergoing HD.

To the best of our knowledge, this is the first study that investigated the suitability for B-lines in lungs and IVC measurements of a handheld ultrasound machine in hospitalized patients requiring HD. The high coefficient *r* =

Fig. 3. Dynamic changes of blood pressure levels during dialysis. **a** Systolic BP decreased significantly at 3 h after dialysis compared to predialysis. **b** Diastolic BP decreased significantly since 3 h after dialysis compared to predialysis. * $p < 0.05$ versus predialysis. BP, blood pressure.

0.92 in the full cohort suggested a significant correlation of TBLN between both ultrasound machines. We demonstrated that the agreement in quantifying B-lines between devices is acceptable. In the Deming and Passing-Bablok regressions, this is indicated by an intercept that is not confidently different from 0 and a slope that is not confidently different from 1 both in the full cohort. The orthogonal fit ratio of 1.04 in the full cohort for TBLN proved that both ultrasound machines did not have remarkably different measurement uncertainties. To determine the limits of agreement between the 2 devices, we performed Bland-Altman analysis. Our analysis showed a small difference in TBLN between both machines. The bias might have been caused by interexaminer variation as interdevice variation was mitigated by the exchanging device protocol after dialysis. Therefore, TBLN measurements between handheld and portable ultrasound machines were in agreement. The mean bias of 1.2 and limits of agreement (95% CI: $-0.35, 0.48$) were also acceptable. Platz et al. [10] also found that there were no significant differences among a small number ($n = 21$) of patients with heart failure in the number of detectable B-lines between the Vscan pocket device and high-end ultrasound systems. In their study, only B-lines number was compared between the 2 devices, while method comparison analysis was not performed [10]. In addition, their findings indicated a substantial difference based on clip duration, with a significantly greater number of B-lines in longer compared with shorter clips [10]. Of note, we used the Vscan Extend, a newer version handheld device, to scan B-lines, and the B-lines number used in our study was not based on clip duration. In addition, we showed a moderate interdevice correlation in IVC measurements between

the 2 ultrasound machines, despite small differences among them. Based on our results, the 2 ultrasound machines could be used interchangeably for TBLN and IVC measurements.

Our study has several limitations. First, this is a single-center study, and the findings should be interpreted within the context of the study design. Second, although many subjects were enrolled in the study, the majority of patients did not have significant EVLW, and the number of patients having more B-lines (TBLN ≥ 4) was small. Third, the comparison of IVC measurements between the 2 devices is limited by its small sample size. Last, the image quality of the B-lines and IVC measurements from the 2 devices was comparable; however, we did not directly assess the image quality.

Taken together, we demonstrated the feasibility and accuracy of handheld ultrasound machine in B-lines assessment and IVC measurements when compared with the portable ultrasound device. Our data also showed that cardiovascular disease and smoking history were strong predictors of EVLW, and that B-lines assessment for dry weight estimation in hospitalized patients requiring HD is feasible. Nevertheless, further investigation is needed on how to guide volume removal using TBLN in HD patients.

Statement of Ethics

The Mayo Clinic IRB approved the study protocol. Informed consent for participation was obtained from each participant. The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

The authors did not receive any funding.

Author Contributions

J.R.G. conceived and designed the study. J.M. and J.P.T.S. conducted the study and contributed data acquisition. J.M. performed statistical analysis and manuscript drafting. K.B.K., Z.Z., M.I., S.M., and H.J. contributed important intellectual content during manuscript drafting. Each author was involved in the approval of the final version of the manuscript.

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