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SYSTEMATIC REVIEW

Assessment of diaphragmatic dysfunction in the critically ill patient with ultrasound: a systematic review

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Abstract

Purpose: Diaphragmatic dysfunction (DD) has a high incidence in critically ill patients and is an under-recognized cause of respiratory failure and prolonged weaning from mechanical ventilation. Among different methods to assess diaphragmatic function, diaphragm ultrasonography (DU) is noninvasive, rapid, and easy to perform at the bedside. We systematically reviewed the current literature assessing the usefulness and accuracy of DU in intensive care unit (ICU) patients.

Methods: Pubmed, Cochrane Database of Systematic Reviews, Embase, Scopus, and Google Scholar Databases were searched for pertinent studies. We included all original, peer-reviewed studies about the use of DU in ICU patients.

Results: Twenty studies including 875 patients were included in the final analysis. DU was performed with different techniques to measure diaphragmatic inspiratory excursion, thickness of diaphragm (Tdi), and thickening fraction (TF). DU is feasible, highly reproducible, and allows one to detect diaphragmatic dysfunction in critically ill patients. During weaning from mechanical ventilation and spontaneous breathing trials, both diaphragmatic excursion and diaphragmatic thickening measurements have been used to predict extubation success or failure. Optimal cutoffs ranged from 10 to 14 mm for excursion and 30–36 % for thickening fraction. During assisted mechanical ventilation, diaphragmatic thickening has been found to be an accurate index of respiratory muscles workload. Observational studies suggest DU as a reliable method to assess diaphragm atrophy in patients undergoing mechanical ventilation.

Conclusions: Current literature suggests that DU could be a useful and accurate tool to detect diaphragmatic dysfunction in critically ill patients, to predict extubation success or failure, to monitor respiratory workload, and to assess atrophy in patients who are mechanically ventilated.

Keywords: Diaphragm, Ultrasonography, Diaphragmatic dysfunction, Thoracic ultrasound, Respiratory monitoring, Critically ill

Introduction

Diaphragmatic dysfunction (DD) has a relatively high incidence in critically ill patients [1, 2] as a result both of disuse/atrophy during mechanical ventilation (ventilation induced diaphragmatic dysfunction, VIDD) [3] and mechanical insults such as cardiac or upper abdominal surgery [4–7].

In the last decade, research focused mainly on causes and mechanisms underlying dysfunction and atrophy of respiratory muscles in the critically ill, but there is still a lack of tools to monitor diaphragm activity at the bedside. Methods to assess diaphragmatic function often have low sensitivity or specificity, as in the case of chest X-rays, or

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are invasive and difficult to obtain at the bedside, as in the case of the gold standard twitch magnetic phrenic nerve stimulation or measurement of transdiaphragmatic pressure with esophageal and gastric balloons [8]. Diaphragmatic ultrasound (DU) in a critical care setting may be of great utility for this purpose. It is noninvasive, easily available, and allows repeated measurements.

There are two acoustic windows to explore the diaphragm. Briefly:

1. At the zone of apposition, between the 8th and 10th intercostal space in the mid-axillary or antero-axillary line, 0.5–2 cm below the costophrenic sinus. To obtain adequate images of diaphragmatic thickness, a linear high-frequency probe (≥10 MHz) is mandatory. At a depth of 1.5–3 cm, two parallel echogenic layers can be easily identified: the nearest line is the parietal pleura, the deeper one is the peritoneum. The diaphragm is the less echogenic structure in between these two lines (Fig. 1a). This approach is utilized to assess thickness of the diaphragm and thickening with inspiration, usually in M-mode (Fig. 1b). In healthy, spontaneously breathing subjects the normal thickness of the diaphragm at the zone of apposition is 1.7 ± 0.2 mm while relaxing, increasing to 4.5 ± 0.9 mm when breath holding at total lung capacity (TLC) [9].
2. In the subcostal area, between the mid-clavicular and anterior axillary lines, using liver or spleen as acoustic windows. Either a cardiac or abdominal probe (2–5 MHz) can be used. Diaphragm is identified as a hyperechoic line (produced by the pleura tightly adherent to the muscle) that approaches the probe during inspiration (Fig. 1c). The inspiratory excursion can be easily measured in M-mode (Fig. 1d). In healthy subject during quiet spontaneous breathing, diaphragm inspiratory excursion was found to be 1.34 ± 0.18 cm [10]. A negative inspiratory excursion indicates paradoxical diaphragmatic movement and is associated with diaphragmatic paralysis and use of accessory muscles [11].

