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Methodological and Clinimetric Evaluation of Inspiratory Respiratory Muscle Ultrasound in the Critical Care Setting: A Systematic Review and Meta-Analysis

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Abstract

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OBJECTIVE: Significant variations exist in the use of respiratory muscle ultrasound in intensive care with no society-level consensus on the optimal methodology. This systematic review aims to evaluate, synthesize, and compare the clinimetric properties of different image acquisition and analysis methodologies.

DATA SOURCES: Systematic search of five databases up to November 24, 2021.

STUDY SELECTION: Studies were included if they enrolled at least 50 adult ICU patients, reported respiratory muscle (diaphragm or intercostal) ultrasound measuring either echotexture, muscle thickness, thickening fraction, or excursion, and evaluated at least one clinimetric property. Two independent reviewers assessed titles, abstracts, and full text against eligibility.

DATA EXTRACTION: Study demographics, ultrasound methodologies, and clinimetric data.

DATA SYNTHESIS: Sixty studies, including 5,025 patients, were included with 39 studies contributing to meta-analyses. Most commonly measured was diaphragm thickness (DT) or diaphragm thickening fraction (DTF) using a linear transducer in B-mode, or diaphragm excursion (DE) using a curvilinear transducer in M-mode. There are significant variations in imaging methodology and acquisition across all studies. Inter- and intrarater measurement reliabilities were generally excellent, with the highest reliability reported for DT (ICC, 0.98; 95% CI, 0.94–0.99). Pooled data demonstrated acceptable to excellent accuracy for DT, DTF, and DE to predicting weaning outcome after 48 to 72 hours postextubation (DTF AUC, 0.79; 95% CI, 0.73–0.85). DT imaging was responsive to change over time. Only three eligible studies were available for intercostal muscles. Intercostal thickening fraction was shown to have excellent accuracy of predicting weaning outcome after 48-hour postextubation (AUC, 0.84; 95% CI, 0.78–0.91).

CONCLUSIONS: Diaphragm muscle ultrasound is reliable, valid, and responsive in ICU patients, but significant variation exists in the imaging acquisition and analysis methodologies. Future work should focus on developing standardized protocols for ultrasound imaging and consider further research into the role of intercostal muscle imaging.

Keywords

intensive care; meta-analysis; respiratory muscles; systematic review; ultrasonography

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Respiratory muscle weakness is prevalent in patients admitted to the ICU and occurs at nearly twice the rate of peripheral muscle weakness (1). It is linked with increased mechanical ventilation (MV) duration (2, 3), higher risk of extubation failure (2), longer ICU length of stay, and mortality (1, 2). Unsurprisingly, there is growing interest in investigating noninvasive bedside ICU tools to evaluate respiratory muscles and detect respiratory muscle weakness accurately.

Use of ultrasound to assess diaphragm and intercostal muscles has seen a rapid growth within the ICU, at admission and for serial imaging, because it is readily available, portable, noninvasive, and free of ionizing radiation (4). Previous systematic reviews within the field have examined accuracy and usefulness of diaphragmatic ultrasound in predicting weaning outcomes and extubation success with the latest review focusing on diaphragm thickening fraction (DTF) and excursion only (5–9). A more recent systematic review by Pałac et al (10) aimed to evaluate the utility of respiratory muscle ultrasound imaging for assessing respiratory function and identify ultrasound variables that best correlate with pulmonary parameters. No systematic reviews to date have comprehensively synthesized and analyzed inspiratory respiratory muscle ultrasound methodology (including acquisition and analysis processes) as well as reporting on clinimetric properties (e.g., reliability, measurement error, construct/predictive validity, and responsiveness). This is an important consideration when selecting what ultrasound parameter may be clinically useful to assess outcomes and for prognostication of patients who may benefit from targeted interventions.

This systematic review aims to understand the methodology for inspiratory respiratory muscle (diaphragm and intercostals) ultrasound imaging within the ICU setting and evaluation of its clinimetric properties (i.e., reliability, validity, measurement error, and responsiveness).

MATERIALS AND METHODS

Protocol and Registration

This systematic review was prospectively registered on the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42021277264). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (11) and COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) (12) were followed.

Information Sources

Five databases (MEDLINE, CINAHL, Embase, Scopus, and Cochrane Library) were accessed through The University of Melbourne and searched from inception to November 24, 2021, using a preplanned search strategy (Supplementary Digital Content File 1, http://links.lww.com/CCM/H250).

Eligibility and Study Selection Process

Eligibility criteria are shown in Table 1. Studies were included if they reported inspiratory respiratory muscle ultrasound (diaphragm or intercostal) assessment of muscle architecture (in form of echotexture, thickening, thickening fraction, excursion, or excursion-derived measures) (defined in Supplementary Table 3, http://links.lww.com/CCM/H250) and included evaluation of at least 1 clinimetric property (i.e., reliability, measurement error, validity, and responsiveness). Only studies with at least 50 adult patients were included, in line with COSMIN guidelines reporting that sample sizes less than 50 are considered of “fair” or “poor” methodological quality (13). Two independent reviewers (one of D.T., S.A., A.N.D., G.N., D.E.-A., C.L.G., and S.M.P.) screened title, abstract, and full-text articles (Fig. 1) against defined eligibility criteria (Table 1), with consultation with third reviewer as needed (S.M.P.).

