Original Article

Role of diaphragm ultrasound in weaning mechanically ventilated patients: A prospective observational study

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ABSTRACT

Background and Aims: Weaning from mechanical ventilation based on clinical parameters and rapid shallow breathing index (RSBI) is associated with a higher weaning failure. Bedside ultrasound of the diaphragm is gaining popularity to assess the diaphragm function. The aim of our study was to determine the use of diaphragm ultrasound in weaning ventilated patients. Methods: This prospective study was done on 200 adult patients on mechanical ventilation for more than 24 h. After meeting the clinical weaning criteria, a spontaneous breathing trial (SBT) was performed. RSBI was recorded and a bedside ultrasound of the diaphragm was performed to measure diaphragmatic excursion (DE) and diaphragm thickening fraction (DTF) before extubation. We assessed the predictability of weaning success of RSBI, DE and DTF by determining the area under the receiver operating characteristic (AUROC) curve and Youden's index. The requirement of non-invasive ventilation or re-intubation within 48 h was considered a weaning failure. Results: Out of the 200 patients studied, 171 were successfully weaned. The AUROC values for RSBI, DTF, DE, RSBI-DTF and RSBI-DE for successful weaning prediction were 0.422, 0.654, 0.809, 0.656 and 0.807, respectively. The predictability using cut-off values were DE >1.21 cm (sensitivity 94%, specificity 71%, Youden's index 0.65), DTF >37% (sensitivity 80%, specificity 52%, Youden's index 0.31) and RSBI <82 (sensitivity 94%, specificity 31%, Youden's index 0.25). Conclusion: Diaphragm ultrasound helps in predicting successful weaning in mechanically ventilated patients. Both DE and DTF showed a higher specificity than RSBI and a combination of RSBI-DE and RSBI-DTF was better than using RSBI alone.

Key words: Diaphragm, extubation, mechanical ventilation, ultrasonography, weaning

INTRODUCTION

Weaning mechanically ventilated patients in the intensive care unit (ICU) is a challenging task for anaesthesiologists. About 20% of ventilated patients have difficulty in weaning.^[1] The diaphragm is the primary muscle involved in active inspiration and its dysfunction leads to inadequate coughing and respiratory failure.

Most patients are weaned based on their subjective clinical assessment by the intensivist and this can lead to mis-judgements at times. Numerous objective measurements and indices such as minute ventilation, rapid shallow breathing index (RSBI), tracheal occlusion pressure 0.1 and the CROP (Compliance, Rate, Oxygenation, Pressure) index have been introduced to improve weaning success, but have their own limitations.^[2] RSBI has gained the most popularity and various studies have demonstrated

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RSBI's usefulness in weaning; however, the suggested cut-off values differ amongst these studies and a few concluded that RSBI is an inefficient tool in weaning ventilated patients.^[3-8]

The tools that can assess the diaphragm function such as fluoroscopy, phrenic nerve conduction study and trans-diaphragmatic pressure measurements are limited by technical difficulty, unavailability and by being expensive.^[9] Diaphragm ultrasound has been employed in the assessment of diaphragm dysfunction following interscalene blocks.^[10,11] Imaging the diaphragm with ultrasound can be done either by measuring the excursion of the diaphragm (DE) or by measuring the contractility of the diaphragm muscle by diaphragm thickening fraction (DTF).^[12] DE more than 1.2 cm and DTF more than 36% were found to predict successful weaning in previous studies.^[13,14] The cut-off values, the area under the receiver operating characteristic (AUROC) curve values, and sensitivity and specificity values of the ultrasound-derived diaphragm parameters (DE and DTF), however, differ among the studies.

We hypothesised that the parameters derived from the ultrasound of the diaphragm, DE and DTF are likely to predict the weaning better than RSBI in predicting weaning success. The primary objective of our study was to determine the diagnostic accuracy of DTF and DE in predicting weaning success. The secondary objectives were to correlate RSBI with ultrasound-derived diaphragm parameters (DTF and DE) and also determine the accuracy of combining RSBI with DTF or DE in predicting successful weaning.

