

# Noninvasive Assessment of Weaning Failure from Mechanical Ventilation in Critically Ill Patients

Radwan WA, El Damrawy MM, El Husseiny RM, Tawfik SE and Abd Elhamed MY

Department of Critical Care Medicine, Faculty of Medicine, Cairo University, Egypt

## Abstract

**Background:** Weaning predictors are used as a point of decision to determine if a patient can progress to a spontaneous respiratory test.

**Aim:** The study aimed to evaluate the role of the following parameters: NT-proBNP, weaning indices (RSBI, Cst and IWI) and echocardiography with use of tissue Doppler imaging (left and right ventricular function was assessed by LVEF, the grade of mitral regurg if any, E/A, DT, E', E/E', TAPSE and RVFAC) as predictor tools of weaning failure in critically ill patients from mechanical ventilation.

**Patients and Methods:** This was a prospective study that was conducted on sixty adult patients of both sexes mechanically ventilated for more than 48 hours and who met the criteria of spontaneous breathing trial (SBT). The studied patients were recruited within a period between May 2016 and November 2017 from the Intensive Care Department in Theodor Bilharz Research Institute.

**Results:** Patients who failed SBT had a higher mortality rate compared to successful SBT. A patient who failed SBT showed a high incidence of weaning failure. Patients who failed SBT showed (before SBT): significantly longer MV duration, the significant decrease in PaO<sub>2</sub>, SaO<sub>2</sub> and PaO<sub>2</sub>/FiO<sub>2</sub>, and the significant increase in RSBI, significant decrease in IWI and significant decrease in Cst. Patients who failed SBT showed (After SBT): Significant increase in MAP, pulse, and RR, Significant increase in NT-pro BNP levels, significant increase CO, no difference incidence of systolic dysfunction. significant shortage in DT, significant lowering E' velocity, significant increase E/E' and diastolic dysfunction incidence, significant increase incidence of moderate and severe MR, significant increase PCOP and a significant decrease in follow up TAPSE and RVFAC.

**Conclusion:** Clinical, laboratory, echocardiography weaning parameters could be considered a sensitive and specific marker for prediction of weaning failure.

**Keywords:** Noninvasive; Weaning; Mechanical; Ventilation and Breathing

\***Correspondence to:** Mohamed Youssef Abd Elhamed, Department of Critical Care Medicine, Faculty of Medicine, Cairo University, Egypt.

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## Introduction

Mechanical ventilation weaning covers the entire process of releasing a patient from the ventilator and the endotracheal tube. Weaning failure is usually defined as an ineffective spontaneous respiratory test (SBT) or ventilator support (including non-invasive ventilation) within 48 hrs. of extubation [1].

During spontaneous breathing, the transition from positive inspiratory pressure during mechanical ventilation to negative airway pressure challenges the physiological reserve of patients. When there is an imbalance between the ventilating needs and capacity of the patients, weaning fails [2].

There are various weaning indexes, all intending to decide the prognosis for this phase, which, contrary to what many believe, cannot be decided by clinical impression and spontaneous breathing test (SBT) alone [3].

Mechanical ventilation (MV) weaning is not an optimal indicator [4]. The cardiac performance was recognized as a common weaning

failure etiology [5]. The occurrence of diastolic dysfunction was independently correlated with weaning failure, so an echocardiography assessment of LV diastolic function before weaning could be useful in identifying patients at risk of weaning failure [6].

## Patients and Methods

A prospective study conducted on sixty adult patients of both sexes. The studied patients were recruited within a period between May 2016 and November 2017 from the Intensive Care Department in Theodor Bilharz Research Institute. The study was conducted on mechanically ventilated patients for more than 48 hours and who met the criteria of spontaneous breathing trial (SBT).

## Inclusion Criteria

Patients with a clear improvement or resolution of the condition that initially necessitated mechanical ventilation, adequate cough, absence of excessive tracheo-bronchial secretion, adequate arterial blood gases and acid base values, adequate oxygenation (partial pressure of arterial oxygen (PaO<sub>2</sub>)/ fraction of inspired oxygen



( $\text{FiO}_2 \geq 200$  on  $\text{PEEP} \leq 8$  cm  $\text{H}_2\text{O}$ ), stable cardiovascular status (heart rate  $\leq 120$ /min, systolic blood pressure higher than 90 mmHg and lower than 160 mmHg) with no or low dose vasopressors or inotropes, adequate pulmonary functions (respiratory rate  $\leq 35$  breathes/min, tidal volume  $> 5$  mL/kg, No significant respiratory acidosis,  $\text{RSBI} < 05$  breaths/min/L.) and Patients on no or only light sedation with stable neurological status.

