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ORIGINAL RESEARCH

Reliability of B-line quantification by different-level observers and a software algorithm using point-of-care lung ultrasound

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Abstract

Quantification of B-lines on lung ultrasonographs is operator-dependent and considered a semi-quantitative method. To avoid this variability, we designed a software algorithm for counting B-lines. We compared the number of B-lines obtained in real-time by observers with three different levels of experience and by the software algorithm, and analyzed intra-rater variability in terms of the estimated number of B-lines in two successive examinations. Forty mechanically ventilated adult (≥ 18 years) intensive care unit patients were included in this prospective study. All patients underwent two consecutive ultrasound examinations for B-lines detection by three human observers (OB1 = high, OB2 = medium, OB3 = low level of experience) and by the software (OBS). Ultrasound scans were obtained on the anterior right and left thoracic side along the midclavicular line, in the second and fourth intercostal space; B-lines counting for each position lasted 10 s. To assess intra-observer variability, a second ultrasound scan was obtained 15–30 min after the first scan. For all lung zones, the intraclass correlation for B-lines counting between OB1 and OB2 was 0.663; between OB1 and OB3, 0.559; and between OB1 and OBS, 0.710. OBS had a better concordance coefficient (0.752) between the first and the second measurements than did the human observers. Our results show that the software algorithm for B-lines counting is a potentially promising alternative when observers have little lung ultrasound experience.

Keywords B-lines · Inter-observer reliability · Intra-observer reliability · Lung ultrasonography

1 Introduction

One of the most significant findings on lung ultrasound (LUS) are B-lines, which have also been called "comet tails" or "lung rockets." B-lines are defined as discrete, laser-like vertical hyperechoic reverberation artifacts that arise from the pleural line (previously described as "comet tails"), extend to the bottom of the screen without fading, and move synchronously with lung sliding [1]. The cause of this phenomenon is fluid-thickening of the interlobular septa, due to increased extravascular lung water. However, this artifact of various etiologies, although most commonly associated with increased interstitial edema, has also been detected in different interstitial lung diseases. The number and frequency of B-lines correlate with the amount of extravascular lung water and the presence of pulmonary edema in critically ill patients [2, 3].

However, B-lines are a relatively operator-dependent sign, and therefore, the quantification of B-lines is defined as a semi-quantitative method [4]. It is frequently difficult to enumerate B-lines exactly in real-time, especially if

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they are plentiful or if they tend to be confluent. Furthermore, there are inter-observer and intra-observer differences in the enumeration of B-lines, which are reported to range from less than 10–30% in several recent studies [4–9]. Thus, the estimated number of B-lines is somewhat uncertain and subjective [8, 9]. To avoid this variability, we designed a computer software algorithm that detects B-lines on the screen and counts them in real-time or in various time intervals [10].

The first aim of our study was to test inter-observer agreement in the estimation of the exact number of B-lines between observers with three different levels of experience and by the software algorithm in real-time. The second aim of our study was to analyze intra-observer variability in the enumeration of B-lines in two successive examinations by the same observers and by the software.

2 Materials and methods

Forty consecutive, mechanically ventilated adult (≥ 18 years) intensive care unit (ICU) patients with sepsis and septic shock were included in this prospective study [11]. The exclusion criteria were: mechanical ventilation < 24 h, inability to perform ultrasound examination due to patients' position or technical reasons, morbidly obese patients (body mass index [BMI] ≥ 40 kg/m^2), and patients with pneumothorax, serious thoracic trauma, and/or major thoracic surgery. Enrollment took place between March 2017 and June 2017 in the ICU of an academic tertiary care facility, with an annual census of 400–500 ICU patients. The study was approved by the University's Hospital Ethics Committee (No.: 2170-29-02/1-16-2). The need to obtain consent was waived by the ethics committee.