METHODS

This was a prospective, observational cohort study conducted in the intensive care unit (ICU) of a tertiary care hospital. The institutional ethics committee approval (IEC no. 1889/IEC/2019) was obtained, and the study was commenced after registration in the Clinical Trials Registry (CTRI/2020/06/025743). The study was conducted following the guidelines of the Declaration of Helsinki.

In total, 200 consecutive mechanically ventilated adult patients in the ICU were enroled in the study from July 2020 to August 2021. The written, informed consent was obtained from the immediate blood relatives of the patients. Patients in the age group between 18 and 60 years with normal performance status before the disease onset (pre-illness frailty score less than 3), who were mechanically ventilated for at least 24 h and with satisfactory clinical weaning parameters such as the ability to tolerate a spontaneous breathing trial (SBT) for 1 h, stable haemodynamics without inotropic support, conscious and oriented, displayed an absence of fever in the last 24 h, had minimal tracheobronchial secretions and effective cough response were included.^[15] Patients with neuromuscular disorders, pneumothorax, pre-existing diaphragmatic palsy, tracheostomised, and those who underwent thoracic and abdominal surgeries were excluded from the study.

This was an observer-blinded study with the ultrasound being done by a single independent anaesthesiologist who had more than 10 years of experience with ultrasound. The intensivist performing the extubation was not aware of the ultrasound findings as well as RSBI, which was calculated by another independent anaesthesiologist and hence, the decision-making on extubation was not influenced.

The patients who were on mechanical ventilation for more than 24 h and the underlying cause resolved, were subjectively assessed for the readiness of weaning by the primary anaesthesiologist in the ICU. They were weaned based on the clinical criteria, which included adequate mentation (Glasgow coma scale [GCS] score of 10T/15), stable haemodynamics (mean arterial pressure 60-110 mm Hg and pulse rate 60-100 beats per minute), adequate spontaneous ventilation (tidal volume (V_{T}) >8mL/kg, respiratory rate (RR) <20/min), adequate muscle strength (sustained head lift for 30 s and handgrip), Visual Analogue Scale (VAS) pain scores <3 and satisfactory arterial blood gas (ABG) reports. At the end of 1 h of SBT, RSBI was calculated from the equation RSBI = f/V_{T} (f = RR in breaths per minute and V_{T} = average tidal volume in litres with no or minimal support of 5cm H₂O) before extubation by a second anaesthesiologist, and this value did not affect the decision of extubation.

Before extubating the patient, another experienced anaesthesiologist performed the bedside ultrasound of the diaphragm with a GE LogiQ machine, China. The patients were placed in a semi-recumbent position at an angle of 45°. A low-frequency 3–5 MHz curvilinear transducer was placed in the right subcostal margin in B-mode and tilted cranially to visualise the dome of the diaphragm. The patient was asked to take a breath from the residual volume (RV) to the total lung capacity (TLC) and then exhale back to the RV (i.e. maximal exhalation followed by a maximal inhalation and then maximal exhalation). The excursion of the diaphragm was measured in M-mode, and the maximum displacement from the baseline was taken as DE in centimetres [Figure 1a]. The paradoxical movement of the diaphragm was ruled out at the commencement. We performed an ultrasound examination of the right hemidiaphragm in all patients because of a better hepatic acoustic window.

A high-frequency 8–13 MHz probe was placed between the anterior and mid-axillary line on the right side at the level of the eighth or ninth intercostal spaces to visualise the diaphragm muscle and the zone of apposition of the diaphragm with the pleura. The diaphragm muscle was visualised as a band with the pleural lining cranially and the peritoneal lining caudally. The thickness of the diaphragm at maximum inspiration (TD_{max}) and maximum expiration (TD_{min}) was measured in M-mode [Figure 1b].The DTF was then calculated using the formula

$$[DTF = (TD_{max} - TD_{min})/TD_{min} \times 100]$$

and expressed as a percentage.

