BNS University
Critical Care Departement

The Egyptian Journal of Intensive Care and Emergency Medicine

Sonographic Assessment of The Impact of Heart Lung Interactions on Success of Weaning from Mechanical Ventilation

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Abstract:

Objective: To evaluate the value of lung ultrasound and echocardiography in the evaluation of weaning induced lung congestion and its impact on the weaning outcome.

Background: Lung ultrasound has been recently introduced in different aspects in medicine; given that it is easily used in the bedside and can give real-time assessment without the risk of patients` transfer or exposure to radiation. Ultrasound can be used in the assessment of the interstitial lung edema that presumably happens during the process of weaning due to the increased cardiac filling pressures while transferring the patient from positive pressure ventilation to spontaneous ventilation.Being a bedside, non-invasive and easy to perform measures with no proposed harm to the patient, make them of value in prediction of weaning results, if their impact is proved by adequate evidence.

Patients and Methods: We performed a prospective study that included critically ill ventilated patients who were deemed ready for weaning as per the readiness criteria. Eligible patients underwent echocardiography, lung ultrasonography, and serum NT-proBNP measurement.

Results: Forty-patients were included. The incidence of weaning failure was 57.5% (n =23 patients); of them, 14 patients (35%) had the failure during the SBT. A statistically significant difference was found between each of lung ultrasound score (LUS) during PPV and SBT and weaning results (P = 0.006 and 0.026) respectively. A cut off value of 5.5 for LUS during PPV predicted weaning failure at a sensitivity of 73.9% and specificity of 64.7 % (AUC=0.752). A cut off value of 5.5 for LUS during SBT predicted the failure of weaning with a sensitivity of 73.9% and a specificity of 64.7% (AUC=0.698). On the contrary, no statistically significant difference was found for NT-proBNP measurements between failed and successful weaning groups. In regard to Echocardiographic parameters, E /e$^{\backslash}$ during PPV and SBT were found to be statistically higher in the failed weaning group than the successful weaning group (P = 0.005 and 0.002) respectively. A cut off value of 7.43 for E/*e*\ during PPV predicted weaning failure at a sensitivity of 69.6% and a specificity of 64.7 % (AUC=0.762). A cut off value of 8 of E/*e*\ during SBT predicted weaning failure at a sensitivity of 82.6% and a specificity of 64.7% (AUC=0.793)

Conclusions: Prediction of weaning failure could be significantly assisted by an integrative, dynamic, and fully bedside ultrasonographic concomitant assessment of the heart and lungs before the start of the weaning process or during SBT.

Keywords: Spontaneous breathing trial; Mechanical ventilation; Ultrasonography; Weaning outcome.

Introduction:

Mechanical ventilation is a life-saving technique for any respiratory failure patient. The length of mechanical ventilation increases the risk of complications; consequently, early weaning is critical in preventing complications [1]. Premature or delayed weaning of a mechanically ventilated patient increases mechanical ventilation duration, ICU stay, morbidity, and death [2,3]. Thus, precise prediction of post-extubation distress and early detection of causes of weaning failure is critical to improving ventilated outcomes [4,5]. Patients who fail the first spontaneous breathing trial (SBT) or who need re-intubation or rescue non-invasive ventilation following extubation are considered weaning failure [4]. Weaning failure is associated with altered lung compliance, lung derecruitment, neuromuscular disorders, and spontaneous breathing induced cardiac dysfunction, including systolic and diastolic dysfunction, as well as pulmonary edema [4–6]. The SBT raises the left ventricular filling pressure (LVFP), causing weaning failure. Currently, transthoracic echocardiography (TTE) may identify cardiac weaning failure. Tissue Doppler imaging (TDI) analyzes myocardial velocities directly and aids in the identification of SBT-associated diastolic dysfunction [7]. Brain natriuretic peptide (BNP) is produced from the ventricles as the mechanical stress or myocardial wall stretch increases [8,9]. It acts as a cardiac protector against the consequences of overload by increasing natriuresis and diuresis, relaxing vascular smooth muscle, inhibiting the renin-angiotensin-aldosterone system, and by counteracting cardiac hypertrophy and fibrosis. As a result, BNP may be used to screen and assess heart failure patients during weaning, although it lacks specificity because to its wide range of physiological responses [10,11].

