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Risk prediction model for difficulty in weaning from mechanical ventilation in critically ill patients: results from a multicentre retrospective study

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ABSTRACT

Objectives We aimed to establish a diagnostic system using retrospective data to predict difficult wean from mechanical ventilation.

Design A multicentre retrospective study

Setting Five tertiary hospitals from China.

Participants Critically ill patients received mechanical ventilation between January 2018 and December 2022.

Primary and secondary outcome measures The primary endpoint was success weaning from mechanical ventilation (>48 hours), reintubation or death, whichever occurred first.

Results Among 1365 initially screened patients, 703 patients (median age: 69 years; 63.02% male) were included. From 42 factors, 22 ($p \le 0.10$) were identified for multivariate analysis. Subsequently, the lung injury score, brain natriuretic peptide level at 24 hours, 24 hour fluid balance, use of dexmedetomidine, spontaneous breathing trial (continuous positive airway pressure vs other) and endotracheal tube reinsertion were included in the predictive model. The area under the curve value was 0.8888 (95% CI: 0.8382, 0.9394). The sensitivity, specificity, positive predictive value, negative predictive value, accuracy, likelihood ratio (LR)+ and LR− were 0.7559, 0.875, 0.9746, 0.3608, 0.7721, 6.0743 and 0.279, respectively. We established a nomogram model based on the optimal model.

Conclusions A model with six factors was established to predict difficult wean from mechanical ventilation in critically ill patients. However, the model should be verified in future well-designed studies before being extended to other populations.

Trial registration ChiCTR1900021432. Registered on February 21, 2019; Post-results.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The retrospective design may introduce biases and limits the ability to establish causality between identified factors and extubation outcomes.
⇒ The study was conducted in a single country, which may limit the generalisability of the findings to different populations and healthcare systems.
⇒ Validation in prospective studies is necessary to confirm the predictive model's accuracy and clinical utility.
⇒ Some relevant clinical variables may not have been included due to data availability constraints.
⇒ Potential inconsistencies in data collection across multiple centres could have affected variable accuracy.

INTRODUCTION

Mechanical ventilation, aided by a ventilator, helps maintain airway patency, improves ventilation and oxygenation, prevents hypoxia and carbon dioxide (CO_2) buildup and helps the body overcome respiratory failure caused by underlying diseases.[1] However, timely liberation from the ventilator is the ultimate goal and a key challenge in clinical practice during mechanical ventilation.

Traditionally, a lack of systematic understanding of weaning from mechanical ventilation has led to reliance on subjective clinical judgement or experience, often resulting in delayed extubation, potential complications, high hospitalisation costs and potential threats to post-discharge quality of life of patients.[2 3] Recently proposed objective criteria-based wean from mechanical ventilation plans aim to reduce mechanical ventilation duration, lower complications such as ventilator-associated pneumonia and decrease hospitalisation costs to some extent.[4] However, these plans lack standardisation, especially for early diagnosis in challenging cases, which may lead to extubation failure or unnecessarily prolonged mechanical ventilation, thereby affecting patient outcomes.[4 5] Further research on patients receiving mechanical ventilation is essential to establish a standardised wean from the mechanical ventilation system.

The mechanical ventilation process generally involves six stages: treating respiratory

Table 1 Baseline characteristics of patients

Variable	Total (n=703)	Outcome of extubation Success (n=584)	Difficult (n=119)	P value
Age (years)	69.00 (56.00, 79.00)	67.00 (55.00, 77.25)	74.00 (63.50, 81.50)	< 0.001
Sex (n, %)				0.403
Male	443 (63.02)	364 (62.33)	79 (66.39)	
Female	260 (36.98)	220 (37.67)	40 (33.61)	
Clinical diagnosis				0.017
Respiratory diseases (n, %)	194 (27.60)	152 (26.03)	42 (35.29)	
Digestive diseases (n, %)	164 (23.33)	141 (24.14)	23 (19.33)	
CVD (n, %)	28 (3.98)	24 (4.11)	4 (3.36)	
Live diseases (n, %)	29 (4.13)	27 (4.62)	2 (1.68)	
Metabolic diseases (n, %)	11 (1.56)	11 (1.88)	0 (0.00)	
Neuro diseases (n, %)	122 (17.35)	95 (16.27)	27 (22.69)	
Kidney disease (n, %)	17 (2.42)	13 (2.23)	4 (3.36)	
Trauma (n, %)	37 (5.26)	31 (5.31)	6 (5.04)	
Surgery (n, %)	32 (4.55)	32 (5.48)	0 (0.00)	
Other (n, %)	69 (9.82)	58 (9.93)	11 (9.24)	
History of smoking (n, %)				0.057
Yes	249 (36.19)	200 (34.66)	49 (44.14)	
No	439 (63.81)	377 (65.34)	62 (55.86)	
Alcohol drinking (n, %)				0.330
Yes	136 (19.91)	111 (19.27)	25 (23.36)	
No	547 (80.09)	465 (80.73)	82 (76.64)	
Charlson comorbidity index	3.00 (1.00, 4.00)	3.00 (1.00, 4.00)	3.00 (2.00, 5.00)	0.011
SOFA score	8.00 (5.00, 10.00)	7.00 (5.00, 10.00)	8.00 (5.00, 12.00)	0.043
GCS score	8.00 (6.00, 13.00)	8.00 (7.00, 13.00)	7.00 (3.25, 10.00)	< 0.001
SAPSII score	38.00 (30.00, 48.00)	37.00 (29.00, 46.00)	41.00 (34.00, 54.50)	< 0.001
APACHE II score	23.00 (20.00, 26.00)	22.00 (19.00, 26.00)	26.00 (22.00, 29.00)	< 0.001