Data Items and Collection

Data were extracted and independently cross-checked by a second reviewer (one of D.T., G.A.W.-W., S.A., A.N.D., C.L.G., and S.M.P.), according to data items, as reported in Supplementary Digital Content File 1 (http://links.lww.com/CCM/H250). The data collection form was informed by previous recommendations (14).

Risk of Bias Assessment

Performed using the COSMIN checklist (15, 16) by two independent reviewers (D.T. and A.N.D.), with discrepancies resolved by third reviewer (S.M.P.).

Statistical Analysis

Clinimetric property results were quantitatively pooled in meta-analyses using inverse variance weighted random effects model, allowing for appropriate weighting to studies and correct confidence estimates in the presence of heterogeneity between studies, with R Version 4.1.2 (R Foundation For Statistical Computing, Vienna, Austria). Cochran Q test and I^2 were computed to quantify heterogeneity. For meta-analyses of correlation, Fisher z transformation (17) was used when combining results from multiple studies (see Supplementary Digital Content File 1, http://links.lww.com/CCM/H250, for full statistical plan).

RESULTS

Flow of Studies

A total of 6,812 studies were identified, resulting in final inclusion of 60 studies, with 39 contributing to meta-analyses (Fig. 1). Strong agreement existed between reviewers (title/abstracts 96% and full-text 94%) (18).

Study Characteristics

Sixty studies, with a total of 5,025 ICU patients, were included (Supplementary Table 1, http://links.lww.com/CCM/H250). All 60 studies involved diaphragm muscle ultrasound (n = 5,025 patients), with three studies (n = 256) also assessing intercostal muscles (19–21). All studies were published since 2011, with most studies (n = 49/60) published in the last 5 years across 19 different countries. More than half of the studies were conducted in a mixed ICU (n = 37/60) and included patients who were MV or undergoing a weaning trial at the time of ultrasound assessment (n = 31/60). Duration of MV across studies ranged from 0.25 to 24 days. Two studies involved patients who were not initially MV, and these studies included patients who were on noninvasive ventilation prior to diaphragm imaging (22) and COVID-19 patients who might require invasive MV (23). The three studies imaging the intercostal muscles included MV patients (19–21).

Forty studies reported information of staff undertaking ultrasound acquisition/analysis, of which 11 studies reported bespoke dedicated training for the purposes of the study (Supplementary Table 1, http://links.lww.com/CCM/H250). The reported background training of investigators performing the ultrasound scans in the studies included in our review was medicine (including physicians from critical care medicine, pulmonology, and radiology) (n = 28/60), formally trained sonographers working under radiology supervision (n = 1/60), and physiotherapy (n = 1/60).

Ultrasound Imaging Acquisition and Analysis Methodology

Full details of individual study ultrasound acquisition and analysis methodologies are reported in Supplementary Table 2 (http://links.lww.com/CCM/H250).

Respiratory Muscle Ultrasound Parameters.—Supplementary Table 3 (http://links.lww.com/CCM/H250) summarizes the ultrasound parameter definitions within this review. The most common diaphragm ultrasound parameter measured was DTF (n = 36/60), followed by diaphragm thickness (DT) (n = 35/60) and diaphragm excursion (DE) (n = 31/60). Thirteen individual studies assessed excursion-derived measures including diaphragmatic rapid shallow breathing index (24–26), rapid shallow diaphragmatic index (27), excursion-time index (28, 29), ULDIMex (28), peak contraction velocity (30, 31), velocity-time integral (30), peak relaxation velocity (30), time-to-peak inspiratory amplitude (32), and contraction velocity (33–36).

In the three studies focused on the intercostal muscle group (19–21), all investigated intercostal thickness (Tic) and two investigated intercostal thickening fraction (TFic) were measured. Assessment of echotexture was not reported for either diaphragm or intercostal muscles within the included studies, though these have been reported in studies with less than 50 patients (37).

Timing and Frequency of Ultrasound Measurements.—Timing of ultrasound measurements varied between studies including a single measure at one point in time (n = 36/60) or serial measures (n = 20/60) performed over the ICU admission. Single measures were mainly taken during a weaning trial (n = 16/60).

Transducer Settings and Technique.—Image acquisition methodology varied between included studies. Diaphragm thickness was most often measured using a linear transducer in B-mode ultrasonography (n = 18/35) though several studies used M mode (n = 11/35). DTF (n = 15/36 studies) was also measured using a linear transducer in B-mode (n = 15/36 studies) with lesser number of studies reporting use of M mode (n = 10/36). The frequency range for linear transducers reported in these studies ranged from 4–9 MHz (38) to 10–15 MHz (39). A curvilinear transducer in M-mode was most used in studies measuring DE (n = 11/31), with transducer frequency ranging from 2–4 MHz (40) to 6.5 MHz (41). A linear transducer in B-mode to measure DE was reported in two studies (25, 42). Details on the transducer settings and type were not completely reported in 19 diaphragmatic studies.