Successful weaning was defined as the ability of the patient to tolerate spontaneous breathing for at least 48 h. Weaning failure was defined as the requirement of non-invasive mechanical ventilation or re-intubation within 48 h of extubation.

The sample size was calculated based on a previous study by Pirompanich *et al.*^[16] considering the predictability of DTF, which was our primary objective in this study with 90% study power and 5% type I error. Finally, 200 patients were included in the study. Data were entered in the MS-Excel spreadsheet (2019) and analysed using the Statistical Package for the Social Sciences version 22 (trial version). Parameters such as RSBI, DE and DTF are represented as mean \pm standard deviation (SD), median, inter-quartile range (IQR) and range values. The Kruskal–Wallis test was used to determine the significance of RSBI, DTF and DE as indicative parameters. A two-tailed *P* value of less than 0.05 was considered statistically significant, and less than 0.001 was considered highly significant.

Sensitivity. specificity, positive and negative predictive values and the Youden's index for RSBI, DTF and DE as weaning prediction indicators were calculated. Receiver operating characteristic (ROC) curve analysis was performed, and the AUROC was calculated to assess the abilities of RSBI, DTF and DE as well as the RSBI-DE and RSBI-DTF combinations to predict weaning success. The cut-off point for all three parameters was chosen as the point that maximised Youden's index (J_{max}) because this provided the optimal trade-off between sensitivity and specificity. The coefficient of determination (R-squared) was used as a measure of the strength of correlation between different variables.

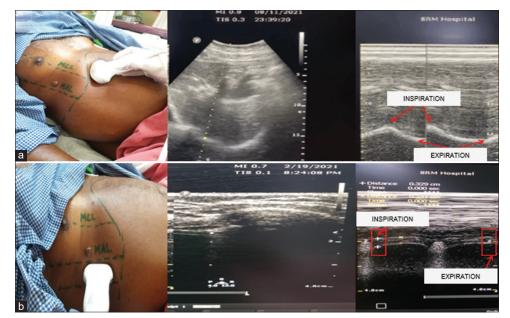


Figure 1: (a) Left: Placement of 3.5–5MHz probe in the right hypochondriac region. Right: Visualisation in B-mode and use of M-mode to measure DE in centimetres. (b) Left: Placement of 8–13 MHz probe at the eighth or ninth intercostal space between the anterior axillary and mid-axillary line. Right: Visualisation in B-mode and use of M-mode to measure DTF

RESULTS

Out of the 200 patients studied, extubation was successful in 171 patients. Weaning failure occurred in 29 patients, of which 16 patients required non-invasive ventilation and re-intubation was done in 13 patients. We included patients with various medical conditions, head injuries as well as postsurgical patients in this study. There was no statistically significant difference in age, gender, body mass index (BMI), pre-illness frailty scores, duration of mechanical ventilation, clinical and laboratory parameters between the patients in the successful and failed weaning groups [Table 1].

The AUROC values obtained were 0.42, 0.81 and 0.66 for RSBI, DE and DTF, respectively. Similar work was done for the RSBI-DTF and RSBI-DE combinations as well [Figure 2]. The sensitivity, specificity, positive predictive value and negative predictive value of each weaning indicator were calculated [Table 2]. Combining RSBI with DTF was found to significantly improve the accuracy of RSBI than when RSBI was used as a standalone parameter. The RSBI-DE combination was found to be better than the RSBI-DTF combination. However, it was noted that the RSBI-DE or RSBI-DTF combination did not alter the weaning prediction much when compared with DE or DTF as a standalone parameter.

The parameter concentration analysis is an effective visual tool to identify the visible cluster differences in weaning success and failure outcomes. It can be visualised from the chart that most failed weaning outcomes had occurred below the DE cut-off value of 1.21 cm but there were no such clear cut-off value conclusions regarding DTF or RSBI. Moreover, the range overlap between failed and successful weaning outcomes for RSBI was very high based on the RSBI concentration cluster [Figure 3].

