B-line by Lung Ultrasound as a Predictor of Re-intubation in Mechanically Ventilated Patients with Heart Failure

Junho Hyun  
Asan Medical Center, University of Ulsan College of Medicine

Ah-ram Kim  
Asan Medical Center, University of Ulsan College of Medicine

Sang-Eun Lee  
Asan Medical Center, University of Ulsan College of Medicine

Min-Seok Kim (✉️ msk@amc.seoul.kr)  
Asan Medical Center, University of Ulsan College of Medicine

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Abstract

There have been few studies on predictors of weaning failure from mechanical ventilation (MV) in patients with heart failure (HF). We sought to investigate the predictive value of B-lines measured by lung ultrasound (LUS) on the risk of re-intubation after MV weaning and in-hospital outcomes. This was a single-center, prospective observational study that included HF patients who were on invasive MV. LUS was performed right before ventilator weaning. A positive exam for B-lines was defined as the observation of two or more regions that had three or more numbers of B-lines located bilaterally on the thorax. Early re-intubation with 72 hours after MV weaning was significantly higher in the positive B-line group (14.1%) than the negative B-line group (2.4%) (p=0.011). The rate of total re-intubation during admission (p=0.004), duration of intensive care unit stay (p=0.004), and hospital stay (p=0.010) were greater in the positive B-line group. The negative predictive value (NPV) of positive B-lines was 97.6% for the primary outcome. B-lines measured by LUS can predict the risk of re-intubation after MV weaning. Considering the high NPV of positive B-lines, it may help guide the decision of extubation in patients on invasive MV due to acute decompensated HF.

INTRODUCTION

A subset of patients with heart failure (HF) experience episodes of decompensation during their clinical course. Approximately 5% of hospitalized patients and 23% of those admitted to the intensive care unit (ICU) due to HF aggravation require invasive mechanical ventilation (MV) because of respiratory failure. To avoid poor outcomes associated with prolonged MV, weaning from MV should be attempted in these patients. However, weaning from MV in HF patients is challenging, and a significant proportion experience weaning failure or re-intubation.

HF itself is a major risk factor for re-intubation after discontinuation of MV, which can occur frequently. During the weaning process, preload and afterload of both ventricles and work of breathing are abruptly altered, which can increase the risk of early re-intubation in HF patients with poor myocardial reserve. In order to avoid the need for re-intubation due to failed extubation, it is crucial to optimize preload by removing excess fluid. An accurate evaluation of remaining pulmonary congestion is essential for this purpose, which is typically done through the use of chest radiography and natriuretic peptides (NPs). However, over 10% of HF patients on MV experience re-intubation with these conventional methods.

B-lines, which can be easily measured using lung ultrasound (LUS), can detect pulmonary interstitial edema and are correlated with NPs and pulmonary capillary wedge pressure (PCWP), making them useful for diagnosing and predicting prognosis in patients with HF. However, the clinical value of B-lines in patients receiving invasive MV due to decompensated HF is unclear. As B-lines can be used to monitor the adequacy of decongestive therapy, they may also provide clinical information about optimizing preload during ventilatory support in patients with HF. Therefore, we aimed to evaluate the prognostic value of B-lines for in-hospital outcomes in HF patients receiving MV.
MATERIALS AND METHODS

