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SYSTEMATIC REVIEW

Signa Vitae

Predictive value of diaphragmatic rapid shallow breathing index in mechanical ventilation weaning: a systematic review and meta-analysis

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Abstract

Background: Mechanical ventilation weaning is a multifactorial process. D-RSBI cannot only reflect the respiratory function but also the diaphragmatic function with the bedside ultrasound technique.

Objective: This review aimed to assess the predictive value of diaphragmatic rapid shallow breathing index (D-RSBI) of weaning outcome.

Method: Databases were systematically reviewed including PubMed, Cochrane Library, Embase, CNKI and WanFang Data. Sensitivity and specificity were pooled with random effects models.

Results: Nine studies met the inclusion criteria and 568 patients were involved. D-RSBI had a pooled sensitivity of 0.84 and a pooled specificity of 0.87 which predicted weaning success. D-RSBI in the success group was significantly lower than the weaning failure group.

Conclusion: D-RSBI is a sensitive and specific predictor for weaning outcomes in spite of the limitations and heterogeneity among the studies. Further studies focusing on particular disease are needed as well.

Keywords

Diaphragmatic rapid shallow breathing index; Mechanical ventilation weaning; Predictive parameters; Ultrasonography; Diaphragmatic dysfunction; Outcomes

1. Introduction

Mechanical ventilation (MV) is a common approach required by patients with respiratory failure. Reducing the duration of MV is of paramount importance for critical care physicians. Premature or delayed extubation is closely linked to increased morbidity, mortality and longer intensive care unit stay [1–3]. However, discovery of reliable predictors to determine the initiation of weaning process still remains a great challenge.

Considering weaning failure from MV is attributable to several factors, diaphragmatic dysfunction plays a major role [4, 5]. Diaphragmatic displacement (DD) reflects the ability of diaphragm in generating force and enhancing tidal volume during the inspiratory phase and can be evaluated with bedside ultrasonography [6]. Ultrasonography is considered as a non-invasive and bedside method and commonly applied in intensive care unit (ICU) to assess diaphragmatic function [7]. The amplitude, force and velocity of contraction, and changes in diaphragmatic thickness have been available with an ultrasonic technique which is sensitive and efficient [8–10].

Rapid shallow breathing index (RSBI) defined as ratio of respiratory rate to tidal volume (RR/VT) is a well-known index for predicting weaning outcome [11–13]. DD is an index reflected diaphragmatic function as well as a predictor of failure to wean according the recent study [14]. Nevertheless, RSBI and DD still have variable sensitivity and specificity. Recent study came up with a novel index for assessing patients with mechanical ventilation, the diaphragmatic RSBI (D-RSBI), by substituting VT with DD in the RSBI (i.e. D-RSBI = RR/DD) [15]. Diaphragm dysfunction is a crucial cause of failure to wean in patients, especially the patients with COPD [16]. D-RSBI can demonstrate the diaphragmatic contribution during spontaneous breathing trial (SBT) as well. Such index avoids ignoring underlying diaphragmatic dysfunction masked by the contribution of the accessory muscles in generating VT [15]. Several studies confirmed that D-RSBI was an accurate index for prediction of extubation [15, 17]. However, results remained variable among the studies.

Due to lack of large sample size researches and variable research findings, we decided to systematically review the literature to evaluate the predictive value of D-RSBI in ventilator weaning. To our knowledge, this is the first review that systematically analyzed the accuracy of D-RSBI for predicting weaning outcomes.