### Exclusion Criteria

Patients suffering any type of dysrhythmias, poor echocardiographic window, patients with mitral stenosis, heavy mitral annular calcification or prosthetic mitral valve where E/E' measurement is not validated for estimation of left ventricular filling pressure in such cases and Patients with constrictive pericarditis were excluded from the study.

### Methodology

**Institutional ethics approval:** After approval of ethical committee of Theodor Bilharz Research Institute, an informed consent was taken from the patient's family.

**General measures:** The selected patients were subjected to the following:

- Full history taking, Complete physical examination, Measurement of Simplified Acute Physiology Score (SAPS II), relevant laboratory investigations including: Complete blood count (CBC), liver enzymes (SGOT and SGPT), serum albumin, renal function checks (blood urea nitrogen and serum creatinine), serum electrolytes including sodium and potassium, blood gases and base acid values.
- Once the inclusion criteria were met the patients were prepared for (SBT) with a T-piece.

**NT-proBNP:** Freshly collected blood samples (2 mL) obtained at initiation and at the end of spontaneous breathing trial (SBT).

Until SBT was initiated, while the patient was in spontaneous mode, press support (PS) was turned zero, and ABG was completed,  $\text{SaO}_2$  and  $\text{PaO}_2/\text{FiO}_2$  registered. Static respiratory system compliance (Cst) was assessed after an inspiratory hold of 0.5 to 1 sec. Tidal volume (TV) and spontaneous respiration were registered and the rapid shallow respiration index (RSBI) was obtained by dividing frequency (f) by spontaneous tidal volume (VT in liters) and integrative weaning index.

- $(\text{IWI}) = (\text{Cst} * \text{SaO}_2) / (f / \text{TV})$  was calculated.

The SBT was conducted with a T-piece over a 30 min duration, while the patient was in a semi-recumbent position ( $45^\circ$ ). During the SBT the heart rate, systolic and diastolic blood pressure, respiratory rate, pulse oximetry, electrocardiographic tracing and consciousness level were closely monitored.

**SBT Failure:** It was defined as the need to connect the patient back to the ventilator prior to its completion due to at least one of the following reasons:

- Agitation and anxiety or depressed mental status.
- Cyanosis, percutaneous oxygen saturation ( $\text{SpO}_2$ ) below 90%.
- Respiratory rate of more than 35 breathes/min.
- Heart rate above 150 beats/min or cardiac arrhythmia, systolic blood pressure above 180 mmHg or below 90 mmHg [7].

**Trans Thoracic Echocardiography (TTE):** With the use of tissue

Doppler imagery on the lateral mitral annulus was performed in each patient under pressure support mode (ranging from 7-12 cmH<sub>2</sub>O) before the ventilator was disconnected and after the spontaneous breathing test (SBT).

### The following parameters were measured:

- Left ventricular systolic function (LVEF), using Simpson's updated law to measure the fraction of the ejection. Systolic instability is less than 50 per cent of EF [8].
- LV stroke volume (SV) was calculated using the Doppler method applied at the level of the LV outflow tract and the cardiac output [9].
- The presence and semi-quantitative severity of the mitral regurgitation (MR) using Color Doppler mapping
- Left ventricular diastolic dysfunction.

LV inflow velocity: Doppler pulse wave was applied to record LV inflow velocities at the tip of the mitral valve leaflets. The average flow rate was determined during the early diastole (E wave) and the atrial phase (A wave) and the E/A ratio was estimated. The E wave (DTE) deceleration time was determined by extending the deceleration slope from the peak wave velocity up to the baseline of zero-velocity.

Tissue Doppler imaging: The maximum velocity of its displacement during early diastole (E' wave) was determined by using pulse-wave tissue Doppler at the lateral portion of the mitral annulus, and the E/E' ratio was estimated. Diastolic dysfunction defined as lateral velocity of 8 cm/sec less or equal to E [10].

The following equation was used to measure the pulmonary capillary coil pressure (PCWP) and the left ventricular filling pressure:

- $\text{PCWP} = (1.9 + 1.24x (\text{E}/\text{E}'))$  [11].

Right ventricular dimensions and function by fractional area change (RFAC) and tricuspid annular systolic plane excursion (TAPSE).

All of the above parameters were measured in patients who passed SBT successfully and those who fail to pass SBT (before and after SBT), in order to obtain the most important and sensitive parameters predicting weaning failures.

## Results

### Demographic and clinical data

The mean age of all patients was  $63.4 \pm 11.53$  years. 68.3% males; while 31.7% females. 50% of patients had previous ICU admission; while 20% had previous mechanical ventilation support.