2.1 Observers

All patients underwent two consecutive ultrasound examinations for the detection of B-lines by three observers with different skill-levels and by the software algorithm. The first observer (observer 1; OB1: A.Š.) had more than 15 years of experience in LUS and B-line assessment, the second observer (OB2: A.P.) had 6 months of experience with LUS, and the third observer (OB3: M.Š.) was a novice at LUS and received very brief (30 min) training on B-line assessment before the beginning of the study. B-line estimation using the software (OBS) was facilitated by bedside nurses without any previous knowledge of ultrasound, while the proper position of the transducer was guided by the attending physician who was blinded to the purposes of the study.

2.2 Chest ultrasound

All ultrasound examinations were performed using the same convex probe and ultrasound device (Shanghai United Imaging Healthcare, Shanghai, China), with the same parameters for gain, frequency (6 MHz), and depth (6–8 cm) of the ultrasound beam. The examinations were performed with patients in the supine (or near supine) position. Ultrasound scans were obtained on the anterior right and left thoracic side in the midclavicular line, in the second and fourth intercostal space, i.e., in four positions for each patient (R1; R2; L1; L2). This was chosen for its ease of application and for the concern of the patients' health condition and also because it is derived from the methodology of the BLUE protocol [2, 12, 13]. For the assessment of inter-observer variability, all examinations were performed in the order: OB1, OB2, OB3, and OBS. After the optimum ultrasound image was achieved, B-line counting for each position lasted 10 s for the observers and for the software during the whole respiratory cycle. The average estimated number of B-lines obtained in a 10-s period was compared. In each intercostal space scan, the number of B-lines was recorded separately, and observers were unaware of each other's results. For the assessment of intra-observer variability, the second ultrasound scan was obtained 15–30 min after the first scan. During the period between the first and second scan, patients did not receive any fluid, diuretics, or significant vasoactive drugs.

B-lines were recognized and counted according to the aforementioned B-line definition. In the case of confluent B-lines (B-lines separated by less than 7 mm [14], we counted them as a single B-line, although there is no standard way to approach this and some subjectivity and discordance exists [7]. If a lung consolidation was present, the number of B-lines was counted at the nearest alternative point in order to favor the B line counting [15].

2.3 Software

We developed a software algorithm that could count B-lines and mark them on the screen [10]. The software counted the B-lines in real-time and also calculated the average number of B-lines in a 10-s period and during the total LUS examination. Input data for the counting algorithm were the ultrasound image (frame) provided by the ultrasound machine software before displaying the frame on the screen. The image data could either be raw data or the final image, after probe transformation has been applied. After the region of interest was determined, vertical integration was calculated inside region of interest boundaries and a one-dimensional array was created. Next, on this array, in order to suppress noise, a digital low-pass filter was applied, which was present in the image data, in order to smooth the array. The next step was to use the peak-detection algorithm, which finds the local maximum in the array and creates a final array that contains the data of the detected B-lines. The numerical data in the final array are the total number of B-lines detected, and the amplitude and width of each B-line detected. The position of the B-lines detected was then overlaid on the image data and the image was displayed on the screen. Lastly, in order to make this process useful in practice, the average number of B-lines in N consecutive data frames or in N consecutive seconds (where N is a user-selectable value) was determined. Then, finally, the number of B-lines detected was displayed on the screen (Fig. 1).

2.4 Statistical analysis

Statistical analysis of data was performed using Statistica for Windows, release 13.3 (Statsoft, INC., Tulsa, OK, USA) and MedCalc (MedCalc Inc., Mariakerke, Belgium). The normality of distribution of age, BMI, and time in ICU was checked using the Kolmogorov–Smirnov test with the Lilliefors correction. Although these data were not normally distributed, we used mean ± standard deviation (SD) to present the data, because it allows easier understanding and comparison with other studies. To test the differences between groups according to age, BMI, and time in the ICU, the Mann–Whitney test was used. We evaluated inter-rater reliability using intraclass correlation coefficients (ICC) according to Cicchetti (less than 0.40—poor; between 0.40 and 0.59—fair; between 0.60 and 0.74—good; between 0.75 and 1.00—excellent) [16]. Two-way random-effects model with absolute agreement and multiple raters/measurements was performed [17]. Two-way random-effects model is used when the raters are randomly selected in order to generalize results to any raters with the same characteristics. Each subject was rated by the same set of raters. In order to test if all the raters assigned the same score to the same subject, absolute agreement was performed. We calculated the concordance correlation coefficient as a measure of precision and accuracy for each observer. All statistical values were considered significant at the level of $P < 0.05$.

