Ultrasonography to Access Diaphragm Dysfunction and Predict the Success of Mechanical Ventilation Weaning in Critical Care

A Narrative Review

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Abbreviations:
AC, Assist control mode of mechanical ventilation; AUC, Area under the curve; COPD, Chronic obstructive pulmonary disease; DE, Diaphragmatic excursion; DTF, Diaphragm thickening fraction; ICU, Intensive care unit; LD, Left diaphragm; LUS, Lung ultrasound; MV, Mechanical ventilation; NPV, Negative predictive value; NIMV, Noninvasive mechanical ventilation; NR, Not reported; PPV, Positive predictive value; PS, Pressure support trial; RD, Right diaphragm; RSBI, Rapid shallow breathing index; SBT, Spontaneous breathing trial; SG, Success group extubation; TPIA, Time to peak inspiratory amplitude diaphragm; TT, T-piece; US, Ultrasound; VIDD, Ventilator-induced diaphragmatic dysfunction

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Introduction—Weaning failure is common in mechanically ventilated patients, and whether ultrasound (US) can predict weaning outcome remains controversial. This review aims to evaluate the diaphragmatic function measured by US as a predictor of weaning outcome.

Methods—PubMed was searched to identify original articles about the use of diaphragmatic US in ICU patients. A total of 61 citations were retrieved initially; available data of 26 studies were included in this review.

Results—To assess diaphragmatic dysfunction in adults, six studies evaluated excursion, five evaluated thickening fraction, and both in nine. Despite heterogeneity in the diagnostic accuracy of diaphragm US among the studies, the sonographic indices showed good diagnostic performance for predicting weaning outcome.

Conclusions—Diaphragmatic US can be a useful and accurate tool to detect diaphragmatic dysfunction in critically ill patients and predict weaning outcome.

Key Words—critically ill patients; diaphragmatic ultrasonography; extubation outcome; ventilator weaning

After recovery of underlying conditions, determining the optimal moment for extubation in critically ill patient receiving invasive mechanical ventilation (MV) is crucial. It has been estimated that the process of weaning is responsible for around 42% of the total time that a patient spends on MV.[1,2]

Predictors of a successful extubation are a topic of debate among specialists since extubation failure contributes to prolonged MV and Intensive Care Unit (ICU) stay, as well as increased hospital mortality, ranging between 40 and 50%.[3,4]

Premature removal of MV entails a high risk of extubation failure and the need for reintubation increases the risk of hospital-acquired pneumonia by 8 times and death by 6–12 times.[5] On the other hand, unnecessary delay in ventilator weaning increases the inherent risks of MV, such as ventilator-induced lung injury, ventilator-associated pneumonia, and ventilator-induced diaphragmatic dysfunction (VIDD).[6]

There are numerous factors such as respiratory and cardiac dysfunction, poor nutritional status, psychological issues, decreased muscle strength associated with weaning failure.[7] Some of them are patients' related, while others may occur due to ICU care. The development of muscle weakness related to sepsis, multiorgan dysfunction syndrome, medications, bed rest, immobilization, and MV, named ICU-acquired weakness, contribute to difficulty in liberation from MV.[8]

Physician's prediction for successful weaning has low accuracy, with positive (PPV) and negative predictive values (NPV) of only 50 and 67%, respectively.[9] Current guidelines[10] recommend the implementation of a spontaneous breathing trial (SBT) as a tool to predict weaning outcome. However, approximately 20% of all mechanically ventilated patients fail their first attempt to wean following a successful SBT,[11,12] since SBT monitoring is insensitive to detect early signs of load-capacity imbalance (the common pathophysiology of weaning failure). Several other parameters have been used extensively in clinical practice to predict weaning failure, such minute ventilation, vital capacity, maximum peak inspiratory pressure, airway occlusion pressure 0.1 seconds and rapid shallow breathing index (RSBI, ie, respiratory frequency/tidal volume), but none proved to be accurate.[13,14]

The diaphragm, the major respiratory muscle, is responsible for approximately 60–80% of the workload[15] with an excursion of 1–2 cm, while during the forced breathing its amplitude is up to 7–11 cm.[4] MV has been proved to induce several diaphragmatic abnormalities, leading to atrophy and contractile dysfunction of diaphragm (VIDD)[16] that is associated with poor prognosis at time of liberation from MV. As a result, diaphragmatic dysfunction remains one of the main causes of difficulty or failure in weaning, with a prevalence of around 30%.[17,18] Hence, an early diagnosis of diaphragmatic dysfunction before extubation is imperative to avoid weaning failure.

Point-of-care ultrasonography is emerging as an important bedside tool to enable expeditious decision-making in critically ill patients. Opposed to invasive methods to access diaphragmatic function, US is noninvasive, easily available at the bedside, and allows repeated measurements. It has been reported as an effective method to provide an estimation of respiratory effort during the weaning process in critically ill patients, to predict extubation success and to detect and monitor VIDD.[19] However, routine evaluation of the functional status of diaphragm is still poorly applied in daily practice.

There are two diaphragm sonographic predictors of weaning outcome: the diaphragmatic excursion (DE), which measures the distance that the diaphragm is able to move during the respiratory cycle, and the diaphragm thickening fraction (DTF), which reflects variation in the thickness of the diaphragm during a respiratory effort.[20] These US measurements can be used to define diaphragmatic dysfunction, although its definition varies widely.

