Combined Use of Lung and Heart Ultrasound: Possible Predictors of Weaning Failure of Ventilated Patients

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ABSTRACT

Background: Lung ultrasonography (LUS) and transthoracic echocardiography (TTE) are reliable tools to predict weaning failure.

Objectives: This study aimed to identify the predictive value of the combined use of pulmonary ultrasonography and TTE in weaning failure.

Patients and Methods: Our work was a prospective cohort observational study. LUS and TTE were performed before (basal) and 30 min after the trial of spontaneous breathing (SBT) (120 min) for fifty patients of both sexes, aged more than 18 years old and had postoperative mechanical ventilation. SBT was done using pressure support (PS) mode (PEEP 5 cmH2O, PS 7 cmH2O, and FIO2 0.5).

Results: LUS score was significantly increased after SBT in group WF (weaning failure) [21±2.7 vs group WS (weaning success) 15.2±2.9, p-value < 0.001]. E/A and E/Ea ratio had a significant increase after SBT in group WF [1.4±0.3 vs group WS 1.2 ± 0.2., p = 0.002], group WF [15.7±5.4 vs group WS 8.4±2.5, p<0.001] respectively. The LUS score and E/Ea ratio after SBT had a high value of the area under the curve in the analysis of the ROC curve (0.917 & 0.904) respectively. The combined use of the LUS score and E/Ea ratio had a high predictive value in weaning failure with 94.1% specificity, and 96.2% positive predictive value. No difference regarding EF, CVP, and fluid balance.

Conclusion: In postoperative mechanically ventilated patients, the combination of LUS and TTE was highly predictive of weaning failure.

Keywords: Lung ultrasound score, Echocardiography, Weaning.

INTRODUCTION

The weaning phase is crucial in mechanical ventilation and contributes as much as 50% of the gross duration. The trial of spontaneous breathing (SBT) significantly impacts lung aeration and hemodynamics [(1)]. Weaning failure concludes two concepts of failure; the failure to pass SBT as well as reintubation within the early 48 h of extubation (extubation failure) [(2)]. Since increased morbidity, mortality, and high cost of care are associated with weaning failure and prolonged ventilation, prediction of this failure and understanding the underlying cause may be important in prognosis [(3, 4)].

Cardiogenic pulmonary edema is considered one of the most convincing explanations for weaning failure, which could be attributed to the increase of the left ventricle (LV) filling pressure [(3)]. Recently, pulmonary edema of cardiac origin could be detected by lung ultrasound and transthoracic echocardiography (TTE) [(4)].

Lung ultrasound could detect extra-vascular lung water (EVLW) through the assessment of B-lines, which substitute A-lines in this condition. Lately, B-lines equal to or more than 6 on the four anterior segments during SBT have been suggested to be a predictor of weaning-induced pulmonary edema (WIPO) [(5, 6)].

Nowadays, transthoracic echocardiography (TTE) is a widespread tool in intensive care [(6)]. It has been used as a weaning failure predictor by estimation of the left ventricle (LV) filling pressure through detecting an increase in the early maximum mitral flow velocity (E wave) / the late maximum mitral flow velocity (A wave) ratio and estimation of the early velocity of mitral annular displacement (Ea wave) using tissue Doppler imaging (TDI) [(7)].

Some previous studies used LUS score and TTE as isolated predictors of weaning failure [(3, 5)]. We hypothesized that the combined use of LUS and TTE is of high predictive value in the weaning failure.

PATIENTS AND METHODS

Between May 2020 and April 2022, this prospective cohort observational study was performed.

A total of 50 patients of both sexes over the age of 18 were considered eligible. They were candidates for the 1st SBT (120 min) after receiving postoperative mechanical ventilation for 48 hours or more. SBT was done using pressure support mode (PS) (PEEP 5 cmH2O, PS 7 cmH2O, and FIO2 0.5). The start of the trial of spontaneous breathing was based on the decision of the treating intensivist and every patient was examined by LUS & TTE before and 30 min after the trial.

Criteria of exclusion: Patients having previous SBT failure, active neuromuscular disease, history of significant COPD, pneumothorax, pleural effusion, ejection fraction < 50% at enrollment, BMI > 35, pregnancy, and tracheostomy.

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Lung ultrasound examination:
LUS was performed by only one trained physician using a **linear transducer (frequency 3.2–11.2 MHz) (Mindray portable ultrasound machine, model Z60, CHINA).**

Each lung was divided through the anterior and the posterior axillary lines into anterior, lateral, and posterior aspects, which were further subdivided into upper and lower segments by horizontal lines. So, six segments were scanned for each lung [8].

