Ultrasound assessment of lung aeration loss during a successful weaning trial predicts postextubation distress*

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**Objective:** Postextubation distress after a successful spontaneous breathing trial is associated with increased morbidity and mortality. Predicting postextubation distress is therefore a major issue in critically ill patients. To assess whether lung derecruitment during spontaneous breathing trial assessed by lung ultrasound is predictive of postextubation distress.

**Design and Setting:** Prospective study in two multidisciplinary intensive care units within University Hospitals.

**Patients and Methods:** One hundred patients were included in the study. Lung ultrasound, echocardiography, and plasma B-type natriuretic peptide levels were determined before and at the end of a 60-min spontaneous breathing trial and 4 hrs after extubation. To quantify lung aeration, a lung ultrasound score was calculated. Patients were followed up to hospital discharge.

**Measurements and Main Results:** Fourteen patients failed the spontaneous breathing trial, 86 were extubated, 57 were definitely weaned (group 1), and 29 suffered from postextubation distress (group 2). Loss of lung aeration during the successful spontaneous breathing trial was observed only in group 2 patients: lung ultrasound scores increased from 15 [13;17] to 19 [16; 21] (p < .01). End spontaneous breathing trial lung ultrasound scores were significantly higher in group 2 than in group 1 patients: 19 [16;21] vs. 10 [7;13], respectively (p < .001) and predicted postextubation distress with an area under the receiver operating characteristic curve of 0.86. Although significantly higher in group 2, B-type natriuretic peptide and echocardiography cardiac filling pressures were not clinically helpful in predicting postextubation distress.

**Conclusion:** Lung ultrasound determination of aeration changes during a successful spontaneous breathing trial may accurately predict postextubation distress. (Crit Care Med 2012; 40: 2064–2072)

**Key Words:** B-type natriuretic peptide; lung ultrasound; mechanical ventilation; postextubation distress; reintubation; weaning

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Pulmonary complications resulting from mechanical ventilation increase with the duration of ventilatory support and require weaning patients quickly. Weaning, which represents up to 40% of the duration of mechanical ventilation, is a critical period (1, 2). Weaning failure includes patients failing the initial spontaneous breathing trial (SBT) and patients with postextubation distress (1). Postextubation distress is defined as reintubation or need for rescue noninvasive ventilation within 48 hrs following extubation (1, 3, 4). Following successful SBT, frequency of reintubation ranges between 3% and 30% (1, 3). Patients failing extubation experience longer stays in the intensive care unit (ICU), higher prevalence of ventilator-associated pneumonia (5, 6), posttraumatic stress disorders (7), and higher morbidity and mortality (8), all factors increasing health costs (1, 8–11). Given the risks associated with delayed or unsuccessful extubation, determining readiness for extubation and predicting postextubation distress is a critical challenge in the ICU.

Identifying patients definitively weaned from mechanical ventilation following extubation remains a difficult issue (12–14). Most proposed predictors of postextubation distress either require special equipment, are too complex for bedside use, or have a limited predictive value (4, 14, 15). Therefore, to date, there are no simple clinical indices known to be powerful predictors of postextubation distress. Many mechanisms whose relative weights vary

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*See also p. 2237.*

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Dr. Soummer initiated the study, participated in the design of the study, carried out the study at La Pitié-Salpêtrière hospital and drafted the manuscript. Dr. Perbet contributed equally to the work. He participated in the design of the study, carried out the study at the Estaing Hospital, and helped to improve the draft. Drs. Brisson and Arbelo participated to the study analysis. Mohammed Bouberima and Laurence Roscayk performed measurements of plasma concentrations B-type Natriuretic Peptide. Drs. Constantin and Lu participated to the conception and analysis of the study. Dr. Rouby participated in the design and conception of the study and helped to improve the draft. The Lung Ultrasound Study Group participated in the study either by contributing to enroll patients or participating to the conception of the study.

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from one patient to another may have an impact on the ability to wean from mechanical ventilation (1, 16). Alteration of lung resistance/compliance, spontaneous breathing-induced cardiac deterioration, and neuromuscular disorders may cause lung aeration loss during SBT. Such a derecruitment, which could be predictive of postextubation distress, has never been directly studied.