Study Design and Participants

This was a prospective observational cohort study conducted at a tertiary center (Asan Medical Center, Seoul, Korea) between March 2020 and December 2022. This study was registered at ClinicalTrials.gov (identifier NCT04322851) and conducted in compliance with the Declaration of Helsinki. The study protocol was approved by the Institutional Review Board of the center (Asan Medical Center, AMC-2020-0164, approved February 06, 2020) and all of the participating patients provided written informed consent. When patients were unconscious or delirious, their legal representatives provided consent for their participation. The study included consecutive patients who had received invasive MV for acute decompensated HF and were eligible for MV weaning with planned extubation. Acute decompensated HF was defined as a sudden or gradual worsening of the signs and symptoms of HF leading to unplanned hospitalization or requiring intravenous therapy to relieve signs and/or symptoms. Patients were included if they met the following criteria: (1) fraction of inspired oxygen (FiO₂) less than 0.4; (2) stable hemodynamic status with no need for or low level of inotropes and/or vasopressors; and (3) stable ventilatory state with a spontaneous breathing trial including a respiration rate less than 35, heart rate lower than 140 beats per minute and increase of heart rate less than 20% of baseline, oxygen saturation higher than 90%, and no signs of respiratory distress. Patients with a tracheostomy state, who received MV not attributable to HF, or who received MV during elective cardiac surgery without evidence of HF were excluded. Most of spontaneous breathing trials were conducted for approximately one hour using a T-piece. Subsequently, all participants underwent extubation. Baseline demographics, clinical data during admission, and laboratory findings including N-terminal pro-brain natriuretic peptide (NT-pro-BNP) on the day of MV weaning were collected. Arterial blood gas analysis was examined before and after weaning from MV.

Lung ultrasound

LUS was performed using the Philips CX50 ultrasound system (Philips Medical Systems, Bothell, WA, USA) with a 3.5-MHz convex probe at a depth of 15–18 cm adjusted to the patient's chest wall depth. The LUS was performed by an investigator (J.H.) who was trained in a standard protocol recommended by the international guideline. All patients were examined with LUS immediately before extubation in a semi-recumbent position and without the support of any positive pressure on a T-piece. B-lines were measured by scanning eight regions of the thorax in a longitudinal plane between two ribs with a distance of adjacent two B-lines < 7 mm. Scanned images were independently adjudicated by two investigators (J.H. and A.K.) who were blinded to the clinical information. A positive region was defined as the presence of three or more numbers of B-lines at each area scanned. A positive B-line result on the LUS examination was defined as having two or more positive regions that existed in both hemithoraces.

Outcomes
The patients were divided into two groups based on the positivity of B-lines. The primary outcome of the study was the rate of early re-intubation within 72 hours. Secondary outcomes included the rates of total re-intubation during admission, in-hospital death, and the duration of ICU and hospital stay. All clinical and outcome data were collected during the index admission. Outcomes were also analyzed according to the total number of B-lines to determine the relationship between B-lines and re-intubation and the correlation of NT-pro-BNP level.

**Statistical analyses**

The rates of re-intubation and in-hospital death were compared using Pearson's Chi-squared test or Fisher's exact test, as appropriate. The hazard ratios of outcomes were analyzed with logistic regression adjusted with variables including age, hypertension, diabetes, chronic kidney disease, body weight change between intubation and extubation, and left ventricular ejection fraction (LVEF). Inter-observer agreement of positive exams and the total number of B-lines was analyzed by Cohen's kappa measure of concordance and intraclass correlation coefficient for agreement, respectively. The correlation between the total number of B-lines and NT-pro-BNP with the log-transformed value, considering its skewed distribution, was estimated with the coefficient of determination ($r^2$) using linear regression. Receiver-operating characteristics (ROC) analysis was used to determine the performance of the B-line result, and the areas under the ROC curve (AUC) were presented with 95% confidence intervals (CI). Sensitivity, specificity, and positive and negative predictive values (PPV and NPV) of the positive B-line result were also analyzed.

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA). All comparisons were two-sided, and P values < 0.05 were considered statistically significant.

**RESULTS**

**Baseline Characteristics**

A total of 146 consecutive patients who received invasive MV due to congestive HF were enrolled. Sixty-four patients (43.8%) had a positive B-line result (positive B-line group), and the remaining 82 (56.2%) had a negative exam (negative B-line group). In terms of baseline characteristics, the positive B-line group had older age, lower body weight at the initiation of MV, lower hemoglobin level, and higher NT-pro-BNP level compared with the negative B-line group ([Supplementary Table S1](#)). The proportion of patients with ischemic etiology of HF was 49.3% (n = 72) in the entire cohort, which was not significantly different between the two groups ($p = 0.851$). The study population received invasive MV for a median of 6 days (interquartile range [IQR], 3–12), and the positive B-line group had a longer median duration (8 days) than the negative B-line group (5 days) ($p = 0.027$). Echocardiography was performed at a median of 4 days (IQR, 2–8) before MV weaning, and the measures were similar between the two groups.