Each of the total twelve lung segments may have one of the following four LUS scores.

- **Score 0:** Normal lung recruitment, (Horizontal artifacts (A-line) or (B-line ≤ 2))
- **Score 1:** Moderate lung decruitment, (Multiple regularly or irregularly spaced B-line)
- **Score 2:** Severe lung decruitment, (Multiple confluent B-lines)
- **Score 3:** Complete lung decruitment, (Lung hepatization or consolidation)

For each lung segment, points were given depending on the worst ultrasound pattern seen. The total LUS score was calculated by adding the scores from the anterior, lateral, and posterior segments, which are ranged from 0-36.

Mitral Doppler study:
All the examinations were done by a cardiologist who is an expert in TTE, the examination was done using **3Sc transducer (GE Healthcare ultrasound system, Vivid T8, CHINA).** Initially, pulsed wave Doppler was used to measure the transmitral flow velocity. E wave and A wave were measured, and the E/A ratio was calculated. After that, the Ea wave was measured with TDI, and the E/Ea ratio was calculated. Lastly, the systolic dysfunction of LV was evaluated by the eye-ball assessment method.

Grouping:
Weaning outcomes included weaning success and weaning failure, so depending on the outcome, we had two groups: Group (**WS**): weaning success & Group (**WF**): weaning failure. Weaning failure may be either SBT failure or extubation failure. **Extubation failure** occurs 48 h after extubation by reintubation, non-invasive mechanical ventilation, or death.

Data collection
Demographic data (age, sex, BMI), hemoglobin, platelets, white blood cells (WBCs), duration of mechanical ventilation, non-invasive mean blood pressure (BP), heart rate (HR), respiratory rate (RR), oxygen saturation (spo2), and SAPS (simplified acute physiology score), were all recorded as baseline data (on admission).

Global LUS score, E/A ratio, E/Ea ratio, ejection fraction (EF), central venous pressure (CVP), and fluid balance, were all recorded just before and 30 Min after SBT.

Ethical considerations:
This study was performed at Mansoura University Hospital after getting approval from The Institutional Research Board, code number: (M.D.20.04.308). The Pan-African Clinical Trial Registration system registered our study protocol with (reference number PACTR 202011718030425). The work was conducted in accordance with the World Medical Association's code of ethics (Declaration of Helsinki) for human studies.

The person in charge of making decisions on the patient's behalf provided informed written consent.

Statistical analysis
Entering and analysis of the data was done using SPSS (Statistical Package for Social Sciences) version 23. Numbers and percentages were used to illustrate the qualitative data and the chi-square test was used when comparing groups. The quantitative data were displayed as means ± SD or medians (range) according to the Shapiro-Wilk test for normality. Variables with normal distribution were compared between groups through an independent sample t-test, whereas the paired sample t-test was used to compare within groups. Variables with non-normal distribution were compared between groups by using the Mann-Whitney test, while the Wilcoxon signed ranks test was used to compare within the groups. To describe the predictive accuracy and define the cutoff point for the most sensitive parameters, the area under the receiver operating characteristic (ROC) curve was determined. Predictive values of screening tests were calculated according to the following formulas**:** PPV (Positive predictive value) = TP (true positive)/ (TP + FP (false negative)) and NPV (negative predictive value) = TN (true negative)/ (TN + FN (false negative)). P. value ≤ 0.05" was considered statistically significant. During the study period between May 2020 and April 2022, the postoperative intensive care unit (I.C.U.) received 250 mechanically ventilated patients. There were inclusion and exclusion criteria utilized, and 50 patients were included in the study to predict weaning failure.

RESULTS
250 mechanically ventilated patients were admitted to the postoperative ICU during the study period. The study included fifty patients after excluding those who did not meet the inclusion criteria. Thirty-three patients succeeded in the weaning trial and 17 failed in the weaning trial. Eleven patients in the failure group had extubation failure and 6 had SBT failure. The extubation

failure group included 7 patients who needed reintubation within 48 h, and 4 patients died (Fig. 1)

We found no statistical significance regarding patients' demographics and basal characteristics between group WS and WF (Table 1). When comparing the groups in terms of fluid balance and CVP, no statistical significance was found, whereas the LUS score in group WF was significantly higher than in group WS (P. value <0.001) (Table 2).

Regarding patients' echocardiographic data (Table 3), After SBT, the value of E/A ratio increased significantly within both groups (P. value <0.001). Also, it was increased significantly in group WF compared to group WS, before and after the trial (P. value =0.037) and (P. value =0.002) respectively.