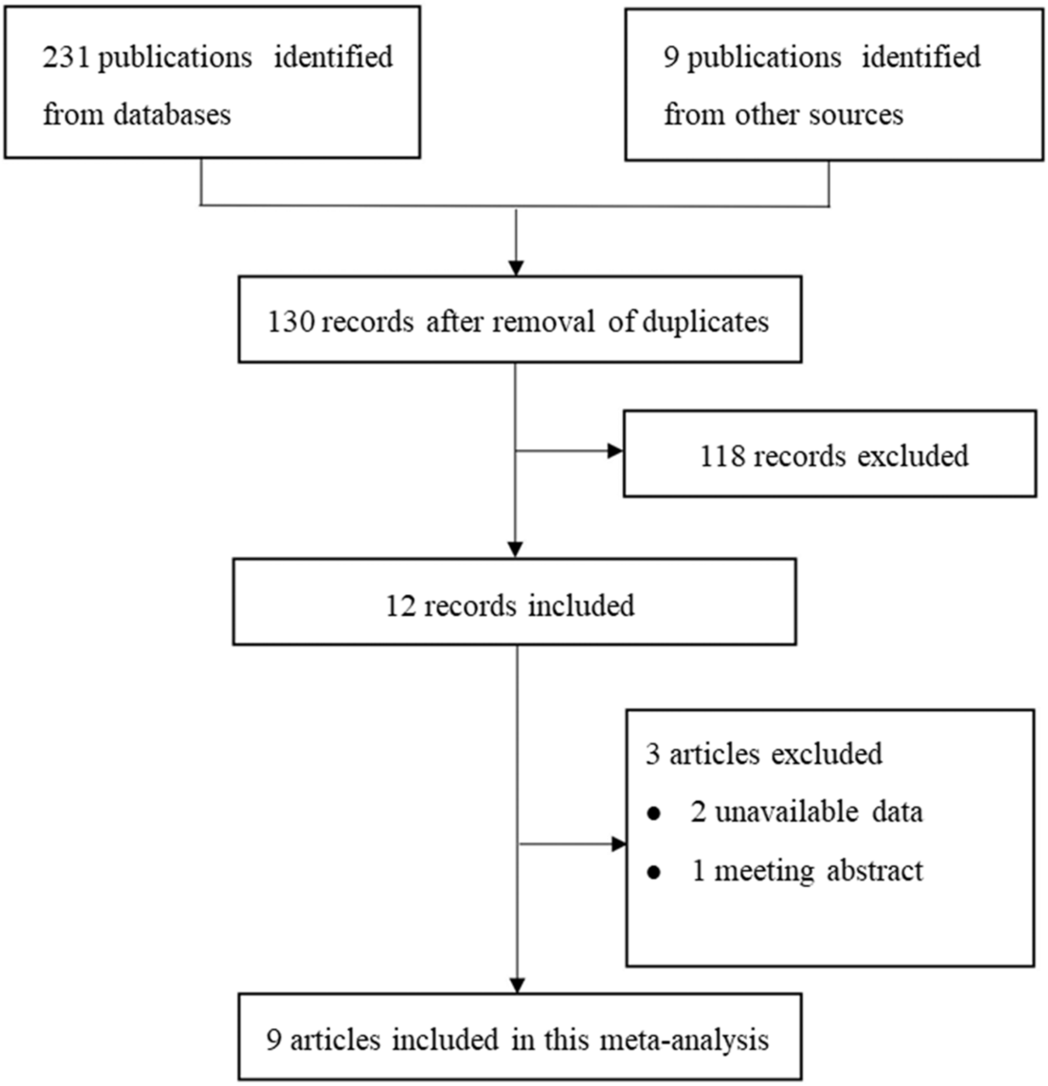

FIGURE 1. Selection of trials in this meta-analysis.

2. Methods

2.1 Search strategy

Two independent investigators searched databases, including Pubmed, Cochrane Library, Embase, CNKI and Wanfang Data (inceptions to March 2020), without regions, publication types and language restrictions. The following keywords: 'D-RSBI' and 'diaphragmatic rapid shallow breathing index' were used for searching. One reviewer (CL) scanned the titles and abstracts to rule out the irrelevant articles. Two reviewers (CL, TW) went through the full texts then. If any difference in opinion, the third reviewer (SL) made the final decision.

2.2 Inclusion and exclusion criteria

The inclusion criteria were as following: (1) Prospective or retrospective study; (2) The subjects underwent invasive MV at least 48 hours; (3) Diaphragmatic displacement was measured by ultrasound, and D-RSBI was calculated during SBT or weaning process; (4) The primary outcome was the accuracy of D-RSBI for predicting weaning success including sensitivity and specificity. SBT failure, need for non-invasive MV or reintubation or death within 48 hours after extubation were considered as weaning failure. Absence of above criteria was regarded as weaning success.

The exclusion criteria were as following: (1) Abstracts, letters, reviews, case reports and expert opinions were not included; (2) Articles without sufficient data were not included.

2.3 Data extraction

Two reviewers (CL, TW) read the texts over and extracted the data independently including the first author's name, publication year, number of subjects, category of patients, study design, SBT, cut-off value, D-RSBI, outcomes and definition of weaning failure, as well as sensitivity and specificity parameters in prediction. All the extracted information was listed in Table 1. Cases with disagreement were conducted and determined by a third reviewer (SL). If necessary, we contacted the authors for more information as well.