The aims of this narrative review are to summarize the technique of ultrasonography in the evaluation of diaphragmatic function and to assess its utility and accuracy for predicting weaning outcomes in critically ill patients on invasive MV.

Methods

Search Strategy

The authors performed a search in PubMed to identify potentially relevant articles, using a preplanned systematic comprehensive and reproducible search strategy with the terms: ("Diaphragmatic ultrasonography" or "Diaphragmatic sonograph*" or "Diaphragm ultrasound" or "Diaphragm ultrasonography" or "Diaphragmatic excursion") combined with ("Ventilator Weaning"[Mesh] or "ventilator weaning" or "extubation success" or "extubation outcome") with no publication data restrictions applied. The search covered all relevant articles published until March 2023.

Study Selection

Title, abstract and full-text articles were screened in a standardized manner to assess their eligibility. The inclusion criteria were: 1) language: articles published in English, Spanish, or Portuguese; 2) type of study: experimental and systematic review articles, published as original studies in peer-reviewed journals, restricted to human studies; 3) population: critically ill adult patients under invasive MV admitted to the ICU and candidates for ventilator weaning; 4) intervention: diaphragm thickness and excursion measured by ultrasound during the weaning process; and 5) predefined outcomes: the accuracy of diaphragm ultrasound to predict weaning outcome. The exclusion criteria were:

1) case reports, opinion papers, editorials; and studies available only as abstract; 2) pediatric studies; 3) studies performed in settings other than critical care (ie, patients ventilated for elective surgery); 4) unusual diaphragm ultrasound methods (ie, indirect measures of diaphragm function).

Data Extraction

After a primary screening of studies, full articles of interest were reviewed and the information to be included in this literature review was extracted. Extracted data included: first author, year of publication, country, population size, ultrasound assessment technique, diaphragm thickness or excursion, and main results.

Ultrasound Assessment for Diaphragmatic Evaluation in ICU Patients

Ultrasonographic examination of the diaphragm can be achieved by two different acoustic windows.[20,21] First, by *the subcostal area*, between the mid-clavicular and anterior axillary lines, using liver or spleen as acoustic windows. A low frequency (2–5 MHz) ultrasound transducer in the longitudinal plane, can be used to identify diaphragm as a hyperechoic line. The B-mode is initially used to obtain the best approach and select the exploration line, then the M-mode is used to show movements and measure diaphragmatic excursion, that appears in a waveform (Figure 1). Inspiration is identified as an upward curvature of the tracing while, expiration is identified as downward curvature.

The values of diaphragmatic excursion in healthy individuals, performed in spontaneous breathing, were reported to be 1.8 ± 0.3, 7.0 ± 0.6, and 2.9 ± 0.6 cm for males, and 1.6 ± 0.3, 5.7 ± 1.0, and 2.6 ± 0.5 cm for females, during quiet, deep breathing, and voluntary sniffing, respectively.[22]

The role of excursion in the functional evaluation of diaphragm contractile activity during patient-triggered MV is far less clear. Under MV, excursion measured with M-mode represents the diaphragmatic contraction plus the pressure applied by the ventilator with no distinction between the active (muscle) and passive (ventilator) forces.[23,24] In the case of mechanically ventilated patients, evaluation of diaphragmatic motion can be used at the time of weaning from MV during a SBT. Interestingly, the same diaphragmatic excursion values (1.8 cm) were found in ventilated patients who succeeded in the weaning trial.[17]

The second possible approach is *at the zone of apposition* of the diaphragm to the rib cage, between the 8th and 10th intercostal space in the antero-axillary and mid-axillary lines at 0.5–2 cm below the costophrenic sinus. A high-frequency linear transducer (≥10 MHz) should be placed directed perpendicularly to the diaphragm at a depth of 1.5–3 cm. In this area, the diaphragm is observed as a structure made of three distinct layers (Figure 2): a non-echogenic central layer bordered by two echogenic layers, the peritoneum and the diaphragmatic pleurae.

This approach is used to assess thickness of the diaphragm, usually in M-mode (Figure 2C). In spontaneously breathing healthy patients, the normal thickness of the diaphragm is 1.7 ± 0.2 mm increasing to 4.5 ± 0.9 mm, while relaxing and when breath holding at total lung capacity, respectively.[25] Diaphragm thickness measured at end inspiration correlates with maximal inspiratory pressure[26] and the change in diaphragm thickness during respiration is strongly related to lung volume.[27]

In clinical practice, thickening reflects the magnitude of diaphragm effort in spontaneously breathing patients and it can also be used during noninvasive MV (NIMV) and to predict extubation failure or success during a SBT. By measuring the muscle thickness at the end of inspiration (DT-end inspiration) and at the end of expiration (DT-end expiration), the DTF can be calculated as [(DT-end inspiration − DT-end expiration)/(DT-end expiration × 100)].[23]

Results

Study Identification and Selection

The process of literature search and selection is shown in Fig. 3. The initial database search yielded 61 references. Screening of the titles and abstracts yielded 36 studies, 10 of which were excluded following full text review and the remaining 26 studies were included in the final analysis.