APACHE II, acute phychologic assessment and health evaluation II; CVD, cardiovascular disease; GCS, Glasgow coma scale; SAPS II, Simplified Acute Physiology Score II; SOFA, Sequential Organ Failure Assessment.

failure and gradually reducing ventilator support, conducting initial assessment for extubation, monitoring physiological indicators such as MIP and rapid shallow breathing index (RSBI), conducting a spontaneous breathing trial (SBT), performing actual extubation and performing reintubation if needed. Prolonged weaning from mechanical ventilation constitutes 40–50% of the total mechanical ventilation time, thereby increasing patient mortality.[5] Some deaths result from complications of mechanical ventilation, especially VAP and airway damage.[6 7] Patients with prolonged ventilation consume 37% of healthcare resources.[8] Unplanned extubation occurs in 0.5–35.8% of cases, with 83% of such cases being self-extubation. Moreover, approximately 50% of these patients do not require reintubation, indicating that many patients spend unnecessary time on mechanical ventilation.[8] In case of no delay, the mortality rate is 12%, whereas it increases to 27% in case of delays.[9] Therefore, daily systematic assessment of extubation potential reduces ventilation duration and mortality, making it an independent predictor of difficult weaning from mechanical ventilation and survival.

Extubation failure, defined as SBT failure or the need for reintubation within 48 hours post-extubation, has various indicators, such as rapid breathing and tachycardia.[10] The prevalence of extubation failure has been reported to be 61%, 41% and 38% in patients with chronic obstructive pulmonary disease, neurological disorders and hypoxemia, respectively.[11] Evidence suggests that various factors are related to extubation failure, including respiratory load, cardiac load, neuromuscular capacity, psychosocial factors and metabolic and endocrine factors.[12] Considering the factors affecting extubation across all body systems, it is important to develop a diagnostic system for the early prediction of difficult wean from mechanical ventilation. Thus, we used retrospective data to establish a diagnostic system based on multiple factors to predict