### Mechanical Ventilation (MV) data

Mean duration of MV for all patients was  $5.95 \pm 2.86$  days; mean pressure support was  $8.81 \pm 1.11$  cm  $\text{H}_2\text{O}$ ; and the mean PEEP was  $5.37 \pm 1.08$  cm  $\text{H}_2\text{O}$ . Regarding causes of MV in all patients, 35% of patients had life threatening hypoxemia, 28.3% had type 2 respiratory failure, 21.6% were shocked, 10% had neurological disorders, and while 3.3% needed heavy sedation and 1.6% had lung collapse.

### Outcome data

Mortality rate was 18.3% and rate of weaning failure was 30%. Causes of weaning failure in failed patients included: pulmonary edema in 44.4%, type-I respiratory failure in 22.2%, and post-extubation stridor in 33.3%



## Comparative Data

Patients were classified according to their weaning outcome in to: Patients with successful SBT (42 patients), Patients with failed SBT (18 patients)

### Demographic and clinical data

No significant difference was detected between patients with successful and failed SBT regarding age and sex. Patients with failed SBT showed significant increase in MV duration; compared to successful SBT ( $p=0.027$ ). No significant difference was detected between patients with successful and failed SBT regarding pressure support, PEEP and causes of MV ( $p>0.05$ ).

### Physiological & vital data

During SBT, patients with failed SBT showed significant increase in MAP, pulse and respiratory rate (RR); compared to successful SBT ( $p<0.05$ ).

No significant difference was detected between patients with successful and failed SBT regarding temperature ( $p>0.05$ ) (Table 1).

No significant difference was detected between patients with successful and failed SBT regarding SAPSII ( $p>0.05$ ).

### Laboratory data

No significant difference was detected between patients with successful and failed SBT regarding all the remaining baseline laboratory variables ( $p>0.05$ ).

No significant baseline NT-proBNP levels (before SBT) ( $p > 0.05$ ). Patients with failed SBT showed; highly significant increase in follow up NT-pro BNP levels (after SBT) compared to successful SBT ( $p < 0.0001$ ).

### Weaning indices data

ABG data (Before SBT) showed no significant difference was detected between patients with successful and failed SBT regarding pH, PaCO<sub>2</sub> and HCO<sub>3</sub> ( $p>0.05$ ). Patients with failed SBT had lower saturation, PaO<sub>2</sub> and PaO<sub>2</sub>/FiO<sub>2</sub>; compared to patients with successful SBT ( $p < 0.05$  respectively).

Regarding weaning indices derived from MV patients with failed SBT showed highly significant increase in RSBI compared to successful SBT patients ( $p=0.001$ ), highly significant decrease in Cst ( $p=0.002$ ) and IWI compared to successful SBT patients; ( $p=0.003$ ) (Table 2).

**Table 1:** Comparison between successful and failed SBT regarding physiological & vital data.

Variable	Successful group (42) Mean±SD	Failed group (18) Mean±SD	P value
MAP (mmHg)	78.26±15.94	87.95±13.84	=0.0289*‡
Pulse (beat/min)	112.33±17.24	121.64±10.98	=0.039*‡
RR (breath/min)	33.67±3.16	36.37±2.89	=0.0029**‡
Temperature (C)	37.98±0.88	38.23±0.94	=0.404‡

**Table 2:** Comparison between successful and failed SBT regarding weaning indices data.

Variable	Successful group (42) Mean±SD	Failed group (18) Mean±SD	P value
RSBI (breath/min/L)	68.98±22.369	95.67±26.992	0.001***‡
Cst (ml/cm H <sub>2</sub> O)	50.243±8.540	42.445±9.436	=0.002**‡
IWI (ml/cm H <sub>2</sub> O/ breaths/min/L)	76.824±33.624	49.376±33.486	=0.003**‡

## Trans-Thoracic Echocardiography (TTE) Data

### Echocardiographic parameters

**LV systolic function:** No significant difference was detected between patients with successful and failed SBT regarding all baseline echocardiographic parameters (before SBT) ( $p>0.05$ ). Patients with failed SBT showed highly significant increase in follow up cardiac output (CO) (after SBT) in failed group compared to successful group of patients ( $p=0.013$ ).

No significant difference was detected between patients with successful and failed SBT regarding follow up EF, SV and LVOT-VTI, in follow up echocardiographic parameters (after SBT) ( $p>0.05$ ).

No significant differences were detected between patients with successful and failed SBT regarding incidence of systolic dysfunction, either (before or after SBT) ( $p>0.05$ ) (Table 3).

**Incidence and severity of mitral regurgitation (MR):** No significant differences were detected between patients with successful and failed SBT regarding Incidence & severity of MR (before SBT) ( $p>0.05$ ).