In the studies on the intercostal muscle group, one study measured Tic in B-mode using a linear transducer (transducer frequency not reported) (21), and the other two studies measured Tic and TFic using a linear transducer in M-mode (10–15 MHz) (19, 20).

Patient and Transducer Positioning During Ultrasound Measurements.—Patient and transducer placement are summarized in Supplementary Figures 1 and 2 (http://links.lww.com/CCM/H250). For evaluation of the diaphragm, three different patient positions were used: semirecumbent between 20° and 60° (n = 30/60), supine (n = 9/60), and upright sitting (n = 1/60). Patient positioning was not reported in 20 studies (n = 20/60). Patients were commonly positioned in semirecumbent for DT (n = 15/35), DTF (n = 18/36), and DE (*n* = 17/31). For evaluation of the intercostals, all studies involved patients in a semirecumbent position.

Unilateral right diaphragm measurement was reported in 57 studies, with only three studies assessing bilaterally. Four different transducer positions were used to assess DT and DTF: midaxillary line, between midclavicular and midaxillary lines, anterior axillary line, and between anterior and midaxillary lines. Most commonly, the transducer was placed in the midaxillary line (between the eighth and 11th rib space) to measure DT (*n* = 23/35) and DTF (*n* = 22/36). DTF measurements were mainly made during both end inspiration and end expiration of tidal breathing (*n* = 33/36). Transducer placement was not reported for DTF in one study (27). Breathing pattern at time of assessment was not reported for DT and DTF in one study (36).

Five different transducer positions were used to assess DE and excursion-derived measures: subcostal margin in the midclavicular line, midaxillary line, between midclavicular and midaxillary lines, anterior axillary line, and between anterior and midaxillary lines. In more than one-third of studies, DE was measured at the subcostal margin in the midclavicular line (*n* = 11/31), and in 68% during tidal breathing (*n* = 21/31). All intercostal studies involved transducer at level of the second right intercostal space.

Image Analysis Process.—Most studies (*n* = 59/60) did not specify the image analysis software used (e.g., ImageJ, National Institutes of Health, Bethesda, MD) (43) or whether measurements were made immediately at or away from the bedside. Twenty-seven (*n* = 27/60) studies reported performing three measurements with 23 studies (*n* = 23/60) taking the average of measures, three studies (*n* = 3/60) taking the highest value (22, 44, 45), and one study taking the median (*n* = 1/60) (38).

Risk of Bias in and Across Studies

Nine studies examined reliability, 54 studies examined validity, five examined measurement error, and eight examined responsiveness (Supplementary Fig. 3, http://links.lww.com/CCM/H250). Twenty-nine studies examined more than one clinimetric property. The COSMIN risk of bias ratings varied across studies from “inadequate” to “very good.” Most reliability studies (87%) were rated as “doubtful”; validity studies (90%) as “very good”; measurement error studies (80%) as “doubtful”; and all responsiveness studies as “inadequate” (Supplementary Digital Content File 1, http://links.lww.com/CCM/H250).

Results of Clinimetric Properties of Ultrasound Measurements

Summary of the clinimetric data is provided in Tables 2 and 3 and Supplementary Figure 3 and Supplementary Table 4 (http://links.lww.com/CCM/H250). Meta-analyzed results are reported here. Where a meta-analysis was not possible, individual study results were described narratively, as summarized in Supplementary Digital Content File 1 (http://links.lww.com/CCM/H250).

Diaphragm Thickness.—A meta-analysis of pooled data (46, 47) demonstrated excellent intrarater reliability (intraclass correlation coefficient [ICC], 0.98) (Supplementary Fig. 4A, http://links.lww.com/CCM/H250).

A meta-analysis of pooled data (48, 49) demonstrated moderate correlation between left and right measurements, with high heterogeneity (r = 0.60) (Supplementary Fig. 4B, http://links.lww.com/CCM/H250).

A meta-analysis of pooled data (49, 50) demonstrated excellent accuracy for predicting weaning outcome after 48 hours, with high heterogeneity due to the mixed patient population, different modes (two studies used M-mode), and different time points of measures (area under the curve [AUC], 0.89) (Fig. 2A).

Diaphragm Thickening Fraction.—A meta-analysis of pooled data (47, 51) showed good interrater reliability (ICC, 0.90) (Supplementary Fig. 4C, http://links.lww.com/CCM/H250).

There was a moderate relationship between DTF taken in B- and M-modes (r = 0.53) (52). Meta-analyses of pooled data found low correlations with lung compliance (r = 0.41) (39, 53), MV duration (r = −0.38) (39, 53), and respiratory distress during an spontaneous breathing trial (SBT) (r = −0.44) (32, 39) (Supplementary Fig. 4D–F, http://links.lww.com/CCM/H250).