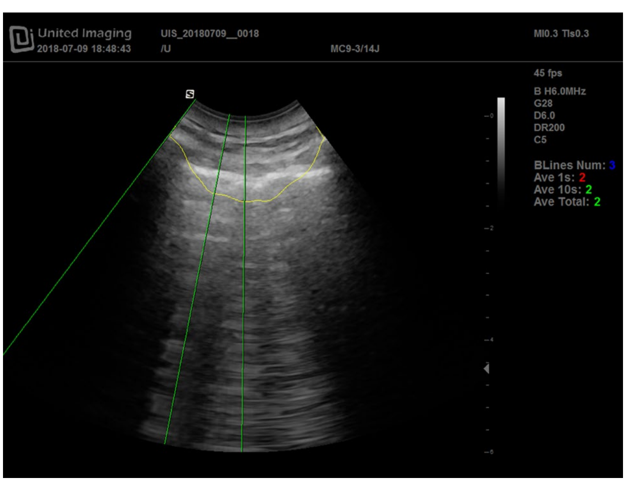

Fig. 1 Display of the screen with active B-line software detection mode. Central two green lines on the screen mark two B-lines. On the right side of the screen are average numerical values of B-lines in one second (Ave 1 s), 10 s (Ave 10 s), and during the entire examination (Ave total)

3 Results

The study was performed on 40 adult, mechanically ventilated, ICU patients (24 males and 16 females). There was no difference between the sexes in terms of age, BMI, and length of stay in the ICU before the study. Descriptive statistics are reported in Table 1.

3.1 Inter-observer reproducibility

ICC for B-lines among observers for the examined lung fields is shown in Table 2. Overall, for all lung zones, the ICC between OB1 and OB2 was 0.663, between OB1 and OB3, it was 0.559, and between OB2 and OB3, it was 0.664. The ICC between OB1 and OBS was 0.710, between OB2 and OBS, it was 0.387, and between OB3 and OBS, it was 0.330.

3.2 Intra-observer reproducibility

Intra-observer reproducibility between the first and second measurements for all for lung regions was 0.723 for OB1, 0.622 for OB2, 0.648 for OB3, and 0.752 for OBS. Therefore, OBS had a better concordance coefficient (e.g., a

Table 1 Descriptive statistics of patient data

Sex[a]	n	%	Age[b] (years) Mean ± SD	BMI[c] (kg/m^2) Mean ± SD	ICU stay (days)[d] Mean ± SD
Male	24	60.0	65 ± 13	29.7 ± 7.0	3.8 ± 2.9
Female	16	40.0	66 ± 15	27.2 ± 7.7	4.4 ± 3.7
All	40	100.0	65 ± 14	28.7 ± 7.3	4.0 ± 3.2

[a]The *t* test for proportions did not show a significant difference according to sex ($P = 0.074$)

[b]The Mann–Whitney test showed no significant difference according to age ($P = 0.722$)

[c]The Mann–Whitney test showed no significant difference according to BMI ($P = 0.301$)

[d]The Mann–Whitney test showed no significant difference according to ICU duration before the study ($P = 0.564$)

Table 2 Intraclass correlation (ICC) for counting B-lines among observers (inter-rater reliability)