For a more accurate description of DU technique, we refer the reader to the related reviews [12, 13].

Ultrasound criteria for evaluation of normal and dysfunctioning/paralyzed diaphragm have been published [10, 11], but routine evaluation of diaphragm excursion and thickness is still poorly applied in daily practice.

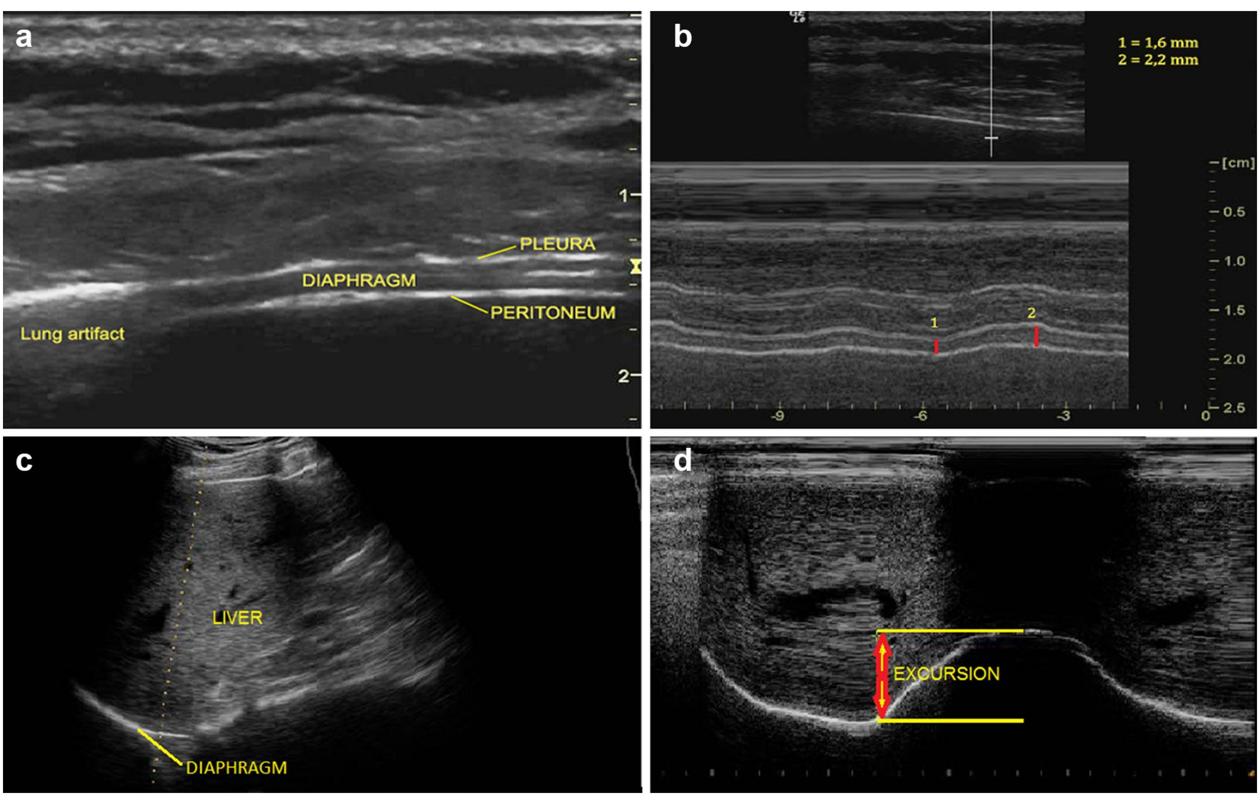

Fig. 1 Diaphragm ultrasonography (DU) at the zone of apposition in **a** B-mode, **b** M-mode. *1* Thickness at end expiration, *2* thickness at end inspiration. DU, right subcostal in **c** B-mode, **d** M-mode

We systematically reviewed the current literature about the use of DU in critically ill patients. The purpose of this systematic review is to answer the following question: is DU a useful and accurate method to assess DD in critically ill patients?