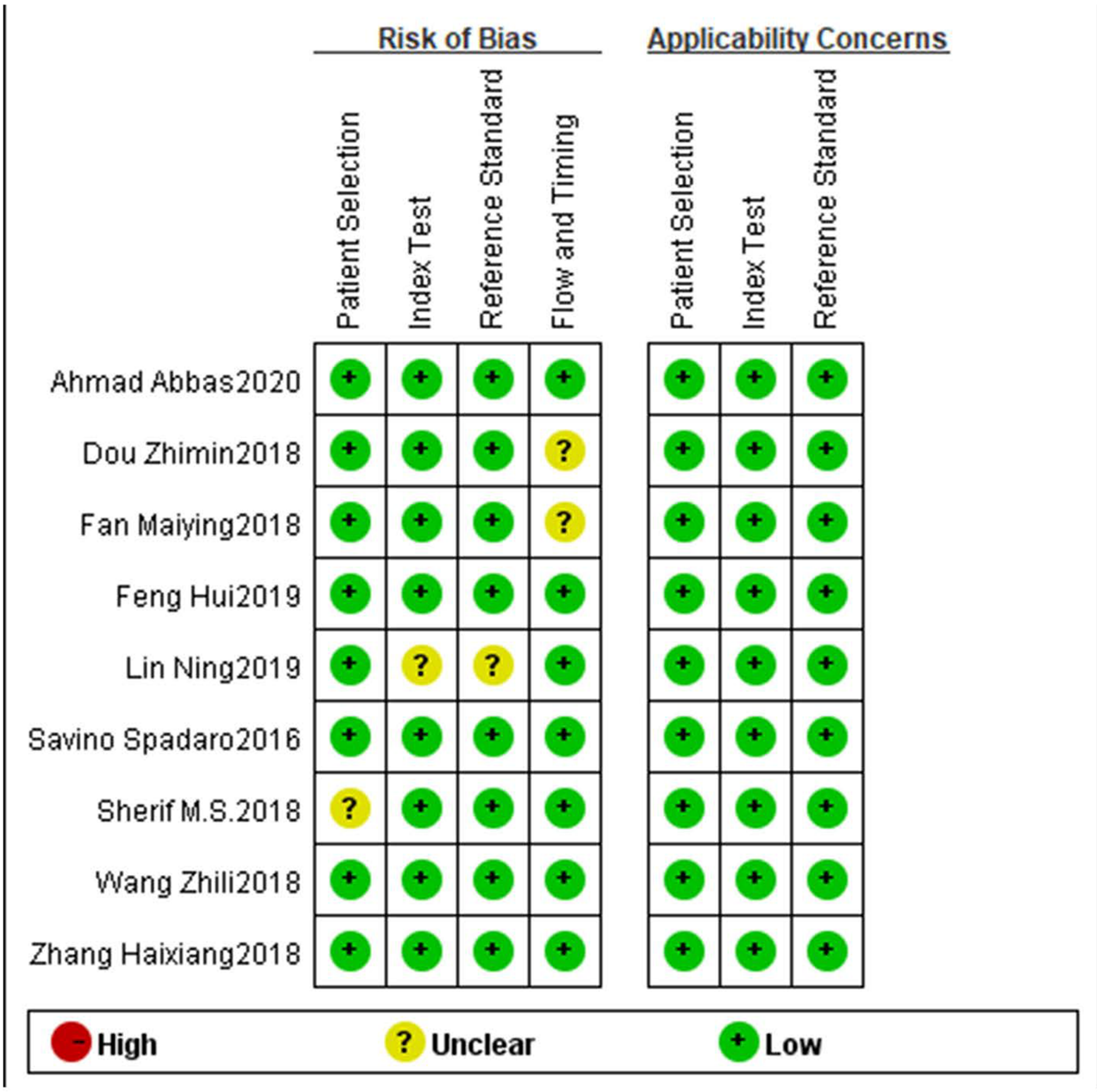

FIGURE 2. Assessment of risk bias of studies with QUADAS-2 tool and a low risk of bias was found. QUADAS-2: Quality Assessment of Diagnostic Accuracy Studies-2.

2.4 Quality assessment and publication bias

The Quality Assessment of Diagnostic Accuracy Studies-2 (QUADA-2) and the funnel plot graph were applied for assessing and demonstrating the risk of bias and publication bias respectively.