Baseline Characteristics of Included Studies

The 20 original studies and 6 systematic reviews included in this narrative review took place between 2014 and 2023. Most of them were carried out in polyvalent ICUs, but 2 studies[28,29] were performed in respiratory ICUs.

The results are presented in Tables 1 and 2, which summarize the most relevant findings regarding ultrasonographic indices to assess diaphragm contractile function in adults. All original studies included were prospective cohort studies (Table 1) except for one which was retrospective.[43] Table 2 describes the

Figure 1. Ultrasonographic assessment of diaphragm displacement. **A**, Ultrasonographic view of the normal diaphragm in the region of the liver dome, with B-mode in the upper part and M-mode in the lower part. **B**, Anatomical structures that can be identified in B-mode scanning. **C**, Anatomical structures that can be identified in M-mode scanning. **D**, Probe placement to explore the diaphragm in the region of the liver dome. [Image reproduced with permission of the rights holder.]

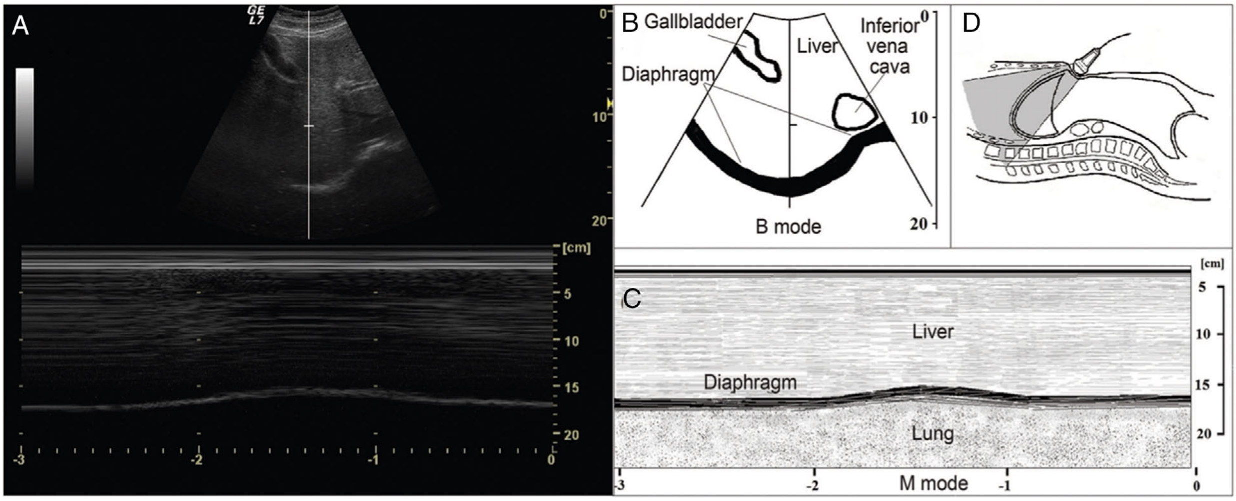
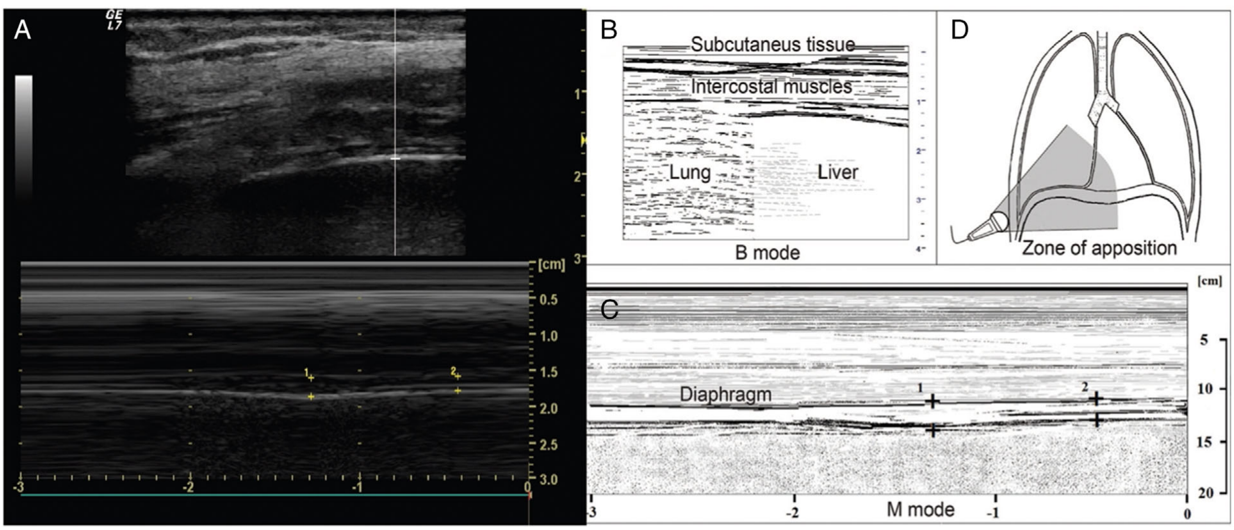


Figure 2. Ultrasonographic assessment of diaphragm thickness. **A**, Ultrasonographic view of the normal diaphragm in the zone of apposition, with B-mode in the upper part and M-mode in the lower part. **B**, Anatomical structures that can be identified in B-mode scanning. **C**, Anatomical structures that can be identified in M-mode scanning. **D**, Probe placement to explore the diaphragm in the zone of apposition. The distance identified by plus signs 1 in A and C is end-inspiratory thickness, whereas the distance between plus signs 2 in the same panels is the end-expiratory thickness. [Image reproduced with permission of the rights holder.]



main findings of the six systematic reviews and meta-analysis included.