Methods

Two independent investigators performed an extensive search in Pubmed, Cochrane Database of Systematic Reviews, Embase, Scopus, and Google Scholar Databases, without language restrictions. References of all retrieved articles were scanned for additional relevant manuscripts.

The research string was "diaphragm*[tiab] AND (ultrasonography[tiab] OR ultrasound[tiab] OR echography[tiab])". The research string was developed to have the widest possible sensitivity, while the specificity was guaranteed by human scanning of retrieved results as follows: one reviewer (SB) examined the titles and abstracts resulting from the electronic search to exclude articles that were obviously irrelevant. Two independent reviewers (MZ and MG) examined the full text of the remaining studies. A third reviewer (SB) was employed to make the final decision when it could not be achieved.

Studies meeting the following criteria were applied: human original studies published in peer-reviewed journals; employed prospective or retrospective design; reported the use of DU as a monitoring/diagnostic tool; enrolled patients admitted to intensive care units (ICU) for any reason. We included both adult and pediatric studies and then discussed the results separately.

Case reports, reviews, editorials, and studies available only as abstracts were excluded. Furthermore, we excluded studies performed in settings other than critical care (i.e., patients ventilated for elective surgery).

Extracted data included first author, year of publication, study design, population size, ultrasound technique used to measure diaphragmatic function (i.e., thickening or excursion, B-mode or M-mode), alternative technique to assess diaphragmatic function, main results.

In a second phase, we added a search of relevant abstracts from the last 3 years to include, as supplementary material, a list of potential relevant issues for the near future (Supplementary file 1).

This study was conducted and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. At a first screening there was no randomized controlled trial to include; therefore, usual quality assessment tools (i.e., Jadad scale) were not applicable.

Therefore, we used the QUADAS-2 tool for the quality assessment of diagnostic accuracy studies. The QUADAS-2 has the advantage of being easily fitted for observational studies investigating diagnostic/monitoring tools, assessing the risk of bias and applicability concerns in four domains: patient selection, index test, reference standard, flow, and timing [14].

The review was registered in PROSPERO International Prospective Register of Systematic Reviews (Registration Number: CRD42016036387).

Results

Twenty studies which included a total of 875 patients were finally selected [15–34]. The study selection process, updated on 31 March 2016, is shown in Supplementary file 2. All included studies were published in peer-reviewed journals. No randomized controlled trials were found. All the included studies were observational, with three case/control studies. The results of quality assessment with QUADAS-2 are reported in Supplementary file 3.

Three studies [21, 24, 25] were conducted on pediatric patients, 17 on adult patients.

To assess DD, 11 studies [15–19, 26, 27, 30–33] measured diaphragmatic thickness, seven of them [15, 19, 26, 27, 30, 31, 33] assessing diaphragmatic contractility as thickening fraction (percentage change in diaphragm thickness with respiratory movement). Five studies [20, 21, 28–30] measured respiratory excursion of the diaphragm in M-mode, five studies [23–25, 29, 34] measured diaphragm excursion in B-mode, and two studies [22, 34] measured liver/spleen displacement as a surrogate for diaphragmatic excursion.

Ten studies compared ultrasound with other methods: two fluoroscopy [24, 25], four transdiaphragmatic pressure [19, 23, 26, 30], four rapid shallow breathing index (RSBI) [15, 20, 22, 33]. Table 1 summarizes the characteristics of the 20 studies selected.

In the selected studies, usefulness and accuracy of DU were investigated in four main settings:

To diagnose dysfunction or paralysis in critically ill patients: six studies reported the use of DU as a clinical monitoring tool to detect diaphragm dysfunction in critically ill patients. The results are summarized in Table 2.

To predict weaning success/failure from mechanical ventilation: four studies aimed to investigate the accuracy of DU in predicting extubation success or failure, two measuring excursion [20, 22] and two measuring thickening fraction [15, 33]. The results are shown in Table 3.