A meta-analysis of pooled data from 16 studies (20, 32, 33, 35, 39, 42, 50, 51, 54–61) found acceptable prediction of weaning outcome after 48 hours, with high heterogeneity due to the mixed patient population, varying imaging modes, and different time points at which measurements were done such as prior to SBT, during SBT, end of an SBT, and during a pressure support weaning trial ± T-piece (AUC, 0.79) (Fig. 2B).

Diaphragm Excursion.—A meta-analysis of pooled data from two studies (26, 62) showed excellent intrarater reliability (ICC, 0.97) (Supplementary Fig. 4G, http://links.lww.com/CCM/H250).

There was a moderate relationship between assessment of left and right DEs (r = 0.648, r = 0.518, and r = 0.548) (49, 63). A meta-analysis of pooled data found a low correlation with DTF (r = 0.49) (61, 63), tidal volume (r = 0.42) (32, 62), and moderate correlation with maximum inspiratory pressure (r = 0.50) (26, 32) (Supplementary Fig. 4H–J, http://links.lww.com/CCM/H250). Two studies (32, 33) were included in the pooled analysis of respiratory distress during an SBT and found negligible correlation (r = −0.22) (Supplementary Fig. 4K, http://links.lww.com/CCM/H250).

A meta-analysis of pooled data from 19 studies (24, 26, 27, 31–35, 42, 44, 49, 50, 58, 59, 61, 62, 64–66) found acceptable prediction of weaning outcome after 48 hours but with high heterogeneity due to the mixed patient population, varying imaging modes, and different time points at which measurements were done such as prior to SBT, during SBT, end of an SBT, postextubation, and during a pressure support weaning trial ± T-piece (AUC, 0.78) (Fig. 2C).

Excursion-Derived Measures.—Predictive validity of excursion-derived measures was assessed in 13 studies (24–31, 33–36, 45). A meta-analysis of pooled data from 10 studies with 12 excursion-derived measures (including diaphragmatic rapid shallow breathing index, rapid shallow diaphragmatic index, excursion-time index, ULDIMex, diaphragm peak velocity, and contraction velocity) found acceptable prediction of weaning outcome after 48 hours (AUC, 0.76) (24–29, 31, 34–36) (Fig. 2D).

Intercostal Thickening Fraction.—Predictive validity of TFic was assessed in two studies. A meta-analysis of pooled data from two studies (19, 20) found excellent ability of TFic to predict weaning outcome after 48 hours (AUC, 0.84) (Fig. 2E).

DISCUSSION

Our review represents the largest body of synthesized data to date on the clinimetric properties of ICU diaphragm and intercostal ultrasound. This review covered a broader range of parameters than previous reviews. We identified that the most measured ultrasound parameters were DT or DTF using a linear transducer in B-mode, or DE using a curvilinear transducer in M-mode. Patients were comwas no consensus on patient positioning, transducer positioning, and timing of image acquisition in the ICU. Furthermore, most studies omitted at least one important methodological parameter of image acquisition and analyses. However, our meta-analysis results help identify quantitative signals that may support improved clinical utility of respiratory muscle ultrasound. We found diaphragm ultrasound to be a reliable and valid tool for predicting weaning outcome within 48 hours of extubation and a responsive diagnostic modality, although noting less data were available to support this. There is also emerging investigation into the use of diaphragm ultrasound-based parameters as surrogate measure of respiratory distress to replace other more invasive measures such as balloon-catheter, ventilator-derived, and magnetic-stimulated measures, and prediction of other patient-related outcomes such as mortality. Less is known about the clinimetric properties of intercostal muscle ultrasound, although early data on predictive validity of TFic and weaning outcome appear comparable.

Previous systematic reviews have demonstrated good diagnostic performance in predicting weaning outcomes 48 hours postextubation, despite high heterogeneity among studies (5–9). These reviews, however, did not evaluate the construct validity of respiratory muscle ultrasound measures, though limited construct validity data were found in this review. The results from our study reflect this, with acceptable to excellent predictive ability of DT (AUC, 0.81), DTF (AUC, 0.79), DE (AUC, 0.78), and excursion-derived measures (AUC, 0.76) in predicting reintubation within 48 hours of extubation. The literature within this review proposes the lowest cutoff of ≥0.17 cm for DT (inspiration), 15.6% of DTF, and 10 mm for DE in predicting weaning outcomes. This should be used with caution, as this contrasts with observations by Vivier et al [43], where low values of DTF and/or DE were not associated with reintubation following extubation. The cohort primarily had chronic heart disease (77%); therefore, diagnostic accuracy of respiratory muscle ultrasound may be more sensitive and useful in populations admitted with primary respiratory pathology necessitating MV. A study found that DE had excellent predictive ability within a respiratory ICU (AUC, 0.975) (24). This highlights that weaning outcomes can be affected by respiratory, but also cardiac, metabolic, and neuromuscular factors (67), indirectly affecting diaphragmatic function (68). There is also growing interest in using combined thoracic ultrasonographic assessment (including heart, lung, and diaphragm), which may help determine the cause of weaning failure (69).