We hypothesized that bedside lung ultrasound (LUS) could be an accurate predictor of postextubation distress by detecting a high lung aeration defect immediately before weaning and/or by evidencing significant lung derecruitment during the SBT. We set up a prospective observational trial in two ICUs to quantify changes in lung aeration during SBT using a recently validated LUS score (17, 18). To determine the potential role of cardiovascular disorders in aeration loss and postextubation distress, cardiac function was assessed using transthoracic echocardiography and B-type natriuretic peptide (BNP) measured before and at the end of the SBT (19–21).

MATERIALS AND METHODS

Supplemental data contains additional information on inclusion criteria, data collection with lung ultrasound, echocardiography, and statistical analysis (Supplemental Digital Content 1, http://links.lww.com/CCM/A482).

Patients

This study was approved by the Ethical and Institutional review Board of the University Hospital of Clermont-Ferrand, France, and written informed consent was required from the patient’s next of kin for inclusion in the study. Consecutive patients mechanically ventilated for more than 48 hrs were included when the underlying respiratory disease that had required intubation was considered by the attending physician as reversed, rendering the patient eligible to a first 1-hr SBT (10). Exclusion criteria were patients aged <18 yrs, patients with tracheostomy, paraplegia with median level above T8, cardiac arrhythmias, severe ICU-acquired neuromyopathy, chronic obstructive pulmonary disease with forced expiratory volume <50% of the theoretical predicted value, patients with planned prophylactic noninvasive ventilation after extubation, and patients who had previously failed a SBT.

SBT

The SBT was performed through a T-tube as previously described (10). Criteria defining successful SBT, failed SBT, and postextubation distress are described in the supplemental data (Supplemental Digital Content 1, http://links.lww.com/CCM/A482). Patients who successfully passed the SBT were extubated, followed up for 48 hrs and classified in the postextubation success group or in the postextubation distress group (1, 3, 4, 22).

LUS

LUS was performed using a 2- to 4-MHz convex probe as previously described (18, 23–25). LUS was performed by trained investigators during a 10-min period, the time required for assessing the whole lung. The same investigator performed the different LUS at each time point of the study. Each intercostal space of upper and lower parts of the anterior, lateral, and posterior regions of the left and right chest wall was carefully examined. Videos were stored on compact disks. Four ultrasound aeration patterns were defined (17, 18): 1) normal aeration (N); presence of lung sliding with A lines or fewer than two isolated B lines; 2) moderate loss of lung aeration: multiple, well-defined B lines (B1 lines); 3) severe loss of lung aeration: multiple coalescent B lines (B2 lines); and 4) lung consolidation (C), the presence of a tissue pattern characterized by dynamic air bronchograms. For a given region of interest, points were allocated according to the worst ultrasound pattern observed: N = 0, B1 lines = 1, B2 lines = 2, C = 3. The LUS score ranging between 0 and 36 was calculated as the sum of points.

Echocardiography

Using transthoracic echocardiography, the left ventricle systolic function was assessed by measuring fractional area change on small axis parasternal view. Left ventricle diastolic function was assessed by measuring mitral inflow velocity (E and A waves and deceleration time of E) and velocities of mitral annulus (Ea) using Doppler tissue imaging (see Supplemental Digital Content 1, http://links.lww.com/CCM/A482).

Protocol

Clinical and biological parameters listed in the supplemental data (Supplemental Digital Content 1, http://links.lww.com/CCM/A482), as well as LUS and echocardiographic parameters, were measured before and at the end of the SBT, and 4–6 hrs after extubation. B-Type natriuretic peptide was analyzed using a Triage BNP test (Biosite, San Diego, CA) and measured before, at the end of the SBT, and 4 hrs after extubation. The attending physician remained blinded to lung ultrasound, echocardiography, and BNP values.

Statistical Analysis

Data are expressed as means ± SD or median quartile [first–third] according to their distribution. Unpaired Student’s t, Mann–Whitney, and paired Wilcoxon tests were used to compare quantitative variables. Comparison of proportions was performed using the Fisher’s exact test. The discriminate power of the LUS score was quantified by measuring the area under the receiver operating characteristic curve. The level of significance was fixed at p ≤ .05.