Table 2 The characteristics of patients in different stages in hospital

Variable	Outcome of extubation			
	Total (n=703)	Success (n=584)	Difficult (n=119)	*P* value
Status of ICU admission				
D-dimer	0.69 (0.39, 1.48)	0.63 (0.38, 1.35)	0.95 (0.44, 2.11)	0.002
ALT	22.00 (13.00, 43.75)	21.00 (12.00, 41.00)	24.00 (15.00, 58.00)	0.056
AST	30.50 (19.00, 65.75)	30.00 (17.00, 59.00)	38.00 (22.00, 90.00)	0.006
Globulin	23.20 (19.40, 26.60)	22.90 (19.20, 26.00)	24.60 (19.90, 27.90)	0.012
LDH	307 (236, 423)	293 (228, 405)	341 (283, 480)	<0.001
EF%	57.00 (54.00, 59.00)	57.00 (54.00, 60.00)	55.00 (50.00, 57.00)	<0.001
BNP	211 (75.4, 690)	197 (66.5, 648)	345 (122, 974)	0.010
24 hours before weaning				
ALT	22.00 (12.00, 40.25)	21.20 (12.00, 39.00)	23.50 (15.00, 55.75)	0.054
ALB	**30.90 (28.40, 33.40)**	**31.00 (28.60, 33.60)**	**29.90 (28.23, 32.28)**	**0.037**
Prealbumin	**11.50 (8.10, 15.50)**	**11.70 (8.40, 16.00)**	**10.30 (7.55, 13.73)**	**0.013**
BUN	**7.81 (5.58, 11.88)**	**7.60 (5.34, 11.36)**	**9.55 (6.91, 15.16)**	**<0.001**
Urine volume	1800 (106, 2900)	1790 (100, 2900)	2100 (180, 2850)	0.835
PHA	7.44 (7.41, 7.47)	7.44 (7.41, 7.47)	7.44 (7.39, 7.48)	0.262
HCO_3^-	**23.50 (20.60, 26.70)**	**23.70 (20.80, 27.00)**	**22.30 (19.40, 25.15)**	**0.001**
BE	**−0.10 (-2.80, 2.98)**	**0.03 (-2.60, 3.10)**	**−0.80 (-4.12, 1.70)**	**0.004**
Lung injury score	**3.00 (2.00, 4.00)**	**3.00 (2.00, 4.00)**	**4.00 (2.00, 4.00)**	**0.010**
RR	**19.00 (16.00, 21.00)**	**18.00 (15.00, 21.00)**	**20.00 (18.00, 22.00)**	**<0.001**
Mechanical ventilation days	**6.00 (3.00, 10.00)**	**6.00 (3.00, 9.50)**	**7.00 (4.00, 12.00)**	**0.025**
Invasive mechanical ventilation days	**5.00 (3.00, 9.00)**	**5.00 (3.00, 9.00)**	**7.00 (3.00, 11.50)**	**0.048**
EF%	**56.00 (53.00, 58.00)**	**56.00 (54.00, 58.00)**	**55.00 (50.00, 57.00)**	**0.001**
BNP	**204 (97.9, 542)**	**184 (90.0, 445)**	**436 (146, 952)**	**<0.001**
24-hour fluid balance/1000 unit	**−139 (−796, 559)**	**−200 (−901, 494)**	**204 (-452, 1170)**	**<0.001**
Use of midazolam				**0.720**
No	460 (67.45)	391 (67.18)	69 (69.00)	
Yes	222 (32.55)	191 (32.82)	31 (31.00)	
Use of dexmedetomidine				0.055
No	577 (84.60)	486 (83.51)	91 (91.00)	
Yes	105 (15.40)	96 (16.49)	9 (9.00)	
72 hours before weaning				
PCT	**0.36 (0.04, 2.62)**	**0.29 (0.04, 2.13)**	**0.92 (0.18, 5.56)**	**0.001**
GCS score	**15.00 (9.00, 15.00)**	**15.00 (10.00, 15.00)**	**10.00 (3.00, 15.00)**	**<0.001**
Invasive mechanical ventilation days	6.00 (3.00, 9.00)	6.00 (3.00, 9.00)	6.00 (3.00, 11.00)	0.194
ICU days	9.00 (5.00, 16.00)	9.00 (6.00, 15.00)	9.00 (4.00, 18.00)	0.890
SBT (n, %)				**0.005**
CPAP	**397 (59.17)**	**351 (61.36)**	**46 (46.46)**	
Others	**274 (40.83)**	**221 (38.64)**	**53 (53.54)**	
Reintubation				**<0.001**
Yes	**46 (6.67)**	**19 (3.30)**	**27 (23.68)**	
No	**644 (93.33)**	**557 (96.70)**	**87 (76.32)**	
Tracheostomy				0.174
Yes	101 (14.64)	89 (15.45)	12 (10.53)	
No	589 (85.36)	487 (84.55)	102 (89.47)	

ALB, albumin; ALT, alanine transaminase; AST, aspartate aminotransferase; BE, Base Excess; BNP, brain natriuretic peptide; BUN, blood urea nitrogen; CPAP, continuous positive airway pressure; EF%, ejection fraction; GCS, Glasgow coma scale; HCO3-, bicarbonate; ICU, intensive care unit; LDH, lactate dehydrogenase; PCT, procalcitonin; PHA, Arterial blood gas PH; RR, respiratory rate; SBT, spontaneous breathing trial.

Table 3 Risk factors of difficult weaning of the mechanical ventilation in patients in ICU