Although respiratory muscle ultrasound has shown promise in predicting weaning success, it should not be used as an isolated surrogate measure of extubation success and is better used as a complementary diagnostic modality alongside available clinical information as weaning outcomes are multifactorial (67, 68). Randomized trials with diaphragm ultrasound embedded within the decision analysis to extubate patients are required to further understand the utility of diaphragm ultrasound in clinical practice. Clinicians are recommended to utilize either B- or M-mode with a high-frequency transducer when measuring DT/Tic or DTF/TFic, and M-mode with a low-frequency transducer when measuring DE (70). Although most studies performed ultrasonography in the semirecumbent position (20–60°) due to feasibility, with extubation usually performed in this position, supine position produced less variability and greater reproducibility (71). Two other factors need to be considered affecting the diagnostic accuracy of ultrasound measures: the learning curve for reproducible images for quantitative ultrasonography (7, 54) and the resolution of the ultrasound machine. Resolution affects the smallest measurable distance (~0.1 mm), which accounts for 5–7% measurement variability, and affects coefficient of variance of muscle measurements (7). Reproducibility of these measures can be affected by observer-dependent variations (e.g., ultrasonography expertise, landmarking, and patient positioning), as well as the ultrasound machine used. The midaxillary line is the preferred landmark, yielding the most consistent measurements, with more ventral landmarks (i.e., the midclavicular line), producing thicker measurements (72). Development of automated accurate measurement of respiratory ultrasound parameters to enable real-time feedback to the bedside clinician would further enhance the transferability of this modality into routine daily clinical decision-making.

Ultrasound methodology and image acquisition reporting are varied and not standardized across studies, affecting comparison between studies and the translation into clinical practice (70). This has been highlighted as a key knowledge gap for the field with a recent international medical expert Delphi consensus. This provided expert recommendations on diaphragm ultrasound methodology (70); however, reporting recommendations were not detailed. Ultrasound imaging has been increasingly used within the ICU multidisciplinary team, by disciplines such as physiotherapists (73, 74) and nurses (75, 76), who are usually part of MV weaning. Therefore, it is critical that a society-level statement and standardized training programs are developed for the interprofessional ICU community to maximize replicability and quality of future studies.

There is a potential for publication bias due to exclusion of non-English articles and exclusion of studies less than 50 patients, where emerging areas of ultrasound (such as echogenicity) were investigated and the exclusion of potential articles that utilized a large number of serial ultrasound exams. Furthermore, studies were not excluded from analyses based on risk of bias assessment. Therefore, caution in interpretation of meta-analyzed data is important particularly when involving small numbers of studies (i.e., two with small overall study sample sizes).

CONCLUSIONS

Research into inspiratory respiratory muscle ultrasound has grown exponentially in recent years. Diaphragm thickness has excellent reliability and predictive accuracy for weaning outcome. DTF, and excursion and excursion derived parameters have good reliability and acceptable prediction of weaning outcomes. There is emerging research in terms of construct validity of diaphragm imaging as a potential surrogate measure and prediction of other important patient related outcomes. Intercostal is a promising emerging tool with further clinimetric evaluation warranted. Future work should focus on developing standardized techniques for image acquisition and analysis as well as developing interprofessional standardized training to maximize replicability and quality of future studies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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KEY POINTS

Question:

To identify how bedside ultrasound is used in critical care to evaluate respiratory muscle thickness, thickening fraction, or excursion; and to evaluate, synthesize, and compare the clinimetric properties of the different image acquisition and analysis methodologies.

Findings:

Diaphragm muscle ultrasound is a reliable, valid, and responsive tool in critically ill patients. Significant variation exists in imaging and analysis methodologies described in research studies. There is emerging research into clinimetric properties of intercostal muscle ultrasound.

Meaning:

Future research should focus on investigating the utility of ultrasound-based parameters as a potential surrogate measure for respiratory clinical outcomes. There is a dire need for standardization of imaging protocols and methodology based on clinimetric properties of respiratory muscle ultrasound.