RESULTS

Patients

One hundred consecutive patients were included in the study and their characteristics are summarized in Table 1. Despite elevated Simplified Acute Physiologic Score 2 and Sequential Organ Failure Assessment scores at admission, ICU-mortality rate was low (8%). Reasons for initiating invasive mechanical ventilation were shock (37%), respiratory failure (21%), non-traumatic coma (15%), multiple trauma (11%), and miscellaneous (16%). As shown in Figure 1, 86 patients were extubated after a successful SBT. Among them, 57 (66%) were definitively weaned (postextubation success) and 29 (34%) patients developed postextubation distress within 48 hrs (postextubation failure). Among them, 14 patients were reintubated for 5 (5–8) additional days, and 15 patients required noninvasive ventilation during 3 (1–6) days (median [first–third]). Six of the 15 patients who required noninvasive ventilation were finally reintubated and mechanically ventilated for 7 (4–10) additional days. Patients with postextubation distress had a significantly higher ICU and hospital mortality than patients with postextubation success. When adjusting to Simplified Acute Physiologic Score 2 and Sequential Organ Failure Assessment scores at admission, postextubation distress was associated with in-ICU death with an odds ratio = 6 [95% confidence interval 1–33, p = .04]. Patients failing SBT and patients with postextubation distress had a significantly greater length of stay in the ICU. Finally, no changes in clinical respiratory and cardiovascular variables were detected in different groups as described in the supplemental data.
Predicting Factors of SBT Failure and Postextubation Distress

Lung Aeration Loss Before and During Weaning Trial. As shown in Table 2, basal LUS score was similar in patients with SBT success and SBT failure. In both groups, LUS significantly increased during SBT. Per-trial derecruitment, however, was more marked in patients with SBT failure. In patients with postextubation distress, basal LUS score was greater than basal LUS score of patients with postextubation success. During SBT, LUS score did not change in patients with postextubation success whereas it markedly increased in patients with postextubation distress, as evidence of significant per-trial derecruitment. An illustrative example is shown in Figure 2. Interestingly, lung derecruitment was predominantly observed in the lower parts of the anterior regions (32% of patients increase LUS score in this region), in upper and lower parts of lateral regions (39% and 38% of patients who develop postextubation distress exhibited an increase of LUS score in this region, respectively), and in upper parts of posterior regions (31% patients who develop postextubation distress increase LUS score in this region). All details for the 29 patients failing extubation are in the Figure S3 in the supplemental data (Supplemental Digital Content 4, http://links.lww.com/CCM/A482). As shown in Figure 4B, inconclusive limits of LUS score to predict postextubation distress was 0.86, 95% confidence interval 0.79–0.93 (Fig. 4A). As choosing a single cut-off is recognized to be insufficiently informative, the analysis was completed by determining positive and negative likelihood ratios (LHR) based on evaluation of inconclusive limits (27). LHR >10 or <0.2 are considered to have the potential to alter clinical decisions (27). Area under curve assessing the ability of end-SBT LUS score to predict postextubation distress was 0.86, 95% confidence interval 0.79–0.93 (Fig. 4A). As shown in Figure 4B, inconclusive limits of LUS score were determined by sensitivity and specificity above 90%. An end SBT-LUS score >17 was highly specific for predicting postextubation distress as associated with postextubation distress, as evidence where it markedly increased in patients with postextubation distress.
to a positive LHR of 11.8, 95% confidence interval, 3.8–36.8. A LUS score ≤12 was highly sensitive for excluding postextubation distress as associated to a negative LHR of 0.20, 95% confidence interval 0.08–0.5, indicating a low risk of postextubation distress (Table 3).

Twenty-two patients among the 86 patients who successfully passed the SBT (25%) had LUS scores between 13 and 17 and were concerned by the inconclusive limits of the end-SBT LUS score. Among them, seven (32%) required a resumption of mechanical ventilation (four reintubations and three rescue noninvasive ventilation). In these 22 patients, the ultrasound analysis of lung derecruitment following extubation appeared helpful to predict postextubation distress. The seven patients with postextubation distress had a higher LUS score 4 hrs after extubation than patients with postextubation success: 19 [15–19] vs. 15 [14–19], p = .07.

