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Predictive value of extubation failure by decrease in central venous oxygen saturation: A systematic review and meta-analysis

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ABSTRACT

Background: The predictive power of extubation failure diagnosed by decrease in central venous oxygen saturation (ΔScvO2) varies by studies. Here we summarized the diagnostic value of extubation failure tested by ΔScvO2.
Methods: A comprehensive online search was performed to select potentially eligible studies that evaluated the predictive power of extubation failure tested by ΔScvO2. A manual search was also performed to identify additional studies. Data were extracted to calculate the pooled sensitivity, specificity, positive likelihood ratio (LR), negative LR, diagnostic odds ratio (DOR), and area under the receiver operating characteristic curve (AUC) to evaluate the predictive power of extubation failure.
Results: Overall, five studies including 353 patients were included in this review, of whom 105 (30%) were extubation failure. The cutoff values of ΔScvO2 varied across studies, ranging from 3.8% to 5.4%. Heterogeneity between studies was assessed with an overall $Q = 0.007$, $I^2 = 0\%$, and $P = 0.498$. The pooled sensitivity and specificity for the overall population were 0.83 (95% CI: 0.74–0.90) and 0.88 (95% CI: 0.83–0.92), respectively. The pooled positive LR and negative LR were 7.2 (95%CI: 4.6–11.2) and 0.19 (95%CI: 0.12–0.31), respectively. The DOR was 38 (95% CI: 17–86). Overall, the pooled AUROC was 0.92 (95% CI: 0.90–0.94).
Conclusions: The ΔScvO2 performed well in predicting extubation failure in adult mechanical ventilation patients. Further studies with a larger data set and well-designed models are required to confirm the diagnostic accuracy and utility of ScvO2 in predicting extubation outcomes in mechanical ventilation patients.

1. Introduction

Weaning from mechanical ventilation is one of the key elements in the care of critically ill intubated patients receiving mechanical ventilation and could represent 40–50% of the total duration of mechanical ventilation [1]. The spontaneous breathing trial (SBT) has been recommended to help determine whether a patient can be weaned from mechanical ventilation [2–4]. After a successful SBT, extubation is recommended. However, 10–20% of patients who successfully complete a SBT experience extubation failure, extubation failure is associated with prolonged mechanical ventilation and extremely high mortality rates of 25%–50% [5,6]. Patients who experience extubation failure were more likely to die in hospital than those who succeeded [7,8]. Therefore, the early identification of critically ill patients who are likely to experience extubation failure is vital for improved outcomes.

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Central venous oxygen saturation (ScvO2) represents the saturation of hemoglobin by O2 from the central venous catheter, provides insight into the balance between oxygen delivered to and consumed by all tissues of the body. ScvO2 monitoring has been used as a prognostic indicator in a variety of conditions in people with cardiac disease, trauma, and sepsis [9,10]. Evidence from published studies [11,12], decreases in ScvO2 (ΔScvO2) during SBT were associated with weaning and extubation failure, and were a useful marker for the reliable prediction of extubation outcomes. However, another study reported that ScvO2 did not differ between patients who experienced extubation success and failure [13]. Given the inconsistent results found by different studies, we reviewed the literature systematically and performed a meta-analysis to assess the efficacy of diagnostic tests that use ScvO2 for the detection of extubation failure.

2. Materials and methods

This meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidance [14,15].

2.1. Registration and protocol

This meta-analysis was registered on PROSPERO(CRD42022325145).

2.2. Search strategy

Relevant studies up to September the 19th 2022 were searched in the PubMed, Embase via OVID, and Cochrane Library databases with the following terms and their combinations: "central venous oxygen saturation or ScvO2" and "reintubation or wean or extubation." All scanned abstracts, studies, and citations were reviewed. We also did manual searches of the reference lists of included articles to identify additional relevant publications.

2.3. Selection criteria

The inclusion criteria were as follows: (1) studies on adult patients were under mechanical ventilation through endotracheal intubation for ≥48 h; (2) a SBT was completed before extubation; (3)studies with SBT-induced decrease in ScvO2 as the index test; (4) studies published with full-text in any language; (5) studies providing sufficient data for constructing 2-by-2 tables, including true positive (TP), false positive (FP), true negative (TN), and false negative (FN). The exclusion criteria were as follows: (1) studies that used the same population or overlapping database; (2) reviews, case reports, editorials, letters, and conference abstracts; (3) articles with no available data for patients with ScvO2 and (4) articles without a definition of extubation failure.