Variable	Unavertable analyses		Multivariable analyses	
	Or (95% CI)	P value	Or (95% CI)	P value
Baseline				
Age, year	1.034 (1.009 to 1.059)	**0.008**		
Males	0.834 (0.426 to 1.631)	0.595		
Clinical diagnosis				
Trauma	1.445 (0.464 to 4.484)	0.5252		
Liver diseases	0.306 (0.038 to 2.475)	0.2669		
Neurological disorders	2.165 (0.862 to 5.435)	**0.1001**		
Kidney diseases	1.486 (0.281 to 7.874)	0.6414		
Digestive system disease	0.48 (0.176 to 13.072)	0.1512		
Others	0.116 (0.015 to 0.904)	**0.0398**		
Smoking status	0.971 (0.488 to 1.934)	0.934		
Alcohol status	0.569 (0.212 to 1.524)	0.262		
Charlson Comorbidity Index	1.105 (0.948 to 1.289)	0.202		
SOFA score	1.015 (0.942 to 1.095)	0.69		
GCS score	0.889 (0.802 to 0.986)	**0.026**		
SAPS II score	1.018 (0.99 to 1.047)	0.203		
APACHE II score	1.057 (0.987 to 1.131)	0.11		
Status of admission ICU				
D-dimer	0.994 (0.962 to 1.028)	0.741		
ALT	0.999 (0.996 to 1.002)	0.456		
AST	0.999 (0.998 to 1.001)	0.451		
Globulin	0.999 (0.991 to 1.007)	0.8		
LDH	1.000 (0.999 to 1.001)	0.799		
EF%	0.966 (0.929 to 1.006)	**0.1**	0.951 (0.905 to 0.999)	0.0444
BNP	1.000 (1.000 to 1.000)	0.934		
24 hours before weaning				
ALT	1 (0.997 to 1.002)	0.706		
AST	1 (1-1)	0.99		
ALB	0.929 (0.847 to 1.019)	0.12		
Prealbumin	0.917 (0.85 to 0.989)	**0.025**		
BUN	1.044 (1 to 1.091)	**0.051**		
Urine volume	1 (0.999 to 1)	**0.026**		
PHA	50 (∞–0.063)	0.251		
HCO3-	1.003 (0.965 to 1.043)	0.871		
BE	1.035 (0.968 to 1.107)	0.314		
Lung injury score	1.425 (1.074 to 1.89)	**0.014**	1.541 (1.093 to 2.174)	0.0137
RR	0.994 (0.929 to 1.065)	0.868		
Mechanical ventilation days	1.033 (0.999 to 1.068)	**0.058**		
Invasive mechanical ventilation days	1.053 (1.009 to 1.098)	**0.016**		
EF%	0.963 (0.921 to 1.008)	**0.108**		
BNP/1000 unit	1.592 (1.183 to 2.141)	**0.002**	1.504 (1.06 to 2.132)	0.0222
24-hour fluid balance/1000 unit	1.399 (1.055 to 1.855)	**0.02**	1.582 (1.129 to 2.217)	0.0077
Use of midazolam	0.435 (0.212 to 0.894)	**0.024**		
Use of dexmedetomidine	0.126 (0.017 to 0.941)	**0.043**	0.111 (0.012 to 1.032)	0.0533

Continued

Table 3 Continued

Variable	Unavertable analyses		Multivariable analyses	
	Or (95% CI)	P value	Or (95% CI)	P value
72 hours before weaning				
PCT	1.003 (0.991 to 1.016)	0.603		
GCS score	0.822 (0.743 to 0.908)	**<0.001**		
Invasive mechanical ventilation days	1.053 (1.01 to 1.098)	**0.015**		
Days in ICU	1.027 (1.005 to 1.048)	**0.014**		
SBT (CPAP vs others)	0.199 (0.088 to 0.451)	**< 0.001**	0.091 (0.034 to 0.244)	<0.0001
Reintubation	20 (6.993 to 55.556)	**< 0.001**	43.48 (13.16 to 142.9)	<0.0001
Tracheostomy	2.101 (0.88 to 5.025)	**0.095**		

ALB, albumin; ALT, alanine transaminase; APACHE II, acute phychologic assessment and health evaluation II; AST, aspartate aminotransferase; BE, Base Excess; BNP, brain natriuretic peptide; BUN, blood urea nitrogen; CPAP, continuous positive airway pressure; EF%, ejection fraction; GCS, Glasgow coma scale; HCO3, bicarbonate; ICU, intensive care unit; LDH, lactate dehydrogenase; PCT, procalcitonin; PCT, procalcitonin; PHA, Arterial blood gas PH; RR, respiratory rate; SAPS II, Simplified Acute Physiology Score II; SBT, spontaneous breathing trial; SOFA, Sequential Organ Failure Assessment.

difficult wean from mechanical ventilation, thereby reducing failure rates and improving patient outcomes.

