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ORIGINAL ARTICLE

Chest Ultrasonographic Assessment of Diaphragmatic Excursion and Thickness as a New Weaning Parameter in Mechanically Ventilated Chronic Obstructive Pulmonary Disease Patients.

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ABSTRACT

Background: Diaphragmatic muscle dysfunction is common among mechanically ventilated COPD patients which leads to weaning failure. Bedsides Diaphragmatic US can be used to predict the extubation outcome. **Aim**: To study the value of chest Ultrasonography in the assessment of both diaphragmatic excursion and thickness as a weaning parameter in mechanically ventilated COPD patients. **Patients and methods**: The study was conducted on 48 mechanically ventilated COPD patients at the time of weaning in the respiratory ICU at Zagazig University Hospitals. The following were done: ABG, and chest X-ray. Ultrasonographic assessment of the right diaphragm (thickness and excursion) during SBT. **The results**: Patients were classified according to weaning outcome into two groups: the successful Weaning group (35 patients), and failed Weaning group (13 patients). Diaphragmatic excursion, tdi at end inspiration, tdi at end-expiration, tdi %, tdi % /f, and tdi % x Vt are significantly higher in the successful group ($p<0.001$). Diaphragmatic excursion and tdi at end inspiration are considered excellent significant discriminators for the success of weaning ($P<0.000$). tdi at end-expiration and tdi % is considered a good significant discriminator for the success of weaning ($P<0.000$). Integration of (Diaphragmatic excursion, tdi %, tdi % /f, tdi % x Vt, RSBI, PI max, PaO_2/FiO_2, and PEEP) can predict weaning success correctly by a percent of 65%. **Conclusions:** Diaphragmatic excursion is the most accurate, sensitive, and excellent discriminator for the prediction of successful weaning among diaphragmatic parameters. Integration of diaphragmatic ultrasound parameters and conventional weaning indices improves the successful weaning predictive value.

Keywords: ultrasound; diaphragm; COPD; Weaning

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is the fourth killer among all diseases worldwide. It can be prevented and treated, so it is an important public health challenge **[1].** Inspiratory muscle weakness has a great clinical association with COPD patients **[2].**

The prolonged mechanical ventilation and weaning failure may be related to diaphragmatic muscle dysfunction **[3].** The traditional weaning parameters (e.g., spontaneous tidal volume (VT), Maximum inspiratory pressure (PI max), and rapid shallow breathing index (RSBI)) are considered useful parameters for weaning. Although, they have unsatisfactory prediction rates **[4].**

Bedside ultrasonography is a non-invasive, safe, and available diagnostic tool for critically ill patients. The prediction of the extubation outcome for mechanically ventilated COPD patients can be assessed using bedside Diaphragmatic US **[5].**

Aim of the Work: To study the value of chest Ultrasonography in the assessment of both diaphragmatic excursion and thickness as a weaning parameter in mechanically ventilated COPD patients and its relation to other traditional weaning parameters to improve the outcome.

METHODS

The setting of the study: The study was carried out at the respiratory ICU, Chest Department, Zagazig University Hospitals in the period from May 2017 to November 2017 after approval of Institutional

Review Board-Zagazig University (IRB-ZU NO. 3701/8-5-2017).

Patients: The study was conducted on Mechanically ventilated COPD patients.

Inclusion Criteria:COPD patients who were on invasive mechanical ventilation and fulfilled the criteria of readiness for weaning trial **[6]:Exclusion criteria:**1) Previous neuromuscular or diaphragmatic disease**, 2)** Morbid obesity (BMI > 40), 3) Intubation due to other medical or surgical causes than COPD, 4) The presence of any mechanical abnormality as (colonic distension, ascites, pulmonary (mass, fibrosis, collapse) or pleural effusion) that may limit the diaphragmatic mobility, 5) Prolonged mechanical ventilation which is the mechanical ventilation for more than 21 successive days, for more than 6 hours per day **[7].**

Study design: Cross-sectional study**.**

Sample size: 48 COPD patients on M.V. at the time of weaning during the period of the study.

Process of the study:

Informed written consent was obtained from relatives of the patients.

Baseline data will be obtained for all patients from their old files.

COPD diagnosis was achieved by fulfilling the presence of the following **[8]: 1)** History of risk factors suggestive of COPD as smoking. 2) Symptoms suggestive of COPD as dyspnea, chest wheezes, chronic cough, and/or sputum. 3) Spirometric functions: the presence of a post-bronchodilator FEV1/FVC less than 0.7, and post-bronchodilator improvement of FEV1 % of predicted less than 12% confirm the diagnosis.

Radiological findings: X-ray chest was done on admission and before weaning.

The mode of mechanical ventilation which was applied for patients was SIMV-VC.

SAPS II, GCS values were assessed at the time of ICU admission **[9] [10].**

Laboratory evaluation: Arterial blood gases (on admission, before Spontaneous Breathing Trial (SBT)), (complete blood count (CBC), Liver enzymes, Coagulation profile, Sodium (Na), Potassium (K), Urea, Creatinine, Tracheal aspirate culture and sensitivity.

Methods:

The weaning process applied for all patients:

Assessment of readiness for weaning [6].

Spontaneous breathing trial (SBT).

SBT was done by applying pressure support of 5 cm H_2O.

The successful SBT was considered when the patient withstands for 30 to 120 minutes.