2.4. Data extraction and quality assessment

All the available data were extracted from each study by two investigators independently according to the aforementioned inclusion criteria, and any differences were resolved by discussion with a third investigator. The following data were collected from each study: (1) basic characteristics of studies, including first author name, publication year, country where the research was performed, selected patients, gender, mean age, number of patients, study design, method and time of SBT, index test device for the ScvO2, definition of extubation failure; (2) diagnostic performance, including cutoff value, sensitivity, specificity, area under the receiver operator characteristic curve (AUROC), TP, FP, FN, and TN. If numbers of TP, FP, FN, and TN were unavailable, we communicated with the corresponding author to obtain these data. The quality of included studies was scored independently by two reviewers using the revised Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) criteria [16]. The quality of studies was assessed using RevMan 5.4.

2.5. Statistical analysis

All analyses were performed using the Stata 16.0 software (Stata Corp., College Station, TX, USA). The bivariate meta-analysis model was employed to summarize sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio (DOR) [17,18]. The sensitivity and specificity of each included study were used to plot the summary receiver operator characteristic (SROC) curve and calculate the area under the SROC curve (AUC). Diagnostic power was good, moderate, and poor if the AUC was more than 0.8, between 0.7 and 0.8, and less than 0.7, respectively [19].

Spearman's correlation coefficient between the logit of sensitivity and logit of 1-specificity was calculated to determine any threshold effect; A strong positive correlation would suggest threshold effect [20]. The between-study heterogeneity was evaluated using Q test and I2 statistics. A P value less than 0.10 for the Q test or I2 value ≥ 50% indicated substantial heterogeneity. A fixed effects model was used if no heterogeneity was observed. A random effects model was selected if significant heterogeneity was observed.

3. Results

3.1. Characteristics of the studies

A total of 118 studies were obtained through electronic database searches, and 2 studies were identified through a manual search. Fig. 1 shows the study selection process. A total of 15 records were initially excluded due to duplicate records; 98 records were excluded due to the source not related to the research topic or being conference abstract or editorial; and 3 records [13,21,22] were excluded because no enough data for constructing 2-by-2 tables. Finally, five studies [11,12,23–25] fulfilled all the inclusion criteria and were considered for analysis. Two of the five studies are multicentric prospective studies, other three studies are single center prospective studies, the main characteristics of the eligible studies are shown in Table 1. The quality of the included studies was assessed using QUADAS-2 available in Fig. 2(a and b).

3.2. Quantitative synthesis

Study data and individual diagnostic estimates are summarized in Table 2. Overall, 353 patients were included in this review, of whom 105 (30%) were extubation failure. The cutoff values of $\Delta ScvO2$ varied across studies, the study by Ashmawi's was >3.8%, the study by Mallat's was ≥5.4%, the study by Helmy's was ≥4%, the study by Shalaby's was >5% and the study by Teixeira's was >4.5%. Three studies gave the AUROC, ranged from 0.856 to 0.87. Heterogeneity between studies was assessed with an overall $Q = 0.007$, $I^2 = 0\%$, and $P = 0.498$, indicated no heterogeneity. Spearman's correlation coefficient was 0.1 ($p = 0.87$), indicating no threshold effect. The pooled sensitivity and specificity for the overall population were 0.83 (95% CI: 0.74–0.90) and 0.88 (95% CI: 0.83–0.92), respectively (Fig. 3). The pooled positive likelihood ratio and negative likelihood ratio were 7.2 (95%CI: 4.6–11.2) and 0.19 (95%CI: 0.12–0.31), respectively. The DOR was 38 (95% CI: 17–86) (Fig. 4). The pooled AUROC was 0.92 (95% CI: 0.90–0.94) (Fig. 5).

4. Discussion

In the last few years, multiple indices and methods such as rapid shallow breathing index, lung and diaphragm ultrasound have been proposed as predictors of weaning outcome, but none has shown more than modest prognostic accuracy [26–28]. To the best of