Lung field	OB1/OB2 ICC (95% CI)	OB1/OB3	OB1/OBS	OB2/OB3	OB2/OB4	OB3/OB4
R1	0.764 (0.555–0.875)	0.695 (0.263–0.858)	0.597 (0.238–0.787)	0.557 (0.031–0.786)	0.248 (–0.439–0.604)	0.150 (–0.265–0.476)
R2	0.644 (0.337–0.810)	0.532 (0.014–0.773)	0.793 (0.606–0.890)	0.751 (0.499–0.872)	0.506 (0.089–0.735)	0.382 (–0.097–0.663)
L1	0.656 (0.358–0.817)	0.456 (0.035–0.715)	0.783 (0.588–0.885)	0.710 (0.369–0.857)	0.479 (0.046–0.720)	0.252 (–0.213–0.566)
L2	0.569 (0.205–0.769)	0.495 (0.053–0.732)	0.644 (0.325–0.809)	0.656 (0.357–0.817)	0.257 (–0.320–0.593)	0.502 (0.025–0.743)
All	0.663 (0.540–0.753)	0.559 (0.177–0.740)	0.710 (0.605–0.788)	0.664 (0.428–0.788)	0.387 (0.169–0.548)	0.330 (0.007–0.541)

Two-way model for absolute agreement

Table 3 Intra-observer variability in B-line counting (intra-rater reliability)

Observer	Concordance coefficient	95% CI
1	0.723	0.641–0.788
2	0.622	0.518–0.707
3	0.648	0.549–0.729
S	0.752	0.676–0.811

similar number of B-lines) between the first and the second measurements than did the other observers (Table 3).

4 Discussion

The detection of B-lines has been suggested as a valuable, rapid, and noninvasive diagnostic tool that physicians can use to estimate index of lung interstitial syndrome and/or extravascular lung water (e.g. pulmonary edema), and the method was proved valuable as a point-of-care diagnostic tool [18].

Although identification of a B-line "pattern" has proved useful in various conditions, some doubt remains about the utility of exact counting of the B-line number in routine clinical practice [8, 19, 20]. The most important reasons for criticism of the applicability of the B-line number is that it is partly an operator-dependent sign [4, 8, 9, 19, 21]. On the other hand, several recent studies have emphasized the clinical significance of the exact number of B lines in the assessment of pulmonary edema, EVLW, or even interstitial lung disease [2, 15, 22]. Ferre et al. find an increase of exactly six Delta-B-lines at the four standardized BLUE points as the threshold value to diagnose weaning-induced pulmonary edema, while Tardella et al. find that the presence of a LUS score superior or equal to ten B-lines is predictive for the presence of significant interstitial lung disease. To address this issue, we designed a novel computer software algorithm that detects B-lines on the screen and counts them in real-time or in various time intervals [10], which leads to faster examination of the patient and spares time in the ICU setting. In this study, we show that this algorithm had good inter-rater comparability with highly experienced observers and intra-rater reliability.

Several recent studies have demonstrated that detection of a B-line "pattern" (e.g., presence of ≥ 3 B-lines, or a similar definition) is a reproducible and easy-to-learn sign for observers with different levels of LUS experience [4, 7, 9, 20]. In a large SIMEU multicenter study, inter-observer agreement of 0.94 and intra-observer agreement of 0.97 and 0.92 were found for recognition of the B-line "pattern," for experts and observers with limited experience, respectively [5]. On the other hand, there are less convincing data for B-line counting; Gullett et al. found overall (for all lung zones combined) agreement in counting B-lines between expert/expert and expert/novice pairs, with coefficients of 0.603 and 0.593, respectively [9]. Additionally, Sparandeo et al. reported a standard deviation higher than 33% in the assessment of B-line number among observers [8].

Two attempts at objective calculation and/or counting B-lines using computer-based analysis or an automated scoring algorithm were recently published. In both of these studies, computer-assisted analysis of B-lines was found to be a useful tool for reducing intra-observer and inter-observer discordance [23, 24].