Ea-wave showed a significant increase after SBT only within group WS (P.value < 0.001) while no change within group WF, however, it was significantly lower in group WF, before and after SBT, compared to group WS (P. value =0.005) and (P. value <0.001) respectively. After SBT, the E/Ea ratio in group WF increased significantly (P < 0.001), whereas there was no change or a slight decrease in group WS, and so, this ratio was significantly higher in group WF than in group WS (P < 0.001). EF had no change, before and after SBT, in both groups and was comparable between both groups.

The potential of the E/Ea ratio, E/A ratio, and LUS score as predictors of weaning failure was evaluated using ROC curve analysis. (Table 4) and (Fig. 2)

The basal lung ultrasound score had an area under the ROC curve (AUC) of 0.900 and (P value < 0.001), as a predictor of weaning failure, with a cutoff value of 16.5 (78.8% sensitivity and 88.2% specificity with 92.9 % PPV and 68.2 % NPV), while LUS score 30 min after SBT had highest AUC 0.917 (P value <0.001) with a cut-off value of 18.5 (81.8% sensitivity and 82.4% specificity with 90% PPV and 70 % NPV).

E/A ratio before SBT had the lowest AUC 0.701 (P =0.021) with a cut-off value of 1.2 (78.8% sensitivity and 64.7% specificity with 81.3 % PPV and 61.1 % NPV), while the AUC for the E/A ratio 30 minutes after SBT was 0.783 (P value < 0.001) with a cutoff value of 1.4 (84.8% sensitivity and 64.7% specificity with PPV 82.4 % and NPV 68.8 %).

E/Ea ratio before SBT had AUC 0.756 (P =0.003) with a cut-off value of 10.6 (81.8% sensitivity and 70.6% specificity with PPV 84.4 % and NPV 66.7 %), while the E/Ea ratio 30 minutes after SBT had a high area under the curve of 0.904 (P value < 0.001) and a cut-off value of 12.8, (93.9% sensitivity and 76.5% specificity with 88.2 % PPV and 81.3 % NPV). The sensitivity, specificity, PPV, and NPV of the combined LUS score and E/Ea ratio (30 min after the trial) were 75.8%, 94.1%, 96.2%, and 66.7% respectively.