**Outcomes**
The median total number of B-lines detected by LUS was 10 (IQR, 6–16) (Supplementary Figure S1), and inter-observer agreement was acceptable (Cohen’s kappa coefficient 0.84, confidential interval [CI] 0.74–0.93; intraclass correlation coefficient 0.91, 95% CI 0.83–0.95). The number of B-lines and the proportion of positive regions (≥ 3 B-lines number in the region) were highest in the lower lateral region of the thorax (Supplementary Table S2), and the details of B-lines in each group are provided in Supplementary Table S3. The rate of early re-intubation was significantly higher in the positive B-line group (14.1%) compared with the negative B-line group (2.4%) (p = 0.011, Fig. 1 and Table 1). The rate of re-intubation during the whole period of the index hospitalization was also significantly higher in the positive B-line group (26.6% vs. 8.5%, p = 0.004). The duration of hospital stay, total ICU stay, and ICU stay after MV weaning was longer in the positive B-line group. In-hospital mortality was not significantly different between the two groups.

### Table 1

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Positive B-line</th>
<th>Negative B-line</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 64</td>
<td>N = 82</td>
<td></td>
</tr>
<tr>
<td>Re-intubation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Within 72 hours (primary endpoint)</td>
<td>9 (14.1)</td>
<td>2 (2.4)</td>
<td>0.011</td>
</tr>
<tr>
<td>During admission</td>
<td>17 (26.6)</td>
<td>7 (8.5)</td>
<td>0.004</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>4 (6.3)</td>
<td>3 (3.7)</td>
<td>0.699</td>
</tr>
<tr>
<td>Duration of stay, days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total admission</td>
<td>34 (19–56)</td>
<td>24 (12–41)</td>
<td>0.010</td>
</tr>
<tr>
<td>ICU</td>
<td>12 (7–21)</td>
<td>9 (5–14)</td>
<td>0.004</td>
</tr>
<tr>
<td>ICU stay after extubation</td>
<td>3 (2–6)</td>
<td>2 (1–3)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Values are presented as patient number (percentage) or median (IQR).

ICU = intensive care unit.

### Association of the Number of B-lines with Outcomes and NT-pro-BNP Level

When divided into three groups according to the tertile of B-line numbers, the total number of measured B-lines showed a proportional increase in the rate of the primary outcome, albeit without statistical significance (p = 0.055) (Supplementary Table S4). The rate of total re-intubation was significantly different according to the groups divided by B-line number tertile (p < 0.001). Patients in the first tertile (total number of B-lines ≤ 7) had the lowest risk of re-intubation within 72 hours (2.0%) and during admission (4.0%), while those in the third tertile (total number of B-lines ≥ 14) had the highest rate of re-intubation within 72 hours (14.6%) and during admission (33.3%) (Fig. 2). NT-pro-BNP level measured on
the day of weaning was weakly correlated with the total number of B-lines ($r^2 = 0.132, p < 0.001$) in the whole study population and in patients not dependent on dialysis ($n = 131 [89.7%]; r^2 = 0.170, p < 0.001$) (Fig. 3).

**Prediction of Re-intubation**

Regression analysis with multivariable adjustment demonstrated that positive B-line was associated with re-intubation within 72 hours (hazard ratio [HR], 6.00; 95% CI, 1.15–31.42; $p = 0.034$) and during the entire admission period (HR, 5.54; 95% CI, 1.60–19.18; $p = 0.007$). ROC analysis showed that the AUC value of the B-line result was 0.71 (95% CI, 0.56–0.85; $p = 0.024$) and that of the NT-pro-BNP value was 0.50 (95% CI, 0.31–0.70; $p = 0.991$) (*Supplementary Figure S2*). The predictive ability for early re-intubation was better with a positive B-line result than with the total number of B-lines as a continuous variable (*Supplementary Table S5*). The NPV of a positive B-line was 97.6% for early re-intubation and 91.5% for re-intubation during the entire admission (Table 2).