To assess the performance of DU measurements as indexes of respiratory effort in mechanically ventilated patients: four studies assessed the accuracy of DU to assess the diaphragm workload during spontaneous or assisted breathing, one measuring excursion [23], two measuring thickening fraction [19, 26], and one measuring both [30]. The results are presented in Table 4.

Table 1 Summary of selected studies

Author (year)	Setting	Study	Aim	Patients (*n*)	Main findings
Balaji [24] (1990)	Pediatric cardiac ICU	Prospective observational	To assess the accuracy of US vs fluoroscopy to diagnose diaphragmatic palsy after surgery	16	US allows one to identify diaphragmatic palsy without fluoroscopy
Urvoas [21] (1994)	Pediatric ICU	Prospective observational	To report and describe US signs of DD in children	27	TM-mode allows one to diagnose diaphragmatic paralysis in children
Jiang [22] (2004)	Medical ICU, adult patients	Prospective observational	To assess if diaphragm excursion can predict successful extubation	55	DU (mean liver/spleen displacement) can predict successful extubation
Lerolle [23] (2009)	Cardiac ICU, adult patients	Case/control	To determine a quantitative ultrasonographic criterion of diaphragm motion for the diagnosis of severe DD	48	DU allows one to identify those with and without severe diaphragmatic dysfunction in patients requiring prolonged MV
Sanchez de Toledo [25] (2010)	Pediatric cardiac ICU	Prospective observational	To assess accuracy of US for diagnosis of DD	25	DU performed by cardiac intensivists allows for an early diagnosis of DD
Kim [20] (2011)	Medical ICU, adult patients	Prospective observational	To detect diaphragmatic dysfunction and to assess its influence on weaning from MV	88	Diaphragmatic dysfunction assessed with DU can predict weaning failure
Grosu [16] (2012)	ICU, mechanically ventilated adult patients	Prospective observational	To quantify rate and degree of diaphragm thinning during MV	7	DU allowed assessment of decrease Tdi during MV
Vivier [19] (2012)	ICU, adult patients under NIV post-extubation	Prospective observational	To assess feasibility and accuracy of DU to assess diaphragmatic function	12	DU was shown to be a valid tool to assess the work of breathing during NIV
Cartwright [17] (2013)	Medical ICU, adult patients	Prospective observational	To detect changes in muscles thickness (included diaphragm) in ICU patients	16	Ultrasound is an informative technique for assessing muscles of patients in the ICU, including diaphragm and respiratory muscles
Baldwin [18] (2014)	ICU septic adult patients	Case/control	To assess relative differences in thickness and strength of respiratory and peripheral muscles	16	Survivors of sepsis and a period of MV may have respiratory muscle weakness without remarkable diaphragm wasting
Dinino [15] (2014)	ICU, adult patients	Prospective observational	To evaluate if diaphragm thickening can be used to predict extubation success or failure	63	TF predicts extubation success of failure during spontaneous breathing or pressure support trials
Ferrari [33] (2014)	Adult high dependency unit	Prospective observational	To test TF as index for weaning from MV	46	TF can predict successful extubation
Goligher [26] (2015)	ICU, adult patients	Prospective observational	To test feasibility and reproducibility of TF in MV patients	96	TF is feasible and highly reproducible
Mariani [29] (2015)	Medical ICU, adult patients	Prospective observational	Assess prevalence of DD through US evaluation, measure reproducibility, compare M-mode and B-mode	34	DD has a 24 % prevalence among ICU patients ventilated for 7 days, but was not associated with a worse prognosis. DD can be easily detected by ultrasound. Agreement higher for M-mode than for 2D images
Valette [28] (2015)	Medical ICU, adult patients	Retrospective observational	To assess feasibility of diaphragmatic ultrasonography in a medical ICU	10	Diaphragmatic ultrasonography enhances detection of DD
Umbrello [30] (2015)	Surgical ICU, adult patients	Prospective observational	Performance of US indices (TF and diaphragm excursion) to assess diaphragm contractility	25	In patients under MV, TF is a reliable indicator of respiratory effort, while diaphragm excursion should not be used to quantitatively assess diaphragm contractile activity