In our study, we analyzed inter-observer and intra-observer variability in quantifying B-lines between observers with three different levels of LUS experience and specifically developed software. The design of this study was partly different from those of previously reported studies. Our study was designed to represent the intensive care medicine reality, where B-line counting and the ensuing clinical decision should be done promptly. B-line counting was performed in real-time and lasted only 10 s, which is generalizable to an acute care clinical setting. In other similar studies, the results were analyzed with a delay, by reviewing previously recorded LUS video clips, rather than in real and limited time [3, 5–7, 9, 25]. It is to be expected that a delayed review would facilitate B-line counting, thus improving accuracy and reducing inter- and intra-observer variability. Consequently, the results of our and other studies are not entirely comparable. However, agreement in counting

B-lines between the observers in our study was similar to the results obtained by Gullett et al. In our study, inter-observer agreement in B-line counting between competent observers (OB1 vs. OB2) was slightly better (0.663 vs. 0.603) than between expert and beginner (OB1 vs. OB3: 0.559 vs. 0593) [9]. Taken together, our results show good ICC (between 0.6 and 0.8) for B-line counting between expert and other observers (including the software algorithm) in most distinct lung fields, and in the whole-lung examination (i.e., cumulative for all four lung fields).

Additionally, intra-rater variability between observers in our study was somewhat comparable with the results of Gullett et al., self-agreement in our study was 0.723 for an expert (OB1) and 0.622 for a competent observer (OB2), while in Gullett et al.'s study, self-agreement for two different experts was 0.676 and 0.586 [9]. Additionally, it is important to emphasize the good intra-rater agreement for the naïve observer (0.648) in our study and, above all, a very good concordance coefficient for the software. The good agreement of the software with the expert observer (0.710) and very good self-agreement (0.752) of the software confirms the encouraging results from comparable studies with computer-based analysis or an automated scoring algorithm for B-line counting [23, 24].

Our study had some important potential limitations. First, like similar previous studies, for technical and ethical reasons the observers' accuracy in semi-quantifying the degree of extravascular lung water by counting B-lines was not compared with results obtained by lung computed tomography, but the main purpose of the study was to compare subjectivity of three providers with different levels of experience and how it relates to the software algorithm. By no means was it supposed to be a definitive diagnostic measure and its utility will need to be compared with other diagnostic modalities before a routine use in the practice. Second, we used the persuasiveness sample of critically ill patients because there is no strength data based on previous studies. Therefore, sample size was not a priori calculated and the number of enrolled patients (examinations) was too small to yield entirely conclusive results. Third, the third observer had almost no experience in LUS at the beginning of the study, but gained experience during the study based on the steep learning curve of LUS. Therefore, the results of the third observer in counting B-lines by the end of the study period are not fully comparable with his results at the beginning of the study. Fourth, there is no "golden standard" for B-line assessment, but this is a common problem in all similar studies on this subject. Fifth, taking into consideration that enrolled patients had the diagnosis of sepsis and septic shock, we acknowledge the fact that B-lines found on ultrasound examination in this population could have been of both non-cardiogenic and cardiogenic origin. Enhanced vascular permeability due to endothelial injury of pulmonary vasculature [26], sepsis induced myocardial stunning, including systolic and diastolic dysfunction [27–29], and possible presence of pneumonia in mechanically ventilated patients, all contribute to the formation of B-line pattern in a septic patient, but this was considered secondary to the purpose of this particular study.

5 Conclusion

In this study we determined the inter-rater and intra-rater reliability for counting B-lines between three observers with different levels of experience in LUS and a novel software algorithm. The software algorithm for B-line counting demonstrated good inter- and intra-rater reliability and is a potentially promising alternative for observers with little LUS experience. Further algorithm iterations may increase its use in both the research and clinical arenas.

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Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the University's Hospital Ethics Committee (KBC Rijeka, Croatia; 12/12/2016, No.: 2170-29-02/1-16-2). All data obtained were handled according to current data protection guidelines.

Informed consent The need to obtain informed consent was waived by the ethics committee.

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