**Cardiovascular Abnormalities Before and During Spontaneous Breathing Trial.** Only 15% of the studied population had a left ventricular systolic dysfunction defined as a fractional area change <40%. Five patients had a fractional area change <30%. At the time of weaning, the mean fluid balance was positive by 2 kg. As shown in Table 1, basal echocardiographic parameters were not different in patients with SBT success and failure except E-wave peak velocity. In contrast, patients with postextubation distress had a significantly lower basal fractional area change and higher E/Ea than patients with postextubation success.

Median BNP values did not differ between patients who passed and those who failed SBT. Among patients who successfully passed the SBT, median BNP values were significantly greater before and after SBT and 6 hrs after extubation in patients with postextubation distress but did not vary during the weaning trial. To determine threshold values of BNP predicting postextubation success and distress, receiver operating characteristic curves were constructed and positive and negative LHR were calculated. As shown in Figures 4C and D, area under curve assessing the ability of end-SBT BNP to predict postextubation distress was low and reached 0.70, 95% confidence interval [0.58–0.82]. Inconclusive limits of the end-SBT BNP were ranging between 66 and 877 pg/mL, a result attesting that BNP was a weak predictor of postextubation distress.

**DISCUSSION**

The present study, performed in 100 patients undergoing SBT for weaning from mechanical ventilation, shows several original findings: 1) a 60-min SBT is associated with significant lung derecruitment, as assessed by transthoracic lung ultrasound; 2) among patients who successfully pass SBT, the derecruitment is greater in patients who develop postextubation distress than in patients who are definitively weaned; 3) in patients who successfully pass the SBT, the derecruitment as assessed by transthoracic ultrasound is associated with significant lung derecruitment, as assessed by transthoracic ultrasound; 4) in patients who successfully pass the SBT, a lung ultrasound score ≤12 at the end of the SBT is highly predictive of postextubation success; 5) in patients who successfully pass SBT, the derecruitment is greater in patients who develop postextubation distress than in patients who are definitively weaned; 6) in patients who successfully pass the SBT, a lung ultrasound score ≤12 at the end of the SBT is highly predictive of postextubation success; 7) in patients who successfully pass the SBT, a lung ultrasound score ≤12 at the end of the SBT is highly predictive of postextubation success.

| Table 2. Spontaneous breathing trial-induced changes in lung ultrasound parameters and B-type natriuretic peptide |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                                 | Overall         | SBT Failure     | SBT Success     | Postextubation  | Postextubation  | Postextubation  |
|                                 | 100 Patients    | 14 Patients     | 86 Patients     | Success         | Distress        |                     |
|                                 | p               |                  |                  | 57 Patients     | 29 Patients     | p                |

LUS, lung ultrasound score; SBT, spontaneous breathing trial; BNP, B-type natriuretic peptide; NS, not significant.

p < .01 for end-SBT vs. before SBT; p < .05; p < .05 for LUS H4 postextubation vs. end-SBT LUS.

p indicates statistical significance between groups. All data are presented as median quartile [first–third].

**Figure 1.** Results of the protocol. MV, mechanical ventilation; COPD, chronic obstructive pulmonary disease; NIV, noninvasive ventilation; T8, eighth thoracic vertebra; LUS, lung ultrasound score; BNP, B-type natriuretic peptide; SBT, spontaneous breathing trial.
predictive of postextubation distress; 5) B-type natriuretic peptide at the end of the SBT is much less accurate than lung ultrasound for predicting postextubation failure.

Such findings suggest that the use of transthoracic ultrasound aimed at assessing lung aeration changes during SBT, a new, easy-to-perform, and noninvasive measurement, may contribute to reducing the occurrence rate of postextubation distress, a clinical condition associated with increased morbidity and mortality (1, 3, 4).