Criteria of successful spontaneous breathing trials [6]: 1) Respiratory rate less than 35 breaths/minute**. 2)** spontaneous breathing trials were adequately tolerated. **3)** Heart rate less than 140 /minute or variability of the heart rate >20%**. 4)** Arterial oxygen saturation (Sao2) more than 90% or PaO2 more than 60 mmHg on FiO2 less than 0.4**. 5)** Systolic blood pressure is more than 80mmHg and less than 180mmHg or less than 20% change from baseline**. 6)** No signs of respiratory distress or increased work of breathing.

Classification of the weaning process according to SBT Outcome [11]: 1) Simple weaning: the first trial of SBT succeeded.2) Difficult weaning: the first trial of SBT is Failed and up to three trials are needed or less than 7 days to become successful SBT.3) Prolonged weaning: more than 7 days are needed for successful SBT.

If SBT failed: Follow up every 24 hours for readiness for another SBT **[12].**

Planning for extubation: After successful SBT, the patient was assessed for airway removal.

***Airway protection capacity*:**

The presence of an effective cough protects the airway from excessive secretions.

The post-extubation stridor can be detected early by A) *Auscultation test:* The endotracheal tube cuff was deflated, and the air leak sound was heard **[13]:** 1) No sound heard by auscultation: No leak, 2) Leak heard by the stethoscope: Mild leak, 3) Sound of leak heard without stethoscope: Significant leak. B) *Cuff leak volume (CLV):* The amount of leak after deflation of the endotracheal tube cuff depends on the degree of laryngeal edema and complete absence of leak means very severe edema. **First step**, the actual exhaled tidal volumes for six ventilated breaths were recorded, **second step:** the oropharynx was suctioned then deflation of the endotracheal tube cuff and **lastly,** the exhaled tidal volumes for six ventilated breaths were measured again. A cuff leak volume of less than 110 ml was a predictor of a significant risk of post-extubation stridor **[14].**

The extubation was canceled if the Patients cannot protect their airways effectively **[15].**

Mental status:Sedation infusion is stopped **[6].** A Glasgow coma score of more than 8 was associated with successful extubation **[16].**

Extubation was done 24h post successful SBT with follow-up 48h.

Diaphragmatic Ultrasound measurement technique: All patients were evaluated in a semi-recumbent position. Ultrasound was performed during SBT using a Sono scape SSI 4000 ultrasound system (China) to assess the right diaphragm.

Diaphragmatic excursion [17].

It was measured with a lower-frequency curvilinear probe (we used a 3.5MHz probe) in the anterior subcostal view. The transducer was placed between the mid-clavicular and anterior axillary lines, directed medially, cranially, and dorsally to visualize the posterior third of the right diaphragm. Measurement was made in the M-mode, from the point of maximal excursion to the baseline in normal breathing.

Normal values of Diaphragmatic excursion are 2.3–4 and 6–7 cm during quiet and deep breathing respectively (there is a mean increase of diaphragmatic excursion by 54% (range 42–78%).

Diaphragmatic thickness [18]

It was measured with a high-frequency linear probe (10 MHz). The diaphragm was visualized by placing the transducer perpendicular to the chest wall, in the eighth or ninth intercostal space, between the anterior axillary and the mid-axillary lines, to observe the zone of apposition of the muscle 0.5 to 2 cm below the costophrenic sinus. The diaphragm was imaged as a structure with three distinct layers, including two parallel echoic lines (the diaphragmatic pleura and the peritoneal membrane) and a hypoechoic structure between them (the muscle itself). The patient was then instructed to perform breathing to total lung capacity (TLC) and then to exhale to residual volume (RV). Several images of the diaphragm were captured and stored, including at least three at the point of maximum thickening at TLC and at least three at minimum thickening at RV. On each frozen B-mode image, the diaphragm thickness was measured from the middle of the pleural line to the middle of the peritoneal line. Then, the tdi % (trans diaphragmatic thickness fraction) was calculated.

$$\mathbf{tdi\% = \frac{Thickness\ at\ end\ inspiration - Thickness\ at\ end\ expiration}{Thickness\ at\ end\ expiration} \times 100}$$

Normal values of diaphragm thickness 2.5- 5 mm, tdi% > 30 %, tdi % /frequency > 0 .01 br/min, tdi % x VT > 100 ml.

Outcome parameters: Successful weaning: When the patient was able to maintain his or her breathing for 48 h without any level of ventilator support **(11).**

Weaning failure: When mechanical ventilation was required within 48 h of self-breathing or failed SBT **(19)**.

STATISTICAL ANALYSIS

Data analysis was performed using IBM SPSS software package version 20.0. Qualitative data were described using numbers and percentages, and comparisons between different groups regarding categorical variables were tested using the Chi-square test. The distributions of quantitative variables were tested for normality using the Shapiro-Wilk test and the D'Agstino test. If it reveals normal data distribution, parametric tests were applied which included the student T-test, and one-way ANOVA. If the data were abnormally distributed,non-parametric tests were used which included the Mann-Whitney test, and the Kruskal-Wallis test. Quantitative data were described using mean and standard deviation for normally distributed data while abnormally distributed data was expressed using median, minimum, and maximum. For normally distributed data comparisons between two groups were done using an independent t-test while for abnormally distributed data, Mann-Whitney Test was used fore normally distributed data comparison between more than two groups was done using one-way ANOVA while abnormally distributed data comparison between more than two groups was done using Kruskal Wallis. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated for ultrasound-derived measurements of diaphragmatic thickness fraction (Δtdi %) at the right side and excursion. Receiver operating characteristic (ROC) curves were used to evaluate the efficacy of ultrasound-derived measurements of diaphragmatic thickness fraction and excursion in predicting extubation success or failure, area under the curve (AUC) interpretation: 0.9-1 (excellent), 0.7-<0.9 (good), 0.5-< 0.7 (fair), Pearson's correlation was done for finding associations. Multiple regression was done for the prediction of success rate from different variables with R^2 (Regression coefficient), SE (standard error) of measured data, and P value <0.05 was considered statistically significant. Boxplot graphs represent the median and interquartile range.