2.5 Statistical analysis

To apply a meta-analysis, Review Manager Software (RevMan V.5.3) was utilized for statistical analysis. The extracted data were also applied to plot summary receiver operating characteristic (SROC) curve to establish the true positivity and false positivity of individual study with RevMan V.5.3. The closer the curve is to the upper left-hand corner, with the exact area under the curve (AUC) of the SROC curve plot, the better the overall accuracy of the test. Mantel-Haenszel random-and-fixed-effect model was performed to obtain the pooled sensitivity and specificity with Stata software (V.12.0). Heterogeneity was significant when $P < 0.05$ and/or $I^2 > 50\%$, and the random-effect model was used, if $P > 0.05$ and/or $I^2 < 50\%$ the fixed-effect model would be applied. To explain the potential heterogeneity, subgroup analyses were performed.

3. Results

3.1 Study inclusion

We identified 231 publications from databases and 9 from other sources which could be involved. A total of 130 publications remained after removal of duplicates. 118 records were ruled out after reviewing abstracts. After reviewing of full text and final adjudication, 9 articles were involved in full meta-analysis (Fig. 1). The main characteristics of each study were summarized and listed (Table 1). All the studies were assessed with QUADAS-2 tool and a low risk of bias was found (Fig. 2). Funnel plot indicated symmetry relatively and did not suggest publication bias with visual inspection. Some plots set outside the 95% confidence interval indicated heterogeneity remained between the studies involved (Fig. 3).

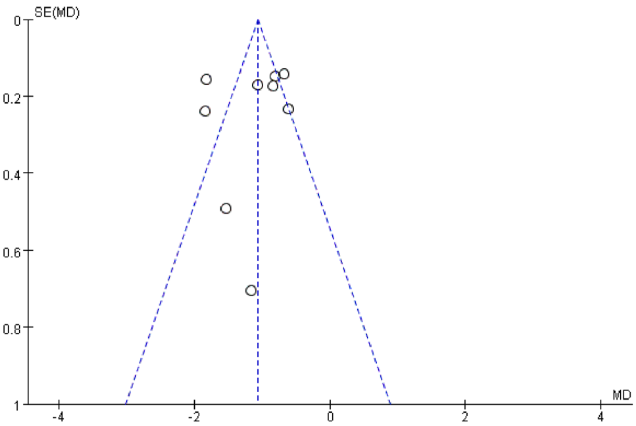

FIGURE 3. Funnel plot showed comparison of D-RSBI between different weaning outcomes by mean difference. Visual analysis of the funnel plot was not suggestive of publication bias.

3.2 Meta-analysis of D-RSBI to predict weaning outcome

Overall, among 568 patients the D-RSBI had a pooled sensitivity of 0.84 (95% CI 0.76 to 0.90) and a pooled specificity of 0.87 (95% CI 0.79 to 0.92) in predicting extubation success (Fig. 4). D-RSBI in weaning success group was significantly lower compared with that in the failure group (mean difference, -1.12; 95% CI; -1.47 to -0.78; $P < 0.00001$). The SROC curve of D-RSBI was shown (Fig. 5). However, there still remained remarkable heterogeneity ($I^2 = 84\%$; $P < 0.00001$) (Fig. 6).

3.3 Subgroup analysis of different SBT

Four studies which used PSV mode for SBT involving 212 patients were obtained in this subgroup analysis [18–21]. Compared with patients that failed to wean, D-RSBI was significantly lower in success group (mean difference, -1.03; 95% CI -1.59 to -0.48; $P < 0.00001$). However, there was high heterogeneity among the included studies ($I^2 = 91\%$; $P < 0.00001$, random-effects model) (Fig. 7).

Four studies which used T-tube test for SBT involving 159 patients were obtained in this subgroup analysis [15, 17, 22, 23]. D-RSBI was remarkably linked to weaning success, with a lower value compared with patients that failed to wean (mean difference, -1.22; 95% CI -1.76 to -0.69; $P < 0.00001$). However, there was heterogeneity among the component studies as well ($I^2 = 84\%$; $P < 0.00001$, random-effects model). Compared between the two subgroups, results demonstrated homogeneity ($I^2 = 0\%$; $P = 0.63$) (Fig. 7).

4. Discussion

Mechanical ventilation weaning is an essential part of ventilator support. Once the cause of respiratory failure is removed, the ventilator should be withdrawn in time to avoid the complications, such as ventilator associated pneumonia which caused by prolonged mechanical ventilation. However, premature extubation may lead to recrudescence or exacerbation of the respiratory failure and increase of the costs, reintubation and mortality. It remains a great challenge for clinicians. Therefore, a variety of indicators should be applied to accurately predict the outcome of weaning process [3]. Single index is insufficient for accurate prediction of weaning outcome. RSBI can reflect the phenomenon of small tidal volume and rapid respiratory frequency during breathing force and load imbalance and is considered to be a predictive parameter of weaning outcome [24, 25]. The advantage of RSBI is simple to operate and does not require complex instruments. However, RSBI lacked adequate predictive value to assess patients with hypercapnia, COPD or heart failure before extubation. Function of diaphragm producing most tidal volume, cannot be judged with this very index [17].

