Diaphragmatic ultrasonography for predicting ventilator weaning
A meta-analysis

Caifeng Li, MSa, Xin Li, MD, Hongqiu Han, MS, Haifong Cui, MSa, Guolin Wang, MSa,* Zhiqiang Wang, MSa,*

Abstract
Background: Weaning failure is common in mechanically ventilated patients. Whether ultrasound can predict weaning outcome remains controversial. This meta-analysis was performed to assess the accuracy of diaphragmatic ultrasonography for predicting reintubation within 48 hours of extubation.

Methods: Literature search was performed in PubMed, Embase, and Cochrane Library to identify all the relevant papers, published in English up to July 16, 2017. Eligible studies were included if data were in adequate details to rebuild 2×2 contingency tables. Methodological quality of the included studies was evaluated using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) in Review Manager 5.3. The sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (DOR), and summary receiver operating characteristic (SROC) curve were pooled using the fixed or random effects model, meanwhile, the heterogeneity was evaluated using Cochran Q test and I² statistics in Meta-DiSc 1.4. Publication bias was assessed using Deeks funnel plot in Stata 12.0.

Results: Thirteen studies with 742 subjects were included in this meta-analysis. The pooled sensitivities for diaphragm excursion (DE) and diaphragm thickness fraction (DTF) were 0.786 and 0.893, and the pooled specificities were 0.711 and 0.796, respectively. The area under curve (AUC) for DE and DTF were 0.8590 and 0.8381. The DORs for DE and DTF were 10.623 and 32.521. No publication bias was observed among these studies.

Conclusions: Diaphragmatic ultrasonography is a promising tool for predicting reintubation within 48 hours of extubation. However, due to heterogeneities among the included studies, large-scale studies are warranted to confirm our findings.

Abbreviations: AUC = area under curve, CI = confidence interval, DE = diaphragm excursion, DOR = diagnostic odds ratio, DTF = diaphragm thickness fraction, NLR = negative likelihood ratio, Pmax = maximum inspiratory pressure, PLR = positive likelihood ratio, QUADAS = Quality Assessment of Diagnostic Accuracy Studies, RSBI = rapid shallow breathing index, SBT = spontaneous breathing test, SROC = summary receiver operating characteristic, VE = minute ventilation, VT = tidal volume.

Keywords: diagnosis, diagnostic accuracy, diaphragmatic displacement, diaphragmatic thickening, mechanical ventilator weaning, ultrasonography, ventilator weaning

1. Introduction

After the recovery of underlying conditions, most patients can be weaned from the mechanical ventilation successfully, given that they have sufficient gas exchange, good neurological and muscular status, and hemodynamic stability. However, weaning failure, defined as the requirement of invasive or noninvasive mechanical ventilation within 48 hours after extubation, is extremely common. About 20% of mechanically ventilated patients confront weaning failure and require reintubation. Weaning failure is associated with prolonged mechanical ventilation and ICU stay, as well as increased hospital mortality ranging between 40% and 50%. Delay in weaning from ventilator increases the inherent risks of mechanical ventilation, such as barotrauma, ventilator-associated pneumonia, and ventilator-induced diaphragmatic atrophy. Thus, patients should be weaned from mechanical ventilation once they are able to cope with the respiratory load to avoid diaphragmatic dysfunction and infection, as well as to decrease the length of ICU and hospital stay.

Current guidelines for weaning recommend spontaneous breathing trial (SBT) as a tool to predict weaning outcome. However, 13% to 26% of patients who are extubated following a successful SBT need to be reintubated within 48 hours. Many other weaning parameters have been used to predict weaning failure, including rapid shallow breathing index (RSBI), minute ventilation (VE), and maximum inspiratory pressure (Pmax), but none has shown great prognostic accuracy.