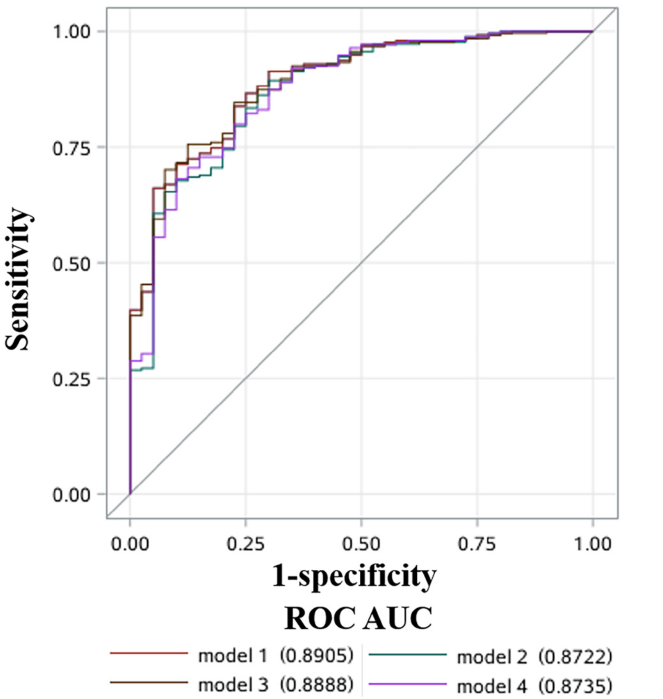
MATERIALS AND METHODS

This multicentre retrospective study was conducted by a collaborative group in China to identify factors affecting wean from mechanical ventilation and establish an early diagnostic prediction system for difficult to wean from mechanical ventilation. The collaborative group included five hospitals in China: Tianjin Third Central Hospital, Beijing Chao-Yang Hospital, Capital Medical University, Hebei General Hospital, TianJin First Center Hospital and Haihe Hospital, Tianjin University.

Patients who received mechanical ventilation in intensive care units (ICUs) at the abovementioned hospitals between 1 January 2018 and 31 December 2022 were included in this study. We included ICU patients who (1) received mechanical ventilation, (2) were aged ≥18 years and (3) underwent at least one SBT. Patients with tracheostomy and those who did not undergo SBT were excluded from this study. The decision to conduct an SBT was made by the ICU physicians based on standard clinical protocols. According to the American Thoracic Society of Intensive Care Medicine, the daily screening for SBT eligibility occurs once patients meet minimal clinical thresholds. The SBT was performed using continuous positive airway pressure (CPAP) and others (including T-tube and PSV), and its success was determined based on clinical signs such as respiratory rate (RR), tidal volume, gas exchange and patient tolerance. In accordance with the Declaration of Helsinki, this study protocol was approved by the Ethics Committees of TianJin Third Central Hospital (IRB Number: IRB2018-031-02). Because this study was retrospective, informed consent was waived.

The primary endpoint was defined as the occurrence of any of the following events: success weaning from mechanical ventilation lasting more than 48 hours, reintubation within 48 hours post-extubation or death after mechanical ventilation, whichever occurred first. According to the difficulty and duration of weaning from mechanical ventilation, the participants were categorised into three groups: simple, difficult and prolonged wean from mechanical ventilation in our clinical practice.[10 12 13] Simple wean from mechanical ventilation involved successful completion of the first SBT and subsequent successful extubation. Difficult weaning from mechanical ventilation required at least three SBTs or successful extubation within 7 days from the first SBT. Prolonged weaning from mechanical ventilation required at least three SBTs or successful extubation >7 days after the first SBT. Extubation failure was defined as SBT failure or the need for reintubation within 48 hours post-extubation. SBT failure was defined using objective indicators, such as rapid breathing, tachycardia, hypertension, hypotension, hypoxaemia, acidosis and arrhythmia, and subjective indicators, such as anxiety, distress, depression, profuse sweating and use of accessory respiratory muscles. The difficult extubation, prolonged extubation, reintubation within 48 hours of weaning and death within 48 hours of weaning are all classified as the difficult weaning group.

Using electronic medical records of hospitals, we obtained patient demographic data (age and sex), human behavioural information (smoking and alcohol status) and clinical information from baseline to ICU admission, 24 hours before weaning from mechanical ventilation and 72 hours before weaning from mechanical ventilation (including baseline characteristics such as clinical diagnosis, Charlson comorbidity index, Sequential Organ Failure Assessment (SOFA) score, Glasgow coma scale (GCS) score, Simplified Acute Physiology Score II (SAPS II) score and acute phychologic assessment and health evaluation II (APACHE II) score; status at ICU admission such as D-dimer, alanine transaminase (ALT), aspartate aminotransferase (AST), globulin, lactate dehydrogenase



ROC models	AUC	95% CI		P
Model 1	0.8905	0.8398	0.9411	Ref.
Model 2	0.8722	0.8123	0.9322	0.0131
Model 3	0.8888	0.8382	0.9394	0.6822
Model 4	0.8735	0.8143	0.9327	0.0354