Diaphragmatic dysfunction was assessed by DE in six studies, DTF in five and both in nine studies. Seven studies compared diaphragmatic US with other methods that have been previously used to predict successful extubation in the ICU: rapid shallow breathing index (RSBI)[33,34,36,37] and Lung US score[11,34,37] in four and three studies, respectively.

Regarding weaning protocols, all the studies assessed patient readiness to be weaned in order to perform a SBT, which was either performed with low pressure support (inspiratory pressure = 5–8 cmH_2O and expiratory pressure = 0–5 cmH_2O) or as T-piece trials. Diaphragm US was mainly performed during a SBT, but three studies also assessed diaphragm function before and after SBT and after extubation.[12,35,40]

The time interval between diaphragm US and extubation was poorly described in the majority of studies.[3,29,31,33,38] In one study, a 24- to 48-hour interval between diaphragm US and extubation was tolerated.[43]

The definition of "weaning failure" is not standard, covering one or more of the following items in the first 48–72 hours after extubation: need for reintubation, need for non-scheduled post-extubation NIMV, tracheostomy requirement, death, and/or SBT failure.

The minimal duration of MV before inclusion in the studies ranged from 24 to 72 hours. One study included patients with complicated weaning (who had failed previous attempts of SBT)[3] and one study included patients at high risk of extubation failure.[42] Some studies focused exclusively on patients with chronic obstructive pulmonary disease (COPD)[5] or COVID-19[41] or patients whose intubation was due to respiratory causes.[28,29,36,39] This aspect could compromise the applicability of the results due to patient selection. Exclusion criteria mostly included conditions affecting diaphragm function or assessment.

Figure 3. PRISMA flow diagram for study identification and selection with reasons for exclusion.

