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# Lung aeration loss as a predictor of reintubation using lung ultrasound in mechanically ventilated patients

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## ABSTRACT

Optimal time to wean from mechanical ventilation remains a challenge in most critically ill patients. There have been studies looking at the factors that aid weaning from mechanical ventilation; however the results have been variable. Recent evidence suggests lung ultrasound can predict successful weaning from mechanical ventilation. This study assesses the ability of the lung aeration scoring using LUS to predict successful weaning in critically ill patients This prospective, observational and non-interventional study was performed in a general ICU in a large university hospital over a period of 6 months. We included all patients who needed mechanical ventilation for more than 48 hours (n=50) and were eligible for Spontaneous Breathing Trial. LUS was performed during SBT and lung aeration Scoring was calculated in 12 lung regions. Points were allocated according to the worst ultrasound pattern observed: N (normal lung pattern) = 0, B1 lines (multiple well-defined B lines) =1, B2 lines (multiple coalescent B Lines) = 2, c (consolidation or atelectasis) = 3. Relevant data were collected from patients, including demographic and LUS aeration scoring in a standardized case report form. Patients were divided into two groups: Group 1 and Group 2 based on the failure and success in weaning, respectively. The LUS aeration scoring was applied to both groups to assess the predictability of weaning failure. Lung aeration scores were significantly higher in patients in Group F compared to Group S (p<0.01). The sensitivity, specificity for failed extubation for an LUS score of more than 18 is 88.89 and 86.96 respectively Lung aeration score using lung ultrasound can predict weaning failure in critically ill patients. Our study showed that an LUS score of more than 18 has a good prediction value. However larger randomized controlled trials are required to validate this pilot study.

**Keywords:** lung ultrasound; mechanical ventilation; reintubation; weaning; spontaneous breathing trial.

## INTRODUCTION

Weaning covers the entire process of liberating the patient from mechanical support and from the endotracheal tube, including relevant aspects of terminal care. There is uncertainty about the best methods for conducting this process, which will generally require the cooperation of the patient during the phase of recovery from critical illness. This makes weaning an important clinical issue for patients and clinicians. (1)

Reintubation after extubation is also associated with many complications like re-infection, prolonged length of stay in ICU, cost implication. Therefore, it is essential to correctly decide the exact time for extubation. (2)

The hypothesis of the current study is to consider the lung ultrasound ( LUS) as a good tool in detecting the degree of lung aeration changes during the spontaneous breathing trial (SBT) through a valid LUS score for lung aeration.(3,4) This score is a global picture of lung aeration and can be regularly monitored. If the score increases, it means that the lung aeration decreases.

SBT is considered as a cardiac stress test, and induces cardiac deterioration in the form of a decrease in intrathoracic pressure which augments venous return, impede left ventricular ejection and increase intrathoracic preload volume.(5,6) Also change in lung compliance and neuromuscular weakness during SBT may cause an increase in lung recruitment.

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Lung aeration can be varying between four regions: normal aeration (lung sliding and horizontal A- lines), moderate loss in lung aeration relates to interstitial syndrome, which is a moderate decrease in lung aeration caused by the thickening of interlobular septa, is detected as the presence of multiple and regularly spaced vertical B-lines, severe loss of lung aeration relates to alveolar interstitial syndrome, which is corresponding to presence of liquid into the alveolar space, and lastly complete loss of lung aeration relates to consolidation and or atelectasis.[4]

## Methods

### Patients:

This study was approved by the Ethical committee of Alexandria University of medicine, Alexandria, Egypt, and written informed consent was required from the patient's next of kin for inclusion in the study. Patients were intubated for ≥ 48 hours and are eligible for SBT according to Statement of the Sixth International Consensus Conference on Intensive Care Medicine. [7] Exclusion criteria were patients aged <18 yrs, patients with tracheostomy, paraplegia with a medullar level above T8, cardiac arrhythmias, severe ICU-acquired neuromyopathy, patients with planned prophylactic noninvasive ventilation after extubation, and patients who had previously failed an SBT.

### Protocol:

All patients included in the study were observed for 48 hours after successful spontaneous breathing trial and extubation for the occurrence of reintubation. All patients were applied initially to: 1) Baseline clinical characteristics (Age mean, Sex ratio, Simplified acute physiologic score 2 median), 2) Complete medical history, 3) Complete physical examination, 4) Vital signs (Heart rate, Blood pressure, Temperature, Respiratory rate), 5) Monitoring of oxygen status by pulse oximetry (SPO2) (Mindray 562A) one hour before SBT, during SBT and six hours after SBT using Mindray 562A, 6) Arterial blood gas measure before SBT, 30 and 2 hours after SBT using GEM Premier 3000 device, 7) Transthoracic echocardiogram (ECHO) will be done for all patients included in the study to exclude systolic and diastolic dysfunction. 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 the mitral annulus (Ea) using Doppler tissue imaging.