Patients with failed SBT showed significant increase in the incidence of moderate and severe MR; compared to successful SBT (before SBT) ( $p = 0.01$ ).

### Left Ventricular (LV) diastolic function

**Doppler parameters:** No significant difference was detected between patients with successful and failed SBT regarding all baseline Doppler parameters (before SBT) ( $p>0.05$ ).

Patients with failed SBT showed significant decrease in follow up Deceleration Time (DT) (after SBT) compared to successful SBT patients; ( $p=0.027$ ).

No significant difference was detected between patients with successful and failed SBT regarding follow up Doppler E/A parameters (after SBT) ( $p>0.05$ ) (Table 4).

**Table 3:** Comparison between successful and failed SBT regarding echocardiographic parameters.

TTE(before SBT)	Successful group (42) Mean±SD	Failed group (18) Mean±SD	P value
EF(%)	55.5±9.2	54.21±11.63	=0.834‡
SV (mL)	72.53±11.86	73.08±13.2	=0.524‡
CO (L/min)	5.89±1.16	5.85±0.93	=0.821‡
LVOT-VTI (cm)	20.74±3.35	20.81±3.49	=0.815‡
Systolicdysfunction (EF<50%) N(%)	20(47.6%)	9(50%)	=0.883‡
TTE (after SBT)	Successful group (42)	Failed group (18)	P value
EF (%)	50.52±12.02	52.37±15.64	=0.620‡
SV (mL)	74.63±11.83	75.74±16.15	=0.371‡
CO (L/min)	6.16±1.63	7.24±1.14	=0.013*‡
LVOT-VTI(cm)	20.662±3.203	20.346±6.338	=0.840‡
Systolic dysfunction (EF<50%) N(%)	19(45.5%)	9(50%)	=0.964‡

**Table 4:** Comparison between successful and failed SBT regarding Doppler (for diastolic dysfunction) parameters.

TTE (after SBT)	Successful group (42)	Failed group (18)	P value
E/A	1.181±0.377	1.31±0.55	=0.305‡
Deceleration Time (DT)	184.21±31.08	120.99±23.3	=0.027*‡



**Tissue Doppler parameters:** No significant difference was detected between patients with successful and failed SBT regarding all baseline tissue Doppler parameters (before SBT) ( $p>0.05$ ).

Patients with failed SBT had statistically lower E' velocity (after SBT) compared to successful SBT patients; ( $p=0.005$ ), statistically higher E/E' ratio compared to successful ( $p<0.01$  respectively) and showed highly significant increase in incidence of diastolic dysfunction compared to successful SBT patients; ( $p<0.001$ ) (Table 5).

**Table 5:** Comparison between successful and failed SBT regarding Tissue Doppler parameters.

TTE (before SBT)	Successful group (42) Mean±SD	Failed group (18) Mean±SD	P value
E' (cm/sec)	11.12±3.05	10.3±2.31	=0.199‡
E/E'	7.16±1.92	8.81±3.08	=0.059‡
TTE (after SBT)	Successful group (42)	Failed group (18)	P value
E' (cm/sec)	10.88±2.86	8.43±3.3	=0.005**‡
E/E'	7.66±2.42	9.95±4.02	=0.008**‡
Diastolic dysfunction (E' < 8 cm/sec)	11(26%)	12(66.6%)	<0.001**‡

**Pulmonary Capillary wedge Pressure (PCWP) parameter:** No significant difference was detected between patients with successful and failed SBT regarding all baseline PCWP (before SBT) ( $p>0.05$ ).

After SBT, patients who failed had statistically higher PCWP compared to successful SBT patients; ( $p<0.0001$ ) (Table 6).

**Table 6:** Comparison between successful and failed SBT regarding PCWP parameter.

TTE (before SBT)	Successful group (42) Mean±SD	Failed group (18) Mean±SD	P value
PCWP (mmHg)	10.87±2.47	12.16±4.23	=0.142‡
TTE (after SBT)	Successful group (42)	Failed group (18)	P value
PCWP (mmHg)	12.03±3.07	19.28±4.96	<0.0001**‡

### Right Ventricular Functions

No significant difference was detected between patients with successful and failed SBT regarding all baseline TAPSE and RVFAC parameters (before SBT) ( $p>0.05$ ). Patients with failed SBT showed highly significant decrease in follow up TAPSE and RVFAC (after SBT) compared to successful SBT patients ( $p<0.0001$  respectively) ( $p>0.05$ ) (Table 7).