The correlation charts between RSBI and diaphragm-derived parameters (DE and DTF) were done post-hoc for RSBI against the other two parameters [Figure 4]. A statistically significant difference was reported between RSBI and DTF values (P-value = 0.024) with a correlation coefficient (ρ) of -0.156. However, the coefficient of determination value (R-squared) was very low and hence no linear dependence was established between RSBI and DTF. In the case of RSBI and DE, the correlation coefficient ρ was -0.06 and there

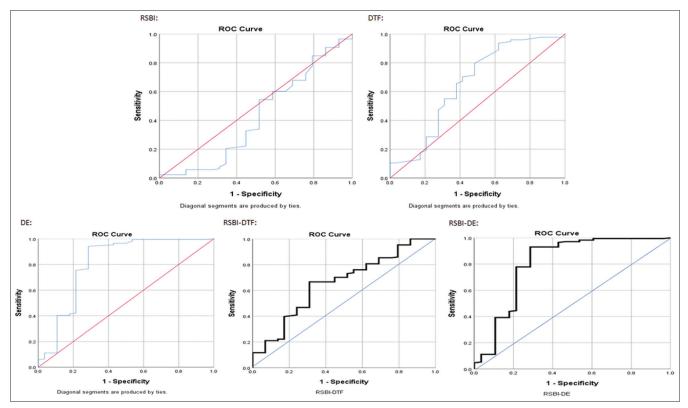


Figure 2: ROC Curves and AUROC values for DE, DTF, RSBI, RSBI-DTF and RSBI-DE. DE – Diaphragmatic excursion, DTF – Diaphragm thickening fraction, RSBI – Rapid shallow breathing index, AUROC – Area under receiver operator characteristic curve

Parameters	Weaning Success (<i>n</i> =171)		Weaning Failure (<i>n</i> =29)		P value
Gender (N/%)					
Female	55/27		13/7		NS
Male	116/58		16/8		NS
	Mean±SD	Median (IQR)	Mean±SD	Median (IQR)	
Age (years)	49±8.98	52 (46-56)	48±10	51 (46-57)	NS
Baseline pulse rate	80±6.69	80 (76.5-85)	79±7.89	78 (76-80)	NS
Baseline systolic blood pressure	124±8.1	124 (120-130)	121±9.87	120 (114-130)	NS
Baseline diastolic blood pressure	76±7.11	76 (70-80)	77±5.91	78 (72-80)	NS
Baseline respiratory rate	15±2.33	15 (14-16)	15±3.54	14 (14-16)	NS
Baseline oxygen saturation	99±0.4	99 (98-99)	99±0.8	99 (98-100)	NS
Pre-illness frailty score	1.6±0.72	2 (1-3)	1.3±0.61	2 (1-3)	NS
P/F Ratio	399±35.74	400 (400-420)	401±26.08	400 (400-420)	NS
BMI (Mean±SD, kg/m²)	25.32±5.73	26 (20-35)	26.71±4.05	27 (21-34)	NS
Electrolytes (Mean±SD)					
Sodium (mmol/I)	139.34±7.22	139 (136-144)	138.93±7.38	139 (135-145)	NS
Potassium (mmol/l)	3.87±0.69	3.8 (3.6-4.4)	3.61±0.49	3.7 (3.5-4.3)	NS
Urea (g/dl)	18.68±8.83	17 (16-25)	21.05±6.82	19 (17-24)	NS
Creatinine (g/dl)	0.81±0.66	0.7 (0.6-0.9)	0.86±0.53	0.7 (0.6-1.0)	NS
Duration of ventilation (h)	51±37.18	48 (35-48)	43±14.87	42 (28-48)	NS
RSBI	52.853±19.995	52.00 (40.00-65.00)	59.630±25.061	60.00 (41.15-85.00)	0.405 (NS)
DTF (%)	54.288±19.202	55.00 (39.00-64.00)	43.578±20.718	37.00 (27.25-62.00)	0.019
DE (cm)	1.933±0.682	1.73 (1.56-2.20)	1.215±0.662	1.12 (0.78-1.52)	<0.001
Case distribution based on underlying aetiology (<i>N</i> /%)					
Poisoning	31 (16%)	4 (2%)			NS
Acute pulmonary oedema	18 (9%)	2 (1%)			NS
Chronic kidney disease	13 (7%)	3 (2%)			NS
Acute exacerbation of COPD	11 (6%)	1 (1%)			NS
Others	106 (53%)	11 (6%)			NS