RESULTS

This study revealed the following results:the baseline characteristics for all the studied patients were the mean age (60±10.97 years) with 79.2% of all patients being males, the mean SAPS II score (43.33 ±13.91), and on admission ABG parameters (pH 7.2±0.07, $PaCO_2$ (mmHg) 80 ± 12.15, PO_2 (mmHg) 57.73 ± 16.09, HCO_3 (m eq/l) 32.71 ± 4.36 **(Data not shown).**

In the present study, the weaning trial was initiated once the patient met the weaning criteria suggested by **Penuelas et al [6].** The mean (HR, Hb, SBP, PaO_2/FiO_2, RSBI, PI max and PEEP) were (85.54±6.55 beat/min, 12.15±1.89 g/dl, 119.7±10.11 mmHg, 294.8±50.22, 99.27±18.93 br/min/l, -29.44±-9.24 cmH_2O and 5.59±0.75 cm H_2O) respectively **(Data not shown).**

Among the 48 studied patients, 37 patients were successful SBT (77.1%) where simple, Difficult, Prolonged, and weaning frequencies were (45.8 %, 16.7%, and 14.6 %) respectively among them, with weaning outcomes (35) patients showing successful weaning (72.9 %). Failed weaning was reported in 13 cases, (9/13) patients (69.2%) because of failed SBT, 2/13 two patients were in need for re intubation and M.V(15.4%), and the remaining two patients died. All cases with simple weaning (22) were successfully extubated contributing to (62.9%) of Successful weaning outcomes **(figure 1).**

Patients were classified according to weaning outcome into two groups:

- Group (I) (Successful Weaning): They were (35) patients act as 72.9%, (28) males and (7) females with a mean age of 57.55± 10.48 years.
- Group (II) (Failed Weaning): They were (13) patients act 27.1%, (10) males and (7) females with a mean age of 65.92± 10.48 years.

Regarding the baseline characteristics of both successful and failed weaning groups: BMI(25.03±1.68 vs 26.66 ± 3.04 Kg/m2) (P-value= 0.03), FEV1 % of the predicted (52.81±11.06 vs 31.91±5.66) (P-value = 0.000), pao_2 (63.65±13.4 vs 41.79 ± 11.31 mmHg) (P-value = 0.000), SAPS II score (36.8±9.43 vs 60.9±6.77) (P-value = 0.000) in groups (I) and (II) respectively **(Data not shown).**

The successful weaning group was associated in a highly significant way (P-value = 0.000) with lower RSBI (83±11.2 vs 98 ±16.2 breath /min /l) and lower PEEP (5.3±0.6 vs 6.4±0.5 cmH2o). While a higher hemoglobin level (12.8±1.7 vs 10.6±1 g/dl), higher PI max (-32.7±7.4 vs-20.2±7.23 cm H2O), and higher PaO2/FiO2 (318±32.8 vs 234±32.8) at time of weaning in comparison to failed weaning **(Data not shown)**.

As regards the Diaphragmatic ultrasound findings to the weaning outcome, **Table (1)** showed that Diaphragmatic excursion, tdi at end inspiration, tdi at end-expiration, tdi %, tdi % /f, tdi % x Vt were significantly higher in the successful group than failed one (P-value = 0.000).

This **table (2)** demonstrated that there was a significant negative correlation between RSBI and (diaphragmatic excursion, tdi%, tdi%\ f and tdi %x Vt), PEEP and (diaphragmatic excursion, tdi%, tdi%\ f and tdi %x Vt). While there was a significant positive correlation between PI max and(diaphragmatic excursion, tdi%, tdi%\ f and tdi %x Vt), PaO2/FiO2 and (diaphragmatic excursion, tdi%, tdi%\ f and tdi %x Vt).

The accuracy of Diaphragmatic ultrasound parameters as predictors of weaning success were shown in **Table (3) as follows:**