**Table 7:** Comparison between successful and failed SBT regarding TAPSE/RVFAC parameters.

TTE (before SBT)	Successful group (42)	Failed group (18)	P value
TAPSE <sub>Mean±SD</sub>	2.03±0.34	1.951±0.325	=0.620‡
RVFAC <sub>N(%)</sub>	49.94±7.34	53.84±9.5	=0.114‡
TEE(after SBT)	Successful group (42)	Failed group (18)	P value
TAPSE <sub>Mean±SD</sub>	19.6±2.73	15.13±1.84	<0.0001**‡
RVFAC <sub>N(%)</sub>	31.11±3.81	22.91±4.25	<0.0001**‡

### Outcome Data

Patients with failed SBT showed highly significant increase in mortality rate compared to successful SBT patients; ( $p=0.002$ ) (Table 8).

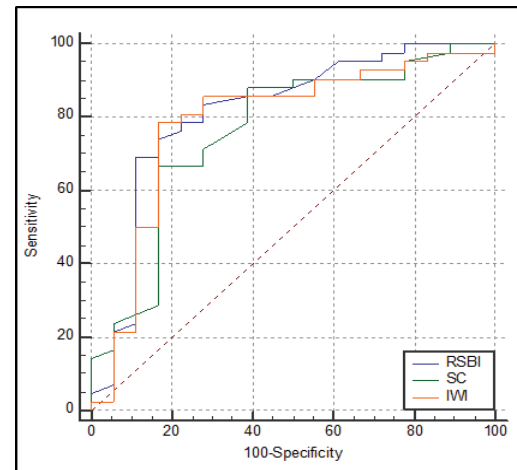
**Table 8:** Comparison between successful and failed SBT regarding outcome data.

Variable	Successful SBT (42)	Failed SBT (18)	P value
Mortality rate <sub>N(%)</sub>	3(7.1%)	8(44.4%)	0.002**‡

### ROC Curve Analysis

By using ROC curve, RSBI at a cutoff point  $\leq 69$  discriminated successfully and failed trials, with good accuracy, sensitivity=69% and specificity=88%, Cstat at a cutoff point  $>46.6$  discriminated successfully

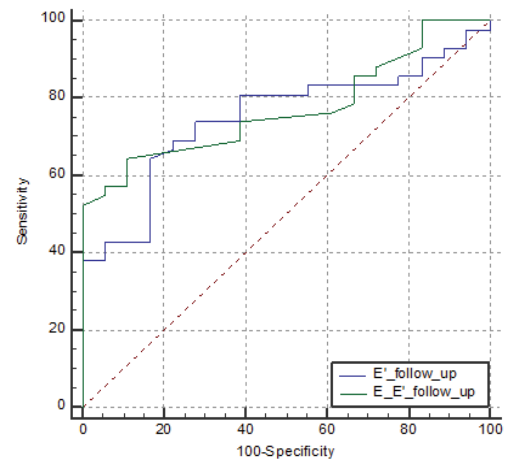
and failed trials, with fair accuracy, sensitivity=66% and specificity=83%. and IWI at a cutoff point  $>54.7$  discriminated successfully and failed trials, with fair accuracy, sensitivity=78% and specificity=83% (Figure 1).



**Figure 1:** ROC curve of RSBI, Cstat and IWI.

ROC-curves of weaning indices cut-off values to discriminate successful SBT patients from failed SBT patients.

By using ROC-curve, E' (after SBT) at a cutoff point  $\leq 9.23$  discriminated successful patients from failed patients, with fair accuracy, sensitivity=64% and specificity=83% and E/E' (after SBT) at a cutoff point  $\leq 9.65$  discriminated successful patients from failed patients, with fair accuracy, sensitivity=64% and specificity=88% (Figure 2).



**Figure 2:** ROC curve of E' and E/E' (after SBT).

### Discussion

The rate of weaning failure in the present study was 30%. This was similar to the incidence reported by Ehab A, et al. (2012) who examined 40 patients, 12 patients (30%) experienced weaning failure and Schifelhain LM, et al. (2011) who enrolled 24 patients did not wean 29 percent for 7 patients [12].

Patients with failed SBT showed significant increase in MV duration; with significant statistical difference ( $p=0.027$ ) compared with successful SBT.

This was agreed with Ghoneim AH, et al. (2017) who recorded



significantly longer MV ( $6.18 \pm 0.9$  days) inpatient with failed SBT than patients with successful SBT ( $4.24 \pm 1.01$  days) ( $P < 0.01$ ) [13].

There was a significant increase in heart rate, mean blood pressure (MAP) and respiratory rate in the failure group compared to performance one ( $p < 0.05$ ) in the current study. These measurements were reported during SBT to predict weaning failure early.