All patients had LUS examination before weaning, during SBT and 6 hours after extubation as the following: 1) LUS was performed using a 2- to 4- MHZ convex probe as previously described (Mindray DP-3300), 2)LUS was performed by trained investigators during a 10-minutes period, the time required for assessing the whole lung. 3) The same investigator performs the different LUS at each time point of the study. 4) 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, making twelve lung regions, 5) Videos were stored on compact disks, 6) Four ultrasound aeration patterns were defined as the following: Normal aeration (N): presence of lung sliding with A- lines or fewer than two isolated B lines. Moderate loss of lung aeration: multiple well-defined B lines (B1 lines). Severe loss of lung aeration: multiple coalescence B-lines (B2 lines). Lung consolidation (C): the presence of a tissue pattern characterized by dynamic air bronchograms, (Figure 1).

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. After 48 hours the patients will be divided into two groups: Group 1: reintubated patients, Group 2: successfully weaned patients.

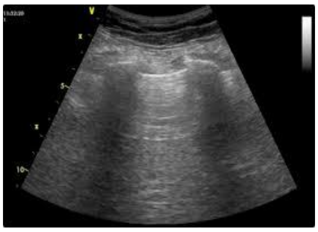
### Outcome measures:

Enrolled Patients were prospectively followed up for the following outcome measures: Primary outcomes (Need for reintubation and mechanical ventilation, Need for non-invasive positive pressure ventilation).

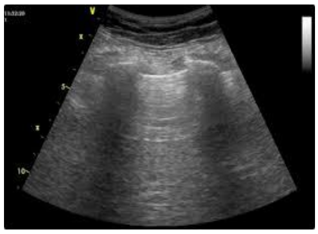
### Secondary outcomes:

ICU length of stay, Duration of mechanical ventilation and 28-days Mortality rate.

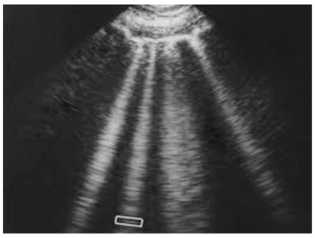
**Figure 1: score of different lung aeration battens**



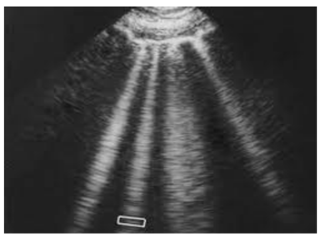
**A lines (score 0)**



**B1- lines (score 1)**



**B2-lines (score 2)**



**Lung consolidation (score 3)**

### Statistical analysis:

A true positive test result correctly predicts reintubation and true negative test result correctly predicts successful weaning from MV. A false positive test result predicts reintubation; however the patient weaned successfully from MV. A false negative test result predicts successful weaning from MV; however the patient reintubated. [8, 9]

The positive likelihood ratio (PLR) indicates the probability of a score resulting in reintubation, divided by the probability of the same score resulting in weaning success. [8, 9]

A negative likelihood ratio indicates the probability of a score resulting in successful weaning, divided by the probability of the same score resulting in weaning failure from MV. A likelihood ratio (LR) of 0.5-2.0 indicates that the parameter is mildly associated with the post-test probability of weaning success or failure. Values for LR of 2.0-5.0 and of 0.3-0.5 correlate with small but potentially important changes in the probability, while Values from 5-10 and 0.1-0.3 correlates with more clinically important changes in the probability. Ratios higher than 10 or lower than 0.1 correlate with the largest changes in the probability.[8, 9]

Positive predictive value (PPV) is the number of patients who had a positive test result and how actually reintubated, and negative predictive value (NPV) is the number of patients who had a negative test result and successfully weaned from MV. A high PPV indicates a strong chance that a person with higher LUS score will reintubated, and a high NPV means that low LUS score will be weaned successfully. [8, 9]

The analysis of receiver operating characteristic curve (ROC curve) allows the ability of an LUS score to discriminate between two groups of patient (those who have been weaned and those who have not), with the advantage of not depending on the cut-off value selected.

