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Association between B-lines detected during lung ultrasound and various factors in hemodialysis patients

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Abstract

Background: In recent years, the use of chest ultrasonography to detect lung water has received growing attention in clinical research. Estimation of the number of B-lines using lung ultrasound is now a standard method for the evaluation of pulmonary congestion. In the present study, we examined the relation between the number of B-lines and clinical parameters in hemodialysis patients.

Methods: A total of 49 consecutive patients receiving maintenance hemodialysis were enrolled in this study. Lung ultrasound was performed using Vscan® (GE Healthcare, Japan). Bilateral scanning of the anterior and lateral chest walls was performed with the patient in a supine position just after the start of the hemodialysis therapy. The total number of B-lines was estimated. We investigated the relationships between the number of B-lines and other clinical parameters.

Results: Patient heart rate and the serum log [NT-proBNP] level were positively correlated ($P = 0.009$ and 0.003, respectively), and body weight and the serum albumin and creatinine level were negatively correlated with the number of B-lines ($P = 0.023$, 0.001, and 0.011, respectively).

Conclusions: The number of B-lines was positively correlated with the serum N-terminal pro-brain natriuretic peptide level. Lung ultrasound can quantify lung edema. Body weight and the serum albumin and creatinine level were negatively correlated with the number of B-lines. Careful attention to the presence of pulmonary edema is needed in patients with a low body weight and a low serum albumin and creatinine level.

Keywords: B-lines, Hemodialysis, Lung ultrasound, N-terminal pro-brain natriuretic peptide

Background

Chronic fluid overloading frequently occurs in hemodialysis patients, so one of the major targets of hemodialysis therapy is to maintain a normal extracellular volume status. Preventing volume overload is a central recommendation when it comes to nephrology best-practice guidelines for dialysis patients [1], as this goal is directly associated with hypertension, increased arterial stiffness, left ventricular hypertrophy, heart failure, and ultimately higher rates of mortality and morbidity [2].

To estimate the volume status, several methods have been proposed, such as evaluating the natriuretic peptide levels [3, 4], the dimensions and collapsibility of the inferior vena cava [5], chest X-ray signs, and bioelectrical impedance analysis techniques [6, 7]. However, each of these methods has significant theoretical and practical limitations.

In recent years, the use of chest ultrasonography to detect lung water has received growing attention in clinical research focused on intensive care patients [8] and patients with heart failure [9]. The most commonly observed finding was a comet tail artifact fanning out from the lung-wall interface and spreading upwards to the edge of the screen, previously named a "B-line" (Fig. 1) [10]. In patients with heart failure, the number of B-lines was correlated with the degree of extravascular lung water [11], and
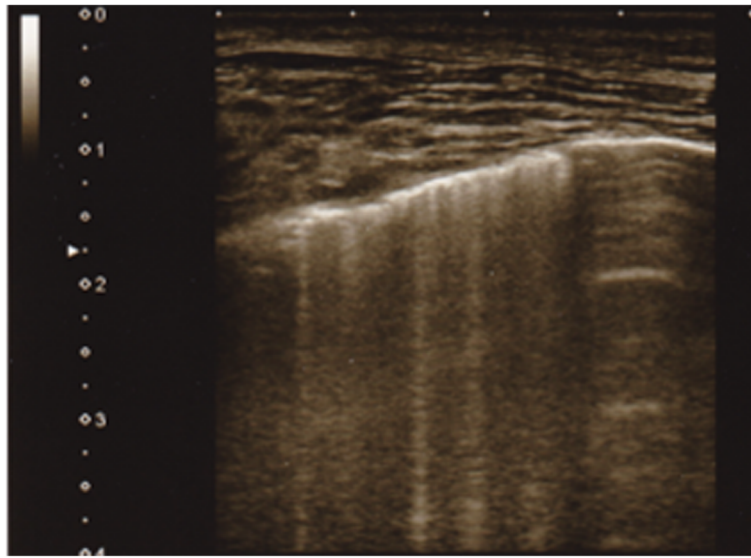
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Fig. 1 B-lines: comet tail artifacts fanning out from the lung-wall interface and spreading upwards to the edge of the screen

a reduction in the number of B-lines reflected the efficacy of treatment [1]. Previous studies have also shown that lung ultrasound can detect extravascular lung water and can be used to show a significant reduction after a dialytic session (both hemodialysis and peritoneal dialysis) [12–15]. Existing data suggest that lung ultrasound characteristics might be suitable for assessing the ideal body weight in hemodialysis patients, since this technique is simple, inexpensive, nonionizing, and can easily be performed at the patient's bedside [16, 17].