index, DTF – Diaphragm thickening fraction, DE – Diaphragmatic excursion, COPD – Chronic obstructive pulmonary disease

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Parameter	Cut off range	Sensitivity %	Specificity %	PPV %	NPV %	Youden's index	AUROC
RSBI	<82	94.0	31.0	89.0	45.0	0.25	0.422
DTF (%)	>37%	79.5	51.7	90.7	30.0	0.31	0.654
DE (cm)	>1.21	93.6	71.4	95.2	64.5	0.65	0.809
RSBI-DTF	>0.854	66.7	69.0	92.7	26.0	0.36	0.656
RSBI-DE	>0.738	93.0	71.4	95.2	62.5	0.64	0.807

RSBI – Rapid shallow breathing index, DTF – Diaphragm thickening fraction, DE – Diaphragmatic excursion, PPV – Positive predictive value, NPV – Negative predictive value, AUROC – Area under receiver operator characteristic curve

was no observed statistically significant correlation (P-value = 0.39).

DISCUSSION

The use of point of care ultrasound (POCUS) as a bedside tool has gained popularity among anaesthesiologists and intensivists.^[16] Apart from clinical assessment of weaning patients from mechanical ventilation and blood investigations including ABG analysis, intensivists regularly perform lung ultrasound and cardiac evaluation. Diaphragm ultrasound has been used for the assessment of diaphragm dysfunction following interscalene blocks and cervical spine injuries. The extended use of ultrasound in assessing the diaphragm function will help predict the weaning success with more accuracy.

DE measured by ultrasound was found to be a predictable and dynamic weaning parameter in our study, having an AUROC of 0.81 with a cut-off value of 1.21 cm. The sensitivity (93.6%) and specificity (73.4%) were also found to be better than both RSBI and DTF. Hayat *et al.*^[13] also observed similar results for DE

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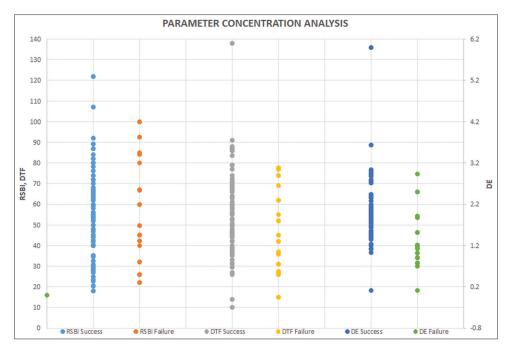


Figure 3: Parameter concentration analysis chart. RSBI - Rapid shallow breathing index; DTF - Diaphragmatic thickness fraction