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Re-intubation within 72 hours</td>
<td>81.8%</td>
<td>59.3%</td>
<td>14.1%</td>
<td>97.6%</td>
</tr>
<tr>
<td>Total re-intubation during admission</td>
<td>70.8%</td>
<td>61.5%</td>
<td>26.6%</td>
<td>91.5%</td>
</tr>
</tbody>
</table>

NPV = negative predictive value; PPV = positive predictive value.

**DISCUSSION**

This study is the first to investigate the predictive value of B-lines detected by LUS in patients receiving invasive MV due to acute decompensated HF. Our findings suggest that a positive B-line result is associated with a higher risk of re-intubation during both the early and the entire period of admission, as well as longer ICU and hospital stay. Moreover, the risk of re-intubation increased with an increase in the total number of B-lines. The B-line number was correlated with the NT-pro-BNP level; however, a positive B-line result, but not the total number of B-lines or NT-pro-BNP, was independently associated with re-intubation risk after weaning. Given the high NPV of a positive B-line, it may serve as a useful parameter to exclude the possibility of re-intubation before deciding on extubation for HF patients on invasive MV.

A subset of patients with HF may develop respiratory failure that requires invasive MV due to either decompensation of pre-existing HF or newly diagnosed HF. HF itself is a risk factor for weaning failure, and positive fluid balance, high levels of NPs, and echocardiographic parameters of diastolic function have been shown to predict weaning failure in patients with HF. Moreover, even though many of these patients can be successfully weaned off with appropriate therapy, a significant proportion may experience re-intubation, which is strongly associated with adverse in-hospital outcomes, including mortality. Adequate decongestion is important to avoid re-intubation in the HF population, as pulmonary
edema reduces lung compliance and can act as a major mechanism of respiratory failure.\textsuperscript{22,23} In contrast, insufficient decongestion, reflected by less body weight reduction, has been associated with a higher risk of re-intubation.\textsuperscript{5} However, it is important to note that parameters such as body weight change are indirect indicators of pulmonary decongestion. Although echocardiography and measuring NPs are useful for evaluating myocardial function and volume status, they are also indirect indicators of pulmonary decongestion.

The LUS is a quick and straightforward method that can be completed within a few minutes. B-line, as measured by LUS, is a hyperechoic artifact that extends vertically from the pleural line and represents a sonographic sign of pulmonary edema with high sensitivity and specificity.\textsuperscript{24,25} It has been well correlated with PCWP and interstitial edema on computed tomography,\textsuperscript{26,27} and its use has been reported in the diagnosis of suspected HF, assessment of adequacy in decongestive therapy, and prediction of prognosis in chronic HF.\textsuperscript{10,11,14,28,29} Although the clinical value of B-line has been previously reported in HF patients with pre-hospital or ambulatory settings, its usefulness in patients with decompensated HF dependent on MV has not been studied extensively. While a previous study showed that B-line by LUS did not predict successful weaning,\textsuperscript{30} this study primarily included patients with non-cardiac causes for initiation of MV. In the present study, we demonstrated that the B-lines detected by LUS were an independent predictor of re-intubation after MV weaning in HF patients. Although the number of early re-intubation in this study was small (a total of 11), the quantitative relationship between re-intubation and the increase in total B-line numbers during the early and entire period of admission supports the interpretation that the observed benefit of B-line by LUS was not due to chance. Furthermore, the high negative predictive value of B-lines suggests that HF patients with negative B-line results who are scheduled for extubation can be safely weaned off without a significant risk of re-intubation.

NPs increase in response to volume overload and are recognized as predictors of prognosis in HF patients. Furthermore, elevated levels of NPs are predictive of weaning failure in patients on MV.\textsuperscript{31} Although NPs can reflect PCWP and subsequent pulmonary edema, the correlation between NPs and PCWP has been reported to be weak in patients admitted to the ICU,\textsuperscript{32} and NPs levels also have a weak-to-moderate correlation with PCWP in HF patients admitted to the ICU.\textsuperscript{33} In addition, NPs can also be elevated in various conditions, including worsening renal function, which is frequently present during episodes of decompensated HF.\textsuperscript{32,34} In our study, we found a significant but weak correlation between B-line and NT-pro-BNP, which is consistent with previous reports. Conventional modalities like chest radiography or NPs have limited value in patients admitted to the ICU. Considering our study results that a positive B-line predicted early re-intubation, B-line measurements may provide valuable information to guide safe weaning decisions.