Table 1 continued

Author (year)	Setting	Study	Aim	Patients (*n*)	Main findings
Haji [34] (2015)	ICU, adult patients	Prospective observational	To evaluate the movement between different parts of each hemidiaphragm and the agreement with liver/spleen displacement	90	Acceptable agreement does not exist for diaphragm and solid organ movement
Goligher [27] (2015)	ICU, adult patients	Prospective observational	Describe the evolution of Tdi over time in patients on MV and its relation to DD	107	Changes in Tdi are common in mechanically ventilated patients and may be associated with DD
Schepens [32] (2015)	ICU, adult patients	Prospective observational	To assess the extent and time course of atrophy in patients on MV	54	Diaphragm atrophy occurs quickly after onset of MV and can be accurately monitored with DU
Zambon [31] (2016)	ICU, adult patients	Prospective observational	To quantify rate and degree of diaphragm atrophy during MV and correlate with the amount of ventilation support	40	There is a linear relationship between ventilator support and diaphragmatic atrophy rate

Tdi thickness of diaphragm, *TF* thickening fraction, *MV* mechanical ventilation, *RSBI* rapid shallow breathing index, *DU* diaphragmatic ultrasound, *DD* diaphragmatic dysfunction, *ICU* intensive care unit

To assess the progression of atrophy in ICU mechanically ventilated patients: six studies investigated the time course of thickness of diaphragm in mechanically ventilated patients. The results are summarized in Table 5.

Reproducibility

Several studies have addressed the subject of reproducibility of ultrasound to measure the diaphragmatic displacement and thickness. Intraclass correlation coefficients (ICC) ranged from 0.876 to 0.999 (intraobserver) and from 0.56 to 0.989 (interobserver). The results are summarized in Supplementary file 4.

Learning curve

Two studies describe learning curves of trainees, one in pediatrics for excursion assessment, and one in adults for thickness measurement.

In a pediatric population, a 4-h hands-on training in ultrasound was reported, focusing on the recognition of normal and abnormal diaphragmatic motion. Semiquantitative assessment of excursion (normal/dysfunction/paralyzed) carried out by a trainee had very high repeatability compared to the one performed by an expert operator skilled in ultrasound [25].

In adult patients, the training of ultrasound operators to identify the diaphragm and measure its thickness was reported to take three to five sessions lasting 10–15 min each [15].

Discussion

This systematic review has several interesting results. First, DU is feasible at the bedside and has excellent intra- and interobserver reproducibility. Second, ultrasound is accurate in investigating diaphragm dysfunction, predicting extubation success or failure, quantifying respiratory effort, and detecting atrophy in mechanically ventilated patients.

To our knowledge, this is the first review that systematically analyzes the use of ultrasound to assess DD in critically ill patients, a composite population including both medical patients, in whom DD is mainly the result of prolonged MV, and surgical patients in whom DD is often caused by acute insults such as trauma or major surgical procedures.

The definition of ventilator induced diaphragmatic dysfunction (VIDD) in the critically ill is relatively recent [3], but its frequency and relevance are strongly enhanced in several publications [1, 35]. DD is responsible for a number of pulmonary complications, including atelectasis and pneumonia, and an early diagnosis of DD (prior to extubation) is mandatory to avoid the risk of extubation failure. Demoule et al. found that DD, defined as a reduced capacity of the diaphragm to produce inspiratory pressure, is as frequent as 64 % on the first day from ICU admission. It is associated with disease severity and sepsis, and it may represent another sepsis-related organ failure. Furthermore, it is associated with a poor prognosis [1].

Despite the widespread use of ultrasound techniques in the ICUs (namely echocardiography and lung ultrasound), DU has only recently been applied in the intensive care setting. DU allows both morphologic assessment (detection of atrophy) and functional evaluation of the muscle (contractility). Furthermore, it allows repeated measurements over time, such as before and after variations in ventilator settings, or before and after the start of noninvasive ventilation.