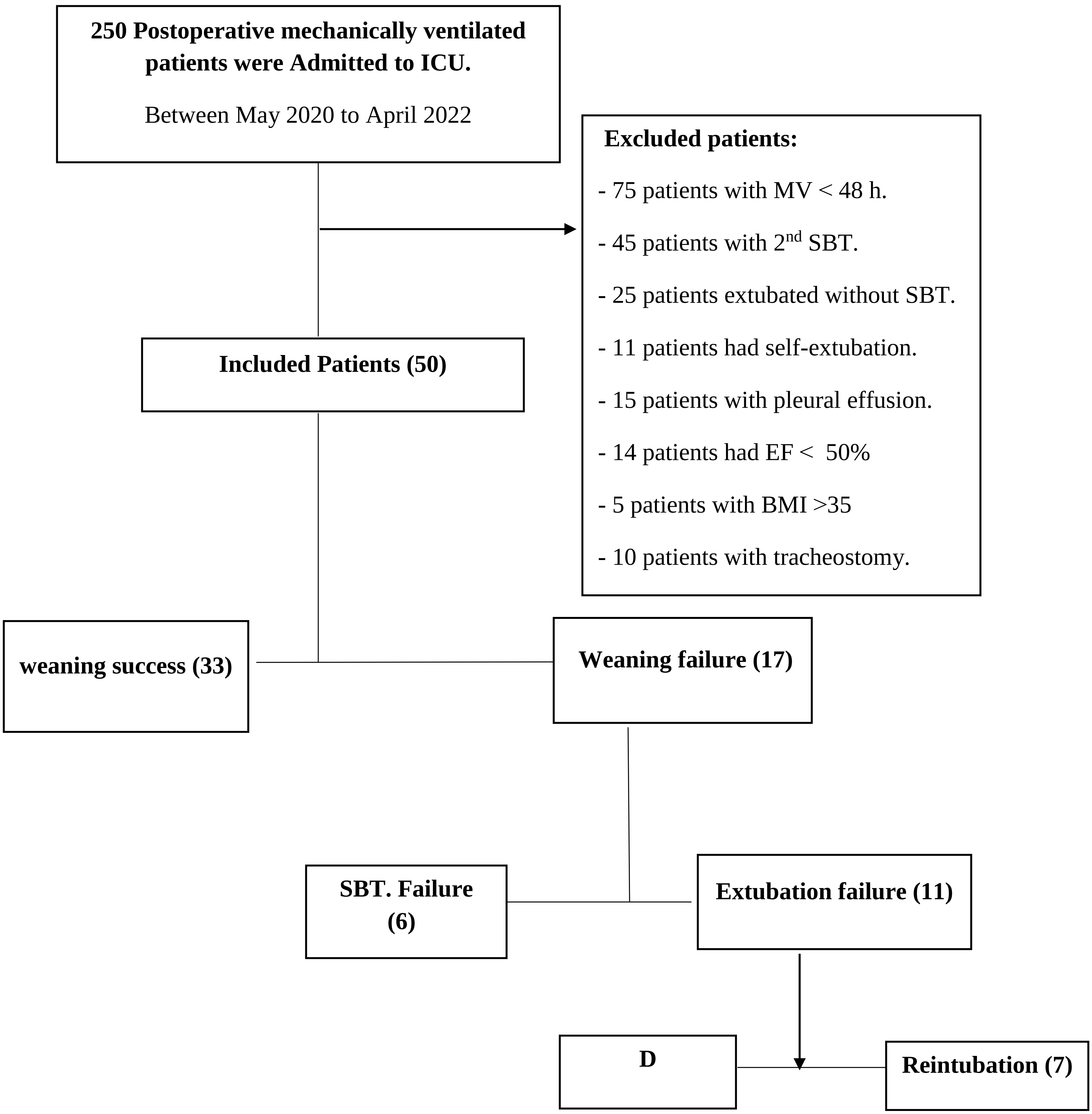


Figure (1): CONSORT flow diagram of patients participating in the study.

Table (1): Patients' demographics and basal characteristics

Variable	Group WS (N=33)	Group WF (N=17)	P-value
Age (years)	54±12.1	55.7±14.5	p=0.7
Gender (M/F)	(17/16)	(8/9)	p=0.8
BMI (Kg/ m^2)	21.4±2.5	20.5±2.8	p=0.2
Hemoglobin (g/dl)	10.2±1.2	10.8±1.4	p=0.1
Platelets (10^3/ul)	284.8±7.2	298.6±9.4	p=0.5
WBCs (10^3/ul)	8.7±1.3	8.3±1.1	p=0.3
Duration of MV (days)	4.7±1.6	5.5±1.6	p=0.08
SAPS II score	55.6±12.3	54.2±13.5	p=0.7
MBP (mmHg)	72.3±7.5	68.5±7	p=0.09
HR (bpm)	85±13.1	83.5±12.4	p=0.7
RR (breath/min)	20.4±2.7	20.5±3.6	p=0.9
SPO_2	97.5±1.3	97.3±1.4	p=0.7

All data were expressed as mean ± SD except gender as number and percentage. P-value ≤ 0.05 is considered significant. **WS:** weaning success, **WF**: weaning failure**, BMI**: Body mass index, **WBCs**: white blood cells, **MV**: mechanical ventilation, **HR:** heart rate, **SAPS II score**: simplified acute physiology score, **MBP**: mean blood pressure, RR: respiratory rate, **SPO2**: peripheral oxygen saturation.

Table (2): The studied group's fluid balance, CVP, and Lung ultrasound scores

Variable	Group WS (N=33)	Group WF (N=17)	P.value
Fluid balance:			
- Basal	390 (-450, 791)	400 (-400, 1100)	p=0.5
- 30 min after SBT	2400 (1450, 3260)	2400 (1400, 6100)	p=0.9
CVP:			
- Basal	7.7±1.8	8±2.2	p=0.6
- 30 min after SBT	9.6±1.6	10.5±1.8	p=0.1
LUS score:			
- Basal	13.7±3	19±2.3	**p<0.001**
- 30 min after SBT	15.2±2.9	21±2.7	**p<0.001**

All quantitative measures were expressed as mean ±SD except fluid balance as median (range), P-value < 0.05 is considered significant, **WS:** weaning success, **WF**: weaning failure, **LUS:** lung ultrasound, **CVP**: central venous pressure, **SBT**: spontaneous breathing trial.