Respiratory muscles weakness is common in patients with mechanical ventilation and is associated with reintubation [26]. Diaphragm dysfunction delayed extubation and prolonged hospital stay which contributed to a poor prognosis [27]. Diagnosis of diaphragm function is based on dynamic imaging with ultrasound that is a non-invasive, convenient and bedside method [28, 29]. Although ultrasonography is an operator-dependent technique, results of previous studies showing good reproducibility of diaphragmatic ultrasonography [30]. There are several approaches to evaluate diaphragm function, such as diaphragm displacement and diaphragm thickening fraction. To record diaphragm displacement, the right hemidiaphragm was examined and the liver served as an acoustic window. Then in M-mode, the diaphragmatic displacement (cm) was measured on the vertical axis during the respiratory cycle. Diaphragm thickening was quantified by the percentage change in right hemidiaphragm thickness from end expiration to peak inspiration during tidal breathing on ventilation (thickening fraction) [14]. Diaphragm thickening revealed the structure and muscle power of diaphragm and usually was measured during mechanical ventilation. Diaphragm displacement was usually examined during spontaneous breathing trial, which revealed the mobility and the active respiratory workload. Relatively low technical requirements were needed for measuring diaphragm displacement. Critically, diaphragm displacement could also reflect the tidal volume. Higher tidal volume is associated with increased excursions of the diaphragm [31]. The both of indexes have a good value for predicting extubation success [32, 33]. Our work found a convenient and accurate index during SBT for predicting weaning outcome. Therefore, D-RSBI (D-RSBI = RR/DD) was considered in our study based on previous studies. D-RSBI combined the two parameters so that a comprehensive assessment is available for clinician. Moreover, it suggested that the index could improve the accuracy through recent researches [15, 17]. Our study showed a pooled sensitivity of 0.84 (95% CI 0.76 to 0.90) and a pooled specificity of 0.87 (95% CI 0.79 to 0.92). A sensitivity of 0.73 and a specificity of 0.75 of RSBI in predicting the weaning failure were reported in a recent study, but our data demonstrated higher accuracy of D-RSBI than RSBI, and the further researches need to be carried out [34]. Two studies without available data and a meeting abstract were excluded from this study [35, 36]. Despite unavailable data including sensitivity and specificity, conclusion of both studies showed a good accuracy of D-RSBI in predicting weaning.

TABLE 1. Main characteristics of the studies included in the systematic review.

Study	N (% male)	Age (year)	Study design	Patient category	Inclusion criteria	SBT	Cut off	Definition of weaning failure	Outcomes (SG vs FG)
Savino Spadaro 2016 [15]	51 (61)	65 ± 13	Prospective cohort	Medical ICU patients	MV for more than 48 h and ready for SBT	T-tube	1.3	SBT failure, reintubation or the use of NIV within 48 h	1.3 ± 0.85 vs 2.83 ± 1.94
Ahmad Abbas 2020 [17]	50 (68)	61.9 ± 7.5	Prospective cohort	Respiratory ICU patients	MV for more than 48 h and ready for SBT	T-tube	1.9	SBT failure, reintubation or the use of NIV within 48 h	1.43 ± 0.32 vs 3.27 ± 0.8
Sherif M.S. 2018 [20]	53 (66)	35.8 ± 9.6	Prospective cohort	Surgical ICU patients	Received MV and passed SBT	PSV	1.61	Reintubation or the use of NIV within 48 h	1.10 ± 0.18 vs 2.93 ± 0.58
Feng Hui 2019 [39]	31 (29)	76.0 ± 8.5	Prospective cohort	Medical ICU patients	MV for more than 48 h and passed SBT	Cuff leak test	1.8	SBT failure, reintubation or the use of NIV within 48 h	1.43 ± 0.31 vs 2.6 ± 1.72
Zhang Haixiang 2018 [21]	131 (73)	71.0 ± 11.3	Prospective cohort	Medical ICU patients	MV for more than 48 h and ready for SBT	PSV	1.65	SBT failure or need mechanical ventilation within 48 h	1.3 ± 0.3 vs 2.1 ± 0.85
Lin Ning 2019 [23]	88 (44)	54.8 ± 11.7	Prospective cohort	Medical ICU patients	MV for more than 48 h and passed SBT	T-tube	1.73	reintubation or the use of NIV within 48 h	1.49 ± 0.47 vs 2.55 ± 0.87
Fan Maiying 2018 [19]	40 (70)	65.9 ± 14.2	Prospective cohort	Emergency ICU patients	MV for more than 48 h and ready for SBT	PSV	1.42	SBT failure, reintubation or the use of NIV or die within 48 h	1.44 ± 0.66 vs 2.06 ± 0.68
Wang Zhili 2018 [22]	48 (60)	63.8 ± 13.2	Prospective cohort	Medical ICU patients	MV for more than 48 h and passed SBT	T-tube	1.23	SBT failure or need mechanical ventilation within 48 h	1.07 ± 0.45 vs 1.75 ± 0.51
Dou Zhimin 2018 [18]	76	65.4 ± 10	Prospective cohort	Medical ICU patients	MV for more than 48 h and passed SBT	PSV	1.13	SBT failure or need mechanical ventilation within 48 h	0.95 ± 0.51 vs 1.79 ± 0.83