Data were fed to the computer using the Predictive Analysis Software (PASW Statistics 18). Continuous variables were expressed by mean ± standard deviation, ordinal variables as median and minimum–maximum, and frequent variables as rates. Comparison between proportions was made using chi-square test comparison between means was made using the F-test; a probability of less than 0.05 was considered significant. [10]

# RESULTS

## Patients:

65 consecutive mechanically ventilated patients were initially recruited in the study, 15 patients were excluded due to a failure of SBT. Fifty Patients were classified into 2 groups according to weaning outcome, and their characteristics are summarized in Table 1. Causes of admission were respiratory failure (52%), cardiovascular failure (33%), trauma (12%) and surgical causes (6%). Patients with past history of respiratory diseases were 24%, and with cardiovascular diseases were 52%. There was no statistically significant difference between both groups regarding sequential organ failure assessment median (5.1±1.7 in group1 compared to 4.7±1.3).

No significant difference in clinical cardiovascular and respiratory variables was detected between both groups before and during the SBT while 6 hours after extubation vital signs were significantly higher in the failed weaning group indicating impending respiratory failure.

Diastolic dysfunction was higher in the failed weaning group which may indicate profound cardiac stress after removal of positive pressure ventilation. The study considered patients with more than 1.5 liters positive balance per day in the last 5 days before SBT. Group 1 had 17 patients with positive fluid balance while group 1 had 4 patients with positive fluid balance.

**Table 1: patient's characteristics**

| | Group 1 (n= 27) | Group 2 (n=23) | P value |
|---|---|---|---|
| *Cause of admission* | | | |
| *Medical disease, n* | 24 | 17 | 0.429 |
| *Surgery, n* | 0 | 3 | 0.09 |
| *Trauma, n* | 4 | 2 | 0.67 |
| *Clinical characteristics* | | | |
| *Age, mean± SD* | 51.89 ± 14.58 | 47.52 ± 14.60 | 0.522 |
| *Sex ratio, male/female* | 14/13 | 14/9 | 0.297 |
| *Pulmonary disease, n (%)* | 6 (22.2%) | 6 (26.1%) | 0.115 |
| *Cardiovascular disease, n (%)* | 17 (63%) | 9 (39.1%) | 0.750 |
| *SOFA score* | 5.1±1.7 | 4.7±1.3 | 0.115 |
| *Vital signs during SBT* | | | |
| *Heart rate* | 91.22 ± 9.58 | 82.52 ± 9.67 | 0.003 |
| *Respiratory rate* | 19.59 ± 2.27 | 16.87 ± 2.69 | <0.001 |
| *Temperature* | 37.49 ± 0.38 | 37.34 ± 0.34 | 0.148 |
| *Mean arterial pressure* | 85.15 ± 9.96 | 94.65 ± 6.66 | <0.001 |
| *Hypoxic index* | | | |
| *during SBT* | 159.26 ± 20.13 | 190.0 ± 21.53 | <0.001 |
| *6 hr after extubation* | 143.50 ± 13.19 | 238.57 ± 37.16 | <0.001 |
| *Positive fluid balance* | 17 (63%) | 4 (17.4%) | 0.001 |
| *Diastolic dysfunction* | 12 (44.4%) | 4 (17.4) | 0.041 |
| *ICU mortality* | 9 (33.3%) | 0 | 0.002 |
| *ICU length of stay* | 17.93 ± 4.40 | 6.35 ± 2.57 | <0.001 |
| *Days on MV* | 9.30 ± 1.79 | 4.26 ± 1.32 | <0.001 |

There was a significant difference between both groups (P=0.001). Secondary outcomes measures (mortality, the length of stay in ICU, days on mechanical ventilation) were significantly higher in weaning failure group compared to weaning success group; it signifies the major impact of extubation failure in morbidity and mortality and cost of management.

### Lung aeration score:

LUS showed a significant difference between both groups; initially, before SBT trial failed weaning group had less aerated lungs compared to successful weaning group (17.67 ± 2.60 versus *10.52* ± 4.29 respectively). During SBT failed weaning group showed an increase in derecruitment and loss of lung aeration, also successful weaned group showed loss of lung aeration but less significantly than weaning failure group. Six hours after extubation, failed weaning group showed some degree of deterioration in the respiratory function and early signs of weaning failure; a significant decrease in the hypoxic index, increase in respiratory and heart rate. These changes were associated with further significant derecruitment in lung aeration (*Table 2).*

Posterior lung regions were already none aerated in most of the patients in both groups; aeration changes observed more in lateral regions and then in the anterior regions.