- **A cut-off value ≥ 1.8 cm for the diaphragmatic excursion** was associated with successful weaning with 91% sensitivity, 85% specificity, 94% PPV, 81.2% NPV, and 89.5% accuracy. The diaphragmatic excursion is considered an excellent significant discriminator for the success of weaning as AUC =0.93 with 95 % CI (0.85-1) (P<0.000)
- **Cut-off value ≥ 3.25 mm for tdi at end inspiration** was associated with successful weaning with 87% sensitivity, 77% specificity, 90.5% PPV, 70.5% NPV, and 83.3% accuracy. tdi at end inspiration is considered as an excellent significant discriminator for the success of weaning as AUC =0.91 with 95 % CI (0.8-0.99) (P<0.000)
- **Cut-off value ≥ 2.5 mm for tdi at end expiration** was associated with successful weaning with 83% sensitivity, 54% specificity, 80.5% PPV, 57% NPV, and 75% accuracy. tdi at end expiration is considered a good significant discriminator for the success of weaning as AUC =0.79 with 95 % CI (0.65-0.94) (P<0.000)
- **Cut-off value ≥ 32 %For tdi %** was associated with successful weaning with 86% sensitivity, 77% specificity, 90% PPV, 70% NPV, and 83% accuracy**.** tdi % is considered a good significant discriminator for the success of weaning as AUC =0.89 with 95 % CI (0.8-0.99) (P<0.000).
- **Cut-off value ≥ 0.02 br /min for tdi % /f** was associated with successful weaning with 83% sensitivity, 85% specificity, 93.5% PPV, 66% NPV, and 83.3% accuracy**.** tdi % / f is considered an excellent significant discriminator for the success of weaning as AUC =0.92 with 95 % CI (0.83-0.99) (P<0.000).
- **Cut-off value ≥ 98.2ml for tdi % x Vt** was associated with successful weaning with 91% sensitivity, 77% specificity, 91.4% PPV, 77% NPV, and 87.5% accuracy**. tdi** % x vt is considered an excellent significant discriminator for the success of weaning as AUC =0.9 with 95 % CI (0.81-0.99) (P<0.000).

Diaphragmatic excursion, tdi %, tdi % /f, and tdi % x Vt were able to predict weaning success in a high significant manner p<0.0001. Integration of diaphragmatic parameters together was able to predict weaning success correctly by a percentage of 61% **(Table 4). Also, table (5)** demonstrated that RSBI, PI max, PaO_2/FiO_2, and PEEP can predict weaning success in a high significant manner p<0.0001. Integration of those weaning indices could predict weaning success by a percentage of 53%. So, Integration of both Diaphragmatic ultrasound parameters and weaning indices for prediction of weaning success (Diaphragmatic excursion, tdi %, tdi % /f, tdi % x Vt, RSBI, PI max, PaO_2/FiO_2, and PEEP) can predict weaning success correctly by percent of 65%

Table 1: Diaphragmatic ultrasound finding in relation to weaning outcome.

Variable	Successful weaning	Failed weaning	Student T-test	p. value
Diaphragmatic excursion (cm)	2.6±0.6	1.5±0.3	6.04	0.000**
tdi at end inspiration(mm)	4.01±0.5	3.01±0.5	5.81	0.000**
tdi at end expiration(mm)	2.8±0.3	2.4±0.4	4.07	0.000**
tdi %	40± 9	26± 8	5.07	0.000**
tdi%\ f (%/br /min)	0.026⸗	0.011⸗	3.76^	0.000**
tdi % x Vt (% ml)	220.16⸗	61.6⸗	3.71^	0.000**

⸗ Median ^ Mann-whitney test

Table 2: Correlation between diaphragmatic excursion, tdi%, tdi%/f, tdi% x Vt and weaning indices.

	diaphragmatic excursion		**tdi%**		**tdi%/ f**		**tdi %x vt**	
	R	**P**	**R**	**P**	**R**	**P**	**R**	**P**
RSBI (br/min /l)	-0.87	0.000	-0.87	0.000	-0.89	0.000	-0.840	0.000
PI max (cmH_2O)	0.79	0.000	0.78	0.000	0.78	0.000	0.78	0.000
PaO_2/FiO_2	0.92	0.000	0.87	0.000	0.89	0.000	0.88	0.000
PEEP (cmH_2O)	-0.84	0.000	-0.8	0.000	-0.84	0.000	-0.84	0.000

Table 3: Accuracy of Diaphragmatic ultrasound parameters in prediction of weaning success**.**

Variable	The best cut of value	Area under curve	Sensitivity	Specificity	PPV	NPV	Accuracy
Diaphragmatic excursion(cm)	≥1.8	0.93	91%	85%	94%	81.2%	89.5%
tdi at end inspiration(mm)	≥3.25	0.91	87%	77%	90.5%	70.5%	83.3%
tdi at end expiration (mm)	≥2.5	0.79	83%	54%	80.5%	57%	75%
tdi %	≥0.32	0.89	86%	77%	90%	70%	83%
tdi%/ f (%/br /min)	≥0.02	0.92	83%	85%	93.5%	66%	83.3
tdi % x Vt (% ml)	≥98.2	0.9	91%	77%	91.4%	77%	87.5

Table 4: Multiple linear regression analysis of the Diaphragmatic ultrasound parameters for prediction of weaning success.

Variable	**Prediction of weaning success**			
	B	**SE**	**Beta**	**Significance**
Diaphragmatic excursion (cm)	0.014	0.009	0.49	0.000
tdi %	0.022	0.01	0.37	0.000
tdi%\f (%/br /min	0.06	0.13	0.13	0.000
tdi % x Vt (% ml)	-0.004	0.004	-0.4	0.000
tdi end inspiration(mm)	0.19	0.17	0.26	0.000
tdi end expiration (mm)	0.001	0.001	0.17	0.000

R^2 =0.61

Table 5: Multiple linear regression analysis of weaning indices for prediction of weaning success.