Consequently, estimation of the number of B-lines using lung ultrasound is now a standard method for the evaluation of pulmonary congestion [18]. In the present study, we examined the relation between the number of B-lines and clinical parameters in hemodialysis patients.

Methods

The proportion of hospitalization for acute heart failure in hemodialysis patients was significantly higher on Monday (approximately 1/3) compared with other days [19]. So we selected patients who underwent hemodialysis therapy on Monday (the first day after weekend interval). A total of 49 consecutive patients receiving maintenance hemodialysis at Sekikawa Hospital on Monday were enrolled in this study. Informed consents were obtained in all patients.

Clinical data including age, sex, duration of hemodialysis therapy, presence of diabetes mellitus and/or hypertension and/or dyslipidemia complications, use of antihypertensive drug, history of coronary artery disease, and the results of biological examinations were collected from the patient's clinical records. Hypertension was defined as a systolic blood pressure of 140 mmHg or higher, a diastolic blood pressure of 90 mmHg or higher, and/or the current use of antihypertensive drugs. Diabetes mellitus was defined as a fasting glucose level ≥126 mg/dL, a nonfasting glucose level ≥200 mg/dL, or the use of medication. Dyslipidemia was defined as a low-density lipoprotein-cholesterol level ≥140 mg/dL, a high-density lipoprotein-cholesterol level <40 mg/dL, a triglyceride level ≥150 mg/dL, or the use of medication.

A peripheral blood sample was obtained before hemodialysis during the first session of the week. The serum N-terminal pro-brain natriuretic peptide (NT-proBNP) level in the pre-dialysis blood sample was measured using an electrochemiluminescence immunoassay on an Elecsys platform (Roche, Basel, Switzerland).

Lung ultrasound was performed at the first session of the week, the same time of peripheral blood sample preparation, using Vscan® (GE Healthcare, Japan), a hand-held ultrasound device with a wide-bandwidth phased-array probe (1.7–3.5 MHz) [20, 21]. Bilateral scanning of the anterior and lateral chest walls was performed with the patient in a supine position just after the start of the hemodialysis therapy. An intercostal scan with maximum extension of the visual pleural line was performed. The chest wall was divided into eight areas (two anterior and two lateral areas per side), and two scan was obtained for each area [22–26]. The anterior zone of the chest wall was designated from the sternum to the anterior axillary line and was then divided into upper and lower halves (from the clavicle to the third intercostal spaces and from the third space to the diaphragm). The lateral zone was positioned from the anterior axillary line to the posterior axillary line and was also divided into the upper and lower

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halves. Cardiologist, who is blind to the result of blood peripheral blood sample, attempted to detect comet tail artifacts fanning out from the lung-wall interface and spreading to the edge of the screen, which were previously named B-lines (Additional file 1: Movie S1) [23, 24]. The total number of B-lines was estimated. Echocardiographic measurements were obtained at the same time and left ventricular ejection fraction (LVEF) was estimated.

We investigated the relationships between the number of B-lines and other clinical parameters. This study was conducted in accordance with the principles of the Declaration of Helsinki and was permitted by the research ethics committee of Sekikawa Hospital (Approved No. H2705). The data were expressed as the means ± SD or median (interquartile range, IQR). A simple and multivariate regression analysis was used to examine the relationship between two continuous variables. Because of the skewed distribution of the NT-proBNP levels, the data were normalized using a logarithmic transformation for further statistical analysis. All the statistical calculations were performed using JMP 5.1 software. P values less than 0.05 were considered statistically significant.

Results

The patient background characteristics are shown in Table 1. The mean age was 74.5 ± 11.2 years. Elderly patients were common in this study. Diabetic nephropathy was the major cause of end-stage kidney disease. Hypertension, diabetes mellitus, and dyslipidemia were present in 83.7, 42.9, and 20.4% of the study participants, respectively. The mean number of B-lines was 10.8 ± 4.6. The results of the biochemistry analyses, including the NT-proBNP level, are shown in Table 2. The serum albumin level was relatively low (3.2 ± 0.5 g/dL), and the serum NT-proBNP level was relatively high (13,404 (4355–28,011) pg/mL) among the study participants.

Table 3 shows the relationships between the number of B-lines and other clinical parameters. Heart rate and the serum log [NT-proBNP] level were positively correlated ($P = 0.009$ and 0.003, respectively), and body weight and the serum albumin and creatinine levels were negatively correlated with the number of B-lines ($P = 0.023$, 0.001 and 0.011, respectively). Patient age tended to be positively associate with the number of B-lines ($P = 0.055$). LVEF tended to negatively relate to the number of B-lines ($P = 0.056$). In multivariate analysis including body weight and heart rate and the serum albumin, creatinine, and log [NT-proBNP] levels, only the serum log [NT-proBNP] level remained significant relation to the number of B-lines ($P = 0.014$).