The diaphragm is the principal respiratory muscle. With an excursion of 1 to 2 cm, the diaphragm provides nearly 75% of the...
Diaphragm thickness measured at end inspiration (Tinsp) and end expiration (Texp) were used to calculate the difference in thickness from inspiration and expiration divided by the thickness on expiration ([Tinsp – Texp]/Texp].[22,23] DTF and DE during respiration reflect diaphragm function and are similar to “thickening fractions and motion amplitude” of the heart. Diaphragm thickness measured at end inspiration correlates with maximal inspiratory pressure.[24] It provides both morphological and functional information in real time. Furthermore, it allows repeated measurements over time. Several ultrasound techniques, such as B-mode and M-mode, have been used to assess diaphragm sonographic predictors: diaphragm excursion (DE), which measures the distance that the diaphragm is able to move during the respiratory cycle, and diaphragm thickness fraction (DTF), which is the ratio between the thickness on inspiration and expiration divided by thickness on expiration. However, the results are still controversial. For instance, some studies reported that DE and DTF had high specificity and accuracy in predicting weaning outcome,[25] while others had opposite results.[26,27] To gain a more reliable conclusion, we performed this meta-analysis to summarize the overall performance of DE and DTF on predicting reintubation within 48 hours of extubation.

2. Methods

We carried out this systematic review following a predefined protocol, which was published in the International Prospective Register for Systematic Reviews with the registration number CRD42017072593. As it is a meta-analysis of the previous works of literature, approval of the ethics committee was not required.

2.1. Literature search

A comprehensive and systematic literature search was conducted by 2 independent researchers (CL and XL) in PubMed, Embase, and Cochrane Library up to July 16, 2017, using the following terms: “Ventilator Weaning,” “Respirator Weaning,” “Mechanical Ventilator Weaning,” “Ultrasonography,” “Diaphragm,” “Diaphragmatic displacement,” “Diaphragmatic thickness,” “Sensitivity and Specificity,” “Diagnosis,” and “Diagnostic accuracy.” In addition, the reference lists of the included studies were hand-screened to find potentially related papers.

2.2. Study selection

Studies that met the following criteria were included: participants aged ≥18 years; focused on ability or accuracy of diaphragmatic ultrasonography on predicting weaning outcome; published in English; provided sufficient data to calculate true-positive, false-positive, false-negative and true-negative numbers; defined weaning failure as the requirement of mechanical ventilation within 48 hours after extubation; protocols[28,29] and conference proceedings published as abstracts[30,31] were excluded.

2.3. Data extraction and quality assessment

Two researchers (CL and XL) independently carried out a primary screening of studies based on the titles and abstracts, then they conducted an examination of full texts in accordance with the eligibility criteria. Data were abstracted from included studies, including first author, year of publication, study period, location, setting, study design, target patient, number of patients, age, gender, patient position, the delay between diaphragmatic ultrasonography and weaning, cutoff value, right or left hemidiaphragm, machine and probe, probe position, number and skills of operator. Study quality was assessed by QUADAS-2, which consisted of 4 domains: patient selection, index test, reference standard, flow and timing. A third author (HC) was invited to resolve any discrepancies between the 2 researchers.

2.4. Statistical analysis

Review Manager 5.3 (Cochrane Collaboration, Oxford, England) was used for quality assessment. Meta-DiSc 1.4 (Romany Cajal Hospital, Madrid, Spain) and Stata 12.0 (Stata Corporation, College Station, TX) were used for analysis. Sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), and diagnostic odds ratio (DOR) were pooled independently. The threshold effect was tested using Spearman correlation analysis. Heterogeneity was judged by Cochran Q test and I² statistics. If significant heterogeneity existed (P < .05 or I² > 50%), the random effect model was used to calculate the pooled effect size; otherwise, the fixed effect model was applied.[34] Source of heterogeneities was detected by meta-regression analysis. Sensitivity analysis was also performed by removing the trials one by one to find the source of heterogeneities and evaluate the reliability of the results. Probable publication bias was estimated by Deeks funnel plot.