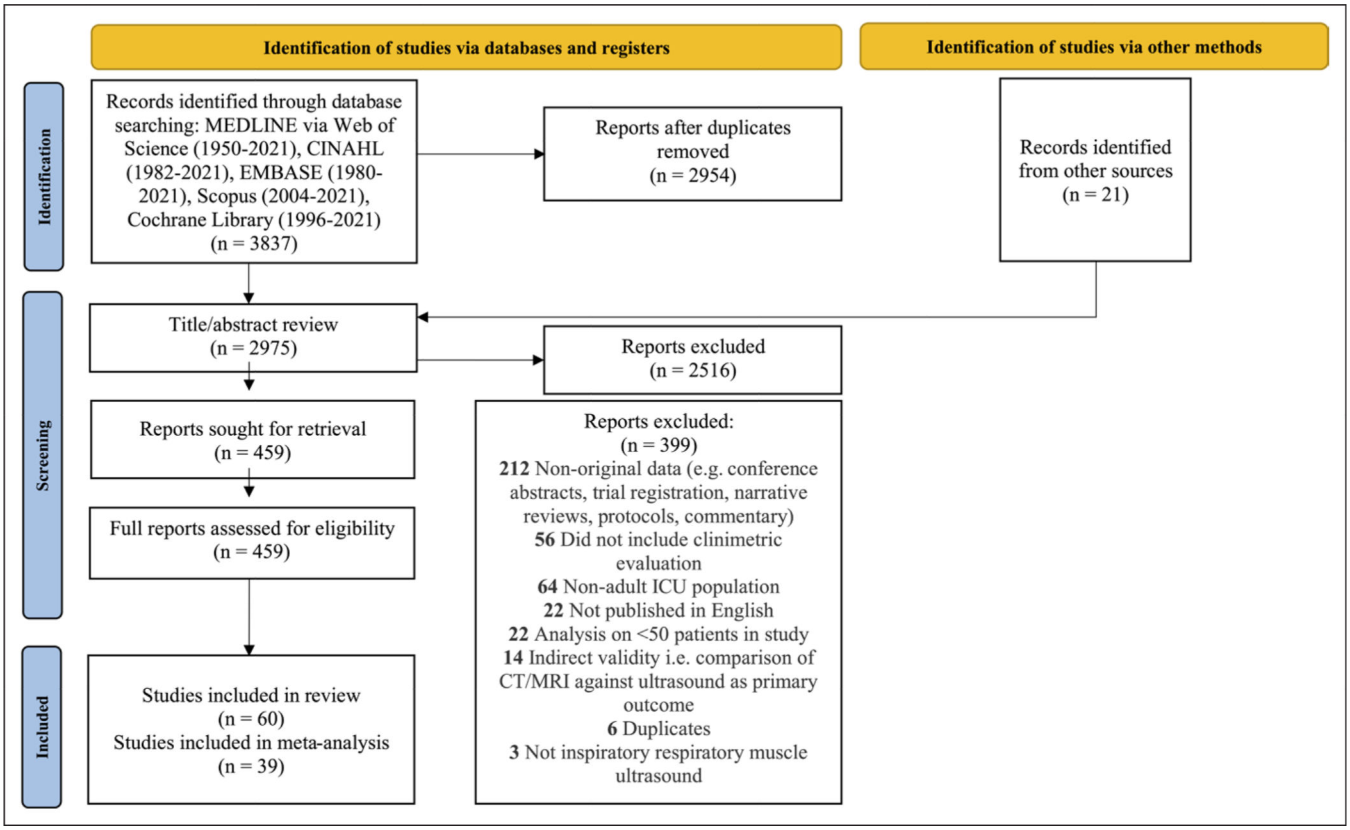

Figure 1.
Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram for study selection.