Table (3): Echocardiographic data of the studied groups

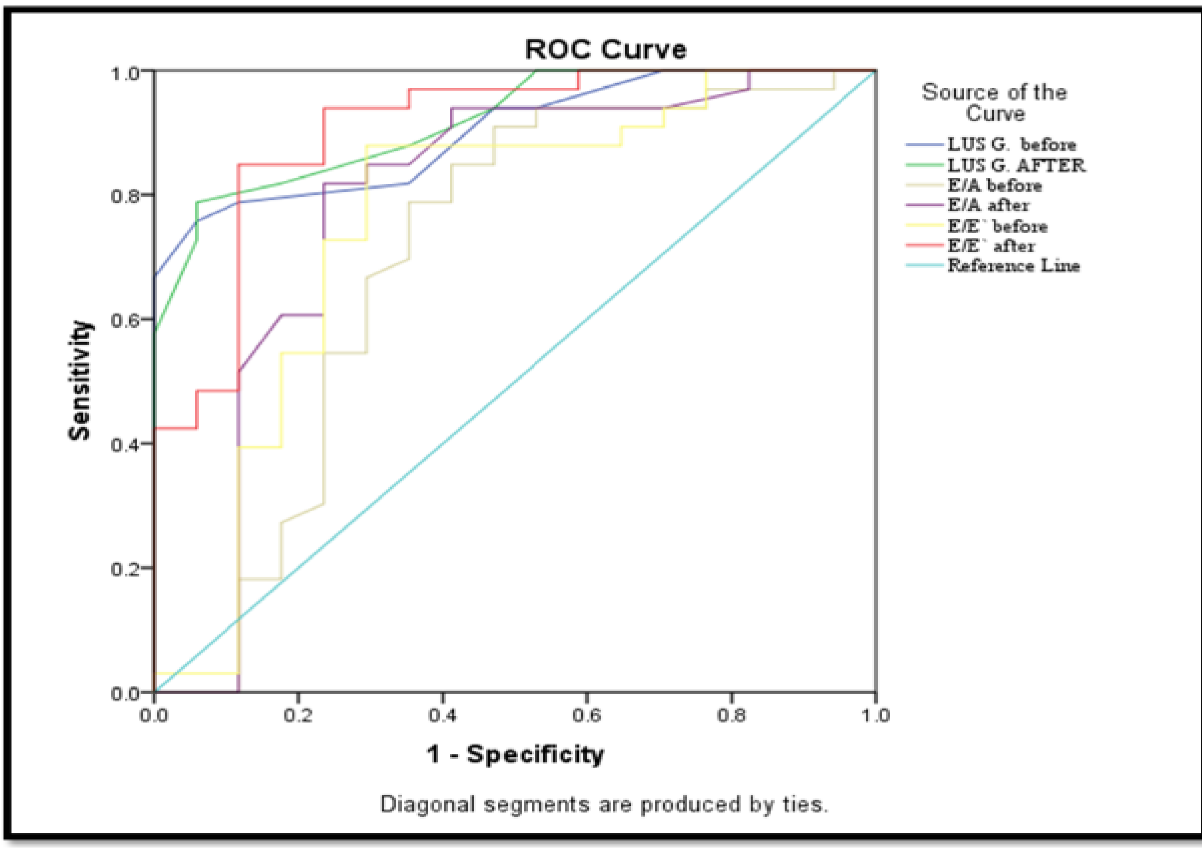
Variable	Group WS (N=33)	Group WF (N=17)	P-value
E/A ratio			
-Basal	1.1±0.2	1.2±0.2	**p=0.037**
- 30 min after SBT	1.2±0.2	1.4±0.3	**p=0.002**
Ea wave (cm/sec)			
-Basal	8.8±2.7	6.6±1.7	**p=0.005**
- 30 min after SBT	11.2±3.5	6.6±1.7	**p<0.001**
E/ Ea ratio			
-Basal	9.3±2.2	13.1±4.6	**p<0.001**
- 30 min after SBT	8.4±2.5	15.7±5.4	**p<0.001**
EF			
-Basal	58.6±7.2	59.1±8.2	p=0.8
- 30 min after SBT	58.4±7.2	59.1±8.3	p=0.8

All data expressed as mean± SD, P-value < 0.05 is considered significant. **WS:** weaning success, **WF**: weaning failure, **E wave**: Peak velocity of early mitral flow (m/sec), **A wave**: Peak velocity of late mitral flow (m/sec), **Ea wave**: early diastolic of components of annular velocities (cm/sec), **E/A ratio**: Ratio between peak velocity of early and late mitral flow, **E/ Ea ratio**: Ratio between Peak velocity of early mitral flow and early diastolic of components of annular velocities, **EF**: Ejection fraction, **SBT**: spontaneous breathing trial.