However, weaning-induced cardiac dysfunction is related with increased EVLW, which affects lung aeration and may be measured using modalities such as CT scan, EIT, and lung ultrasonography [12]. For many years, lungs were not considered to be easily visualized by ultrasound; as air does not allow for the transmission of ultrasound waves. However, ultrasonography can easily identify artefacts produced at the lungs' contact with other substances (masses and fluids). However, by identifying reduced lung aeration just before weaning and severe alveolo-interstitial edema during SBT, lung ultrasonography may be a reliable predictor of post-extubating suffering and weaning failure [12,13]. This study aimed to evaluate the value of lung ultrasound and echocardiography in the evaluation of weaning induced lung congestion and its impact on the weaning outcome.

Patients and Methods:

The study gained ethical clearance from the responsible committee in the Faculty of Medicine, Beni-Suef University. All patients were required to sign informed consent before deeming eligible for the present study.

I- Subjects:

We performed a prospective study that included critically ill ventilated patients admitted to the Critical Care Department of Beni-Suef University Hospital from December 2018 to August 2019. We included mechanically ventilated patients for at least 48 hours who were deemed ready for weaning as per the readiness criteria. We excluded the pediatric age group, patients with lesions in the chest wall or any other impairments in the acoustic windows that interfere with imaging, heart failure and atrial fibrillation patients, significant valve lesion or history of valve replacement, patients with interstitial pulmonary fibrosis, pneumonectomy or extensive bronchiectasis, and patients with traumatic lung injury or pneumothorax.

II- Methods:

Each patient was evaluated during the positive pressure ventilation (PPV) for history and clinical examination findings, electrocardiography (ECG) findings, fluid balance, routine laboratory investigations, radiological findings, and arterial blood gas (ABG) parameters. Besides, eligible patients underwent echocardiography, lung ultrasonography, and serum NT-proBNP measurement. All patients were ready for SBT, which lasted for 30 minutes using the pressure support ventilation (PSV).

The echocardiography was performed using a *Vivid S5 General Electric®*, with a 3.5 MHz transducer, with parasternal, apical 4-chamber, or subcostal views according to the echocardiographic window of the patient.

The lung ultrasonography was performed with either 5.5 or 3. 5 MHz probes of the *EDAN DUS 60* ultrasound device. The probe was situated perpendicular on the intercostal spaces of each region while patients were lying flat or in the semi-recumbent position. We excluded the posterior chest from the assessment. The examination was conducted to develop the Lung Ultrasound Score (LUS), identifying four aeration patterns. A total of 12 regions were scored using the LUS to develop the total LUS, ranging from 0 (normal aeration) to 24 (complete loss of aeration).

The serum NT-proBNP was measured from the venous blood using the immunofluorescence assay technique.

All of the abovementioned parameters were evaluated during PPV just before the start of SBT and were repeated at the end of this phase. The study's investigators had no impact on the patients' care and were blinded to the patients' data.

Study's Outcomes:

We primarily assessed the incidence of SBT failure as defined by the developing of any of the following events: distributed mentality, diaphoresis, hypoxia, cyanosis, increased accessory muscle activity, dyspnea, respiratory acidosis, or cardiovascular instability. We also assessed the incidence of **r**espiratory distress requiring re-intubation or re-ventilation. The secondary outcomes included length of hospital stay, duration of mechanical ventilation, and in-hospital mortality.

Statistical Analysis

Retrieved data were summarized and processed with IBM SPSS statistical software (version 25). Frequencies were used to describe categorizes and numeric were summarized into median (range). The hypothesize of significant associations between various parameters and weaning was tested by Chi-square test for categorical variables and Mann-Whitney test for continuous variables. The prediction utilities of LUS and NT-proBNP were explored by receiver operator characteristic and the outputs were presented diagnostic accuracy measures. P-value <0.05 was regarded as statistically significant

Results:

Forty-patients were included. The age of the studied patients ranged from 18 to 92 years with a mean ± SD of 53.08 ± 19.39 years; overall, 21 (52.5%) of the patients were females. The risk factors and causes of admission are present in **Table 1**. Pneumonia accounted for the vast majority of the causes for mechanical ventilation (55%), followed by stroke (20%) and intracranial hemorrhage (7.5%). More than 40% of the patients had renal impairment. In terms of fluid balance, 32.5% and 25% of the patients had positive and negative balance, respectively. The mean PH of the patients was 7.39 ± 0.06. The mean NT-proBNP during PPV and SBT was 1422 ±429.2 and 1446.3 ± 517.6 pg/ml, respectively. The mean LUS during PPV and SBT was 6.9 ± 2.5 and 6.95 ± 3.4, respectively. The mean echocardiography parameters during PPV and SBT are present in **Table 2.**

Table 1: Characteristics of the included patients

			Mean ± SD/ No.	**Range/%**
Age of studied patients			53.08 ± 19.39	18-92
Female			21	52.5
Risk Factors		**HTN**	20	50%
		DM	12	30%
		Smoking	3	7.5%
Causes of ICU admission	**Infectious causes (No. 30)**	**Pneumonia**	22	55%
		CNS infection	3	7.5%
		Urosepsis	4	10%
		Soft tissue infection	1	2.5%
	Non-infectiouscauses (No. 10)	**DKA**	2	5%
		Hypertensive crisis	3	7.5%
		IHD	2	5%
		AKI	3	7.5%
Causes of Mechanical ventilation	**Pulmonary causes (No. 27)**	**Pneumonia**	22	55%
		COPD	2	5%
		Asthma	2	5%
		Pulmonary embolism	1	2.5%
	Extra pulmonary causes (No. 13)	**Stroke**	8	20%
		ICH	3	7.5%
		Postoperative	2	5%
Comorbidities		**Ischemic heart disease (IHD)**	2	5%
		Renal impairment	17	42.5%
		Liver impairment	9	22.5%
		Autoimmune disorders	6	15%
Fluid balance		**Balanced**	17	42.5%
		Positive	13	32.5%
		Negative	10	25%

Clinical data	**MAP**	89.6 ± 12.9	60– 120
	Respiratory rate	21.4±5.6	11 – 30
	Temperature	37.45 ± 0.33	37 – 38
	Pulse	100.5 ± 13.8	61 – 122

Table 2: Characteristics of the included patients during PPV and SBT

Parameters (Mean ± SD)		During PPV (1)	During SBT (2)
ABG	**PH**	7.39 ± 0.06	7.37 ± 0.06
	PaCO2 (mmHg)	36.2 ± 6.9	37.6 ± 6.6
	PaO2 (mmHg)	104.01 ± 33.6	89.9 ± 26.8
	Sao2 %	97.6±1.8	96±2.2
	PaO2/FiO2	206.6 ± 61.9	44.98 ± 13.5
Mechanical Ventilation	**RSBI**		50.2±21
	Pressure support		9.2 ± 0.83
	PEEP		4.2 ± 0.86
	Tidal volume		380.54 ± 143.26
	FiO2		42.38 ± 8.09
NT-proBNP (pg/ml)		1422.1 ± 429.2	1446.3 ± 517.6
LUS		6.9 ± 2.5	6.95 ± 3.4
Echocardiography	**EF**	69.6±10.5	67.4 ± 9.5
	PASP (mmHg)	35.8 ± 12.2	35.5 ± 12.3
	RV (cm)	3.5 ± 0.58	3.5 ± 0.44
	TAPSE (cm)	2.1 ± 0.45	2.06 ± 0.48
	E/A	1.04 ± 0.39	1.08 ± 0.45
	E /e$^{\backslash}$	8.7 ± 3.7	8.8 ± 3.6

The incidence of weaning failure was 57.5% (n =23 patients); of them, 14 patients (35%) had the failure during the SBT (**Figure 1**). The overall in-hospital mortality was 65% (27 patients). The mean days of ventilation was 12.4±7.4, while the mean length of stay was 16.7±7.5 days.