The present study provides compelling evidence that shifting a patient from mechanical ventilation to spontaneous breathing is associated with lung aeration loss. This derecruitment is the result of lung aeration abnormalities persisting at the time of the first SBT. Selection criteria for a weaning trial rely on the assumption that the initial respiratory condition has been sufficiently reversed to allow spontaneous breathing (1, 4, 10). Therefore, the process of weaning from the ventilator is undertaken far before normalization of lung function. Here, it is highly likely that SBT as well as extubation failures result either from an insufficient lung reaeration at the time of SBT and/or a per-trial excessive derecruitment. Transthoracic lung ultrasound offers the unique opportunity to assess regional lung aeration (17, 18, 23, 28). SBT-induced derecruitment was mostly observed in all anterior, lateral, and upper-posterior lung regions. Interestingly, derecruitment was made of partial loss of lung aeration rather than appearance of new consolidation: normally aerated lung regions were transformed into poorly aerated lung regions (normal to B1 or B1 to B2 lines) whereas the transformation of poorly aerated into nonaerated lung regions was rarely observed. This result suggests that prophylactic noninvasive ventilation could prevent such partial derecruitment. At the beginning of SBT, lower and posterior lung regions were already consolidated in more than half of the patients and remained nonaerated at the end of the trial. Very likely, resumption of an active contraction of both diaphragms during the SBT did not increase transpulmonary pressure enough to re-aerate posterior lung regions (29).

It has been shown that shifting a patient from mechanical ventilation to spontaneous breathing is associated with increased cardiac preload and afterload (30–32). In a series of 100 critically ill patients undergoing a SBT, BNP significantly increased during SBT in 14 patients with SBT failure caused by heart failure, whereas patients with postextubation distress had a significantly higher basal BNP than patients with postextubation success (33). The present study also shows significant increases in BNP in patients failing SBT, reflecting an increase in left cardiac filling pressures and suggesting a cardiac participation to SBT failure. The present study also confirms that patients with postextubation distress have a significantly higher basal level of BNP compared to patients successfully extubated. However, because only 15% of patients included in the present study had a history of cardiac failure, basal BNP and the variation of E/Ea during SBT were not discriminating enough to predict SBT failure and postextubation distress in a general population of critically ill patients.

Up to now, indices proposed to predict extubation failure are indirect testimonies of compromised lung aeration, oxygen saturation defect, mental disturbances, hemodynamic instability, and reflect

Figure 2. Lung derecruitment during spontaneous breathing trial (SBT) in a patient with postextubation distress. Lung ultrasound score (LUS) was 16 at the beginning of SBT and increased to 28 at the end of SBT. A_up and A_low correspond to the upper and lower parts of anterior thoracic regions, L_up and L_low to upper and lower parts of lateral thoracic regions, and P_up and P_low to upper and lower parts of posterior thoracic regions. The value displayed in the left and lower corner of each picture corresponds to the pattern of lung aeration characterizing the region: Normal = 0, B1 lines = 1, B2 lines = 2, Consolidation = 3.
physiological compensatory mechanisms, frequency to tidal volume ratio, and tachycardia, that are patient-dependent. The possibility of directly quantifying lung aeration before and at the end of a SBT offers a decisive advantage for predicting postextubation distress because compromised aeration is one of the critical pathophysiological factors. Transthoracic lung ultrasound has several advantages over conventional radiological means for assessing lung aeration: it is reliable and accurate (17, 18, 23), highly reproducible (34), noninvasive, and easily repeatable at the bedside. Several studies have demonstrated that lung ultrasound is accurate for assessing positive end-expiratory pressure and prone position-induced lung recruitment (17, 35–37), lung reaeration following antimicrobial therapy in ventilator-associated and community-acquired pneumonia (18), and lung reaeration associated with resolution of various forms of pulmonary edema (38–44). Although the ultrasound detection of SBT-induced lung derecruitment does not give any indication about the cause of aeration loss, upper airway obstruction, persisting pneumonia, congestive heart failure, aspiration of secretions, cough inefficient to remove excessive bronchial secretions, and muscle weakness as observed in critically ill patients with polyneuropathy, it can be used as a predictor of extubation failure. Patients with an end-SBT LUS <13 can be extubated with a very low risk of extubation failure, whereas patients with an end-SBT LUS >17 are at high risk of extubation failure. An end-SBT between 13 and 17 however, does not allow an accurate prediction of extubation success and failure. It has to be outlined that continuation of lung derecruitment 4 hrs after extubation is predictive of extubation failure.