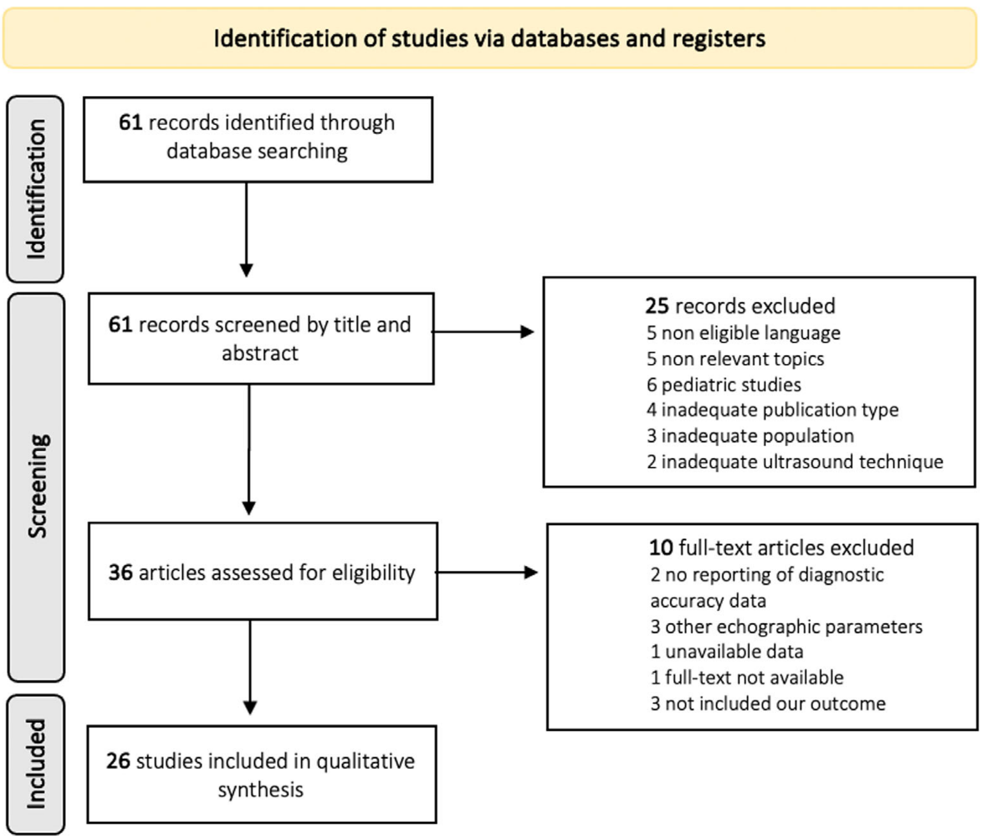


Table 1. Characteristics of Included Studies

Study (Year)	Country	n	Age[a] (Years)	Major Reason for Admission	Type of SBT During US	Timing of US	Cut-Off Values for Successful Weaning	Diagnostic Accuracy to Predict Extubation Success	Main Findings
Alam et al, 2022[30]	Bangladesh	31	42 ± 16	NR	TP	Obtained at 0′ and 10′ of a SBT and before extubation	DE >1.14 cm DTF >22.33%	DE: sensitivity 77.8% specificity 84.6%, PPV 84.6%, NPV 73.3%; DTF: sensitivity 61.1%, specificity 84.6%, PPV 87.5%, NPV 61.1%	DE and DTF can therefore be useful parameters in predicting extubation success. Among these two, DE outperformed DTF. Both were better than RSBI.
Carrie et al, 2017[31]	France	67	66 (58–74)	Medical and surgical condition	PS	During SBT	DE_{max} > 2.7 cm	The sensitivity and specificity of diaphragm US in predicting weaning failure were 59 and 71%. AUC 0.65	A decrease in DE values may be associated with an unfavorable weaning outcome. DE measured is however unable by itself to predict weaning failure.
DiNino et al, 2014[32]	USA	63	66.0 ± 19	Medical condition	PS / TP	Within the first 5′ of SBT	DTF≥30%	DTF: sensitivity 88%, specificity 71%, PPV 91%, NPV 63%, AUC 0.79	US measures of DTF may be useful to predict extubation success or failure during SBT.
Eltrabili et al, 2019[33]	Egypt	30	52.0 ± 13.2	Abdominal sepsis	PS	Obtained at 30′ of a SBT	DTC >30.7% DE >1.0 cm RSBI <44	DTF: sensitivity 94.1%, specificity 100%, AUC 0.97; DE: sensitivity 94%, specificity 85%, AUC 0.85; RSBI: sensitivity 76%, specificity 100%, AUC 0.9	Diaphragmatic US indices could be useful parameters for assessment of success of extubation in patients with abdominal sepsis.
Elshazly et al, 2020[28]	Egypt	62	65 (55–70)	Respiratory disease	TP	During SBT	DE >1.25 cm DTF >21.5%	DE: sensitivity 97.1%, specificity 82.1%; DTF: sensitivity 91.2%, specificity 60.7%	The diaphragmatic US was found to be a promising tool for predicting the extubation outcome.
Farghaly et al, 2016[29]	Egypt	54	65 (55–70)	Respiratory disease	PS	During SBT	DE ≥1.05 cm DTF ≥34.5%	DE: sensitivity 87,5%, specificity 71.5%; DTF: sensitivity 90%, specificity 64.3%	US evaluation of DE and DT_{ins} could be a good predictor of extubation outcome. Combining DE and Tdi_{ins} decreased sensitivity to 64.9% but increased specificity to 100%.
Flevari et al, 2016[3]	Greece	27	65 (54–73)	Medical, surgical and trauma condition	PS / TP	During SBT	DE ≥1 cm for RD DE ≥0.7 cm for LD	DE ≥1 cm for LD was the best index to predict weaning success (sensitivity	DE threshold of 1 cm and 0.7 cm for RD and LD respectively could be used as adjunct tool in the

								86%, specificity 85%, NPV 94%)	predictive of weaning in difficult to wean patients.
Gok et al, 2021[34]	Turkey	62	57.6 ± 14.1	Trauma	TP	Obtained at 30′ to 1 h of a SBT	DE >1.3 cm DTF ≥27.5% LUS <6.5; RSBI <64	DE: sensitivity 69%, specificity 67.5%, AUC 0.79; DTF: sensitivity 67.5%, specificity 66.6%, AUC 0.8	The US examination accompanied by an RSBI will increase extubation success in the weaning process.
Hayat el at, 2017[35]	Pakistan	100	40.5 ± 25.7	Medical condition	Oxygen	After extubation	DE >1.2 cm	DE: sensitivity 78.9%, specificity 70.8%, PPV 82.3%, NPV 60.0%	US measurement of DE is a good method for predicting weaning outcome from MV.
Lalwani et al, 2022[36]	India	54	41.8 ± 17.0	Respiratory disease	PS/TP	During SBT	DTF > 29.71% RSBI <93.75	DTF: sensitivity 93.33%, specificity 66.67%; RSBI: sensitivity 93.33%, specificity 22.22%	Diaphragmatic US is better than RSBI in predicting weaning outcomes.
Li Shigang et al, 2021[37]	China	101	70 (65–87)	Medical condition	TP	Obtained at the beginning of SBT	DE >1.3 cm DTF ≥30% LUS ≤11; RSBI ≤102	DE: sensitivity 85%, specificity 62%; DTF: sensitivity 94%, specificity 84%; LUS: sensitivity 71%, specificity 55%	DTF has highest sensitivity and specificity, making it superior to other parameters. However, the combination of all indices allows the most accurate prediction of weaning outcome.
Lozano et al, 2018[11]	Spain	69	66 (53–78)	Medical condition	PS/TP	Within the first minutes of SBT	DTF ≥24% LUS <7	DTF: sensitivity 93%, specificity 58%	A low DTC value or high LUS value indicates high risk of weaning failure.
Luo et al, 2017[38]	China	60	66.5 ± 18.9	Medical and surgical condition	TP	Obtained at 5′–15′ of a SBT	DE >1.26 cm	A DE <12.6 mm showed the highest diagnostic accuracy with sensitivity and specificity of 80 and 68.4%, respectively.	Diaphragm US could help identify patients with high risk for re-intubation. DE could help predict re-intubation within 1 week in the FG.
McCool et al, 2020[39]	USA	32	55.8 ± 14.8	Pneumonia	PS	Within the first 5′–10′ of a SBT	DTF ≥30%	sensitivity 90.9%, specificity 86.7%, PPV 90.0%, NPV 86.7%	The time from US to extubation was shorter in patients with normal function diaphragm.
Palkar et al, 2018[12]	USA	73	72.5 ± 17.0	Medical condition	PS	During AC, SBT, and after extubation	DE >1 cm	DE <1 cm during SBT is highly specific (92.5%) to predict failure extubation, but no sensitive (30%).	DE did not differ between the SG or FG on A/C, but during STB the difference approached statistical significance