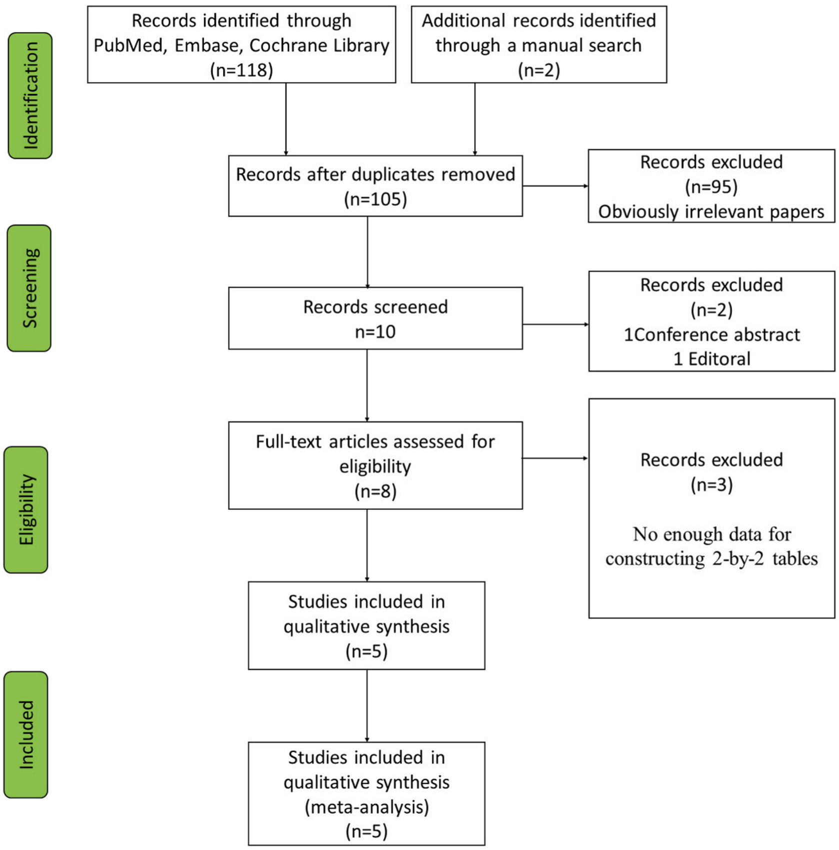

Fig. 1. Flow diagram of identification of studies.

Table 1
Characteristics of the studies included in this meta-analysis.

First author/ Year of publication	Country	Patients	Gender (M/f)	Age (year) Mean ± SD	Cases	Method and time of SBT	Index test device	Definition for failure extubation	Study design
Ashmawi/ 2020 [26]	Egypt	Patients intubation and mechanical ventilation ≥2 days and meeting the weaning criteria	37/13	64.7 ± 8.6	50	PSV≤ 7 cmH2O 30min	Blood gas analyzer	Reintubation within 2 days	Single central prospective study
Mallat/2020 [12]	France	Patients received MV for at least 48 h and satisfied the weaning criteria	56/19	68 ± 11	75	T-tube trial 60min	Blood gas analyzer	Mechanical ventilation within 48 h	Multicentric prospective study
Helmy/2014 [25]	Egypt	COPD patients intubated and ventilated ≥48 h and meeting the weaning criteria	31/4	56.51 ± 6.05	35	PSV≤ 7 cmH2O 30min	Blood gas analyzer	Reintubation in 48 h	Single central prospective study
Shalaby/2014 [24]	Saudi Arabia	Patients mechanically ventilated for >48 h and meeting the weaning criteria	68/52	54 ± 20	120	T-tube trial 30min	Blood gas analyzer	Reintubation in 48 h	Single central prospective study
Teixeira/2010 [11]	Brazil	Patients mechanically ventilated for >48 h and meeting the weaning criteria	39/24	57 ± 19	73	T-tube trial 30min	Blood gas analyzer	Reintubation within 48 h	Multicentric prospective study

COPD, chronic obstructive pulmonary disease; PSV, pressure support ventilation.