El-Beheidy RM, et al. (2018) Concluded that clinical weaning parameters (blood gases, vital signs and respiratory mechanics) can be used to evaluate the results of weaning [14].

Numerous studies evaluated the diagnostic accuracy of calculating circulating NT-proBNP levels to predict weaning failure before and during SBT [15].

No significant difference in baseline NT-pro BNP levels (before SBT) ( $p > 0.05$ ) was observed in the present work between patients with positive and failed SBT ( $p > 0.05$ ); patients with failed SBT showed; very significant increase in follow-up NT-pro BNP levels (after SBT) compared to successful SBT levels ( $p < 0.0001$ ).

This was agreed with Farghaly S, et al. (2015) who studied 30 patients, (46.6% of patients had failed to wean) to determine the value of BNP levels measured at initiation and end of SBT as a predictor of successful weaning and (after SBT) were significantly higher in patients with failed weaning compared to those with successful weaning ( $P = 0.031$ ). Nevertheless, there was no statistically significant BNP rates (before SBT) between the 2 groups ( $P = 0.722$ ) [16].

During SBT sedation is removed and cardiopulmonary stresses are produced as the increased fan drive changes intrathoracic pressure, increases venous return, increases left ventricular Trans mural pressure and increases afterload. Such stimuli cause naturriuretic peptide secretion with cardiac volume and pressure overload in minutes [17].

With regard to weaning indices, data (ABG) were reported before SBT was started as separate from any normal weaning protocol. The importance of (ABG) to determine when to extubate after SBT is unclear [14]. In the current study,  $\text{SaO}_2$ ,  $\text{PaO}_2$  and  $\text{PaO}_2/\text{FiO}_2$  were lower in patients who failed SBT relative to patients with positive SBT ( $p < 0.05$ ).

This was agreed with the study conducted by Keyal N, et al. (2018) who found similar results during the review of 108 patients and concluded that ABG may help identify patients who may suffer weaning failure [18].

Patients with failed SBT showed highly significant increase in RSBI Compared to active patients with SBT; with a highly significant statistical difference ( $p = 0.001$ ); agreed with Habacon GP, et al. (2016) weaning was successful in 59 patients who studied 71 patients (failed weaning in 12 patients) to assess the function of RSBI as a predictor of weaning outcome, and found that RSBI predicts weaning outcome significantly ( $p < 0.001$ ) [19].

By using the ROC curve, RSBI at a cut-off point = 69 breath/min/L discriminated successfully and failed tests with good accuracy, sensitivity = 69% and specificities = 88%. This was agreed with Youssef HA, et al. (2016) who enrolled 84 patients to evaluate RSBI's predictive value relative to the weaning outcome and reported 67 cutoff point with 67% sensitivity and 72 percent specificity [20].

Although the original RSBI cut-off value is 100-105 breath/min/L, studies using 60 and 76 breath/min/L cut-off values have achieved greater accuracy than the original cut-off value [21].

These variations can be due to the sample size or the absence of a global weaning description and the use of various RSBI measurement methods [22].

Failed SBT patients reported a highly significant reduction in Cst relative to active SBT patients; ( $p < 0.01$ ). This was in agreement with Mahmoud H, et al. (2011) who examined 100 patients to classify the condition, reporting that unsuccessfully weaned patients had lower Cst and also substantial association between longer MV and lower Cst length ( $P < 0.001$ ) [23].

By using ROC-curve, Cst a cut-off point  $> 46.6$  ml/cm  $\text{H}_2\text{O}$  discriminated successfully and failed tests with equal precision, sensitivity = 66% and specificity = 83%. This was accepted with Borges DL, et al. (2014) who registered cut-off point over 43.3 ml/cm  $\text{H}_2\text{O}$ , sensitivity = 74% and specificity = 92% [24].

Patients with failed SBT showed a significant decrease in IWI compared to successful SBT patients; ( $p < 0.01$ ). This was agreed with El-Baradei GF, et al. (2015) who studied 120 patients to assess the efficacy of IWI as a predictor of weaning success and found that IWI had a high sensitivity of 97%, specificity of 78% [25].

By using ROC-curve, IWI at a cutoff point  $> 54.7$  ml/cm  $\text{H}_2\text{O}$ /cycles/min/L discriminated successfully and failed trials, with fair accuracy, sensitivity = 78% and specificity = 83%; which came in agreement with Hassanein E, et al. (2014) who reported that cut-off point of IWI for prediction of successful weaning more than 65.178 with good sensitivity (80.65%) and moderate specificity (77.78%) [26].