(Continues)

Table 1. Continued

Study (Year)	Country	n	Age[a] (Years)	Major Reason for Admission	Type of SBT During US	Timing of US	Cut-Off Values for Successful Weaning	Diagnostic Accuracy to Predict Extubation Success	Main Findings
									($P = .06$). DE measured during STB has some utility to predict the outcome of extubation.
Theerawit et al, 2018[40]	Thailand	62	66.4 ± 16.7	Medical and surgical condition	TP	At the end of a 2 h SBT	DE >1.2 cm DTF ≥36% TPIA >1.2seg	DE and DTF non-significant results. TPIA: sensitivity 92%, specificity 46%, PPV 89%, NPV 56%.	The TPIA exhibits good performance as predictor of weaning and performed better than all other parameters.
Vetrugo et al, 2022[41]	Italy	57	65 (56–71)	COVID-19	PS	During SBT	DTF >28%	NR. DTF did not differ between the SG or FG.	DTF was found to be unrelated to weaning outcome in COVID-19 patients.
Viver et al, 2019[42]	France	191	68 ± 4	Medical condition	TP	During SBT just prior to extubation	DE >1 cm DTF ≥30%	NR. Values of DE and DTF did not differ between the SG or FG.	Diaphragmatic dysfunction assessed by US was not associated with an increased risk of extubation failure.
Yoo et al, 2018[43]	Korea	60	69 (57–76)	Medical and surgical condition	PS / TP	During SBT	DE >1 cm DTF ≥30%	DE: sensitivity 80.9% specificity 69.2%, PPV 90.5%, NPV 50.0%; DTF: sensitivity 68.1%, specificity 61.5%, PPV 86.5%, NPV 34.8%	Diaphragm US may be a useful tool to predict successful extubation. DE seems more accurate than DTF to predict extubation success.
Zhang et al, 2019[5]	China	58	74 ± 8.0	COPD	PS	Obtained at 0′, 5′ and 30′ of a SBT	DE_{30} >1.72 cm, $\Delta DE_{30\text{-}5}$ >0.16 cm	DE_{30}: sensitivity 76%, specificity 75%, PPV 86.4%, NPV 60%; $\Delta DE_{30\text{-}5}$: sensitivity 84%, specificity 83.3%, PPV 91.3%, NPV 71.4%	The combination of DE_{30} and $\Delta DE_{30\text{-}5}$ could improve the predictive value and could be used as the predictor of extubation outcome in COPD patients.

$\Delta DE_{30\text{-}5}$, the variation of DE between 5 and 30 minutes of SBT; AC, assist control mode of MV; AUC, area under the ROC curve; COPD, chronic obstructive pulmonary disease; DE, diaphragm excursion; DTF, diaphragm thickening fraction; DT_{ins}, diaphragmatic thickness at end inspiration; FG, failure group extubation; LD, left diaphragm; LUS, lung ultrasound score; MV, mechanical ventilation; NPV, negative predictive value; NR, not reported; PPV, positive predictive value; PS, pressure support trial; RD, right diaphragm; RSBI, rapid shallow breathing index; SBT, spontaneous breathing trial; SG, success group extubation; TPIA, time to peak inspiratory amplitude diaphragm; TT, T-piece; US, ultrasound.
[a]Age is expressed according to data extracted from each study as mean ± standard deviation or median (interquartile range).