3. Results

3.1. Literature search

The process of literature search and selection is shown in Figure 1. Forty-two papers were obtained according to the search strategy, then 5 duplicates were removed. After screening for the titles and abstracts, 23 papers were excluded due to the irrelevant contents. Among the remaining articles, 8 were excluded because of reviews (n = 5), abstracts (n = 2), and protocol (n = 1). Finally, 6 studies[1,2,3,22,25,31,36] and 7 hand-screened studies,[24,26,27,37–40] which met the selected criteria, were included in our meta-analysis.

3.2. Characteristics and qualities of included studies

Thirteen prospective observational trials, with 742 adult participants, were included in the final meta-analysis and...
systematic review. These studies, published between 2011 and 2017, were from different countries, such as Egypt, France, Greece, Italy, Korea, and the USA. Nine studies reported data for DE (n = 469), while 8 studies for DTF (n = 485). Most of the studies were conducted in ICU, while 3 studies took place in the respiratory ICU. 1 study was conducted in a high dependency unit. Usually ultrasounds were performed on patients during the SBT, while 3 studies took place in the supine position in 4 studies, but during the forced breath. Ultrasounds and measurements were evaluated according to QUADAS-2. The results of quality assessment are shown in Figure 2.

3.3. Predicting value of DE and DTF on weaning outcome

The threshold effect was estimated using the Spearman correlation coefficient. No threshold effect was detected in DE (Spearman correlation coefficient: −0.234, P = .544) and DTF (Spearman correlation coefficient: 0.144, P = .734), therefore, a further combined analysis could be performed. The sensitivities of DE were homogeneous (P = .075, I² = 44.0%), thus, the fixed effect model was used and the pooled specificity of DE was 0.786 (95% confidence interval (CI): 0.734–0.832). Due to significant heterogeneity in sensitivities of DTF (P = .009, I² = 62.6%), the random effect model was used and the pooled sensitivity of DTF was 0.893 (95% CI: 0.854–0.924). Similarly, because of significant heterogeneity in specificities of DE (P = .000, I² = 76.3%), the random effect model was used and the pooled specificity of DE was 0.711 (95% CI: 0.637–0.777); however, the specificities of DTF were homogeneous (P = .075, I² = 45.6%), thus, the fixed effect model was used and the pooled specificity of DTF was 0.796 (95% CI: 0.723–0.857). Significant heterogeneities were detected in NLRs of DE (P = .015, I² = 57.9%) and DTF (P = .029, I² = 55.2%), so the random effect model was performed, the pooled NLRs of DE and DTF were 0.287 (95% CI: 0.190–0.443) and 0.157 (95% CI: 0.094–0.259). Owing to significant heterogeneity in PLRs of DE (P = .000, I² = 84.6%), the random effect model was used, and the pooled PLR of DE was 2.854 (95% CI: 1.474–5.527); conversely, PLRs of DTF were not heterogeneous (P = .393, I² = 4.8%), the fixed effect model was applied, and the pooled PLR of DTF was 4.257 (95% CI: 3.113–5.822). Moreover, owing to heterogeneity (P = .003, I² = 65.2%) in DORs of DE, the random effect model was used, and the pooled DOR of DE was 10.623 (95% CI: 4.169–27.068). On the contrary, the DORs of DTF exhibited consistency (P = .127, I² = 37.9%), therefore, the fixed effect model was used and the combined DOR of DTF was 32.521 (95% CI: 18.618–56.807). The diagnostic performances of DE and DTF on weaning outcome are presented in Table 2 and Figure 3. The summary receiver operating characteristic (SROC) curve was applied to evaluate the comprehensive diagnostic performance. Figure 4 shows the SROC curves, with area under curve (AUC) of 0.8590 for DE and 0.8381 for DTF, indicating the high level of overall accuracy. Fagan nomogram, presented in Figure 5, was also used to analyze the diagnostic value of DE and DTF on weaning outcome.