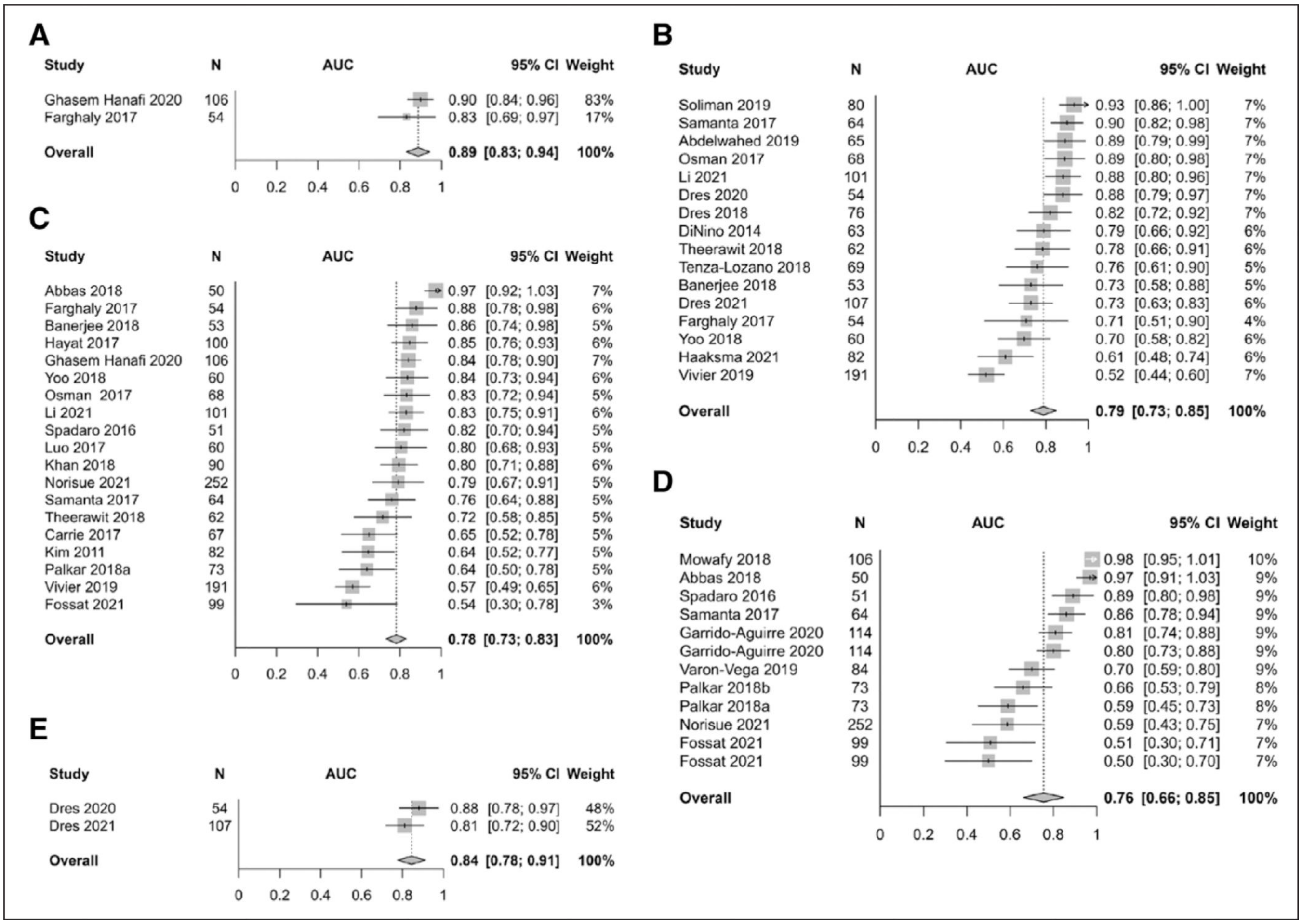

Figure 2.

Meta-analysis of individual studies investigating specific ultrasound parameters of predictive ability of diaphragm thickness (**A**), diaphragm thickening fraction (**B**), diaphragm excursion (**C**), diaphragm excursion-derived measures (Garrido-Aguirre 2020 [area under the curve (AUC), 0.81]—excursion-time index, Garrido-Aguirre 2020 [AUC, 0.80]—ULDIMex, Fossat 2021 [AUC, 0.51]—diaphragmatic rapid shallow breathing index, and Fossat 2021 [AUC, 0.50]—rapid shallow diaphragmatic index) (**D**), and intercostal thickening fraction (**E**), to predict weaning outcomes within 48–72 hr postextubation. Only studies with analyses conducted on 50 or more participants were included in meta-analyses.

TABLE 1.

Eligibility Criteria

Characteristics	Inclusion	Exclusion
Design	Quantitative studies including RCTs, pseudo-RCTs, cohort studies, case-control studies, or case series as per National Health and Medical Research Council classification	Studies not published in a peer-reviewed journal Studies without original participant data (such as reviews, editorials, and narratives) and conference abstracts
Participants	Adults ≥ 18 yr who have been in critical care	< 50 patients in study
Intervention	Did not form part of the eligibility criteria	
Outcomes	Ultrasound imaging of inspiratory respiratory musculature measuring any characteristic of muscle architecture (quality, quantity, and/or motion/excursion) and included evaluation of clinimetric property (reliability, measurement error, validity, and/or responsiveness)	Other forms of diagnostic imaging such as MRI, CT, or fluoroscopy Indirect validity—e.g., comparison of CT/MRI against ultrasound as primary outcome Surrogate measurement of diaphragm function/mvt assessed via mvt of solid organs such as spleen or tidal mvt of liver/portal vein Expiratory muscle (active), i.e., abdominal muscles
Publication	No publication date or language restriction applied on initial search	Non-English language studies

mvt = movement, RCT = randomized controlled trial.

TABLE 2.

Narrative Synthesis of Evidence Regarding Construct Validity

Ultrasound Parameter	Construct Validity[a]
DT	Negligible correlation between diaphragm thickness difference with spirometry, respiratory distress, ventilator derived diaphragmatic measures (32) Negligible correlation between DT at end expiration with body mass index (45) Negligible correlation with magnetic stimulated diaphragmatic measures at initiation of MV or switch to PSV (56) Low correlation of diaphragm thickness at end expiration with CT imaging (38) Moderate correlations between left and right measurements (48, 49) High correlations for tidal inspiratory and expiratory thickness between B- and M-mode (52)
Diaphragm thickening fraction	Negligible to moderate correlations with spirometry (32, 77), respiratory distress (20, 32, 33, 39) Negligible correlation with MV duration, dynamic compliance (53) and ICU length of stay (39) Negligible correlation with ventilator-derived diaphragmatic measures (32) or muscle strength (Medical Research Council) (1) Moderate correlation with P/F ratio and static compliance (39) Moderate to high correlations with magnetic stimulated diaphragmatic measures (56, 77) Moderate to high correlations with balloon catheter diaphragmatic measures (22, 77) Moderate correlation for tidal inspiratory and expiratory thickness with B- and M-mode (52)
Diaphragm excursion	Negligible to low correlations with spirometry (32, 62), cough peak flow (31), respiratory distress (32, 33), dynamic lung compliance (53) and magnetic stimulated diaphragmatic measures (56) High correlation with ventilator-derived diaphragmatic measures (32) Low to moderate correlations with diaphragm thickening fraction (61, 63) Low correlation with severity of illness and MV duration (53) Moderate correlation between left and right measurements (49)
Diaphragm excursion-derived	Moderate correlation between time to peak inspiratory amplitude and spirometry (32) Low correlation between peak contraction velocity and cough peak flow (31) Low to high correlations between time to peak inspiratory amplitude, diaphragmatic rapid shallow breathing index, and contraction velocity with respiratory distress (26, 32, 33) High correlation with balloon catheter derived diaphragmatic measures (30) Negligible correlation with ventilator-derived diaphragmatic measures (32)
Intercostal thickness	Nil studies
TFic	Negligible correlations with respiratory distress for TFic and TFic/thickening fraction of diaphragm (20) High correlation with balloon catheter derived diaphragmatic measures (19)