MV: mechanical ventilation. PSV: pressure supported ventilation. NIV: Non-invasive ventilation. SG: success group. FG: failure group.

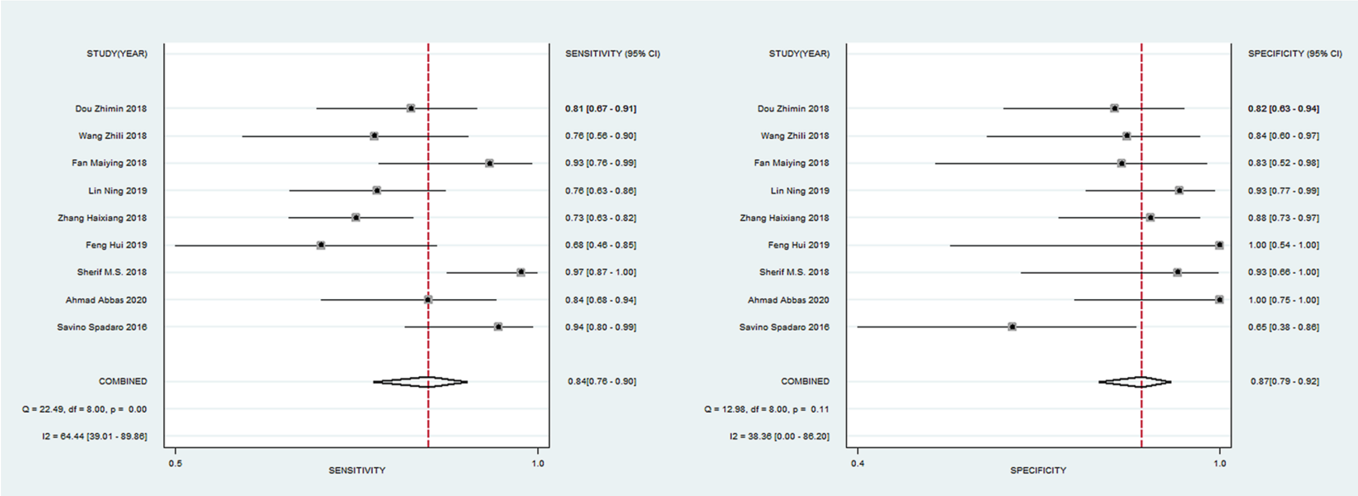

FIGURE 4. Pooled sensitivity and specificity of D-RSBI in predicting weaning success.

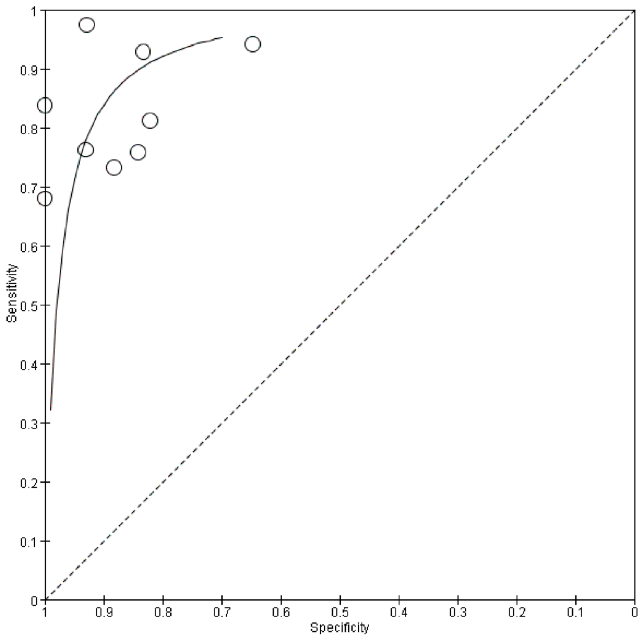

FIGURE 5. Summary of receiver operating characteristic curve plotting of accuracy of D-RSBI.