Figure 1 Receiver operating characteristic curves of four predictive models for difficult weaning from mechanical ventilation. Model 1: EF% at ICU admission, lung injury score, BNP-24 h, 24 hours fluid balance, use of dexmedetomidine, SBT (CPAP vs other) and endotracheal tube reinsertion. Model 2: EF% at ICU admission, lung injury score, BNP-24 h, 24 hours fluid balance, SBT (CPAP vs other) and endotracheal tube reinsertion. Model 3: Lung injury score, BNP-24 h, 24 hours fluid balance, use of dexmedetomidine, SBT (CPAP vs other), and endotracheal tube reinsertion. Model 4: Lung injury score, BNP-24 h, 24 hours fluid balance, SBT (CPAP vs other), and endotracheal tube reinsertion. The final model was model 3.

(LDH), ejection fraction (EF%), brain natriuretic peptide (BNP); status at 24 hours before extubation such as ALT, AST, albumin (ALB), prealbumin, blood urea nitrogen (BUN), urine volume, PHA (Arterial blood gas PH), bicarbonate (HCO_3), BE (Base excess), lung injury score, RR, mechanical ventilation days, invasive mechanical ventilation days, EF%, BNP, 24 hours fluid balance, use of midazolam, and use of dexmedetomidine; Status at 72 hours before extubation such as procalcitonin (PCT), GCS score, invasive mechanical ventilation days, ICU days, SBT, endotracheal tube reinsertion, and tracheostomy).

Statistical methods

We evaluated 10 factors at baseline, 7 factors at ICU admission, 18 factors within 24 hours before weaning from mechanical ventilation and 7 factors within 72 hours before weaning from mechanical ventilation using univariate and multivariate logistic regression models. We first selected significant factors using a univariate logistic regression model and then used stepwise multivariate logistic regression to determine the three best models. We compared the receiver operating characteristic (ROC) curve and area under the ROC curve (AUC) values of the predictive models and calculated the sensitivity, specificity, accuracy, positive predictive value (PPV), negative predictive value (NPV) and likelihood ratios (LRs) for each model under the best cut-off point indicated by the Youden index. Using the best model, we established a nomogram model to predict difficult weaning from mechanical ventilation among patients admitted to ICU. The complete case analysis was used to deal with the missing data.

All statistical analyses were performed using SAS software (version 9.4, SAS Institute, Inc, Cary, NC, USA), with a statistically significant level (two-sided) of 0.05.

Patient and public involvement

None.

RESULTS

Among 1365 initially screened patients, 703 patients aged 56–79 (median: 69) years with 63.02% males (n=443) were included in this study (table 1). Of these patients, 584 with a median age of 67 (range: 55–77) years were successfully weaned, and 119 with a median age of 74 (range: 64–82) years experienced difficult weaning from mechanical ventilation. Those with difficult weaning were more likely to be older; have respiratory, neurological or kidney diseases; have higher Charlson comorbidity index, SOFA, SAPS II and APACHE II scores; and have lower GCS scores (all P values <0.05).

At the time of ICU admission, patients in the difficult group exhibited more severe organ dysfunction, higher BNP levels and lower EF% than those in the success group (table 2). The D-dimer, AST, globulin, LDH and BNP levels were significantly higher in the difficult group than in the success group (all P values <0.05). The EF% was significantly lower in the difficult group than in the success group (p<0.001). Within 24 hours before weaning, the levels of ALB, prealbumin, BUN, HCO_3^-, BE and BNP as well as lung injury score, RR, mechanical ventilation time, invasive mechanical ventilation time, EF% and fluid balance all showed statistically significant differences between the difficult and success groups (all P values <0.05). The difficult group had more severe organ dysfunction, poorer nutritional status, higher 24 hours fluid balance and longer mechanical ventilation and invasive mechanical ventilation times. Within 72 hours before weaning, significant differences in PCT, GCS score, SBT mode and reintubation rate were observed between the difficult and success groups (all P values <0.05). Patients who were difficult to wean from mechanical ventilation showed higher infection indicators, lower GCS scores, lower usage of CPAP mode during SBT and higher reintubation rates.

Table 4 Estimated parameters and 95% CI for the final model

Values	Estimates	Lower limit	Upper limit	P
Sensitivity/TPR/Recall	0.7559	0.7031	0.8087	<0.0001
Specificity/TNR	0.875	0.7725	0.9775	<0.0001
PPV/Precision	0.9746	0.9527	0.9966	<0.0001
NPV	0.3608	0.2653	0.4564	<0.0001
FPR/FDR	0.02538	0.003418	0.04734	0.0235
FPR	0.125	0.02251	0.2275	0.0168
FNR/FOR	0.6392	0.5436	0.7347	<0.0001
FNR	0.2441	0.1913	0.2969	<0.0001
Accuracy	0.7721	0.7242	0.8201	<0.0001
LR+	6.0473	1.0711	11.0234	0.0172
LR–	0.279	0.2103	0.3476	<0.0001

FDR, false discovery rate; FNR, false negative rate; FOR, false omission rate; FPR, false positive rate; LR–, negative likelihood ratio; LR+, positive likelihood ratio; NPV, negative predictive value; PPV, positive predictive value; TNR, True negative rate; TPR, True positive rate.