Discussion

We showed that the number of B-lines was positively correlated with heart rate and the serum NT-proBNP

Table 1 Background characteristics of the study participants

Characteristic	Quantity
Gender (M/F)	24/25
Age (year)	74.5 ± 11.2
Duration of HD (year)	3.4 (2.1–7.2)
Primary cause of ESKD, *n* (%)	
Chronic glomerulonephritis	8 (16.3)
Diabetic nephropathy	22 (44.9)
Nephrosclerosis	10 (20.4)
Unknown and others	9 (18.4)
Hypertension, *n* (%)	41 (83.7)
Diabetes mellitus, *n* (%)	21 (42.9)
Dyslipidemia, *n* (%)	10 (20.4)
Atrial fibrillation, *n* (%)	6 (12.2)
Use of antihypertensive drug, *n* (%)	38 (77.6)
History of coronary artery disease, *n* (%)	
PCI	4 (8.2)
CABG	3 (6.1)
Vascular access	
Arteriovenous fistula	43 (87.8)
Arteriovenous graft	2 (4.1)
Subcutaneously fixed superficial artery	2 (4.1)
Venous catheter	2 (4.1)
Body weight (kg)	52.7 ± 11.5
Systolic blood pressure (mmHg)	141 ± 26
Diastolic blood pressure (mmHg)	73 ± 16
Heart rate (beat/minute)	75 ± 13
Ejection fraction (%)	60 ± 12
B-lines (number)	10.8 ± 4.6

Mean ± SD, median (interquartile range: IQR)
HD hemodialysis, *ESKD* end-stage kidney disease, *PCI* percutaneous coronary intervention, *CABG* coronary artery bypass grafting

Table 2 Background characteristics of laboratory data

Characteristic	Quantity
Albumin (g/dL)	3.2 ± 0.5
Urea nitrogen (mg/dL)	51.8 ± 19.0
Creatinine (mg/dL)	7.57 ± 2.41
Sodium (mEq/L)	137 ± 4
C-reactive protein (mg/dL)	0.26 (0.10–0.91)
Hemoglobin (g/dL)	10.4 ± 1.2
NT-proBNP (pg/mL)	13,650 (4355–28,011)
log [NT-ProBNP (pg/mL)]	9.26 ± 1.33

Mean ± SD, median (interquartile range: IQR)
NT-proBNP N-terminal pro-brain natriuretic peptide

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Table 3 The relationship between the number of B-lines and other clinical parameters

	r	P value
Age (years)	0.276	0.055
Duration of HD (year)	0.026	0.576
Body weight (kg)	−0.325	0.023
Systolic blood pressure (mmHg)	−0.103	0.479
Diastolic blood pressure (mmHg)	0.013	0.928
Heart rate (beat/minute)	0.371	0.009
Ejection fraction (%)	−0.275	0.056
Albumin (g/dL)	−0.444	0.001
Urea nitrogen (mg/dL)	−0.159	0.276
Creatinine (mg/dL)	−0.360	0.011
Sodium (mEq/L)	−0.248	0.085
C-reactive protein (mg/dL)	0.063	0.666
Hemoglobin (g/dL)	−0.197	0.175
NT-ProBNP	0.523	<0.001
log [NT-ProBNP]	0.447	0.002

HD hemodialysis, NT-proBNP N-terminal pro-brain natriuretic peptide

level, while it was negatively correlated with the body weight and the serum albumin and creatinine level.

Lung ultrasound assessments of extravascular lung water based on the number of B-lines provide an excellent diagnostic alternative, expanding the already established role of transthoracic echocardiography for patients with heart failure [2, 27–29]. Bedetti et al. compared lung ultrasound information obtained by experienced echocardiologists and by inexperienced echocardiographer with very limited (30') dedicated training on B-lines assessment and reveal, there was a significant, tight correlation ($r = 0.958$, $p < 0.001$) between the two observations in the same patient [30]. B-lines can be evaluated anywhere (including extreme environmental conditions using pocket-sized instruments to detect high-altitude pulmonary edema), anytime (during dialysis), by anyone (even a novice sonographer after 1 h of training), and on anybody (since the chest acoustic window usually remains patent even when an echocardiography is not feasible) [18]. The pre-dialysis number of B-lines significantly correlated with a whole body bioimpedance spectroscopy device-derived extracellular water in hemodialysis patients [31]. Vitturi et al. investigated lung and bioimpedance spectroscopy results immediately before and after dialysis and reported that a reduction in the number of B-lines was correlated with fluid loss as a result of hemodialysis, conforming that lung ultrasound can identify extravascular lung water. The number of post-dialysis B-lines is correlated with the residual weight assessed using bioimpedance, suggesting a role for ultrasound in the management of

hemodialysis patients [32]. The serum NT-proBNP level is influenced not only by heart function but also by the volume status. Among nondialysis patients, lung congestion was correlated with the NT-proBNP level [22]. Natriuretic peptides may directly enhance capillary permeability, an effect that may explain the association in addition to filling pressure alone [33]. In this study, we also showed a positive and independent relationship between the number of B-lines and the serum NT-proBNP level in hemodialysis patients.