LUS demonstrates significant changes in lung aeration during SBT in the failed group; a score above 19 shows 100% positive predictive value, 100% specificity for reintubation and positive likelihood ratio > 10. Score more than 18 shows positive likelihood ratio of 6.81. Receiver operating characteristics curve for diagnosis of weaning failure shows the area under the curve of 0.95, *(*Figure 2). Low LUS score also showed high accuracy in excluding weaning failure, since a score of less than 10 illustrates 100% negative predictive value; no patients with a score less than 10 reintubated, negative likelihood ratio was 0. Score less than 11 showed a negative likelihood ratio of 0.06, (*Table 3*). Therefore, it is concluded that score above 18 and score less than 11 have high sensitivity and specificity to predict weaning outcomes. Score in between showed less predictive value and inconclusive in terms of weaning outcomes. Non-invasive ventilation was used in 15 patients to treat post extubation stress. Five patients end up by reintubation and ten patients successfully weaned. The mean score of patients treated with NIV were 17 and 15 in group 1 and group 2 respectively.

## Discussion

The study presents an evidence of using LUS as a bedside tool to help intensivists in their weaning decision. The study shows that LUS can predict weaning success or failure through detection of aeration changes after removal of positive pressure ventilation during SBT.

**Table 2: Comparison between two studied groups according to lung ultrasound score.**

| LUS score | Weaning after 48 hr | | P |
|---|---|---|---|
| | **Group 1 (n = 27)** | **Group 2 (n = 23)** | |
| **During MV** | | | |
| Min. – Max. | 10.0 – 21.0 | 2.0 – 18.0 | |
| Mean ± SD | 17.67 ± 2.60 | 10.52 ± 4.29 | <0.001 |
| Median | 19.0 | 11.0 | |
| **During SBT** | | | |
| Min. – Max. | 11.0-25.0 | 3.0 - 19.0 | |
| Mean ± SD | 20.47 ± 2.75 | 12.52 ± 4.61 | <0.001* |
| Median | 21.0 | 13.0 | |
| **6 hr after extubation** | | | |
| Min. – Max. | 12.0-26.0 | 3.0-20.0 | |
| Mean ± SD | 21.41 ± 2.86 | 12.65 ± 4.70 | <0.001* |
| Median | 22.0 | 13.0 | |

**Table 3: Diagnostic accuracy of different LUS scores.**

| LUS score 30 min from SBT | Weaning failure | Weaning success | False +ve | False –ve | Sensitivity | specificity | PPV | NPV | Likelihood Ratio | Accuracy |
|---|---|---|---|---|---|---|---|---|---|---|
| ≥19 | 21 | 23 | 0 | 6 | 77% | 100% | 100% | 79% | 0.2->10 | **88%** |
| 18 | 24 | 20 | 3 | 3 | 88.8% | 86.9% | 88.8% | 86.8% | 0.13-6.81 | **88%** |
| 17 | 25 | 19 | 4 | 2 | 92% | 82% | 86% | 90% | 0.08-5.3 | **88%** |
| 16 | 26 | 18 | 4 | 2 | 92% | 81% | 86% | 90% | 0.08-5.1 | **88%** |
| 11->15 | 26 | 14 | 9 | 1 | 96% | 60% | 74% | 93% | 0.06-2.4 | **88%** |
| ≤10 | 27 | 19 | 14 | 0 | 100% | 39% | 65% | 100% | 0-1.6 | **72%** |

**PPV**: positive predictive value**; NPV:** negative predictive value

A Predictive parameter for weaning is a criterion that evaluate a given physiological aspect of respiratory failure, with the objective of distinguishing between patients who will successfully weaned from MV and those who will fail the weaning process.[11] Substantial literature exists about weaning predictors and outcomes; most being inaccurate in predicting extubation outcome. [11] To predict extubation failure is essential, as both delayed and failed extubation have detrimental consequences such as prolonged ventilation and ICU stay, need for tracheostomy, increased cost of treatment and mortality. [12-14]

The study hypothesis was built on the assumption that LUS can accurately detect extravascular lung water and also quantify the degree of aeration loss. Studies illustrates that LUS can detect extravascular lung water accurately, since they compared LUS result with the result of PICCO and pulmonary artery catheter and it was closely similar.[15,16]

CT is the gold stander method for measurement of lung aeration changes; however it requires transportation of patients outside ICU and exposes patients to high radiation hazards. [17]There are different lung ultrasound patterns corresponding to different lung aeration degrees. In a study by Bouhemad et al, they examined the accuracy of LUS in detection of the efficacy of antimicrobials in treatment of VAP and occurrence of lung reaeration, the results confirmed the ability of LUS to detect aeration changes. [3] Another study showed significant reduction of the B lines by LUS after hemodialysis [18]

This study provides evidence that SBT is associated with per-trial derecruitment. Weaning failure patients have much loss of aeration than successfully weaning patients. LUS provide a chance for assessing each lung regions in details, most of aeration loss was observed in anterior and lateral regions, posterior regions were already none aerated.