Table (4): Results of the ROC CURVE analysis of potential predictors

Variable	AUC	p-value	95% CI	Cut-off	Sensitivity	Specificity	PPV	NPV
LUS score - Before SBT	0.900	<0.001	0.819-0.982	16.5	78.8%	88.2%	92.9%	68.2%
- 30 min after SBT	0.917	<0.001	0.844-0.99	18.5	81.8%	82.4%	90%	70%
E/ A ratio - Before SBT	0.701	0.021	0.523-0.878	1.2	78.8%	64.7%	81.3%	61.1%
- 30 min after SBT	0.783	0.001	0.624-0.943	1.4	84.8%	64.7%	82.4%	68.8%
E/ Ea ratio - Before SBT	0.756	0.003	0.594-0.917	10.6	81.8%	70.6%	84.4%	66.7%
- 30 min after SBT	0.904	<0.001	0.811-0.997	12.8	93.9%	76.5%	88.2%	81.3%
Combined lung ultrasound score and E/Ea ratio after SBT.					75.8%	94.1%	96.2%	66.7%

P-value < 0.05 is considered significant, **AUC:** area under the curve, **ROC:** receiver operating characteristic, **SBT**: spontaneous breathing trial, **LUS:** lung ultrasound, **PPV:** positive predictive value, **NPV:** negative predictive value.