Variable	prediction of weaning success			
	B	**SE**	**Beta**	**Significance**
RSBI (br \min \l)	-0.49	0.25	0.65	0.000
PI max (cm H2O)	-3.6	3.6	-0.79	0.000
PaO_2/FiO_2	0.003	0.003	0.5	0.000
PEEP(cm H2O)	1.3	1.34	1.6	0.000

R^2 =0.53

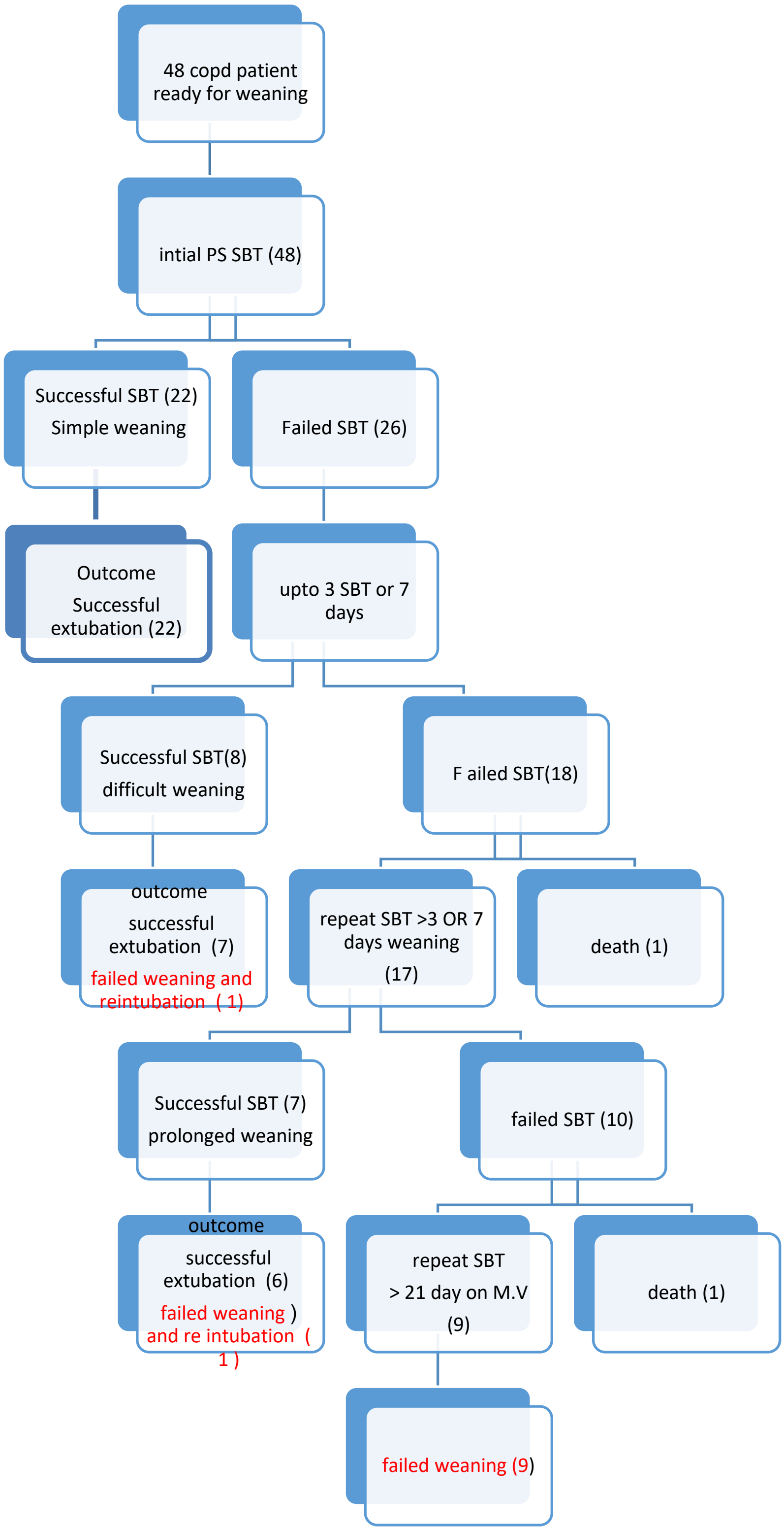

Figure 1: Flow chart of the weaning outcome of the current study

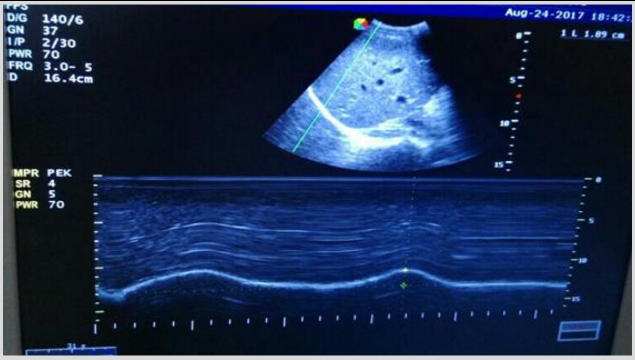

Fig. (2a)

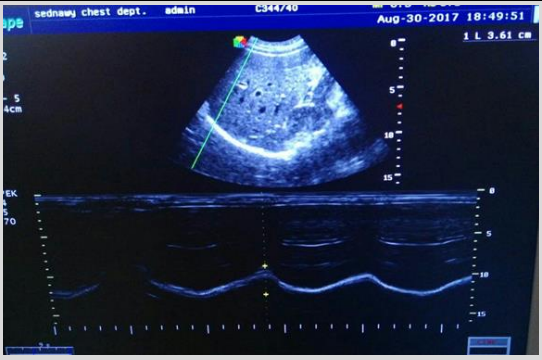

Fig. (2b)