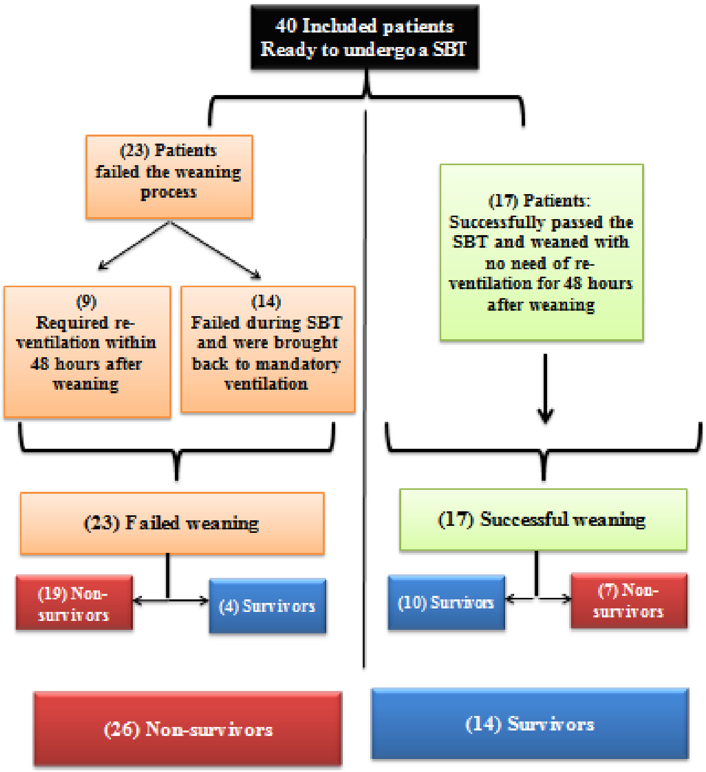

Figure 1: Weaning outcome of the studied patients

There was a statistically significant relation between failure of weaning and infectious causes of ICU admission (P=0.006). On the other hand, the non-infectious causes of ICU admission were found to be significantly associated with weaning success (P=0.005). A statistically significant relation was found between the cause of mechanical ventilation and the weaning result where pulmonary causes of ventilation were associated with higher failure of weaning; whether the extra-pulmonary causes were associated with high degree of success of weaning (P = 0.002). Likewise, a statistically significant difference was found between PaO2/FiO2 ratio measured during PPV and during SBT for patients who failed weaning and that for who were successfully weaned (P = 0.046 and 0.05) respectively. Also, PaCO2 measured during PPV was found to be lower in the failed weaning group (P = 0.03). As regard to ventilation and oxygenation parameters during SBT**,** RSBI was found to be significantly lower in successful weaning patients (P = 0.027). Additionally, TV was found to be significantly higher in the successful weaning group (P = 0.045), **Table 3**.

Table 3: Comparison between study parameters and weaning results

Variables		**Weaning**		**P-value**
		Failure	**Successful**	
Risk factors	**Smoking**	2 (8.7%)	1 (5.9)	0.738
	HTN	12 (52.2%)	8 (47.1%)	0.749
	DM	7 (30.4%)	5 (29.4%)	0.944
Cause of admission	**Infectious causes**	21 (91%)	9 (53%)	**0.006**
	Non-infectious causes	2 (7%)	8 (47%)	**0.005**
Cause of Ventilation	**Pulmonary causes**	20 (87%)	7 (41%)	**0.002**
	Extra pulmonary causes	3 (13%)	10 (59%)	
Comorbidities	**IHD**	1 (4.3%)	1 (5.9%)	0.826
	Renal impairment	11 (47.8%)	6 (35.3%)	0.428
	Liver impairment	7 (30.4%)	2 (11.8%)	0.162
	Autoimmune disorders	5 (21.7%)	1 (5.9%)	0.165
Fluid Balance	**Balanced**	8 (34.8)	9 (52.9)	0.46
	Positive	9 (39.1)	4 (23.5)	
	Negative	6 (26.1)	4 (23.5)	
ABG	**PH (1)**	7.37 ± 0.07	7.37 ± 0.05	0.792
	PaCO2 (1) (mmHg)	34.2 ± 5.5	38.95 ± 7.8	**0.03**1
	PaO2 (1) (mmHg)	97.7 ± 29.7	112.5 ± 37.6	0.173
	Sao2 (1) %	97.4 ± 2.1	98 ± 1.5	0.352
	PaO2/FiO2 (1)	189.9 ± 49.02	229.21 ± 71.5	**0.046**
	PH (2)	7.41 ± 0.07	7.37 ± 0.04	0.07
	PaCO2 (2) (mmHg)	36.3 ± 6.1	39.4± 7.1	0.149
	PaO2 (2) (mmHg)	86.7 ± 24.8	94.2 ± 29.7	0.388
	Sao2 (2) %	96.3 ± 2.5	95.6 ± 1.6	0.352
	PaO2/FiO2 (2)	173.4 ± 49.6	188.5 ± 59.4	**0.05**
	RSBI	56.41 ± 21.66	41.76 ± 15.33	**0.027**
	Pressure support	9.1 ± 0.8	8.5 ± 0.5	0.421
	PEEP	4.6 ± 0.3	4 ± 0.9	0.327
	Tidal volume	327.7 ± 70.9	420.1 ± 101.2	**0.045**
	FiO2	39.7 ± 8.2	31 ± 6.3	0.175