Rather than using a single LUS cutoff for predicting postextubation distress, using two cutoffs and interval likelihood ratios offers a more clinically relevant approach. Indeed, interval likelihood ratios are not influenced by disease’s prevalence and quantify the increase in knowledge about the risk of postextubation distress that is gained through end-SBT LUS score. This method of analysis results in less distortion and loss of information than choosing a single cutoff and may improve clinical decision making (45). As discussed above, per-SBT derecruitment is essentially made of transformation of normally aerated lung regions into poorly aerated ones, an aeration loss that can be easily reversed and prevented by positive end-expiratory pressure (17). Therefore, in patients who successfully pass the SBT and whose end-SBT is ≥13, the systematic administration of noninvasive ventilation after extubation could be proposed to prevent further derecruitment and postextubation distress. Simultaneously, factors implicated in SBT-induced lung derecruitment, fluid overload, large pleural effusion, lung superinfection, deterioration of cardiac function, accumulation of abundant bronchial secretions, ventilator-induced diaphragmatic dysfunction (46, 47), should be systematically screened and treated when possible.

Limitations

The overall rate of extubation failure was relatively high (29%) as patients who needed rescue noninvasive ventilation after extubation were included in the failure group. The rate of reintubation following extubation (14%) was, however, comparable to what has been reported before (1). Whether patients requiring noninvasive ventilation after extubation should be considered as extubation failure remains unclear. Recently, it has been recommended to classify these patients in an intermediary category called “weaning in progress” (1). In the present study, LUS scores, mortality, and length of stay in the ICU were not different between extubated patients who needed noninvasive ventilation or reintubation. This result pleads in favor of including both categories of patients in the same group.
The results of the present observational study obtained in 100 patients have not been validated prospectively. Therefore, before generalizing the results of the present study, a multicenter randomized interventional study is required to assess the impact of an algorithm based on lung ultrasound score on postextubation distress rate, length of stay, and in ICU-mortality.

The ultrasound method has also intrinsic limitations. Obese patients are frequently difficult to examine because of the thickness of the rib cage’s subcutaneous tissue. The presence of subcutaneous emphysema or large thoracic dressings precludes the propagation of ultrasound beams to the lungs and makes for difficult lung ultrasound examination. Like all techniques of ultrasonography, bedside lung ultrasound can be operator-dependent, however, a high intra- and interobserver reproducibility was reported (18, 28). In the present study, only experienced physicians performed ultrasound examinations. It has been shown that the learning curve to acquire skills in general lung ultrasound ranges from 3 wks to 7 months (48–50) depending on the level of expertise (51).

CONCLUSIONS

Bedside lung ultrasound provides critical information about aeration during a spontaneous breathing trial. Such information is highly relevant for predicting postextubation distress in patients who successfully pass the spontaneous breathing trial because it allows assessment of the common final pathway of extubation failure, i.e., loss of lung aeration, whatever its cause. An end-SBT LUS <13 is predictive of extubation success. An end-SBT LUS >17 is predictive of postextubation distress.

Figure 4. Ability of lung ultrasound score and B-type natriuretic peptide (BNP) measured at the end of spontaneous breathing trial (SBT) to predict postextubation distress. a, Receiving operating characteristic curve showing a cutoff value for lung ultrasound score >14 estimated by maximizing the Youden index with an area under the curve of 0.8667. B, Inconclusive limits of lung ultrasound score measured at the end of the spontaneous breathing trial (dashed area). C, Receiving operating characteristic curve showing a cutoff value for end-SBT BNP >267 estimated by maximizing the Youden index with an area under the curve (AUC) of 0.7. D, Inconclusive limits of end-SBT BNP measured at the end of the spontaneous breathing trial (dashed area).
Table 3. Interval likelihood ratios for the prediction of postextubation distress using lung ultrasound score measured at the end of spontaneous breathing trial

<table>
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<th>End-Spontaneous Breathing Trial Lung Ultrasound Score</th>
<th>Failure Number of Patients</th>
<th>Success Number of Patients</th>
<th>% of Postextubation Distress</th>
<th>Likelihood Ratio</th>
<th>95% Confidence Interval</th>
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