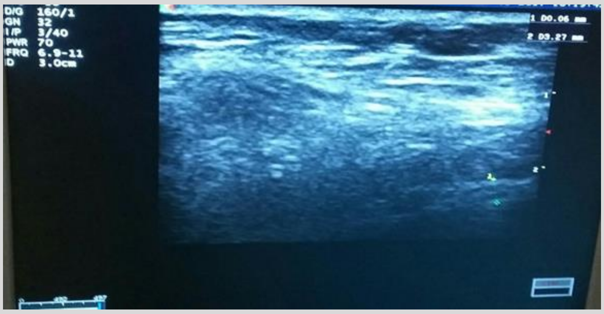

Fig. (2c)

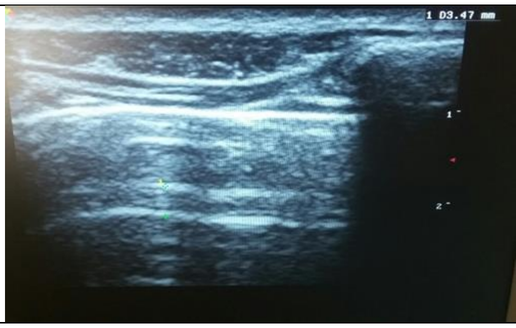

Fig. (2d)

Figure 2: showed ultrasonographic images of some diaphragmatic measures during the current study: Fig (2a) demonstrated the Diaphragmatic excursion measurement (1.89 cm). Fig.(2b): Diaphragmatic excursion measures (3.61 cm). Fig. (2c): Diaphragmatic thickness at end-expiration measures (3.27 mm). Fig. (2d): Diaphragmatic thickness at end inspiration measures (3.47 mm).

DISCUSSION

One of the most crucial periods for mechanically ventilated COPD patients is the period of weaning. Patients with chest overinflation, respiratory muscle weakness, and inadequate nutrition have more liability for developing difficult spontaneous breathing trials. So, many factors might affect COPD patients and lead to weaning failure from mechanical ventilation (MV) **[20].**

In COPD patients, the hyperinflation of the lung causes abnormal diaphragmatic contraction due to a decrease in the pressure-generating capacity of the diaphragm, as the diaphragm muscle fibers become shorter, so the diaphragm will contract on the steep part of its length-tension curve which is a mechanical disadvantage for the diaphragm. Therefore, acquired diaphragm dysfunction had a significant negative impact on the duration of mechanical ventilation (MV), weaning outcome, and survival **[21].**

Ultrasound is commonly used as a diagnostic tool by critical care physicians. For mechanically ventilated patients. It can detect diaphragm dysfunction and assess diaphragmatic mobility during spontaneous breathing weaning trials. Ultrasound is an available, fast, and non-invasive test that can be used frequently without radiation hazards **[22].**

The Present study was conducted on 48 mechanically ventilated COPD patients admitted to the Respiratory Intensive Care Unit of the Chest Department at Zagazig University Hospitals. Aiming to study the value of chest Ultrasonography in the assessment of both diaphragmatic excursion and thickness as weaning parameters in mechanically ventilated COPD patients and their relation to other traditional weaning parameters to improve the outcome.

Many studies had evaluated diaphragmatic excursion and thickness in mechanically ventilated COPD patients as **Fayed et al [23]and Saeed et al [24]** who assessed the diaphragm US in invasively mechanically ventilated COPD patients. Other studies evaluated the diaphragmatic ultrasound (US) as additive new parameters for the weaning process but on different intensive care unit (ICU) patient groups, **DiNino et al [25]** recruited patients from medical intensive care units with different respiratory failure causes. Also, **Ferrari et al [18]** assessed patients on pressure support ventilation through a tracheostomy tube after one or more failed attempts of weaning. **Osman and Hashim**

[26] studied patients from different ICUs who were admitted due to different causes, mainly post-major surgeries.

The current work assessed the Rt dome of the diaphragm as it is the preferable side by most authors as **DiNino et al [25] and Ferrari et al [18]** as the liver lies below the right hemidiaphragm and hence provides a better acoustic window for the right dome with easy measurement of tdi.

In the present study, the following Diaphragmatic U.S findings were assessed during SBT for all patients (Diaphragmatic excursion, tdi at end inspiration, tdi at end-expiration, tdi%, tdi % /f and tdi % x VT) with mean values of (2.27±0.73cm, 3.74±0.68 mm, 2.71±0.38 mm, 38±0.11%, 0.02±0.008%/br/min, 163±84.94%ml) respectively which are nearly comparable to **Fayed et al [23]** findings whose RT hemidiaphragm measures among COPD patients were: tdi at end-inspiration 4.89 ± 1.0 mm, tdi at end-expiration 3.61 ± 0.74 mm, tdi % 35 ± 0.09. However, **Saeed et al [24]** found that the mean diaphragmatic displacement in mechanically ventilated COPD patients was 1.3 cm, this discrepancy may be because we used M-mode to evaluate the diaphragmatic excursion as it was easier than the B-mode during dealing with non-cooperative-ICU-patients. While **Saeed et al [24]** assessed the mobility using B-mode.

As regards weaning outcome, Successful weaning was reported in 35 patients (72.9%) while weaning failure was reported among 13 patients (27.1%) where out of the 13 failed patients 9 patients showed failed SBT,2 patients were re-intubated and the remaining 2 patients were died". This is consistent with **Saeed et al [24]**, and **Osman and Hashim [26]** who showed failure rates of about 20%, 26.7%, and 23.3% respectively. This is controversial to **Ferrari et al [18]** who reported a 63% failure rate, which may be due to different study populations with different causes for mechanical ventilation as well as different ventilation periods before starting a weaning process which may affect the weaning outcome.