In our meta-analysis, significant heterogeneities were observed. Meta-regression analysis was carried out to find the source of heterogeneities, however, due to the small number of included studies, no significant result was found in target patient (the difficult weaning patient or not), sample size (N ≥ 50 or not), index test (maxDE/maxDTF during the forced breath or DE/DTF during the resting breath) and timing of index test (before/during SBT or after extubation). The results of meta-regression analysis are presented in Table 3. Sensitivity analysis, exhibited in Table 4, was also performed to explore the source of heterogeneities. After removing the trials one by one, the results remained consistent; however, the heterogeneities between studies were not significantly decreased, thus, additional large-scale trials are needed to confirm the findings of this study.

3.4. Publication bias

Publication bias was evaluated by Deeks funnel plot. Shown in Figure 6, the slope coefficient was −5.345298 and −32.12883, the associated P-value was P = .782 and P = .054, respectively, indicating no evidence of publication bias.

4. Discussion

Diaphragmatic ultrasonography has gained more and more attention from clinicians all over the world. As it is a noninvasive, painless and convenient bedside method, it might provide more accurate and reliable information regarding the prediction of weaning outcome. However, the findings of related studies are inconsistent and lack statistical power, and the clinical significances of DE and DTF still remain controversial. Lerrolo et al demonstrated that DE correlated well with trans-diaphragmatic pressure and suggested that DE could reflect diaphragmatic dysfunction. On the contrary, Umbrello et al believed that DTF rather than DE was a reliable index of respiratory effort and diaphragmatic contractile function. In our meta-analysis, the pooled sensitivities for DE and DTF were 0.786 and 0.893, and the pooled specificities were 0.711
| Study | Period | Location | Setting | Design | Patient | N | Age | Gender, m/f | Patient position | Delay between diaphragmatic excursion and weaning | Quotient | Right or left hemidiaphragm | Machine | Probe | Probe position | Number of and skills of operator |
|-------|--------|----------|---------|--------|---------|---|-----|-------------|----------------|--------------------------------|---------|--------------------------|---------|-------|----------------|--------------------------------|
| Ali and Mohammeed[34] | January to June 2015 | Egypt | ICU | Prospective | Patients who were mechanically ventilated | 60 | 54 | 46/15 | Supine | Within 24h before extubation | DE = 1.5 cm, DTF = 30% | Right | Echoplace 128 Ki | 4 and 10 MHz probe | Diaphragmatic dome | N/A |
| Barou et al[26] | January to June 2015 | Egypt | General and respiratory ICU | Prospective | Patients who were planned for weaning | 30 | 59.17 | 15/15 | Semi- recumbent | During the SBT or the PS trial | DE = 1cm, DTF = 30% | Right | Philips Healthcare Andover, MA | 2–4 MHz phased array probe | Diaphragmatic dome | Physicians |
| Blumenfeld et al[17] | July 2014 to August 2015 | Philadelphia, USA | ICU | Prospective | Patients mechanically ventilated for greater than 24h | 52 | 62 | 28/25 | Semi- recumbent | Within 48h before extubation | DTF = 30% | Right | SonoSite M-Turbo, Fujifilm, Tokyo, Japan | 7.5–10 MHz transducer | N/A | Trained clinicians |
| Carre et al[22] | December 2014 to April 2015 | France | ICU | Prospective | Patients who met the criteria for the SBT after at least 48h of mechanical ventilation | 67 | 66 | 37/30 | Semi- recumbent | Before the start of SBT | DTF = 2.7 cm | Right | Vivid S5TM ultrasound machine (GE Healthcare, Waukesha, WI) | 48 Hz cardiac probe | Diaphragmatic dome | Two experts |