Table 2. Characteristics of Included Systematic Reviews and Meta-Analysis

Study (Year)	Country	n	Diagnostic Accuracy to Predict Extubation Success	Main Findings
Le Neindre et al, 2021[44]	France	816	The pooled sensitivities for DTF and DE were 0.70 and 0.71, specificities were 0.84 and 0.80, and AUC were 0.82 and 0.82, respectively. The review detected a sensitivity lower and specificity higher for DTF.	Diaphragm US predicts extubation failure with high specificity. However, sensitivity was low because absence of diaphragm dysfunction does not imply no risk of extubation failure (weaning is also affected by non-diaphragm-related factors).
Li Caifeng et al, 2018[4]	China	742	The pooled sensitivities for DE and DTF were 0.786 and 0.893, specificities were 0.711 and 0.796, and AUC were 0.859 and 0.831, respectively. The review detected a lower sensitivity and specificity for DE as compared with DTF.	The review data indicates a satisfactory diagnostic accuracy in predicting extubation outcome. Diaphragmatic US is a promising tool for predicting reintubation within 48 hours of extubation.
Llamas-Álvarez et al, 2017[45]	Spain	1071	The review detected a significantly higher specificity for DTF and higher sensitivity for DE in studies with applicability concerns. The AUC were 0.87 for DTF. The pooled sensitivity for DE were 75%.	Lung and diaphragm US can provide valuable information for predicting weaning outcome, but taken alone, they may not perform as well as individual studies suggest. Its accuracy may vary depending on the patient subpopulation.
Mahmoodpoor et al, 2022[19]	Iran	1114	The pooled sensitivities for DTF and DE were 0.89 and 0.79, specificities were 0.81 and 0.69, respectively. The pooled sensitivity and specificity for RSBI were 0.74 and 0.73, respectively.	The meta-analysis showed the superiority of the diagnostic accuracy of DTF in comparison to the DE and the RSBI. Among the different US methods for prediction of weaning outcome, DTF seems to be most accurate.
Qian et al, 2018[46]	China	436	The DE or DTF had a pooled sensitivity of 0.85 and a pooled specificity of 0.74 for predicting weaning success.	Both DE and DTF showed good diagnostic performance to predict weaning outcomes in spite of limitations included high heterogeneity among the studies. DD was found to be a predictor of weaning failure.
Zambon et al, 2016[47]	Italy	875	Optimal cutoffs ranged from 1.0 to 1.4 cm for DE and 30–36% for DTF.	Diaphragmatic US could be a useful tool to detect DD, to predict extubation success or failure, to monitor respiratory workload and to assess atrophy in patients under MV.

AUC, area under the ROC curve; DD, diaphragmatic dysfunction; DE, Diaphragm excursion; DTF, diaphragm thickening fraction; MV, mechanical ventilation; RSBI, rapid shallow breathing index; US, ultrasound.

Predicting Value of DE and DTF on Weaning Outcome

To predict weaning outcome from MV either DE or DTF measurements performed during weaning process or around STB were employed as the test index. Sensitivity and specificity of both indices found in each study are shown in Tables 1 and 2 summarizes the pooled sensitivity and specificity of all studies.

In the studies that used DE ≥10 mm as a cutoff point to predict extubation success, sensitivity ranged from 69 to 97.1% and specificity from 62 to 85%. One study reported a high specificity (92.5%) to predict failure of extubation with a cutoff of DE <10 mm, but with low sensitivity (30%).[12] DE was significantly lower in patients who fail compared with the successfully extubated group.[12,46]

DTF was measured in 12 studies. In the studies that used a cutoff point of DTF ≥30%, sensitivity ranged from 68.1 to 94.1% and specificity from 61.5 to 100%. Qian et al further showed that DTF in the successfully weaning group was significantly higher than in failure group.[46]

Optimal cutoff to diagnose diaphragmatic dysfunction ranged from 10 to 14 mm for DE and from 30 to 36% for DTF during SBT.[47] In Eltrabili's study, cutoff value to predict successful weaning was DE >10 mm and DTC >30.7%, with a sensitivity of 94 and 94.1%, a specificity of 85 and 100%, and an area under the curve (AUC) of 0.85 and 0.97, respectively.[33]

In the systematic reviews, despite the remarkable heterogeneity among the studies, the diagnostic performance, evaluated by the AUC for DE and DTF was 0.82–0.859 and 0.82–0.87, respectively, suggesting a high level of overall accuracy diagnostic performance.

Discussion

The diaphragm is a fundamental respiratory muscle whose dysfunction is common in critically ill patients.[48] Demoule et al[49] found that VIDD occurs in 64% of the patients on the first day of ICU admission. This was confirmed by Schepens et al[50] that also observed that diaphragm atrophy develops rapidly, within the first 24 hours of MV initiation in adults.

In recent years, ultrasonography emerged as a new method for assessment of diaphragm function, prevailing over other techniques. Diaphragmatic ultrasound is a non-invasive, cost-effective, safe, and easy-to-perform technique, thus representing an attractive and suitable diagnostic tool for ICU patients.[16] It allows a morphological and functional evaluation of the diaphragm in real time and can be repeated overtime at the bedside.[4]

Predicting the optimal time for extubation is challenging, especially in patients with diaphragm dysfunction that has been increasingly recognized as the primary reason for difficult weaning or weaning failure from MV, and measurement of diaphragm function using US has the potential to predict weaning's outcome from MV.[20] McCool et al showed that incorporating information of diaphragm US into usual ICU care allowed clinicians to identify patients with a normally functioning diaphragm and decreased the time from US to extubation.[39]

Some recent studies have reported that reduced DE and DTF were associated with weaning difficulties in patients who are mechanically ventilated,[3,11,31] while others found opposite results.[12,41,42] The most recent studies suggest that diaphragm US enables the prediction of extubation outcome.[28,32,35,45]

According to some authors, diaphragmatic movement correlates well with transdiaphragmatic pressure. Measurement of the DE could, therefore, be an important tool to evaluate the respiratory endurance of a patient and, by extension, predict successful extubation.[17,35,40,43] Furthermore, Flevari et al concluded that this index may also be a reliable tool to assess patients with difficult and prolonged weaning, in whom the diaphragm has some degree of atrophy due to prolonged MV.[3] Kim et al found that DE of <10 mm or paradoxical movement during SBT identified patients at a higher likelihood of extubation failure.[17] Similar results were found in the study of Farghaly et al[29] According to this author, a cut-off of >10.5 mm for DE at the time of SBT predicts successful extubation with a sensitivity of 87.5% and a specificity of 71.5%.[29]