Several studies have compared ultrasound of the diaphragm with reference methods (i.e., transdiaphragmatic

Table 2 Summary of studies reporting DU to diagnose diaphragmatic dysfunction in the critically ill

Author (year)	Setting	Measures	DU criteria for dysfunction	Comparison	Main findings	Accuracy
Balaji [24] (1990)	Pediatric cardiac ICU	Diaphragm excursion, B-mode	Paralysis: absence of movement or upward movement during inspiration	Fluoroscopy	US allows one to identify diaphragmatic palsy without fluoroscopy	NA
Urvoas [21] (1994)	Pediatric ICU	Diaphragm excursion, M-mode	Paralysis: paradoxical motion. Dysfunction: excursion ≤4 mm	X-rays, fluoroscopy	M-mode allows one to diagnose diaphragmatic paralysis in children	NA
Lerolle [23] (2009)	Cardiac ICU, adult patients	Diaphragm excursion, B-mode	Excursion <25 mm (at maximal inspiratory effort) was considered severe dysfunction	Transdiaphragmatic pressure (Gilbert index)	DU allows one to identify those with and without severe diaphragmatic dysfunction in cardiac patients requiring prolonged mechanical ventilation	AUC 0.93, sensitivity 100 %, specificity 85 %
Sanchez de Toledo [25] (2010)	Pediatric cardiac ICU	Diaphragm excursion, B-mode	Semiquantitative. Diaphragmatic motion was classified as (1) normal; (2) hypokinetic; (3) akinetic; and (4) paradoxical	Fluoroscopy	DU performed by intensivists allows for an early diagnosis of DD in a pediatric cardiac population	Performed by specialist: sensitivity 100 %, specificity 100 %. Performed by a trainee: sensitivity 86 %, specificity 94 %
Mariani [29] (2015)	Medical ICU, adult patients	Diaphragm excursion, B-mode and M-mode	Excursion <10 mm (right) and <11 mm (left)	None	Bilateral DD has a 24 % prevalence among ICU patients ventilated >7 days. No association was found between DD and extubation failure. Agreement higher for M-mode than for 2D images	NA
Valette [28] (2015)	Medical ICU, adult patients	Diaphragm excursion, M-mode	Paralysis: paradoxical or no movement. Dysfunction: excursion <10 mm during unassisted deep breathing	None	Diaphragmatic ultrasonography enhances detection of DD in a medical ICU population	NA

Tdi thickness of diaphragm, *TF* thickening fraction, *MV* mechanical ventilation, *DU* diaphragmatic ultrasound, *DD* diaphragmatic dysfunction, *ICU* intensive care unit, *NA* not assessed

pressure) in healthy subjects, finding diaphragmatic excursion and thickening fraction very effective in assessing the diaphragmatic function [36, 37].

In our systematic review, we found DU successfully applied in four different settings:

1. To diagnose dysfunction or paralysis in critically ill patients. DD diagnosed with ultrasound was found in 29 % of mechanically ventilated patients without history of diaphragmatic or neuromuscular disease [20]. This finding indicates that DD is probably underestimated in ICU patients.
2. To predict weaning success/failure from mechanical ventilation. Either diaphragm excursion or thickening fraction measurements performed during a spontaneous breathing trial in intubated patients have shown good performance as weaning indexes.
3. To assess respiratory effort in mechanically ventilated patients. When compared to invasive techniques such as diaphragm and esophageal time–pressure product (PTPdi and PTPes), the thickening fraction has shown significant correlation, thus emerging as a new noninvasive tool to monitor respiratory workload during assisted mechanical ventilation.

Table 3 Summary of studies assessing the performance of DU in predicting weaning outcome

Author (year)	Setting	Measures	Comparison	Main findings	Best cutoff to identify DD	Accuracy
Jiang [22] (2004)	Medical ICU, adult patients	Diaphragm excursion (liver/spleen displacement)	Traditional weaning indexes (included RSBI)	DU (mean liver/spleen displacement) can predict successful extubation	11 mm	Sensitivity 84.4 %, specificity 82.6 %
Kim [20] (2011)	Medical ICU, adult patients	Diaphragmatic excursion, M-mode	RSBI	Diaphragmatic dysfunction assessed with DU can predict weaning failure	14 mm (right) and 12 mm (left)	Sensitivity 60 %, specificity 76 %, AUC 0.68
Dinino [15] (2014)	ICU, adult patients	Tdi and TF	RSBI	TF predicts extubation success or failure during spontaneous breathing or pressure support (Δ5/5) trials	30 %	Sensitivity 88 %, specificity 71 %, AUC 0.79
Ferrari [33] (2014)	Adult high dependency unit	TF	RSBI	TF can predict successful extubation	36 %	Sensitivity 0.82, specificity 0.88