This is the first review that systematically analyzed the accuracy of D-RSBI for predicting weaning outcomes. Value of D-RSBI in different weaning outcome groups is helpful to clinical application. However, this reported index remains some limitation as well. It was reported that different SBT affected the outcome of extubation. PSV may be associated with lower weaning failure rates and T-tube may be related to a shorter weaning duration [37, 38]. In order to find whether the sources of heterogeneity are different SBTs, we purposely compared D-RSBI between the different SBT groups (PSV and T-tube), and no significant subgroup difference was detected. D-RSBI showed high accuracy in each subgroup analysis and the heterogeneity still exists in each subgroup. The high level of heterogeneity of the included studies might attribute to variety of diseases or comorbidities involved in the studies and a lack of objective criteria to judge the success of withdrawal from MV. One study included use cuff leak test for SBT [39]. The sensitivity analysis performed with removal of this study still demonstrated heterogeneity (I^2 = 86%; $P <$ 0.00001, random-effects model). It suggested that pattern of SBT was not the factor contributing to the heterogeneity, since the subgroup analysis performed within different SBT (PSV and T-tube) showed homogeneity. Some diseases, such as COPD causing impaired lung function might have influence in the evaluation before extubation and this might contribute to the heterogeneity as well [40]. Diaphragmatic displacement was greater in noninvasive ventilation success than in failure, while diaphragm thickening fraction and thickness had no significance between the groups [41]. Their results also suggest that diaphragmatic displacement might be a critical parameter to assess COPD patients who required mechanical ventilation.

We hypothesize D-RSBI combining diaphragmatic displacement with respiratory rate can be an effective parameter in predicting the outcome of mechanical ventilation in COPD patients. More researches need to be conducted to explore the value of D-RSBI in COPD patients. Researches focusing on particular diagnosis remained to be implemented. Moreover, this study was generally comprised with small trials and large trials with high quality are expected to be carried out.

5. Conclusions

In conclusion, D-RSBI can predict the weaning outcome and may identify patients at risk of weaning failure. The accuracy does not depend on SBT. MV weaning is a multifactorial process. To accurately predict weaning result, the clinicians still need to combine the clinical manifestations and other indicators of the weaning prediction to make a comprehensive analysis. The subsequent research should focus on specific cause of respiratory failure.

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Ahmad Abbas2020	1.43	0.32	37	3.27	0.84	13	11.6%	-1.84 [-2.31, -1.37]
Dou Zhimin2018	0.95	0.51	48	1.79	0.83	28	12.9%	-0.84 [-1.18, -0.50]
Fan Maiying2018	1.44	0.66	28	2.06	0.68	12	11.7%	-0.62 [-1.08, -0.16]
Feng Hui2019	1.43	0.31	25	2.6	1.72	6	4.3%	-1.17 [-2.55, 0.21]
Lin Ning2019	1.49	0.47	59	2.55	0.87	29	12.9%	-1.06 [-1.40, -0.72]
Savino Spadaro2016	1.3	0.85	34	2.83	1.94	17	6.8%	-1.53 [-2.50, -0.56]
Sherif M.S.2018	1.1	0.18	39	2.93	0.58	14	13.2%	-1.83 [-2.14, -1.52]
Wang Zhili2018	1.07	0.45	29	1.75	0.51	19	13.4%	-0.68 [-0.96, -0.40]
Zhang Haixiang2018	1.3	0.3	97	2.1	0.85	34	13.3%	-0.80 [-1.09, -0.51]
Total (95% CI)			**396**			**172**	**100.0%**	**-1.12 [-1.47, -0.78]**

Heterogeneity: Tau² = 0.21; Chi² = 50.67, df = 8 (P < 0.00001); I² = 84%
Test for overall effect: Z = 6.43 (P < 0.00001)