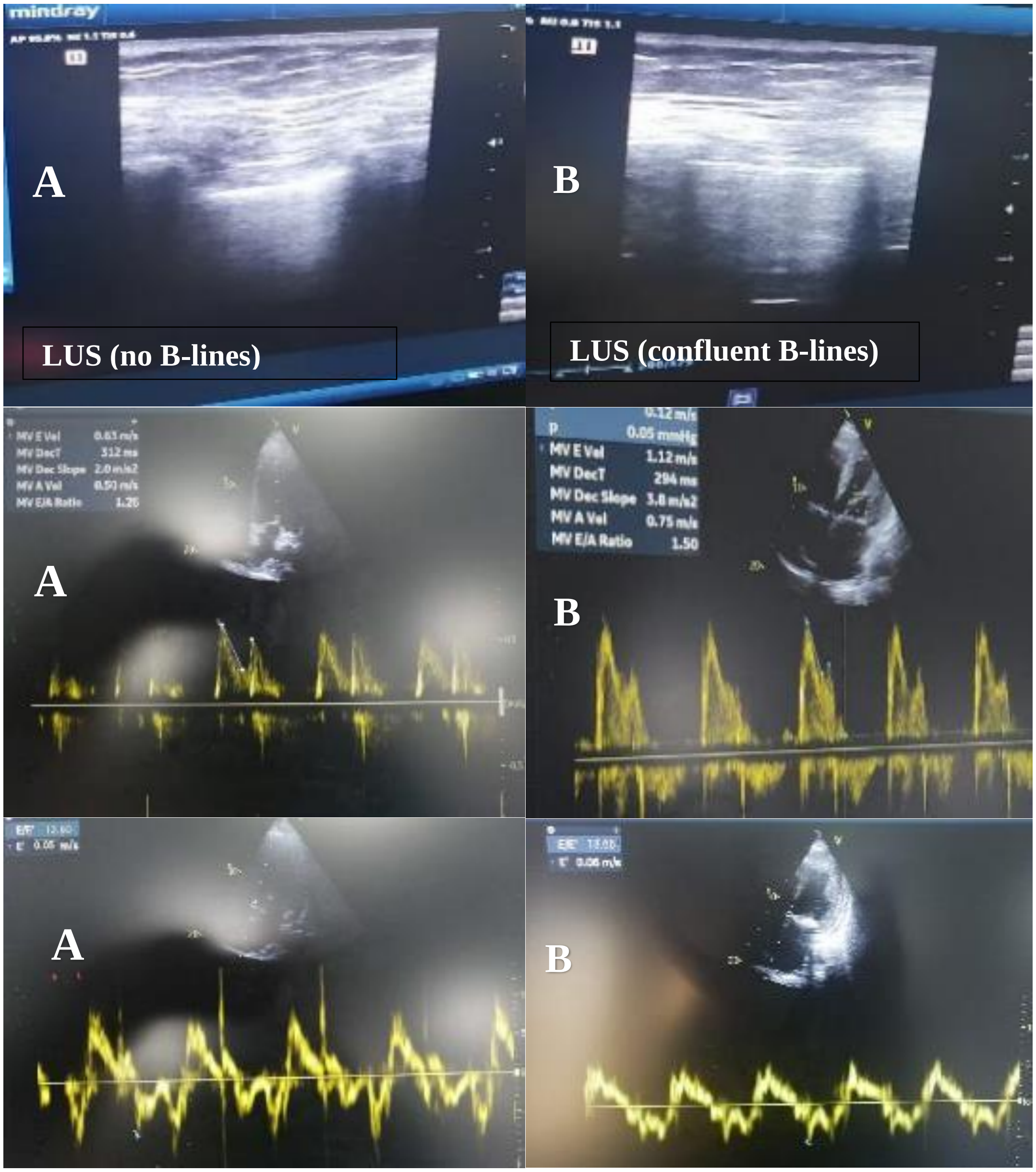


Figure (3): There was an increase of B-lines, E/A ratio, and E/Ea ratio after SBT in the failure group.
(A): show (no B-lines), E/A ratio was (**1.26**), and E/Ea ratio was (**12.60**), **before SBT**.
(B): show (confluent B-lines), increase of E/A ratio (**1.50**), and E/Ea ratio (**18.66**), **after SBT.**

DISCUSSION

Our study demonstrated that the failure rate of weaning from mechanical ventilation was 34% and the predictive values of the combined use of LUS score and E/Ea ratio (30 min after SBT) were 75.8% sensitivity, 94.1% specificity, 96.2% PPV, and 66.7% NPV, respectively. Furthermore, the LUS score, E/Ea ratio, and E/A ratio in group WF were significantly higher than in group WS, although the ejection fraction (EF) revealed no statistically significant difference between the two groups. Additionally, LUS score and E/Ea ratio after SBT had the greatest AUC in the ROC curve for potential predictors of weaning failure (0.917 & 0.904). Weaning causes lung derecruitment as shown by the findings of the recent study, where the LUS score was significantly lower in group WS [13.7±3 (basal) vs 15.2±2.9 (after SBT) (P < 0.001)] than in group WF [19±2.3 (basal) vs 21±2.7 (after SBT) (P < 0.001)]. This is consistent with **Riddhi *et al.*** [9] who stated that the successful group had a lower LUS score (15.06 ± 2.16) vs (16.12 ± 2.17) (P < 0.001) before and after the SBT than the failure group (17.44 ± 2.59) vs (19.85 ± 2.56) (P < 0.001). Likewise, **Bouhemad *et al.*** [7] showed that LUS can predict weaning outcomes, with the failure group having a significantly higher LUS score (median [IQR]) (20.5 [17–23]) than the successful group (16 [13–18]) (P=0.0014) at the end of SBT. On the other hand, **Ana *et al.*** [10] revealed that LUS is a non-reliable predictor of weaning failure, with a sensitivity 47%, specificity 64%, PPV 25%, and NPV 82%. This difference could be attributed to T-tube as a technique of weaning, as well as the assessment approach for B-lines in their study (the anterior thoracic surface divided into four sections), which differed from ours (12 zones approach).

Weaning is a stressful condition, like exercise, and has the same effects on the cardiovascular system, which could be detected using TTE [11]. Following the weaning trial, we evaluated E/A ratio, Ea wave, and E/Ea ratio, and as indicators of diastolic dysfunction based upon the most recent guidelines for grading LV diastolic function published by the American Society of Echocardiography [12]. In respect of the **E/A ratio**, group WF had a significantly higher E/A ratio [(1.2 ± 0.2 versus 1.1 ± 0.2., (P.value <0.037) (basal) and (1.4±0.3 versus 1.2 ± 0.2 (P.value <0.002) (after SBT)] than group WS, which was consistent with that of **Mayo *et al.***[4] who reported in a review article for evaluation of lung, pleura, heart and diaphragm using ultrasound during the weaning process, that the E/A ratio increased during and after SBT. Interestingly after SBT, **Caille *et al.*** [13] reported a significant increase in the E/A ratio (median [IQR]) 0.94 (0.82–1.05) vs 1.00 (0.88–1.15) (P<0.003) through the performance of TTE just before SBT and 30-min after. In contrast, **Amarja *et al.*** [14] showed that the E/A ratio increased insignificantly after SBT in a study of 161 patients. This could be because the echocardiography was performed pre- and six hours post-extubation rather than the current pre and 30 min after SBT. Likewise, **soummer *et al*.** [15] found no statistical significance in the E/A ratio between the success and failure ones, which could be attributable to the different weaning methods used, which was T-tubes.