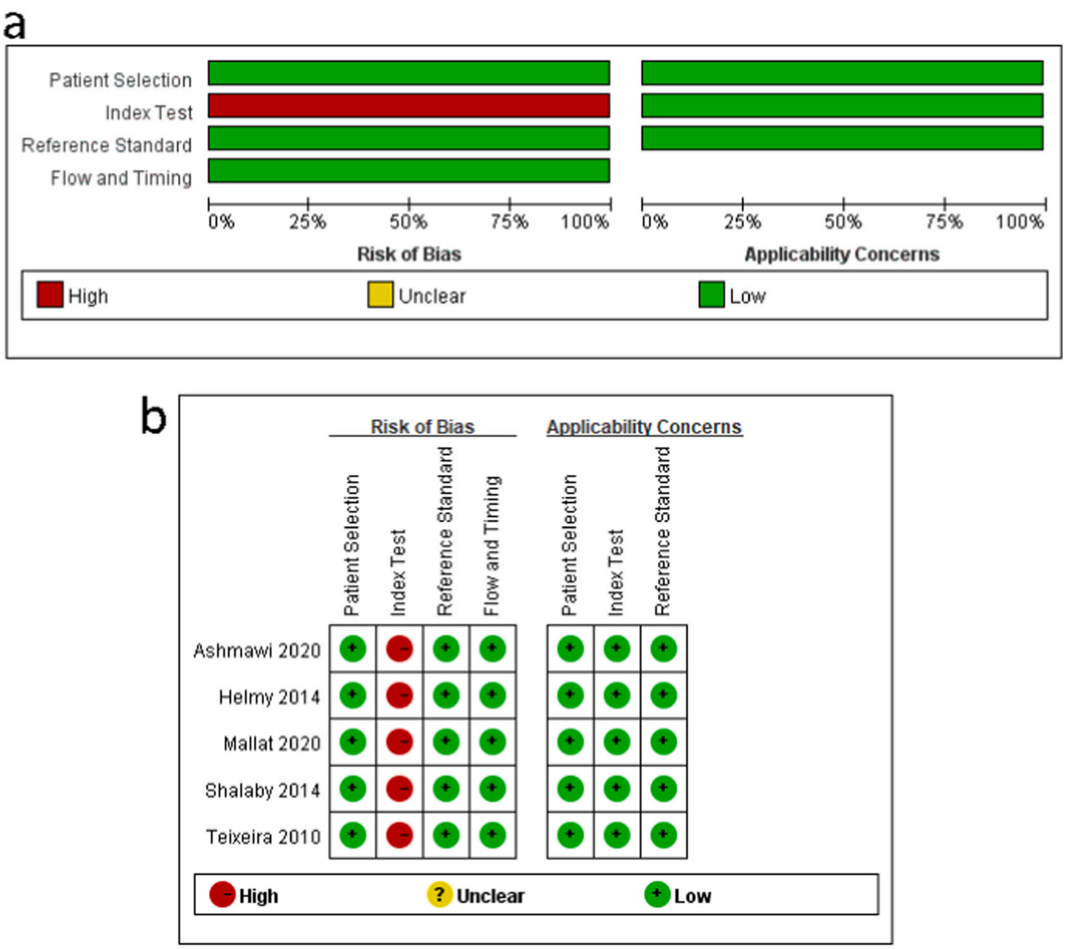

Fig. 2. Risk of bias and applicability concerns for the studies included in the meta-analysis. (a) Risk-of-bias graph; (b) Risk-of-bias summary.

Table 2
Summary of results of the studies included in this meta-analysis.

First author/Year of publication	Sample size	Cutoff value	Subject numbers could be calculated				Sensitivity (%)	Specificity (%)	AUROC (95% CI)
			TP	FP	FN	TN			
Ashmawi/2020 [26]	50	>3.8%	10	4	1	35	89.7	90.9	NA
Mallat/2020 [12]	75	≥5.4%	12	8	6	49	67	86	0.856 (0.756–0.926)
Helmy/2014 [25]	35	≥4%	7	7	1	20	87	74	0.861 (0.702–0.954)
Shalaby/2014 [24]	120	>5%	32	8	5	75	87	90	NA
Teixeira/2010 [11]	73	>4.5%	27	2	4	40	88	95	0.87(NA)

AUROC, Area under the receiver operator characteristics curve; CI, confidence interval; FN, false negative; FP, false positive; TN, true negative; TP, true positive; NA, no available.