A statistically significant difference was found between each of LUS during PPV and SBT and weaning results (P = 0.006 and 0.026) respectively. On the contrary, no statistically significant difference was found for NT-proBNP measurements between failed and successful weaning groups. TAPSE during PPV was found to be significantly lower in the failed weaning group than the successful weaning group (P = 0.004). Also, E /e$^{\backslash}$ during PPV and SBT were found to be statistically higher in the failed weaning group than the successful weaning group (P = 0.005 and 0.002) respectively (**Table 4**).

Table 4: Comparison between LUS measurements and weaning [1: During PPV, 2:During SBT]

	Failure	**Successful**	**P-value**
	Mean ± SD		
LUS (1)	8.22 ± 3.58	5.18 ± 1.74	**0.006**
LUS (2)	8.26 ± 3.81	5.18 ± 2.04	**0.026**
NT-proBNP (1) (pg/ml)	1,830.26 ± 384.81	869.82 ± 277.23	0.221
NT-proBNP (2) (pg/ml)	1,859.43 ± 430.88	887.35 ± 370.08	0.232
EF (1)	70.09 ± 11.13	68.94 ± 9.84	0.73
PASP (1) (mmHg)	39.39 ± 10.32	30.88 ± 11.43	0.08
RV (1) (cm)	3.49 ± 0.59	3.52 ± 0.57	0.86
TAPSE (1) (cm)	1.96 ± 0.39	2.36 ± 0.43	**0.004**
E/A (1)	1.07 ± 0.43	1.01 ± 0.34	0.648
E /e\ (1)	10.05 ± 2.94	6.85 ± 1.24	**0.005**
EF (2)	69.09 ± 10.98	65.18 ± 6.65	0.20
PASP (2) (mmHg)	39.09 ± 12.33	30.53 ± 11.24	0.08
RV (2) (cm)	3.53 ± 0.5	3.49 ± 0.36	0.80
TAPSE (2) (cm)	1.96 ± 0.45	2.21 ± 0.5	0.12
E/A (2)	1.12 ± 0.51	1.02 ± 0.36	0.49
E /e\ (2)	10.24 ± 3.73	6.86 ± 1.42	**0.002**

A cut off value of 5.5 for LUS during PPV predicted weaning failure at a sensitivity of 73.9% and specificity of 64.7 % (AUC=0.752). A cut off value of 5.5 for LUS during SBT predicted the failure of weaning with a sensitivity of 73.9% and a specificity of 64.7% (AUC=0.698). A cut off value of 512.5 for NT-proBNP during PPV predicted weaning failure at a sensitivity of 65.2% and a specificity of 70.6 % (AUC=0.662). A cut off value of 575 for NT-proBNP during SBT predicted the failed weaning with a sensitivity of 70.6% and a specificity of 70.6% (AUC=0.665). A cut off value of 7.43 for E/*e*\ during PPV predicted weaning failure at a sensitivity of 69.6% and a specificity of 64.7 % (AUC=0.762). A cut off value of 8 of E/*e*\ during SBT predicted weaning failure at a sensitivity of 82.6% and a specificity of 64.7% (AUC=0.793) (**Table 5**).