| Dineu et al[23] | N/A | USA | Medical ICU | Prospective | Patients who were ready for SBT | 63 | 66 | 31/32 | Semi- recumbent | Within the first 5min of the SBT or the PS trial | DTF = 30% | Right | LOGIQ Book GE Healthcare Waukesha, WI | 7–10 MHz linear ultrasound probe | Zone of apposition of the diaphragm | Well-trained operator |
| Otage and Harcao[5] | April 2015 to November 2015 | Egypt | Respiratory ICU | Prospective | Patients with underlying pulmonary disease causing aSBI who had successfully passed the SBI | 54 | 55 | 65 | F, 62.5 | Semi- recumbent | Obtained at 30 min of a SBT | DTF = 34.2% | Right | Samsung Medison SonoAce R3 | 3.7 and 5.5 MHz | N/A | Two experts |
| Raguel et al[29] | December 2010 to December 2011 | Turin, Italy | High dependency unit | Prospective | COPD patients who failed one or more attempts of weaning not the criteria met for a SBT | 112 | 62,61 | 97/15 | Supine | During the SBT | Right DTF > 30% | Both | Mindray DP-10 | 10 MHz linear ultrasound probe | Zone of apposition of the diaphragm | Well-trained researchers |
| Sebati et al[35] | N/A | Egypt | ICU | Prospective | Patients with difficult and/or prolonged weaning not the criteria met for a SBT | 46 | 64 | 64 | 34/12 | Semi- recumbent | During the SBT | Right DTF > 30% | Both | Esaote MyLab 40 ultrasound system | 10 MHz linear ultrasound probe | N/A | N/A |
| Rehavi et al[1] | January to December 2014 | Athens | Adult ICU | Prospective | Patients who were mechanically ventilated to perform an SBT | 27 | 65 | 13/14 | Semi- recumbent | During the SBT | Right and left | N/A | Esaote ultrasound machine (Biotech Lab 5000, Genoa, Italy) | 3.5 MHz ultrasound probe | N/A | N/A |
| Hik et al[28] | October 2009 to March 2009 | Seoul, Korea | Medical ICU | Prospective | Patients who required mechanical ventilation for 48h, not the criteria met for a SBT | 82 | 66 | 55/32 | Supine | At the start of SBT | Right and left | Esaote ultrasound machine (Biotech Lab 5000, Genoa, Italy) | 3.5 MHz ultrasound probe | Diaphragmatic dome | One well-trained expert |
| Omeren and Harcao[2] | August 2015 to August 2016 | Cairo, Egypt | ICU | Prospective | Patients in different ICU with various reasons for ventilation not the traditional weaning criteria | 68 | 56 | N/A | Semi- recumbent | After extubation | DTF = 10mm | Right | Esaote M-7000 | 3.5 MHz ultrasound probe | N/A | N/A |
| Solari et al[31] | November 2012 to October 2014 | Cairo, Egypt | Respiratory ICU | Prospective | COPD patients who were prepared for weaning | 30 | 59 | N/A | Supine | During the SBT | DTF = 1.1 cm | Right | Mindray DP 1100 ultrasound machine | 3.5 GHz convex probe | N/A | N/A |
| Spadaro et al[27] | July 2014 to March 2015 | Ferrara, Italy | ICU | Prospective | Patients requiring mechanical ventilation for more than 48h who were ready to perform an SBT | 51 | 65 | 35/30 | Semi- recumbent | During the SBT after 30min from the beginning of the SBT, before reconnecting to the ventilator in the case of SBT failure | Right and left | SonoSite M-Turbo, SonoSite Inc., Bothell, WA | 3.5–5 MHz convex ultrasound probe | Diaphragmatic dome | One well-trained intensivist |

**Notes:** DE = diaphragmatic excursion, DTF = diaphragmatic thickness fraction, FG = failed group, ICU = intensive care unit, m/f = male/female, N = number, N/A = not available, PS = pressure support, SBT = spontaneous breathing test, SG = successful group.
and 0.796, respectively. The SROC curve and the AUC were used to assess the overall diagnostic performance. The AUC for DE and DTF were 0.8590 and 0.8381, respectively. Our data indicate a satisfactory diagnostic accuracy in predicting extubation outcome. The DOR was also analyzed to evaluate the diagnostic accuracy. The DOR is the ratio between PLR and NLR, the larger the DOR is, the greater the diagnostic accuracy is. In this meta-analysis, the DORs for DE and DTF were 10.623 and 32.521, illustrating a high diagnostic accuracy.