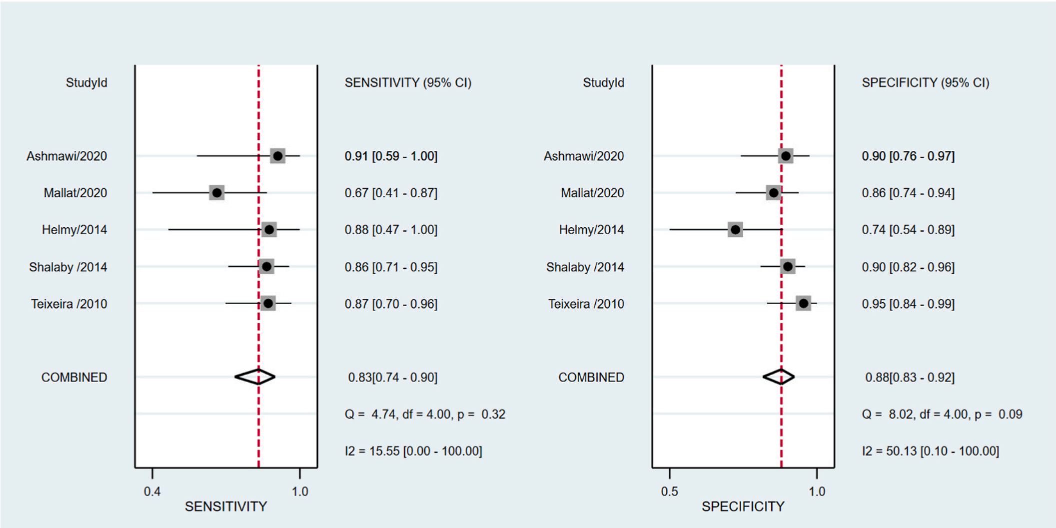

Fig. 3. Forest plots of the pooled sensitivity and specificity. Each solid square represents an individual study. Error bars represent 95% CI. Diamond indicates the pooled sensitivity and specificity for all of the studies.

our knowledge, this is the first systematic review and meta-analysis to explore the diagnostic accuracy of $\Delta ScvO_2$ in predicting extubation failure in adult mechanical ventilation patients. The results confirmed that, overall, the $\Delta ScvO_2$ performed well diagnostic power for predicting extubation failure, with a pooled AUROC of 0.92 (95% CI: 0.90–0.94). A significant decrease in ScvO2 was well predictive of extubation failure, with a pooled sensitivity of 0.83 (95% CI: 0.74–0.90). The absence of a significant decrease in ScvO2 also was used well to rule out extubation failure, with a pooled specificity of 0.88 (95% CI: 0.83–0.92). Our results are clinically important and add significant data to the existing literature, for patients with central venous catheter during SBT, the tracking of ScvO2 showed excellent predictability in extubation outcomes. Further diagnostic studies are warranted to obtain the appropriate cutoff value and validate the pooled results.

Weaning from mechanical ventilation is usually associated with increased oxygen consumption (VO2) linked to the augmented work of breathing [29,30]. To meet the metabolic demand during SBT, increases in VO2 should be accompanied by increases in cardiac output and oxygen delivery (DO2). Mixed venous oxygen saturation (SvO2) well reflects the balance between VO2 and DO2. Although ScvO2 is less accurate than SvO2, it has been successfully used as a target for adequate resuscitation in critically ill patients [31,32]. Earlier studies [10,33,34] had demonstrated adequate correlation between ScvO2 and SvO2, as such, measurement of ScvO2 using central venous catheters seems to be a simple method and an attractive alternative to measurement of SvO2 for the evaluation and monitoring of critically ill patients, since it can be obtained in an easier, less risky and less costly manner.

Using SvO2 to predict weaning failure has been well described [35–37],. Teixeira et al. [11], first described a decrease in ScvO2 during the SBT was able to predict accurately extubation failure in difficult-to-wean patients, they found decrease of ScVO2 by>4.5% was an independent predictor of reintubation, and could reflect the increase of respiratory muscles oxygen consumption. Similarly, other studies [11,12,21–25] also found the similar results in different critical ill patients. However, Chittawattanarat et al.'s [13] findings are not in agreement with those of aforementioned studies. The discrepancy between Chittawattanarat et al.'s findings and those of previous studies could stem from several factors: First, the study populations were dissimilar, they are all post-cardiac surgical patients in Chittawattanarat et al.'s study. Second, in Chittawattanarat et al.'s study, patients were ventilated for less than 24 h. Anyway, our meta-analysis demonstrated that ΔScvO2 performed well diagnostic power for predicting extubation failure.

The present systematic review and meta-analysis had some limitations. First, this analysis included only five studies with a