B-mode = brightness mode, DT = diaphragm thickness, M-mode = motion mode, MV = mechanical ventilation, TFIC = intercostal thickening fraction.

[a] See Supplementary Digital Content File 1 Statistical Analysis (http://links.lww.com/CCM/H250) for further details on cutoffs used.

TABLE 3.

Narrative Synthesis of Evidence Regarding Predictive Validity

Ultrasound Parameter	Predictive Validity[a]
DT	No/poor discrimination of predictive ability of weaning outcomes when measuring diaphragm thickness at end expiration (50, 54) Excellent predictive ability of weaning outcomes when measuring diaphragm thickness at end inspiration and difference between end expiration and end inspiration (32, 49, 50) Decreasing DT associated with increasing risk of prolonged MV duration, ICU and hospital LOS (21) Acceptable predictive ability of ICU-acquired weakness and excellent predictive ability of inhospital and 90-d mortality (78) No discrimination of detecting diaphragm dysfunction (56) Acceptable predictive ability of adverse outcomes, such as death or the need for invasive MV (23) Thinner baseline DT associated with higher chance of extubation (HR, 0.832–0.875) (45)
Diaphragm thickening fraction	Acceptable to outstanding predictive ability of weaning outcomes (19, 20, 32, 33, 35, 39, 40, 50, 51, 54, 55, 58–60), no discrimination to excellent predictive ability depending on ventilator settings (79) No discrimination of weaning outcomes (42, 57, 61) No discriminative predictive ability of identifying diaphragm dysfunction at the initiation of MV, and outstanding predictive ability during pressure support ventilation (56) Excellent predictive ability of noninvasive ventilation failure in individuals with acute exacerbation of chronic obstructive pulmonary disease (22) Poor discrimination of predicting postoperative pulmonary complications after cardiac surgery (48)
Diaphragm excursion	Acceptable to outstanding predictive ability of weaning outcomes (24, 26, 29, 31–33, 40, 49,50, 58, 59, 61, 64–66), and no discrimination to acceptable predictive ability depending on mode of ventilation (34). No/poor discriminative predictive ability of weaning outcomes (34, 42, 44, 62) No/poor discrimination of detecting diaphragm dysfunction (56) Poor discriminative predictive ability for reintubation and weaning failure at Day 7 (27)
Diaphragm excursion-derived	Outstanding predictive ability of diaphragmatic rapid shallow breathing index for weaning outcomes within 48 hours (24–26) No predictive ability of diaphragmatic rapid shallowing breathing index or rapid show diaphragmatic index for prediction of reintubation within 72 hours, prediction of reintubation or weaning failure at Day 7 (27) Excursion-time index had poor discriminative to excellent predictive ability of weaning outcomes (28, 29) ULDIMex index prior to spontaneous breathing trial had excellent predictive ability of weaning outcomes (28) Conflicting results for contraction velocity with no discriminative to outstanding predictive ability of weaning outcomes (31, 33–36) Time to peak inspiratory amplitude had no discriminative predictive ability of weaning outcomes (32)
Intercostal thickness	Decreased intercostal thickness associated with increased mechanical ventilation duration (HR, 2.87), and increased critical care LOS (HR, 2.58), compared to increased thickness (21)
Intercostal thickening fraction	Excellent predictive ability of weaning outcomes (19,20) Ratio of intercostal thickening fraction to diaphragm thickening had excellent predictive ability of weaning outcomes (20)

DT = diaphragm thickness, HR = hazard ratio, LOS = length of stay, MV = mechanical ventilation.

[a]See Supplementary Digital Content File 1 Statistical Analysis (http://links.lww.com/CCM/H250) for further details on cutoffs used. Data included in table if reported area under the curve, with other studies reported narratively in Supplementary File 1 (http://links.lww.com/CCM/H250) (i.e., studies that reported sensitivity, specificity, positive predictive value, and negative predictive value).