Table 5: Results of ROC curve analysis of different variables

Test Variables	Cut off	Sensitivity	Specificity	AUC	Asymptotic 95% Confidence Interval	
					Lower Bound	Upper Bound
LUS (1)	5.5	**73.9%**	64.7 %	0.752	0.600	0.904
LUS(2)	5.5	**73.9%**	64.7%	0.698	0.543	0.862
BNP (1)	512.5	65.2%	**70.6 %**	0.662	0.489	0.835
BNP (2)	575	**70.6%**	**70.6%**	0.665	0.489	0.841
E/e\ (1)	7.43	69.6%	64.7 %	0.762	0.615	0.909
E/e\ (2)	8	**82.6%**	64.7%	0.793	0.652	0.934

Discussion:

In this study, successful weaning was achieved in 42.5%, while post-extubation failure and failure during SBT were reported in 22.5% and 35%, respectively. The mortality rate was 65%, and about 61.5% of the mortality cases were attributed to sepsis, and 23% were due to stroke. By comparing successful and failed weaning, successful weaning was significantly associated with non-infectious causes of ICU admission, extrapulmonary causes of MV, elevated $PaCO_2$ during PPV, and elevated PaO_2/FiO_2 ratio during PPV. Successful weaning was associated with non-infectious ICU admission, extrapulmonary MV, high PaCO2 during PPV, and raised PaO2/FiO2 ratio during PPV. In the failed weaning group, PaCO2 during SBT was observed to be greater than during PPV (p=0.038), while PaO2 was lower during SBT than PPV (P=0.016). Moreover, PaO2/FiO2 ratio was found to be significantly lower in the failed weaning group than that for those who were successfully weaned when measured during PPV and during SBT (P = 0.046 and 0.05) respectively. Several studies have attempted to identify an oxygenation level that best predicts weaning failure, with PaO2/FiO2 120, PaO2 60 mmHg, or SaO2 90% being used as rough predictors. However, no single parameter can predict weaning failure, as the process is complex and requires multiple factors to be assessed [14]. Roche-Campo et al. revealed that short weaning increased PaO2/FiO2 [15]. Similarly, El-Dehily et al. reported that effective weaning had a higher PaO2/FiO2 ratio [16]. Successful weaning was shown to have a higher mean PaO2 than failed weaning, according to Osman et al.[17]. Likewise, effective weaning patients exhibited higher PaO2 and SaO2 (P = 0.04 and 0.01), according to Schifelbain et al.[18]. In the study of El Khoury et al., they found that PaO2/FiO2 ratio is similar between the patients who experienced effective weaning and those who experienced reintubation. Moreover, they reported that the sensitivity and specificity of the PaO2/FiO2 ratio were 70% and 56%, respectively, indicating that PaO2/FiO2 ratio cannot predict successful weaning independently [19].

RSBI was found to be significantly lower in successful weaning patients (p = 0.027). The low RSBI values in the included patients may be explained by the degree of assistance provided by PSV rather than T-Piece. Patel et al. observed that a minimum amount of support exhibited lower levels of RSBI than zero or minimal support [20]. Banerjee et al. observed that RSBI was greater in the failed group than the successful group [21]. Moreover, Haji et al. found a statistically significant increase in the median value of RSBI in the failed group (P = 0.03) [22]. Also, Osman et al. observed that successful weaning had lower RSBI than failure weaning [17]. El-Dehily et al. demonstrated that RSBI was greater in unsuccessful weaning than in successful weaning (P=0.001) [16]. TAPSE was observed to be greater in the short weaning group than the extended weaning group (P = 0.03) [15]. According to Daif et al., RVSP was greater in the failed weaning group (P=0.001), possibly owing to RV failure linked with transition from PPV to negative pressure ventilation resulting in increased preload against a high RVSP [23]. Dehily et al. showed a negative correlation between TAPSE during PPV and TAPSE during SBT and ventilation duration (P = 0.002). They also found that the extended weaning group also had increased PASP during SBT (P = 0.008) [16].