Our data suggest a lower sensitivity and specificity for DE as compared to DTF in predicting weaning outcome. DTF reflects the active contraction of the diaphragm during the mechanical ventilation,[44] whereas DE is primarily related to the inspired volume,[45] regardless of whether it depends on the muscle effort or the ventilatory support. Therefore, DTF should be measured to estimate the diaphragm function in patients undergoing mechanical ventilation, while DE is meaningful in the absence of the ventilatory support. Moreover, diaphragm dysfunction is

| Parameter | DE (95% CI) | DTF (95% CI) |
|-----------|-------------|--------------|
| SEN       | 0.786 (0.734–0.832)* | 0.893 (0.854–0.924)* |
| SPE       | 0.711 (0.637–0.777)* | 0.796 (0.723–0.857)* |
| PLR       | 2.854 (1.474–5.527)* | 4.257 (3.113–5.822)* |
| NLR       | 0.287 (0.190–0.435)* | 0.157 (0.094–0.259)* |
| DOR       | 10.623 (4.169–27.066)* | 32.521 (16.618–66.807)* |
| AUC       | 0.8590 | 0.9064 |

AUC = area under the curve, CI = confidence interval, DE = diaphragm excursion, DOR = diagnostic odds ratio, DTF = diaphragm thickness fraction, NLR = negative likelihood ratio, PLR = positive likelihood ratio, SEN = sensitivity, SPE = specificity.  
* Fixed effect model was used.  
† Random effect model was used.
the main cause of weaning failure, but not the only one, it is essential to contextualize the information derived from diaphragmatic ultrasound with clinical and laboratory data, as well as information obtained from other imaging technologies such as X-ray, CT scans, and echocardiography.

RSBI and VE, widely used in clinical practices, are the weaning parameters that measure the volume generated by all the respiratory muscles without especially assessing the contribution of the diaphragm.\textsuperscript{[23]} Under the circumstance of diaphragm dysfunction, the diaphragm motion is inhibited and the accessory muscles take on a greater role in the production of tidal volume (VT).\textsuperscript{[46,47]} Therefore, diaphragm dysfunction can be disguised by the compensatory action of other respiratory muscles during SBT.\textsuperscript{[30]} However, the accessory muscles are weaker and more fatigable than the diaphragm, so the compensatory effect cannot be sustained for a long time.\textsuperscript{[48,49]} Thus, weaning failure may

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**Figure 3.** The diagnostic performance of DE and DTF on weaning outcome: (A) sensitivity, (B) specificity, (C) PLR, (D) NLR, (E) DOR. CI = confidence interval, DE = diaphragm excursion, DOR = diagnostic odds ratio, DTF = diaphragm thickness fraction, NLR = negative likelihood ratio, PLR = positive likelihood ratio.
occur despite an initially acceptable RSBI and VT. Spadaro et al. reported many patients failed the weaning attempt, though RSBI was much lower than the threshold predicting weaning failure described in the paper by Yang and Tobin. Poor endurance is an important cause of failed weaning. DE and DTF reflect the ability of the diaphragm to generate inspiratory volume, hence, the true diaphragmatic contribution to VT. There are other traditional ways to evaluate diaphragm dysfunction, such as fluoroscopy, electrical or magnetic phrenic nerve stimulation, and trans-diaphragmatic pressure measurement. However, all of these methods possess serious shortcomings, for instance, ionizing radiation, high cost, difficult
execution, invasiveness, and inconvenience. What is more, transportation of critical patients to the radiology department is difficult and dangerous.