Non-invasive ventilation was used in patients who could tolerate it. We considered patients who weaned through NIV as a successful weaning; mean scores of patients used NIV and weaned were 11 to 17. These is the score with low sensitivity and specificity in predicting weaning outcomes; therefore, therapeutics interventions like NIV or diuretics could be trailed in patients with score between 13 and 17 to prevent further aeration loss.

Treatment of many critical ill patients requires volume resuscitation at the early phases of the illness. Institution of MV itself commonly causes hypotension due to reduced venous return. [19] In a previous study demonstrated that negative fluid balance during weaning improves survival in septic shock patients.[19] it is advisable that fluid administered during resuscitation in early phases of the disease must be retrieved before attempt to wean from MV.

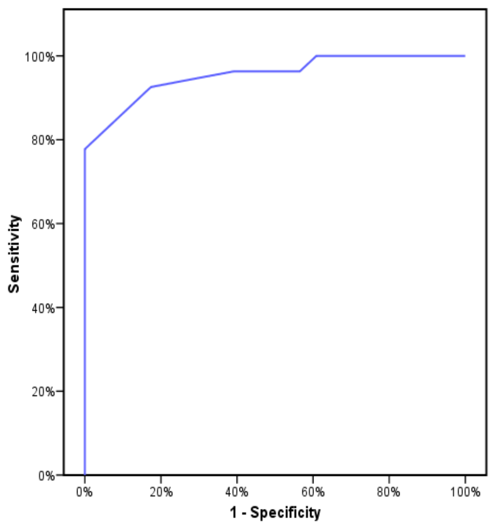
We observed in our study that patients with positive fluid balance (inputs> outputs) in the last five days before attempt weaning were more likely to failed weaning (63% of failed weaning patients had positive fluid balance compared to 17% in the successful group). This results match with a result published in a study where positive fluid balance in the 24, 48, and 72 hours and cumulative balance since hospital admission were significantly greater in weaning failure group than successful weaning group.[20]

Weaning from MV imposes additional work on the cardiovascular system and can provoke or unmask left ventricular diastolic dysfunction with consecutive pulmonary oedema or systolic dysfunction with inadequate increase in cardiac output. [21] Left ventricular diastolic dysfunction is characterized by decrease myocardial compliance for variety of reasons:

coronary artery disease, myocardial hypertrophy, age, acidosis and hypoxia.[21] The number of patients in the failed group in the current study diagnosed with diastolic dysfunction before SBT was outweighed the number of their counterparts in successful group. This may contribute to increase risk of weaning failure.

However, LUS can detect aeration changes during SBT; it cannot detect the cause of derecruitment. Recognizing the causes of weaning failure, like diastolic dysfunction and positive fluid balance, and sorting them out will increase the chances of weaning success. It is crucial also to assess the upper airway patency and protection before removal of the tub.

**Figure 2: ROC curve for LUS 30min from SBT for diagnosing weaning failure.**




### Limitations:

Also the study were conducted prospectively on 50 consecutive patients, most of them were admitted due to medical reasons. This can affect the percentage of weaning outcomes since surgical patients known to be easily weaned from mechanical ventilation. [22] The number of failed weaning patients outweighed the number of successfully weaned ones.

The study conducted on 50 patients showed high predictive value for LUS to predict weaning outcomes, the LUS score needs to be validated through multicenter randomized control study. Bedside LUS is operator dependant and there is variability in the results. In the current study only one trained intensive care physician performed the examination; therefore, we avoided personal variability in the results. Poor LUS view is a problem especially in obese patients and COPD patients, since thick thoracic wall and subcutaneous emphysema stand against the ultrasound beams to be propagated appropriately.

## Conclusion

Lung ultrasound is an appropriate tool to assess aeration changes during SBT. Score more than 19 is highly predictive for weaning failure, and score less than 11 is highly predictive of weaning success. Score between 11 and 19 inconclusive in weaning outcomes, NIV can be tried to avoid further aeration loss.

## Conflict of Interests

Authors declare that there is no conflict of interests regarding the publication of this paper.

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