However, Carrie et al showed discordant results in their study, concluding that, although a decrease in DE values may be associated with an unfavorable weaning outcome, DE measured is not an accurate index by itself to predict weaning failure.[31] This study has the particularity of using the maximal and not the mean DE as the US measurement. Nevertheless, mean values of maximal DE were significantly higher in patients who succeeded at their first weaning attempt (4.1 ± 2.1 vs 3 ± 1.8 cm, $P = .04$). Another study reported that, although DE was not statistically different between the success and failure groups, ΔDE (30–10 minutes during SBT) was higher in failure group than in the success group (1.07 ± 0.64 mm vs 3.33 ± 3.17 mm, $P < .05$).[5] The difference can be attributed to the timing of the US measurements (DE at 0, 10, and 30 minutes after initiation of SBT).

On the contrary, some available data suggest a lower sensitivity and specificity for DE as compared with the DTF in predicting weaning outcome.[4] Umbrello et al believe that DTF rather than DE is a reliable index of respiratory effort and active contraction of the diaphragm during MV, and reported a significantly higher DTF in the weaning success group, compared with the failure group.[21] This study evaluated both indices during assisted breathing and concluded that DE should be limited to patients on SBT. DiNino et al found that DTF ≥30% had a PPV for extubation success of 91% in patients undergoing SBT with low levels of pressure support (PS of Δ5/5).[32] McCool et al reported similar results for PPV, NPV, and AUC for DTF ≥30%.[39] By contrast, Vivier et al found that TDF was not useful to distinguish between patients who were and were not successfully extubated.[42] Different from the prior studies, they included patients under prolonged MV (at least 1 week), older patients (aged >65 years) and at high risk for re-intubation. Furthermore, they studied both hemidiaphragms and found unilateral dysfunction in 140 of 160 patients.[40]

According to three systematic reviews DTF is more accurate than DE to predict weaning outcome.[4,23,42] Llamas-Álvarez et al, based on 19 studies, showed a significantly higher specificity for DTF and higher sensitivity for DE.[45] Recently, Mahmoodpoor et al also showed a higher diagnostic accuracy of DTF compared with DE and RSBI.[19]

However, some studies found that DE has higher sensitivity and specificity than DTF.[28,30,43] This can be explained by the ventilator mode at the timing of US since, in these studies, measurements were made during a SBT without positive-pressure ventilation. The data obtained from measurements made during positive-pressure ventilation would affect the measured DE that is derived from adding the patient's effort to the pressure generated by the ventilator. Therefore, DTF is suitable to estimate the diaphragm function in patients under MV, while DE should be reserved to cases in the absence of the respiratory support, as the downward displacement of the muscle may reflect passive insufflation by the ventilator.

Nevertheless, two studies demonstrated that both indices are useful to predict successful extubation.[4,34]

Weaning is also affected by non-diaphragm-related factors. Le Neindre et al concluded that diaphragm US predicts extubation failure with high specificity (0.84 for DTF and 0.82 for DE, respectively).[44] However, sensitivity was low (0.70 for DTF and 0.71 for DE) because absence of diaphragm dysfunction does not imply no risk of extubation failure. Therefore, a single diaphragmatic index may not be a perfect predictor. This supports several studies that emphasize the interest of combining diaphragmatic US with other traditional parameters to predict weaning outcome.[11,34,37]

Conclusions

Diaphragm US is a novel method for measuring diaphragmatic function in mechanically ventilated patients and an attracting and a promising tool to predict weaning outcome.

The increased routine use of ultrasonography in the ICUs as a fast, inexpensive and noninvasive test is expected to lead to a timely identification of critically ill patients at risk of weaning failure.

Both ultrasonography indices, DE and DTF, showed a good predictive ability for successful liberation from MV in different populations, however DTF seems to be most accurate method to estimate the diaphragm function in patients undergoing MV, while DE should be reserved to cases in the absence of the breathing support (T-piece or low PS). Optimal cutoffs ranged from 1.0 to 1.4 cm for DE and 30–36% for DTF.

This technique may be a reliable and helpful tool to predict extubation outcome, however due to significant heterogeneities among studies, clinicians should be aware of its utility and limitations.

Additional high-quality randomized controlled trials are needed to standardize sonographic diagnostic criteria for diaphragmatic dysfunction and its use in daily clinical decisions in the weaning process.

Ethics Statement

All authors read and approved the final manuscript. This work has not been supported by public grants or financial support. No sources of funding were used to assist in the preparation of this study. Each author certifies that he has no commercial associations that might pose a conflict of interest in connection with the submitted article. We certify that this research was conducted in conformity with ethical principles of our institution. This work, figures and tables, have not been previously published and reproduced from another source.

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

IRB Statement

The study was conducted in accordance with the Declaration of Helsinki and Ethical approval for this review was waived.

Data Availability Statement

The authors confirm that the data supporting the findings of this study are available from the corresponding author upon reasonable request.

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