In the current study, Regarding RSBI at the time of weaning**,** its value was significantly lower (83±11.2 breaths/min/ml) in patients with successful weaning than in patients with failed weaning (98 ±16.2breaths/min/ml) which were consistent with many studies among COPD patients as **Ferrari et al [26]** who detected that RSBI had a median 70 in the success group and 120 in the failure group with a *p*-value (<0.0001) also, **Fayed et al [23]** who found that RSBI had a median of 60 and 100 in success and failure group respectively with a *p*-value (<0.001).On the contrary, **Tanios et al [27]** and **Elgazzar et al [28]** reported no significant difference regarding RSBI between successfully weaned patients and failed weaning patients in their studies.

Although all participants in the present study had RSBI <105 according to weaning criteria and were eligible for weaning, 13 patients failed. This was consistent with the result of **DiNino et al [25]** who previously explained that RSBI is an integrative function of all inspiratory muscles. So, during the diaphragmatic fatigue, the contraction of the other inspiratory muscles will be adequate to preserve the tidal volume which will mask the diaphragm weakness initially but later, the intercostal muscles become more fatigable than the diaphragm, and adequate ventilation cannot be maintained. So, at the time of weaning, patients may have an initial acceptable RSBI but later fail. **Fadaii et al [26]** who assessed the RSBI as a predictor of weaning in the respiratory care unit, reported that RSBI of less than 105 breaths/min/ml was a good weaning index, but its application alone may be delusive; other factors as general patient status, poorly controlled comorbidities, and ICU length of stay should be considered for successful weaning.

In the present study, at the time of weaning, the value of PI max in the group with successful weaning was more negative (-32.7±7.4) than the value in the group with failed weaning (-19.5±7.23), revealing the ability of the respiratory muscles of the group with successful weaning to create more negative pressure than the group with failed weaning. However, PI max still needs a cooperative patient to be able to exert a maximal respiratory effort other than diaphragmatic displacement measured in quiet breathing **[18].** These results matched with **Saeed et al. [24] and Youssef et al [30]** who revealed statistically significant higher negative values of PI_{max} in the success group compared with the failure group in their studies.

In contrast, **Mabrouk et al [31]** who studied many predictors for successful weaning from mechanical ventilation, found no significant difference between the two groups as regards PI max, which may be due to the recruitment of patients with non-respiratory causes of respiratory failure; moreover, their weaning methods from mechanical ventilation were different. Indeed, the measurement of PI_{max} alone could not predict the weaning outcome mainly in patients with a $PI_{max} \geq$ -20 to -30 cm H2O as the patient's cooperation can not be confirmed at that time as they are mostly so ill. On the contrary, normal muscle with a normal PImax may become fatigued if loaded by excess respiratory work which causes respiratory failure as agreed with **El-Khatib et al [32]**

Regarding the Diaphragmatic excursion as a predictor for the weaning outcome, In the present stu dy, the value of Diaphragmatic excursion in the group with successful weaning was significantly higher (2.6±0.6 cm) than the value in the group with failed weaning (1.5±0.3cm) with cut off value for weaning success ≥ 1.8 cm to be an excellent significant discriminator with (91 % SN, 85% SP, 94%PPV, and 81.2% NPV). In agreement with those findings despite the variations in the reported values **Saeed et al. [24]** concluded that the mean value of diaphragmatic displacement in the group with successful weaning was 1.4 cm, which was higher than the mean value in the group with failed weaning, which was 1.05 cm in COPD patients, with sensitivity 86.8%, specificity 87.5%, and accuracy of 89% using cutoff value 1.1 cm.

Jiang et al [33] Evaluate the movements of the Liver / Spleen and extubation outcome, The cut-off value for predicting successful extubation was 1.1 cm by ROC curve analysis. Using this cut-off value, the sensitivity, and specificity of this method to predict successful extubation were 84.4% and 82.6%, respectively. The positive and negative predictive values were 81.8% and 86.4%, respectively. The accuracy was 83.6%. Similar data had been reported by **Makhlouf et al [34]** and **El Hoffy and Khamis [35].** Despite the different cut-off values, the previous studies of mechanically ventilated COPD patients agreed that diaphragm excursion is a significant predictor of successful extubation. However, many other factors might affect the diaphragmatic motion as tidal volume, the proximity of the rib cage, and the abdominal organs **[36]**

In the present study, tdi at end expiration (mm) as a predictor for weaning was significantly NPV)higher in the group with successful weaning (2.8±0.3mm) than the group with failed weaning (2.4±0.4mm) with cut-off value ≥ 2.5 mm which is a good significant discriminator for weaning success with (83 % SN, 54 % SP, 80.5 %PPV, and 57 % NPV) and AUC=0.79 (P<0.002). The previous results were in accordance with **McCool et al [37]** who stated that tdi measurement at end-expiration reflected the diaphragmatic strength in healthy individuals. Hence, a strong diaphragm would achieve successful extubation. On the contrary, **DiNinio et al [25]** showed that in their pressure support group, tdi at end expiration on the right side can predict the weaning outcome with (84 %SN, 18 %SP,70 % PPV, and 33% NPV), with the area under the ROC curve was 0.61. Measuring tdi at end expiration failed to improve extubation predictions. This discrepancy with our results may be due to the variability of tdi among individuals and the different patient groups in their study.