Similar systemic reviews and meta-analyses have been published recently, however, the inclusion criteria, reference standard and major clinical endpoints of these meta-analyses are different from our study. Our study focuses on diaphragmatic ultrasound for predicting weaning failure within 48 hours after extubation in adults, which makes it much more specific and reliable. In addition, the latest trials are included in our paper, so the results are more powerful.

| Table 3 | Possible sources of heterogeneity (meta-regression analysis). |
|---------|---------------------------------------------------------------|
| **Index test** | **Covariate** | **Coefficient** | **P** | **RDOR** |
| DE | Target patient (the difficult weaning patient or not) | 1.041 | 0.3977 | 2.83 |
|    | Sample size (N ≥ 50 or not) | 0.223 | 0.8502 | 0.80 |
|    | Index test (maxDE/maxDTF in the forced breath or DE/DTF in the resting breath) | 1.098 | 0.3710 | 0.33 |
|    | Before/during SBT or after extubation | 1.216 | 0.5949 | 3.37 |
| DTF | Target patient (the difficult weaning patient or not) | 1.060 | 0.2005 | 2.89 |
|    | Sample size (N ≥ 50 or not) | 1.153 | 0.3927 | 3.17 |
|    | Index test (maxDE/maxDTF in the forced breath or DE/DTF in the resting breath) | 0.419 | 0.7846 | 1.52 |
|    | Before/during SBT or after extubation | 3.819 | 0.9883 | 45.56 |

**Table 4**

The diagnostic performance of DE and DTF after omitting each trial (sensitivity analysis).

| Index tests | Study excluded | SEN (95% CI)/F | SPE (95% CI)/F | DOR (95% CI)/F | PLR/NLR |
|-------------|----------------|----------------|----------------|----------------|--------|
| DE | Ali and Mohamad[41] | 0.775 (0.719–0.824)/41.0% | 0.687 (0.605–0.761)/77.2% | 8.58 (3.320–22.17)/61.3% | 2.541/0.311 |
|    | Baess et al[28] | 0.794 (0.740–0.841)/46.8% | 0.735 (0.661–0.809)/70.1% | 13.673 (5.826–32.088)/65.9% | 3.211/0.269 |
|    | Carrie et al[29] | 0.800 (0.744–0.849)/44.4% | 0.728 (0.650–0.796)/76.2% | 12.966 (4.500–37.360)/64.7% | 3.270/0.261 |
|    | Farghaly and Hasan[39] | 0.772 (0.715–0.829)/40.0% | 0.711 (0.634–0.780)/70.3% | 10.031 (3.500–28.750)/68.1% | 2.876/0.305 |
|    | Flevari et al[1] | 0.781 (0.736–0.827)/44.4% | 0.722 (0.650–0.798)/78.2% | 12.966 (4.500–37.360)/64.7% | 3.270/0.261 |
|    | Kim et al[23] | 0.790 (0.736–0.830)/50.2% | 0.765 (0.678–0.830)/75.3% | 10.411 (3.717–29.157)/66.4% | 3.516/0.264 |
|    | Osman and Hashim[27] | 0.775 (0.717–0.826)/46.9% | 0.677 (0.601–0.750)/70.1% | 8.616 (3.320–22.17)/61.3% | 2.541/0.311 |
| DTF | Ali and Mohamad[41] | 0.886 (0.845–0.929)/63.9% | 0.786 (0.704–0.854)/51.4% | 28.403 (15.931–50.640)/33.7% | 4.036/0.170 |
|    | Baess et al[28] | 0.908 (0.872–0.946)/75.5% | 0.802 (0.726–0.862)/52.3% | 39.908 (22.127–71.367)/25.9% | 4.402/0.120 |
|    | Blumhof et al[40] | 0.897 (0.857–0.939)/69.9% | 0.802 (0.721–0.867)/52.9% | 36.376 (19.621–67.437)/44.4% | 4.356/0.147 |
|    | Dinino et al[35] | 0.865 (0.824–0.909)/67.7% | 0.804 (0.726–0.862)/51.1% | 35.648 (19.278–65.919)/44.1% | 4.665/0.150 |
|    | Farghaly and Hasan[39] | 0.892 (0.850–0.925)/67.9% | 0.812 (0.736–0.873)/45.0% | 35.898 (19.489–66.123)/43.2% | 4.632/0.154 |
|    | Fayed et al[38] | 0.891 (0.850–0.925)/67.9% | 0.812 (0.736–0.873)/45.0% | 35.898 (19.489–66.123)/43.2% | 4.632/0.154 |
|    | Ferrari et al[22] | 0.899 (0.859–0.931)/65.7% | 0.785 (0.706–0.851)/49.5% | 27.122 (15.588–49.189)/32.7% | 4.079/0.147 |
|    | Osman and Hashim[27] | 0.895 (0.855–0.935)/67.5% | 0.769 (0.688–0.857)/0.0% | 27.672 (15.588–49.189)/32.7% | 3.745/0.158 |