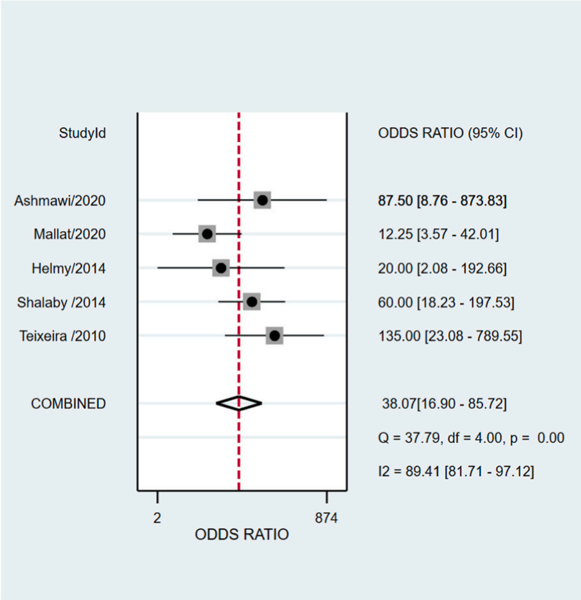

Fig. 4. Forest plots of the pooled diagnostic odds ratio. Each solid square represents an individual study. Error bars represent 95% CI. Diamond indicates the pooled diagnostic odds ratio for all of the studies.

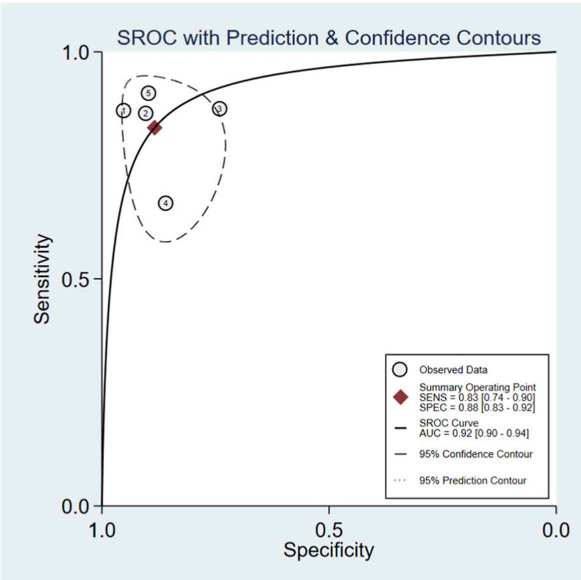

Fig. 5. SROC curve of decrease in central venous oxygen saturation for predicting extubation failure. Each circle represents individual study estimates. The diamond is the summary point representing the average sensitivity and specificity estimates. The ellipses around this summary point are the 95% confidence region (dashed line) and the 95% prediction region (dotted line). The cutoff value of included studies: (1) Ashmawi/2020 [26]:> 3.8%; (2) Mallat/2020 [12]:≥5.4%; (3) Helmy/2014 [25]:≥ 4%; (4) Shalaby/2014 [24]:> 5%; (5) Teixeira/2010 [11]:>4.5%.

relatively small sample size. Therefore, the power and precision of the results were limited. Second, the quality assessment showed a high risk of bias in the index test due to insufficient information to judge whether their test results were interpreted blind for all the included studies. This bias might have restricted the interpretation of the true diagnostic efficacy of ΔScvO2 in predicting extubation failure. Third, different types and durations of SBTs were performed in the enrolled studies. The rate of successful SBTs was higher when they were performed under pressure support ventilation than under T-piece [38]. But, extubation failure did not vary by type and duration of SBT [39–41]. Therefore, the type of SBT is unlikely to affect the outcome between Scvo2 and extubation failure. Finally, the patients included in the study were mainly of internal diseases, and complicated with cardiopulmonary problems. Therefore, the interpretation of the above results should be cautious and its application should not be expanded.

5. Conclusions

This meta-analysis confirmed that the ΔScvO2 performed well in predicting extubation failure in adult mechanical ventilation patients. Further studies with a larger data set and well-designed models are required to confirm the diagnostic accuracy and utility of ScvO2 in predicting extubation outcomes in mechanical ventilation patients.

Author contribution statement

Haijun Huang, Chenxia Wu: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote and revised the paper.

Hua Xu, Luoxia Hu and Qinkang Shen: Analyzed and interpreted the data; Performed the experiments.

Data availability statement

PROSPERO, Registration Number: CRD42022325145.

Ethics approval and consent to participate

Not applicable.

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e18227.

List of abbreviations

ScvO2	Central venous oxygen saturation
ΔScvO2	Decrease in central venous oxygen saturation
SBT	Spontaneous breathing trial
DOR	Diagnostic odds ratio
CI	Confidence interval
TP	True positive
FP	False positive
TN	True negative
FN	False negative
AUROC	Area under the receiver operator characteristic curve
QUADAS-2	Quality Assessment of Diagnostic Accuracy Studies
SROC	Summary receiver operator characteristic
AUC	Area under the SROC curve
VO2	Oxygen consumption
DO2	Oxygen delivery
SvO2	Mixed venous oxygen saturation

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