We also showed that the number of B-lines was positively correlated with heart rate and negatively correlated with body weight and the serum albumin and creatinine level. Volume overload results in lung congestion and also activates the sympathetic nervous system which increases the heart rate. Hypoalbuminemia is common in heart failure patients [34, 35]. Two mechanisms have been proposed to explain the relationship between hypoalbuminemia and congestion. On the one hand, an increase in vascular permeability mediated by an increase in hydrostatic venous pressure may increase the transcapillary escape rate of albumin from the intravascular to the extravascular space [36]; on the other hand, it is possible that intestinal congestion favors albumin enteric losses [37]. It is well documented that a decrease in the body mass index is correlated with an increased mortality rate in patients with heart failure [38, 39]. Serum level of albumin was positively related to body weight in our study participants ($r = 0.332$, $P = 0.020$, data not shown). Both hypoalbuminemia and body weight loss are result of malnutrition. That may be the reason of the relationship between B-lines and body weight. Giuseppe et al. previously reported that physical functioning was inversely associated with the number of B-lines and patient age and was positively associated with the serum albumin level [40]. In our study, patient age tended to be positively associate with the number of B-lines ($P = 0.055$). In elderly patients, hypoalbuminemia, body weight loss (which results in reduction of serum creatinine level), and a low level of physical functioning are known to affect each other. Under such conditions, lung congestion, which can be detected by lung ultrasound as B-lines, should be considered.

Left ventricular systolic dysfunction may cause overhydration which result in lung congestion. On the other hand, overhydration may cause lung congestion and increase venous return volume and ventricular filling, thereby increase the stroke volume by the Frank-Starling mechanism when LVEF is preserved. There are conflicting result about the relationship between the number of B-lines and LVEF. Mallamaci et al. [12] used this technique in a population of 75 hemodialysis patients and showed the number of B-lines was negatively associated with an LVEF. But in other study, Siriopol et al. reported the

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number of B-lines was not related to LVEF [31]. The differences are most certainly the result of differences in study populations. In Siriopol et al.'s study, the patients (being younger and possibly with less comorbidities) had a preserved left ventricular systolic function (only 6.3% of the patients had an LVEF of <50%) [31]. In our study, 11 (22.4%) of the patients had an LVEF of <50%. In hemodialysis patients, the relationship between hydration status, B-lines, and left ventricular systolic function is complex. Accordingly, additional investigation will be needed to clarify the mechanism underlying the association between overhydration and B-lines in hemodialysis patients with a preserved or reduced LVEF.

Our study had some limitations. The sample size was relatively small, and the study was performed at a single institution. B-lines represent the volume status of extravascular lung water. There are some markers of intravascular volume such as cardiothoracic ratio, inferior vena cava, and serum level of atrial natriuretic peptide. Bioimpedance spectroscopy device enables to derive the extracellular water and intracellular water. But we did not have such data, so we could not discuss the relation between these markers. Another limitation of this study was that the investigator who performed lung ultrasound was not blind for the clinical information of the patients such as age, gender, or clinical diagnosis. In addition, the limitations of lung ultrasound are essentially patient-dependent. Obese patients may be more difficult to examine because of the thickness of their ribcages and soft tissues. Furthermore, the cross-sectional design prevented us from making any conclusions regarding the effects of treatment. The study participants were also relatively old, their serum albumin levels were relatively low, and their serum NT-proBNP levels were relatively high because of the specificity of our institution.

Conclusions

The number of B-lines was positively correlated with the serum NT-proBNP level. Lung ultrasound can quantify lung edema noninvasively in real time and in a radiation-free manner, enabling the direct imaging of extravascular lung water. Patient age tended to be positively correlated and the body weight and the serum albumin and creatinine levels were negatively correlated with the number of B-lines. Careful attention to the presence of pulmonary edema is needed in elderly patients with a low body weight and a low serum albumin and creatinine level.

Additional file

Additional file 1: Movie S1 B-lines detected by lung ultrasound using Vscan® (GE Healthcare, Japan). (mp4 2009 kb)

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