Our study had several limitations. First, weaning failure and subsequent re-intubation is a complex outcome that is influenced by various factors, including cardiac condition, interstitial edema, neuromuscular, metabolic, psychological, and nutritional factors.\textsuperscript{15} Therefore, the B-line result alone cannot be the sole determinant in deciding the adequacy of weaning. Nevertheless, adequate
decongestion is essential for HF patients before being weaned off from MV, and this can be easily detected through LUS. Second, we measured B-lines in a semi-recumbent position. As the number of B-lines can be affected by the position, the position during LUS scanning may affect the outcomes. However, it is unclear which position is optimal for B-line measurement. While many studies have reported the clinical value of B-lines measured in the supine position, some have also used the semi-recumbent position. Furthermore, as many ICU patients have pleural effusion that may interfere with B-line measurement at lateral regions during the supine position, we opted for the semi-recumbent position. Third, there are numerous methods to obtain the LUS images from various regions. We chose scanning eight regions which includes lateral side of the thorax. Sonographic distribution of B-lines in cardiongeic pulmonary edema infrequently is not even, possibly accentuated in basal part of the lung, which can be detected by examining lateral side of the thorax during supine position. Fourth, the correlation between the total number of B-lines and NT-pro-BNP level was weak and the significance was higher in the study population not dependent on dialysis than dialysis-dependent patients. However, NT-pro-BNP levels can be falsely elevated in dialysis-dependent patients, which limits the use of NT-pro-BNP for making weaning decisions in these populations. Last, the study population was limited to individuals with HF. Consequently, our study findings cannot be extrapolated to encompass all ICU patients with MV. Sixth, despite of high NPV, low positive predictive value may limit clinical utility for finding high-risk subset for re-intubation necessitating further decongestive therapy.

CONCLUSIONS

The study demonstrated that B-lines, measured by LUS before extubation in patients receiving invasive MV due to acute decompensated HF, can predict the risk of re-intubation. Also, a negative B-line result was found to be highly predictive of safe weaning from MV without significant risk of re-intubation. Therefore, B-line measurement may assist in guiding decisions on MV weaning in this population.

Abbreviations

\( \text{FiO}_2 \)
- fraction of inspired oxygen

HF
- heart failure

ICU
- intensive care unit

IQR
- interquartile range

LUS
- lung ultrasound

MV
- mechanical ventilation
NP
natriuretic peptide

NT-pro-BNP
N-terminal pro-brain natriuretic peptide

PCWP
pulmonary capillary wedge pressure

Declarations

ACKNOWLEDGMENTS

None.

AUTHOR CONTRIBUTIONS

J.H., M.S.K. contributed to conceptualization, design, methodology, formal analysis and investigation, and writing of original draft. J.H. performed statistical analysis. All authors were involved in review, editing, and supervision. All authors read and approved the final manuscript.

FUNDING

None.

COMPETING INTERESTS

None reported.

DATA AVAILABILITY STATEMENT

The data analyzed on the current study are available by the corresponding author upon reasonable request.

References


**Figures**

![Figure 1](image-url)

**Figure 1**

*Rates of re-intubation according to the B-line positivity*

(A) Re-intubation within 72 hours. (B) Re-intubation during the entire period of admission.
Figure 2

Rates of re-intubation according to the tertiles of the total number of B-line

(A) Re-intubation within 72 hours. (B) Re-intubation during the entire period of admission.

* p<0.05 for the comparison with the first tertile (number of B-line ≤ 7).
† p<0.001 for the comparison with the first tertile (number of B-line ≤ 7).

Figure 3

Correlation Between the Number of B-line and NT-pro-BNP level

(A) Whole study population. (B) Patients not dependent on dialysis.

*NT-pro-BNP level was transformed into log value due to skewed distribution.
NT-pro-BNP = N-terminal pro-B-type natriuretic peptide.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementarymaterialScientificReports.docx