Moreover, our finding showed that E /e\ during PPV and E /e\ during SBT were statistically higher in the failed weaning group than the successful weaning group (P = 0.005 and 0.002) respectively. Additionally, our study showed that both of e\ during PPV and e\ during SBT were significantly higher in survivors than non-survivors (P = 0.005 and 0.018) respectively. These findings would explain that the impaired relaxation, which becomes evident during mechanical ventilation and at the start of SBT, may express the severity of the condition or maybe an addition of a risk factor for included patients causing a worse outcome. Daif et al. used the T-Piece methodology to predict weaning outcomes using cardiac and lung ultrasonography, and they concluded that diastolic dysfunction was linked to more failure weanings [23]. Similarly, El-Dehily et al. showed that the extended weaning group had considerably greater E/e than the problematic weaning group (P = 0.031) [16]. Our findings matched those of Liu et al. who investigated weaning-induced pulmonary edema as a cause of weaning failure. The E/e ratio of mitral flow was greater in individuals who failed SBT (P =0.001) [24]. Moschietto et al. observed that the failed group had considerably greater E/e during PPV and SBT (P 0.001 and 0.0001, respectively). Both PPV and SBT were considerably greater in the successful group (P 0.01 and 0.0003), confirming the hypothesis that decreased cardiac relaxation affects outcome [25].

A statistically significant difference was found between each of LUS during PPV, LUS during SBT, and weaning results (p= 0.006 and p=0.026), respectively. Similarly, conducted diaphragmatic and LUS 20 minutes after SBT. Weaning success and LUS were shown to be correlated in the study of Banerjee et al.[21] and Antonio et al.[26]. Aeration scores were calculated for all patients before weaning, during SBT, and 6 hours after extubation by Shoaeir et al. The unsuccessful weaning group exhibited fewer aerated lungs than the successful weaning group (P=0.001). The unsuccessful weaning group lost more lung aeration than the successful weaning group (P=0.001). Six hours after extubation, the failed weaning group showed significant lung derecruitment and decreased aeration (P=0.001) [27].

Regarding cardiac biomarkers, NT-proBNP measurements were found to be higher in the failed weaning group during PPV and during SBT; however, this difference couldn't reach a statistical significance, with (P = 0.22 and 0.23) for the first and the second measurements respectively. To predict weaning outcomes, Roche-Campo et al.[15] used echocardiography and serum BNP. Unlike our study, echocardiography was performed during baseline ventilator settings, and patients were followed for 72 hours to detect re-intubation. The BNP measurements were the same in both the short and prolonged weaning groups. Similar to these findings; Chien et al found no statistically significant difference between BNP measurements of the failed and successful weaning groups before the start of the weaning process. However, patients with failed SBT had higher levels of serum BNP measured during SBT (P<0.001) [28]. On the contrary to our findings, El Maraghi et al. conducted a prospective observational study on 40 ventilated patients. BNP sampling was performed immediately before SBT and at the end of SBT. It was found that SBT-BNP was significantly lower than that before SBT in the extubation success group (P=0.004) [29].

Regarding echocardiographic measurements, EF assessment was not significant in separating the two weaning groups or in predicting the study population's outcome. Similarly, Zapata et al. found no difference in LVEF between failed and successful patients [30]. Lamia et al.[7] and Mekontso et al.[25] found similar results. Weaning failure was shown to be associated with reduced EF in the failed group [23,31]. There are many explanations for this, including a significant number of patients with poor EF in both trials, which may impair the weaning process.

Regarding ROC analysis of LUS, we found that a cut-off point of 5.5 was the best for both LUS during PPV and LUS during SBT in the prediction of the failure of weaning with a sensitivity of 73.9% and a specificity of 64.7 % and (AUC=0.752) and (AUC=0.698) respectively. Low cut-off values for both PPV and SBT LUS may be attributed to excluding posterior chest wall ultrasonography, which often raises the LUS score. Notably, posterior chest wall LUS is difficult to use on a severely sick ventilated patient, not to mention the problems that may develop during this technique. Similarly, Tenza et al. 2018 used a modified score (LUSm) to assess four lung areas on each side, ranging from 0 to 24. The ROC curve predicted weaning success. To wean successfully, a sensitivity of 76% and specificity of 70% were found (AUC= 0.80). In a similar way, Soummer et al. used the ROC curve for prediction of weaning results and found that LUS at the end of SBT >17 was highly specific for predicting postextubation distress with (AUC=0.86) and an LUS score <12 was highly sensitive for excluding postextubation distress [13]. Also, Osman et al. used the ROC curve and found that LUS during SBT (<12) has a high probability for success, (12-17) intermediate probability for success, and (>17) high probability for failure [17]. Shoaeir et al. performed the ROC curve for LUS score 30 minutes from SBT and found that LUS at a cut-off value of (19) could predict re-intubation with 100% positive predictive value, 100% specificity.