In the current study, we used medial mitral valve annulus velocity (Ea wave) because the expansion of the lung during controlled mechanical ventilation may confuse the penetration of the ultrasound beams into the lateral annulus. The recent study found that **Ea wave** was significantly lower in group WF (6.6±1.7 vs 8.8±2.7., p=0.005 (basal), 6.6±1.7 vs 11.2±3.5., p<0.001 (After SBT)] than in group WS that is also consistent with the findings of **Moschietto *et al.*** [11] who performed ECHO for 68 patients before and 10 min after the SBT and found that Ea wave after SBT was increased significantly in the successful group (median [IQR]) (10 (8 - 12)) than in the failure one (7 (6 - 8)) (P < 0.0003)**.** Additionally, only the successful group showed a significant rise in Ea wave [(8.8±2.7) vs (11.2±3.5), P value <0.001], even though and after SBT, the failure group showed no change [(6.6±1.7) vs (6.6±1.7), P=0.2]. **Ha *et al.*** [12] stated that the weaning trial is like exercise and thus increases the Ea velocity in healthy people, whereas the Ea wave did not change in patients of diastolic dysfunction**.** On contrary to the recent study, **Tongyoo *et al.*** [13] declared that the success and failure groups differed insignificantly considering Ea wave [M (6.8 ± 2.8) vs (6.4 ± 3.9), P.value 0.67respectively]. This could be related to the different types of study populations who were acute respiratory failure patients with more than 72 h of mechanical ventilation.

Higher **E/Ea** ratios are associated with weaning failure. This is consistent with recent guidelines for diagnosing LV dysfunction and the fact that during the weaning, there is an increase of the venous return to the LV, which cannot be compensated by the poorly functioning LV, resulting in an increased E/Ea ratio [6]. In line with our findings, **Sanfilippo *et al.*** [17] and **de Meirelles *et al.*** [18] conducted a meta-analysis and a systematic review to evaluate the role of diastolic dysfunction in the prediction of weaning failure, both reported that higher E/Ea ratio was associated with weaning failure.

Regarding **LVEF**, we observed no significant changes between the success and failure groups [58.6±7.2 vs 59.1±8.2, p=0.8, respectively]. This is consistent with ***Zapata's et al.*** [19](18) findings of no significant differences in LVEF at the end of the SBT [(57 ± 9) (49 ± 14)] and supported by **Dres *et al.***[20] and **Goudelin *et al.***[21]. **Sanfilippo *et al.*** [17] found no correlation between weaning failure and LVEF in another meta-analysis. We may clarify that the LVEF of the majority of patients complaining of heart failure is normal, and the associated congestion is attributed more to the ventricle's diastolic function than its systolic function [9]**.** There was no statistical significance between group WS and group WF considering fluid balance and CVP, which is consistent with **Antonio *et al.*** [22] who found that, in a medical-surgical intensive care unit population, the fluid balance did not predict weaning outcomes. In contrast, **Maezawa *et al.*** [23] found in their study that more positive fluid balance before the weaning process is related to the weaning failure, this could be attributed to longer duration (24 h.) for fluid assessment. Before and after the trial, we observed that CVP values were higher in group WF than in group WS. This could be attributed to the more hypervolemia of patients who are prone to weaning failure, and this agrees with the findings of **Dubo *et al.*** [24], which revealed that an initial increase of CVP after commencing an SBT was predictive of extubation failure. Finally, ROC curve analysis for lung ultrasound and echocardiographic clinical variables having the potential to predict weaning failure revealed that a LUS score greater than 18.5 and an E/Ea ratio greater than 12.8 at the end of SBT, with AUCs of 0.917 and 0.904, are highly predictive of weaning failure. **Mayo *et al.*** [4] observed that LUS score > 17 was a strong predictor of extubation failure, which is consistent with our findings. While,

Tongyoo *et al.* [13] showed that in patients with preserved systolic function of LV, E/Ea ratio ≥ 14 is a significant predictor of weaning failure. In the same way, **Moschietto *et al.*** [11] stated that a reliable predictor of weaning failure is E/Ea ratio >14.5.

Limitation: The first limitation, was the small sample size of the current study, as we included 50 critically ill patients with preserved systolic function of the LV. Second, we used PS mode only as a method of weaning. Finally, our study was limited to postoperative ICU patients not medical ones.

CONCLUSION

We concluded that the lung and heart ultrasound are reliable predictors of weaning failure, and the combined use was of high predictive value in the weaning process of postoperative mechanically ventilated patients.

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