The univariate analysis screened all 42 factors at baseline, ICU admission, 24 hours before weaning and 72 hours before weaning; 22 factors were selected (p≤0.10) for further multivariate analysis (table 3). After stepwise selection, the EF% at ICU admission; lung injury score, BNP at 24 hours, 24 hours fluid balance and dexmedetomidine use within 24 hours before weaning; and SBT and endotracheal tube reinsertion within 72 hours before weaning were selected as independent risk factors for difficult weaning from mechanical ventilation in patients admitted to the ICU (all P values <0.05).

Based on the results of variable selection and clinical experience, we established four predictive models (figure 1). Model one comprised EF% at ICU admission, lung injury score, BNP-24 h, 24 hours fluid balance, use of dexmedetomidine, SBT (CPAP vs other), and endotracheal tube reinsertion. Model two included EF% at ICU admission, lung injury score, BNP-24 h, 24 hours fluid balance, SBT (CPAP vs other), and endotracheal tube reinsertion. Model three consisted of lung injury score, BNP-24 h, 24 hours fluid balance, use of dexmedetomidine, SBT (CPAP vs other), and endotracheal tube reinsertion. Model four comprised lung injury score, BNP-24 h, 24 hours fluid balance, SBT (CPAP vs other), and endotracheal tube reinsertion. The corresponding AUCs of the four models were 0.8905 (95% CI: 0.8398, 0.9411), 0.8722 (0.8123, 0.9322), 0.8888 (0.8382, 0.9394), and 0.8735 (0.8143, 0.9327). Compared with model one (full model), only model two was not significantly different (p=0.6822), exhibiting both fewer variables and good predictive value. The highest sensitivity, specificity, PPV, NPV, accuracy, LR+, and LR– were 0.7559 (0.7031,

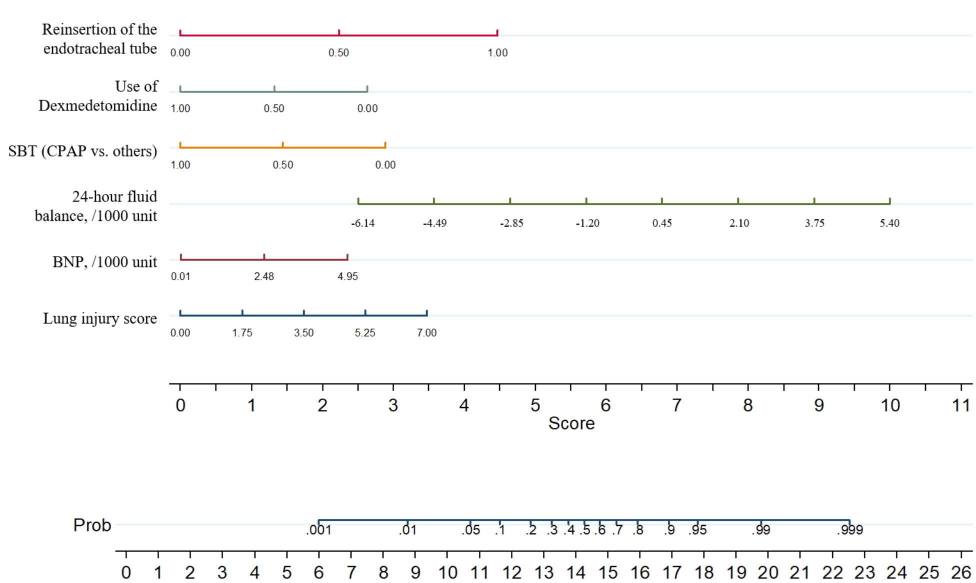


Figure 2 Nomogram model for predicting difficult weaning from mechanical ventilation in critically ill patients based on the final model (model 3).

0.8087), 0.875 (0.7725, 0.9775), 0.9746 (0.9527, 0.9966), 0.3608 (0.2653, 0.4564), 0.7721 (0.7242, 0.8201), 6.0743 (1.0711, 11.0234), and 0.279 (0.2103, 0.3476), respectively (table 4). Finally, we established a nomogram model based on model 3 (figure 2).