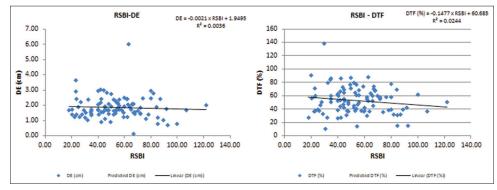


Figure 4: Correlation of RSBI with DTF and DE. RSBI – Rapid shallow breathing index, DTF – Diaphragm thickening fraction, DE – Diaphragmatic excursion

with 74% sensitivity and 71% specificity when a cut-off value of 1.2cm was considered. In a pilot study on 20 patients by Ramakrishnan et al.,^[17] a higher AUROC of 0.92 was obtained for DE compared to an AUROC of 0.58 for RSBI. Unlike our research, RSBI was considered a weaning parameter and patients with RSBI more than 105 were excluded from this study. However, DE can be affected by factors such as abdominal compliance and muscular activity of the rib cage and abdominal wall.^[18] Not withstanding these confounding factors, DE represents the actual diaphragmatic strength, which does not get reduced even in chronic obstructive pulmonary disease (COPD) patients.^[19] The predictability of DE was found to be better in other studies with various cut-off values.[20-22] Further, the combination of RSBI-DE in our study showed the greatest improvement relative to RSBI as a standalone parameter. However, it was noted that there was no discernible improvement of the RSBI-DE combination over standalone DE as a weaning indicator.

In this study, the cut-off range for DTF was 37% with a sensitivity of 79.5% and specificity of 51.7%. The AUROC for DTF was 0.65, which, though inferior to DE, was better than RSBI. In a similar study by Ferrari *et al.*,^[14] with a cut-off value of 36% DTF, the sensitivity and specificity were reported to be 82% and 88%, respectively, with an AUROC of 0.95. However, this study was done on a smaller sample size of 46 patients. In our study, the combination of RSBI-DTF improved the specificity to 69% and Youden's index to 0.36, which was similar to the results reported by Pirompanich *et al.*^[16] DTF represents the shortening of the diaphragm and is analogous to the ejection fraction of the heart. The weaning predictability of DTF as a standalone parameter was demonstrated in various other studies. $^{[20,23]}$

Before the ultrasound era, RSBI was the standard tool for assessing weaning, introduced in 1984 by Yang and Tobin. With a cut-off value of 82 in our study, we found that the sensitivity and specificity were 94% and 31%, respectively. The AUROC was 0.422, which was similar to other studies.^[24-26] The lower the cut-off value, the higher the predictability in RSBI. It has the advantage of considering the balance between respiratory load and effort. However, the compensation by the easily fatigable accessory non-diaphragmatic muscles may lead to weaning failure. This was demonstrated in various studies and the 2 h RSBI performed better than immediately after SBT.^[6-8]

The parameter concentration analysis chart is unique to the current study and because we observed 200 patients, the sample size of the study was significantly higher than most other previous works and therefore, it generated a densely populated parameter concentration chart. The concentration of cases with a cut-off value of 1.21 cm for DE was observed from the chart, whereas DTF and RSBI exhibited no clear cluster concentration.

In our study, the RSBI-DTF correlation was found to be clinically significant, whereas the RSBI-DE correlation was not. The negative correlation between RSBI and diaphragm-derived parameters was also reported by Theerawit *et al.*^[23] There is no statistically significant correlation between RSBI and weaning outcomes as evident from *P* value (0.405). Hence, combining DE with RSBI rather than DTF as an indicator for weaning will be ideal as DE is statistically not correlated to RSBI.

The major strengths of our study include a large sample size including medical and surgical patients. Both DTF and DE were assessed in all patients. Because all the measurements were done by a single anaesthesiologist, inter-observer variability was avoided. Parameter concentration analysis, accuracy and correlation coefficients, wherever applicable, were all studied.

Our study has a few limitations. This was a single-centre study involving only adult patients, and patients on tracheostomy were excluded. The other contemporary parameters such as maximum inspiratory pressure (PImax) and the time to peak inspiratory amplitude of the diaphragm (TPIA $_{dia}$) were not studied. There is a scope for future research based on these parameters in weaning ventilated patients.

CONCLUSION

DE proved to be the best standalone predictor of weaning outcome. DE or DTF alone can better predict weaning success than combining with RSBI. However, combining RSBI with either of the diaphragm ultrasound-derived techniques (DTF or DE) improved the accuracy in predicting weaning outcomes than using RSBI alone.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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