In the present study, **tdi %** as a predictor for weaning outcome was significantly higher in the group with successful weaning (0.4±0.09) than the group with failed weaning (0.26±0.08) with cut-off value for **tdi %**≥ 32 % as a predictive for success which is a good significant discriminator for weaning success with (86 %SN, 77% SP, 90% PPV, and 70% NPV). **DiNino et al [25]** have used ultrasound for measuring the diaphragmatic thickness to predict extubation outcome in any patient ventilated due to respiratory failure regardless of the cause. The resulting sensitivity and specificity were 88% and 71%, respectively. The PPV of a Δtdi% ≥ 30% for extubation success was 91% and the NPV of a Δtdi < 30% for extubation failure was 63%.Also, **Fayed et al [23]** evaluated the tdi % as a new predictive index of weaning in COPD, The cut-off value of tdi>29% at the right side was associated with successful weaning with 97% sensitivity, 73% specificity, 0.90 positive predictive value (PPV), 0.91 negative predictive value (NPV) and 91% accuracy.

Integration between different parameters was done to increase the predictive value of weaning success as tdi%/f and tdi% x Vt. Regarding t**di %/f** as a predictor for weaning In the present study, the median value of **tdi %/f** in the group with successful weaning was significantly higher (0.026 br/min) than the median value in the group with failed weaning (0.011 br/min) with a cut-off value For **tdi %/f** ≥ 0.02 br/min which is an excellent significant discriminator for weaning success with (83% SN, 85%SP, 93.5% PPV, and 66% NPV) with AUC= 0.92.

Regarding **tdi %x Vt** as a predictor for weaning in the current study, the median value of **tdi %xVt** in the group with successful weaning was significantly higher (220.16 ml) than the median value in the group with failed weaning (61.6 ml) with a cut-off value for **tdi % x Vt** is ≥ 98.2 ml which is an excellent significant discriminator for weaning success with (91% SN, 77% SP, 91.4% PPV, and 77% NPV) with AUC =0.9. So, combined measures of Δtdi% with components of breathing pattern (Vt or f) in the current study, were better than **tdi %** alone in the prediction of weaning outcome. It can be explained as a shortening of the Diaphragm is responsible for most of the change in inspiratory volume. For a given degree of diaphragm shortening, an ‘efficient’ diaphragm will produce a larger tidal volume and lower frequency of breathing than a diaphragm which contracts at a mechanical disadvantage **[25].**

This result was not matched with **DiNino et al [25]** who concluded that combing either Vt or f with Δtdi % did not improve extubation predictions, as in their study, the cut-off value for Δtdi%×Vt was ≥80 ml with (88% SN,71% SP, 91%PPV, and 63% NPV) AUC was 0.76. A cut-off value for Δtdi %/f was ≥0.008 with (92%SN, 67% SP, 90%PPV, and 71%NPV) AUC was 0.75. This difference may be due to different patient populations (which had different causes of respiratory failure) and different weaning methods used "PS and SB" in the latter study.

In the current study, analysis of the Diaphragmatic ultrasound parameters for prediction of weaning success (Diaphragmatic excursion, tdi%, tdi%/f, and tdi% x Vt) was able to predict weaning success correctly by a percent of 61%. While, analysis of traditional weaning indices for prediction of weaning success (RSBI, PI max, PaO2/FiO2, and PEEP) were able to predict weaning success correctly by percent of 53%.No studies show integration results between further weaning indices but, **Nemer et al [38]** reported a new integrative weaning index (IWI) that may predict the weaning outcome accurately. The IWI is the product of static compliance and arterial oxygen saturation divided by the f/Vt. Using a threshold of 25 ml/cmH2O/breaths/l/minute gave a sensitivity of 0.97 and a specificity of 0.94. However, the static compliance of the respiratory system was measured with difficulty in the spontaneously breathing patient in the latter study. Another study by **Boniatti et al [39]** concluded that the modified IWI as well as other weaning predictors do not accurately predict extubation failure.

The current study revealed that Integration of both Diaphragmatic ultrasound parameters and traditional weaning indices for prediction of weaning success (Diaphragmatic excursion, tdi %, tdi % /f, tdi % x Vt, RSBI, PI max, PaO2/FiO2, and PEEP) can predict weaning success correctly by percent of 65%.In a multiple linear regression analysis**, Numis et al [40]** reported that diaphragm excursion only was significantly associated with longer weaning time (p=0.003). ROC curve with a weaning time longer than 36 hours was considered a positive state. The AUC value was 0.912(p<0.001). The higher sensitivity rate (100%) was achieved with a specificity rate of 86.7%and a cut-off value of 3.165 cm, so patients with an excursion lower than 3.165 cm were better to be weaned after at least 36 hours, while patients with an excursion higher than 3.165 cm could be weaned within 36 hours.

CONCLUSIONS

1-Diaphragmatic ultrasound parameters (Diaphragmatic excursion, tdi %, tdi % /f, tdi % x Vt) have higher predictive values than the conventional weaning indices (RSBI, PI max, PEEP, Pao2/FIo2) for prediction of successful weaning among mechanically ventilated COPD patients.

The 2-Diaphragmatic excursion is the most accurate, sensitive, and excellent discriminator for the prediction of successful weaning among diaphragmatic parameters.

3-Integration of ventilator parameters (Vt,f) to tdi % improves the accuracy, sensitivity, and power of discrimination to predict successful weaning.

4-Integration of diaphragmatic ultrasound parameters and conventional weaning indices improves the successful weaning predictive values.

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