Differences in IWI's cut-off point could be explained by difficulties in calculating Cst during the weaning process, as the motivating effort of the patient during the supported breath could conflict with the inspiring pressure calculation of the plateau and this can lead to different values. Variations in  $\text{FIO}_2$  values can also cause variations in  $\text{SaO}_2$  and thus affect IWI values [27].

With regard to TTE data, no significant difference in EF, SV, CO, and LVOT-VTI (before SBT) was observed between patients with positive and failed SBT; these results came in accordance with Caille V, et al. (2010) [7].

No significant difference was found in the frequency of systolic dysfunction ( $\text{EF} < 50$ ) in the follow-up echocardiographic parameters (after SBT) ( $p > 0.05$ ) between patients with active and failed SBT. This was in line with the results obtained by Roche-Campo F, et al. (2018) who studied 67 patients in order to evaluate systolic and diastolic function during the weaning phase and identified systolic dysfunction as  $\text{LVEF} < 50$  per cent with no difference in the incidence of systolic dysfunction between groups ( $p = 0.12$ ) [8].

That may be clarified in many studies by the fact this. It has been shown that 40 to 50 per cent of patients with typical signs of heart failure have an abnormal or slightly reduced LVEF, so the LVEF is not a good predictor of clinical disability and suggests that congestive symptoms are more closely related to the ventricle's diastolic properties than to its systolic properties [28].

Patients with failed SBT showed a marked increase in follow-up CO (after SBT) in the failed group compared to the successful patient group ( $p = 0.013$ ). The increase in CO was correlated with tachycardia due to the unchanged amount of LV stroke. This finding was agreed with Caille V, et al. (2010) who studied 117 patients (20% with weaning failure) and recorded an increase in CO in 6.0 L/min (5.4-6.7) failed SBT patients compared to 5.8 L/min (5.2-6.2) ( $p = 0.004$ ) successful



SBT patients. They also found increases in HR in failed SBT patients (0.00001) [7].

No significant difference in incidence and frequency of MR, (before SBT) between successfully and failed SBT, was observed in the present work. Although after SBT, failed SBT patients showed a significant increase in incidence and severity of MR relative to active SBT; ( $p=0.01$ );

Patients with failed SBT showed a significant increase in the incidence of moderate and severe MR after SBT compared with successful SBT; ( $p=0.01$ ); This finding came in agreement with Gerbaud E, et al. (2012) [29].

With respect to Doppler echocardiographic parameters for assessment of diastolic activity, no significant difference was observed between patients with positive and failed SBT with regard to normal velocities of mitral annulus before or after SBT ( $p>0.05$ ).

This was agreed with Konomi I, et al. (2016) who studied 42 patients and noted that E/A was not associated with the main result [6].

Six observational studies (all of them cohort studies) were included in the systemic review by de Meirelles Almeida CA, et al. (2016) stating that the E/A was not associated with weaning failure (mean difference 0.07, 95% CI -0.04 to 0.18;  $p=0.22$ ) [5].

In follow-up deceleration period (DT) (after SBT) patients with unsuccessful SBT showed significantly shorter compared to active SBT patients; with significant statistical difference ( $p=0.027$ ); this was accepted with Moschietto S, et al. (2012). They found DT values to be significantly shorter in those patients they failed to wean compared to those obtained in successfully weaned patients (median value 215 vs. 170 ms,  $p=0.03$ ) [10].

When relaxation is anomalous, the DT is characteristically prolonged and becomes shorter when relaxation is rapid or high ventricular filling pressures. Its absolute value is inversely related to pulmonary capillary wedge pressure (PCWP). So DT provides precise estimate of left ventricular filling pressure [30].

As for TDI, no significant difference was observed as E' (before SBT) ( $p>0.05$ ) between patients with positive and failed SBT. Nonetheless, patients with ineffective SBT reported a very significant decrease in E' follow-up relative to active SBT patients; with a highly significant statistical difference ( $p=0.005$ ). This was accepted with Roche-Campo et al., who observed that E' velocity decreased by a higher (93.3%) number of patients who failed to wean tests relative to successes ( $p<0.001$ ) and reported that this decrease in E's velocity during failed weaning tests is consistent with reduced diastolic relaxation in these patients [8].

By using ROC-curve analysis, E (after SBT) at a cutoff point of approximately 9.23 cm/sec effectively discriminated against failed SBT with good precision, sensitivity=64% and specificity=83%.

This result was consistent with the cutoff point E' velocity below 10cm/s recorded by Thille AW, et al. (2015) and Papanikolaou J, et al. (2011) who analyzed 50 patients in the general critical care unit, 28 patients (56%) failed to wean and found a cutoff point of 10.5 cm/sec with 71% sensitivity and 73% specificity [31,32].