Tdi thickness of diaphragm, *TF* thickening fraction, *MV* mechanical ventilation, *DU* diaphragmatic ultrasound, *DD* diaphragmatic dysfunction, *ICU* intensive care unit, *RSBI* rapid shallow breathing index

Table 4 Summary of studies evaluating the accuracy of DU to assess the diaphragm muscular workload

Author (year)	Setting	Measures	Comparison	Accuracy
Lerolle [23] (2009)	Cardiac ICU, adult patients	Diaphragm excursion at maximal inspiratory effort (through pleural effusions)	Transdiaphragmatic pressure (Gilbert index)	Maximal excursion significantly correlated with Gilbert index ($\rho = 0.64$)
Vivier [19] (2012)	ICU, adult patients under NIV post-extubation	TF	Diaphragmatic pressure–time product (PTPdi)	TF significantly correlated with PTPdi ($\rho = 0.74$)
Goligher [26] (2015)	ICU, adult patients	TF	Diaphragm electrical activity and transdiaphragmatic pressure	TF significantly correlated with diaphragm electrical activity and transdiaphragmatic pressure ($r^2 = 0.32$ and 0.28)
Umbrello [30] (2015)	Surgical ICU, adult patients	TF and diaphragmatic excursion	Diaphragm and esophageal time–pressure product (PTPdi and PTPes)	TF significantly correlated with PTPdi and PTPes ($r = 0.701$ and 0.801). No significant correlation for diaphragmatic excursion

Tdi thickness of diaphragm, *TF* thickening fraction, *MV* mechanical ventilation, *DU* diaphragmatic ultrasound, *DD* diaphragmatic dysfunction, *ICU* intensive care unit

4. To assess the progression of atrophy in ICU mechanically ventilated patients. Measuring thickness at the zone of apposition in mechanically ventilated patients is the best tool to detect atrophy, one of the main features (even if not synonymous) of dysfunction [2].

The technique to measure diaphragm performance varied from subcostal assessment of inspiratory excursion to assessing the muscle at the zone of apposition for thickness and thickening fraction measurements. The two techniques have indeed different features.

Thickening fraction has shown the best performance to estimate respiratory muscle workload during non-invasive mechanical ventilation and to predict extubation failure or success during a spontaneous breathing trial. The reported cutoff to predict extubation success or failure ranged between 30 and 36 % during spontaneous breathing trials [15, 33]. Nevertheless, thickness and thickening fraction measurements are not always easy to perform. First, the mean thickness values are about 1.5–2 mm and therefore it needs a high frequency probe (usually a 10 MHz “vascular” probe). Second, technical difficulties with some patients (i.e., obese patients) should be expected. Third, the smallest measurable distance of most machines is 0.1 mm, which means about 5–7 % of the measurement; therefore, small operator-dependent variations could influence the measurement. Fourth, it is not always possible to assess the left hemidiaphragm [26, 31]. Finally, there is a lack of data about the learning curve to measure the thickening fraction; nevertheless, in our experience it is longer than the one to measure respiratory excursion.

On the other hand, ultrasonographic assessment of diaphragmatic excursion is relatively easy to perform. A convex cardiac or abdominal probe should be used. The probe is placed between the mid-clavicular and anterior axillary lines, in the subcostal area, and directed medially, cranially, and dorsally, so that the ultrasound beam reaches perpendicularly the posterior third of the diaphragm. The inspiratory and expiratory cranio-caudal displacement of the diaphragm respectively shortens and lengthens the probe–diaphragm distance. To measure diaphragmatic excursion, M-mode has been shown to be more reproducible than B-mode [29].

Movement is usually better appreciated on the right side, while on the left side the descending lung, bowel, and gas interposition during inspiration often hide the diaphragm.