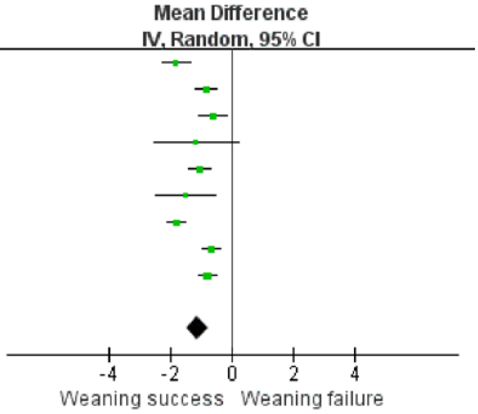

FIGURE 6. Mean difference of D-RSBI between weaning failure and success groups.

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
3.4.1 PSV								
Dou Zhimin2018	0.95	0.51	48	1.79	0.83	28	13.4%	-0.84 [-1.18, -0.50]
Fan Maiying2018	1.44	0.66	28	2.06	0.68	12	12.2%	-0.62 [-1.08, -0.16]
Sherif M.S.2018	1.1	0.18	39	2.93	0.58	14	13.7%	-1.83 [-2.14, -1.52]
Zhang Haixiang2018	1.3	0.3	97	2.1	0.85	34	13.9%	-0.80 [-1.09, -0.51]
Subtotal (95% CI)			**212**			**88**	**53.3%**	**-1.03 [-1.59, -0.48]**
Heterogeneity: Tau² = 0.29; Chi² = 31.98, df = 3 (P < 0.00001); I² = 91%								
Test for overall effect: Z = 3.63 (P = 0.0003)								
3.4.2 T-tube								
Ahmad Abbas2020	1.43	0.32	37	3.27	0.84	13	12.1%	-1.84 [-2.31, -1.37]
Lin Ning2019	1.49	0.47	59	2.55	0.87	29	13.4%	-1.06 [-1.40, -0.72]
Savino Spadaro2016	1.3	0.85	34	2.83	1.94	17	7.2%	-1.53 [-2.50, -0.56]
Wang Zhili2018	1.07	0.45	29	1.75	0.51	19	14.0%	-0.68 [-0.96, -0.40]
Subtotal (95% CI)			**159**			**78**	**46.7%**	**-1.22 [-1.76, -0.69]**
Heterogeneity: Tau² = 0.23; Chi² = 18.49, df = 3 (P = 0.0003); I² = 84%								
Test for overall effect: Z = 4.48 (P < 0.00001)								
Total (95% CI)			**371**			**166**	**100.0%**	**-1.12 [-1.48, -0.77]**

Heterogeneity: Tau² = 0.21; Chi² = 50.65, df = 7 (P < 0.00001); I² = 86%
Test for overall effect: Z = 6.19 (P < 0.00001)
Test for subgroup differences: Chi² = 0.24, df = 1 (P = 0.63), I² = 0%

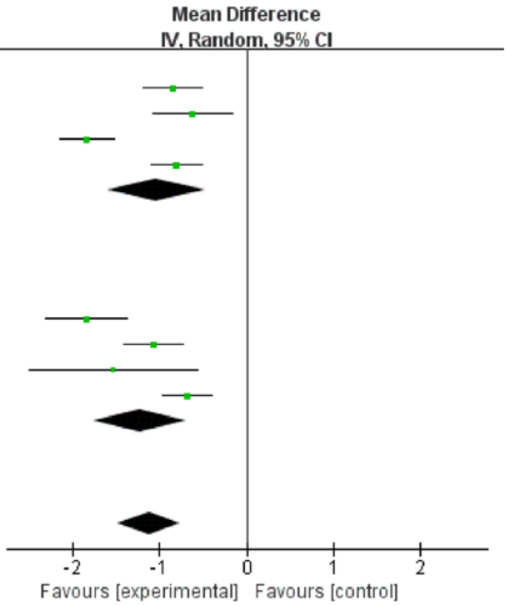

FIGURE 7. PSV and T-tube SBT Subgroup analysis of mean difference of D-RSBI between weaning failure and success groups.

AUTHOR CONTRIBUTIONS

Liuzhao Cao and Linli Sang designed the study. Jie Yang, Liuzhao Cao and Weiyun Teng searched the literature. Liuzhao Cao and Weiyun Teng collectted the data. Liuzhao Cao, Weiyun Teng and Jie Yang analized the data. Liuzhao Cao, Weiyun Teng and Linli Sang prepared the manuscript. LIuzhao Cao and Linli Sang reviewed the manuscript.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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