**Figure 6.** Deeks funnel plots for publication bias.
In this meta-analysis, significant heterogeneities were observed. However, sensitivity analysis showed the result of this meta-analysis was robust and reliable. Although meta-regression analysis was performed, we could not explore the source of potential heterogeneities due to the limited number of included studies. It is generally known that the measuring result could deviate as the position of probe changes. Moreover, DE may differ relying on the posture, demonstrating higher values when patients are supine than seated. In addition, DTF may vary as STB progresses owing to diaphragmatic fatigue, that is to say, an early test would show lower accuracy to predict weaning failure. In our meta-analysis, with a coefficient of 3.819 and RDOR of 45.56, the timing of measurement was very nearly significant. Therefore, the exact position of probe, patient posture and the timing of ultrasound should be considered as factors that need to be solved in future studies. Moreover, we might hold that the accuracy of diaphragmatic ultrasound on predicting weaning outcome depends on the number and experience of the operators. Despite being an observer-reliant technique, the available evidence shows that both DTF and DE are replicable measures.

In addition, we were also concerned about the effect of publication bias because positive results were more likely to be published. However, Deeks funnel plot indicates no publication bias in our meta-analysis.

There are some limitations in our meta-analysis. First, only articles published in English were included. Second, the influence of gender was not considered, since the excursion and thickness fraction were larger in men than in women. Third, the number of included studies was small and may not have fully assessed the diagnostic accuracy and could not find the source of heterogeneities. Thus, further large-scale studies are needed to investigate the diagnostic accuracy of DE and DTF.

5. Conclusion

Despite the limitations mentioned above, the results of our meta-analysis indicated that diaphragmatic ultrasonography may be a reliable, noninvasive and convenient way to predict re-intubation within 48 hours of extubation. However, due to significant heterogeneities among the included studies, clinicians should be aware of the utilities and limitations of this tool. Additional high-quality, large-scale studies are required.

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Author contributions

Conceived and designed the experiments: CL. Performed the experiments: CL, XL, HC. Analyzed the data: CL. Contributed reagents/materials/analysis tools: CL, XL, HC, HH, GW, ZW. Wrote the manuscript: CL.

Conceptualization: Caifeng Li, Guolin Wang, Zhiqiang Wang. Data curation: Caifeng Li. Formal analysis: Caifeng Li, Xin Li. Investigation: Caifeng Li, Xin Li, Hongqiu Han, Hailong Cui. Methodology: Caifeng Li, Hailong Cui, Guolin Wang. Project administration: Caifeng Li.

Resources: Caifeng Li, Hongqiu Han. Software: Caifeng Li, Xin Li.

Supervision: Guolin Wang, Zhiqiang Wang. Validation: Caifeng Li. Visualization: Caifeng Li.

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