The best cutoff to diagnose DD with diaphragmatic excursion measurements ranged from 10 to 14 mm during normal spontaneous breathing and 25 mm for maximal inspiratory effort. It should be noted that excursion as an index of diaphragmatic function should be limited to patients on spontaneous breathing. Only one study assessed both thickening of diaphragm and excursion to evaluate inspiratory muscle effort during assisted breathing and concluded that excursion should not be used to assess diaphragm contractility [30]. In fact, excursion is mainly related to the inspired volume [37], regardless of whether it depends on muscle workload or ventilator support. Therefore, to estimate the diaphragm workload during assisted breathing thickening fraction should be measured.

Limitations

This systematic review has some limitations. The existing studies are observational, and no randomized controlled trials have been published so far on the utilization of DU in critical care; furthermore, they are relatively small and heterogeneous, and this does not allow one to perform pooled data analysis. Even if excellent reproducibility has been reported in most of the studies, attention should be drawn to the fact that statistical gold standard to assess reproducibility (i.e., Bland–Altman limits of agreement) was reported only in one publication [34]. Data on learning curves for DU are lacking, especially for thickening fraction measurements.

Only three studies compare DU with transdiaphragmatic pressure, a measure of the diaphragm's force-generating capacity. Therefore, the relationship between diaphragm thickening or inspiratory excursion and strength of the diaphragm should be further investigated. Nevertheless, clearly all the retrieved articles support DU as a useful tool for respiratory muscle monitoring in critically ill patients.

Table 5 Summary of studies assessing diaphragm atrophy in mechanically ventilated patients

Author (year)	Setting	Patients (*n*)	Main findings
Grosu [16] (2012)	ICU, mechanically ventilated adult patients	7	DU allowed assessment of decrease in Tdi during MV. Diaphragm thickness decreased on average 6 % per day of MV
Cartwright [17] (2013)	Medical ICU, adult patients	16	Diaphragm thickness did not vary significantly
Baldwin [18] (2014)	ICU septic adult patients	16	Survivors of sepsis and a period of mechanical ventilation may have respiratory muscle weakness without remarkable diaphragm wasting
Goligher [27] (2015)	ICU, adult patients	107	Changes in Tdi are common in mechanically ventilated patients and may be associated with DD. Over the first week of MV, thickness decreased in 44 %, did not vary in 44 %, and increased in 10 % of patients. Thickness did not vary in nonventilated patients
Schepens [32] (2015)	ICU, adult patients	54	Diaphragm atrophy occurs quickly after onset of MV and can be accurately monitored with DU. Mean baseline thickness was 1.9 mm, and mean nadir was 1.3 mm, corresponding to a mean change in thickness of 32 %. Length of mechanical ventilation was associated with the degree of atrophy
Zambon [31] (2016)	ICU, adult patients	40	There is a linear relationship between ventilator support and diaphragmatic atrophy rate. Daily atrophy rate ranged from −7.5 % under CMV to +2.3 % during SB

Tdi thickness of diaphragm, *TF* thickening fraction, *MV* mechanical ventilation, *CMV* controlled mechanical ventilation, *SB* spontaneous breathing, *DU* diaphragmatic ultrasound, *DD* diaphragmatic dysfunction, *ICU* intensive care unit

Conclusions

DU has shown to be useful and accurate in diagnosing diaphragmatic dysfunction with a cutoff of 10–14 mm for diaphragmatic excursion and 30–36 % for thickening fraction. Current literature suggests the use of DU to detect diaphragmatic dysfunction in critically ill patients, to predict extubation success or failure, to monitor respiratory workload, and to assess atrophy in patients who are mechanically ventilated. Randomized controlled studies are needed to assess if the use of DU to guide clinical decisions may influence outcomes in critically ill patients.

Electronic supplementary material

The online version of this article (doi:10.1007/s00134-016-4524-z) contains supplementary material, which is available to authorized users.

Abbreviations

DD: Diaphragmatic dysfunction; DU: Diaphragm ultrasonography; ICU: Intensive care unit; RSBI: Rapid shallow breathing index; MV: Mechanical ventilation.

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Conflicts of interest

All authors report no financial or other conflict of interest relevant to the subject of this article.

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