DISCUSSION

In this retrospective study, we analysed 42 factors at different time points (baseline, ICU admission, 24 hours and 72 hours before weaning) and established a six-factor predictive model for difficult to wean from mechanical ventilation in ICU patients. Our model, which included EF% at ICU admission, lung injury score, BNP-24 h, 24 hours fluid balance, SBT (CPAP vs other) mode and endotracheal tube reinsertion, demonstrated an AUC of 0.8722, with a sensitivity of 0.7559 and specificity of 0.875, suggesting good predictive performance.

Previous studies have attempted similar predictive models. A study based on body mass index at admission, occlusion pressure at 0.1 s (P0.1) and heart-rate analysis parameters (LF/HF; both measured before SBT), and heart rate during SBT (global performance 62%–83%) reported an AUC of 0.74.[13] Machine learning models have also been used to predict ventilation duration, with key predictors including vasopressor use, pH, and SOFA score.[14] Other studies have highlighted the significance of ABG variables, such as $PaCO_2$ and PaO_2, in predicting prolonged mechanical ventilation.[15] Our model expands on prior work by incorporating a broader range of clinical parameters spanning the ICU course.

Lung injury is a critical factor influencing extubation outcomes in ICU patients. While previous studies have identified P/F ratio and alveolar-arterial oxygen difference as predictors of extubation failure,[16 17] our model suggests that a higher lung injury score is a protective factor, potentially indicating closer monitoring and intervention in these patients.

BNP-24 h has been widely recognised as a predictor of extubation failure, particularly in patients with cardiovascular dysfunction.[18 19] BNP and N-terminal prohormone BNP (NT-proBNP) levels reflect ventricular stress and correlate with weaning failure due to cardiac dysfunction. Studies have shown that BNP levels increase during heart failure and decrease with diuresis, making it a valuable biomarker for predicting extubation outcomes.[20–22] Notably, changes in BNP levels before and after SBT can indicate cardiac stress responses, further influencing weaning outcomes.

Fluid balance is another significant factor in predicting weaning outcomes. Specifically, a more positive 24 hours fluid balance before weaning has been linked to extubation failure.[23] However, cumulative fluid balance since admission may have an even higher impact on predicting wean outcomes.[24] Moreover, studies suggest that achieving a negative fluid balance (NFB) is beneficial for weaning success, though excessive fluid removal does not necessarily improve wean outcomes.[25] Another study revealed that patients with a cumulative NFB are more likely to be successfully weaned than those with positive cumulative balance.[26] These findings underscore the importance of carefully managing fluid status before weaning.

SBT parameters also play a crucial role in wean success. High RSBI, positive fluid balance and pneumonia-related mechanical ventilation have been linked to extubation failure following a successful SBT.[27] The duration and mode of SBT are significant considerations, with studies showing that shorter, less demanding trials (eg, 30 min of pressure support ventilation) may improve weaning success compared with more prolonged T-piece trials.[28] Current predictive models for extubation failure within the first 24 hours post-extubation have an accuracy of approximately 70%, emphasising the complexity of predicting weaning outcomes.[29]

Endotracheal tube reinsertion is a crucial indicator of extubation failure, occurring in up to 20% of ICU patients after failed extubation attempts.[30] Factors such as cuff leak tests have been explored as predictors of extubation failure, but current assessment methods remain imprecise.[31] Strategies such as using a supraglottic device or tube exchanger may mitigate the risks associated with failed extubations, emphasising the need for improved predictive tools in ICU settings.[31]

Although EF% is not widely reported as a direct predictor for extubation failure in ICU patients, various studies have identified predictors such as prolonged mechanical ventilation, advanced age and secretion burden as key contributors to weaning difficulties.[32 33] EF% should be considered alongside other clinical variables when assessing weaning readiness.

This study systematically evaluated 10 baseline factors, seven ICU admission factors, 18 factors within 24 hours before weaning and seven within 72 hours before weaning, leading to the development of a six-factor nomogram model for predicting extubation failure from mechanical ventilation in ICU patients. However, several limitations must be acknowledged. The retrospective nature of the study may introduce potential biases and limit the ability to establish causality between the identified factors and wean outcomes. The study's findings are based on data from a single country, which might limit the applicability of the results to different populations and healthcare systems globally. Validation of the predictive model in prospective studies and diverse patient populations is necessary to confirm its utility and accuracy in broader clinical practice.

CONCLUSIONS

We established a model comprising six factors (AUC of 0.8722) to predict difficult weaning from mechanical ventilation in ICU patients. The highest sensitivity and specificity were 0.7559 and 0.875, respectively. However, well-designed studies are warranted to determine whether the model can be extended to other populations.

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