Moreover, a score of less than (10) showed high accuracy in excluding weaning failure with a 100% negative predictive value [27].

NT-proBNP during PPV and SBT was proven to be a predictor for failure weaning. NT-proBNP had a sensitivity of 65.2% and a specificity of 70.6% (AUC=0.662) at a cutoff value of 512.5. NT-proBNP cutoff 575 during SBT had 70.6% sensitivity and specificity to indicate failure weaning (AUC=0.665). Patients with HF were excluded from the study, which explains the study's low and weak NT-proBNP cut-off point. Zapata et al. revealed that a baseline NT-ProBNP of 1,343 ng/L had a lower sensitivity (67%) to predict SBT failure than BNP (83%) [30]. These findings explain why NT-proBNP is less accurate than BNP in predicting weaning failure in cardiac patients.

With a cut-off value of 7.43, E/e during PPV predicted failure weaning with 69.6% sensitivity and 64.7 % specificity (AUC=0.762). A cut-off point of 8 for E/e during SBT also predicted failure weaning with 82.6 % sensitivity and 64.7 % specificity (AUC=0.793). AUC = 0.474 for E/e during SBT predicted the failure of weaning during SBT by El-Dehily et al [16]. Similarly, Moschietto et al. showed that the E/e ratio at SBT 14.5 might predict failure weaning with 75% sensitivity and 958 specificities. The failed group had much higher E/e values prior to SBT, however, the ROC curve findings were non-significant. The study's main conclusion is that repeated E/e measurements correctly predict weaning failure [25].

We acknowledge that our study has some limitations, including the small sample size and the single-center design, which may hinder the generalizability of our findings. Diastolic dysfunction is a common disorder seen in critically ill patients and our findings maybe not be related to the failed weaning process only but may express the severity of the case and association of various risk factors. Exclusion of many patients due to the poor echocardiographic window and the difficulty to perform lung ultrasonography in some patients under mechanical ventilation. The diagnosis of weaning-induced cardiac dysfunction and pulmonary edema was made using non-invasive techniques without the use of other invasive methods i.e. PAOP that can confirm the findings.

In conclusion, cardiac dysfunction is a predisposing factor for weaning failure rather than a result of the weaning process. Prediction of weaning failure could be significantly assisted by an integrative, dynamic, and fully bedside ultrasonographic concomitant assessment of the heart and lungs before the start of the weaning process or during SBT. Predisposed patients breathing spontaneously, even during PPV, can express cardiac dysfunction and weaning-induced pulmonary edema even before the start of an SBT. NT-proBNP is a weak predictor of weaning outcomes and it is better not to guide the weaning process except in patients with known heart failure. The early assessment of cardiopulmonary changes during PPV can direct the management to a fluid restrictive strategy to help in decongestion of the lung and facilitate the success of the SBT. Future interventional studies are required to validate the impact of integrating thoracic ultrasound data on post-extubation distress, length of ICU stay, and mortality.

Abbreviations:

AKI: Acute kidney injury, **BNP:** B- type natriuretic peptide**, EIT:** Electrical impedance Tomography**, EVLW:** Extra vascular lung water**, HF:** Heart failure**, ICH:** Intracranial hemorrhage, **IHD:** Ischemic heart disease**, LUS:** Lung ultrasound - Lung ultra sound score**, LV:** Left ventricle**, MV:** Mechanical ventilation**, NIV:** Non- invasive ventilation**, PAOP:** Pulmonary artery occlusion pressure**, PPV:** Positive pressure ventilation**, PSV:** Pressure support ventilation**, RSBI:** Rabid shallow breathing index**, RV:** Right ventricle, **SBT:** Spontaneous breathing trial**, TAPSE:** Tricuspid annular plane systolic excursion, **TTE:** Trans thoracic echocardiography

Work of breathing

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