Patients with failed SBT reported a very significant increase in E/E' (after SBT) follow-up compared with positive SBT patients; ( $p<0.01$ ). This result was also in line with Gerbaud E, et al. (2012) who examined 44 patients (10 patients (22.7%) who failed their SBT) and found that

E/E' increased significantly in those who failed the SBT, as compared to the weaning performance category in which they remained unchanged ( $P=0.006$ ) [29].

ROC curve analysis of E/E' (after SBT) revealed; a cutoff point A9.65 had successfully discriminated against and failed patients with fair accuracy, sensitivity=64% and specificity=88%; This was in agreement with Wang H, et al. (2017) who predicted E/E after SBT greater than 7.9 predicted weaning failure with sensitivity and specificity (82.6% and 91.3%) respectively [33].

The threshold values of E/E' to predict SBT failure differ between studies (range: 7.8 to 14.5) due to different sites of E' measurement, different characteristics of study populations, and cumulative variable fluid balance at SBT time [32].

A dynamic change in diastolic function during weaning stress in patients with a lack of diastolic reserve could be a potential weaning failure mechanism, independent of baseline cardiac function. It means that diastolic dysfunction is a key factor for weaning failure [8].

Patients with failed SBT reported a highly significant increase in incidence of diastolic dysfunction (defined as lateral E' wave velocity less than or equal to 8 cm/sec (after SBT) relative to patients with active SBT; ( $p<0.01$ ).

This was in agreement with Moschietto S, et al. (2012) who studied 63 patients and reported high incidence of diastolic dysfunction in failed SBT patients ( $p=0.0003$ ) [10].

It was also accepted with Konomi et al. who observed 42 patients (15 patients were unable to wean) and noted that LV diastolic dysfunction (a decrease in E' wave and a concomitant rise in E/E') was significantly associated with weaning failure ( $P<0.001$ ) [6].

In the current study, PCWP estimated to estimate LVFP based on E/E in patients with normal sinus rhythm and specific cardiac conditions based on an equation developed by Nagueh SF, et al. (2001) [11].

No significant difference in all baseline PCWP (before SBT) ( $p>0.05$ ) was observed between patients with active and failed SBT. Patients with failed SBT reported a highly significant improvement in PCWP (after SBT) follow-up relative to active SBT patients; ( $p<0.0001$ ).

This was accepted with Lamia EJ (2013) who reported an E/E' >8.5 value calculated with TTE predict weaning-induced PAOP elevation and this allowed precise, non-invasive detection of weaning-induced PAOP elevation and also with Abdelbary A, et al. (2011) who found a correlation between Doppler-derived diastolic filling variables with weaning-induced PAOP elevation (defining the PAOP >18 mmHg after SBT) in failed SBT patients [4,34].

RV function assessed by TAPSE and RVFC, no significant difference was detected between patients with successful and failed TAPSE and RVFAC (before SBT) parameters ( $p>0.05$ ); whereas (after SBT) patients with failed TAPSE and RVFAC showed a highly significant decrease ( $p<0.0001$ ).

Which agreed with Papaioannou VE, et al. (2010) who enrolled 32 mechanically ventilated patients, and observed patients with failed weaning ( $n=12$ ) had decreased TAPSE ( $14.59\pm 1.5$  6SBT vs. failed  $19.13\pm 2.59$  mm ( $p<0.001$ )), decreased RVFAC (percent) ( $11.31\pm 1.02$  in successful SBT vs.  $8.98\pm 1.70$ , failed  $p<0.001$ ); and Increased/E' ( $11.31\pm 1.02$  vs.  $8.98\pm 1.70$ ,  $p<0.001$ ); also in agreement with Roche-Campo F, et al. (2018) who assessed TAPSE for RV and observed a



reduction in TAPSE in patients with failed SBT (after SBT) [8,35].

This could be explained by a rise in weaning-induced RV after load due to hypoxemia or deterioration (PEEPi), in addition to the corresponding increase in systemic venous return, increased RV afterload during weaning, thus preventing the diastolic filling of the left ventricle by a biventricular interdependence mechanism [15].

Regarding mortality, it was 18.3 percent in all patients. Comparative study revealed between successful and failed SBT patients; highly significant mortality rise in failed SBT patients (44.4 percent) compared to successful SBT patients ( $p=0.002$ ).

Shin HJ, et al. (2017) Total mortality rates were registered in 127 patients with prolonged mechanical ventilation (86 patients with weaning failure) at 55.1% who observed very significant differences between positive (13.6%) and failed (77%) SBT [36].

## Conclusion

Clinical, laboratory, echocardiography weaning parameters could be considered a sensitive and specific marker for prediction of weaning failure.

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