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Development and validation of a mechanical power-oriented prediction model of weaning failure in mechanically ventilated patients: a retrospective cohort study

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ABSTRACT

Objective To develop and validate a mechanical power (MP)-oriented prediction model of weaning failure in mechanically ventilated patients.

Design A retrospective cohort study.

Setting Data were collected from the large US Medical Information Mart for Intensive Care-IV (MIMIC-IV) V.1.0, which integrates comprehensive clinical data from 76 540 intensive care unit (ICU) admissions from 2008 to 2019.

Participants A total of 3695 patients with invasive mechanical ventilation for more than 24 hours and weaned with T-tube ventilation strategies were enrolled from the MIMIC-IV database.

Primary and secondary outcome Weaning failure.

Results All eligible patients were randomised into development cohorts (n=2586, 70%) and validation cohorts (n=1109, 30%). Multivariate logistic regression analysis of the development cohort showed that positive end-expiratory pressure, dynamic lung compliance, MP, inspired oxygen concentration, length of ICU stay and invasive mechanical ventilation duration were independent predictors of weaning failure. Calibration curves showed good correlation between predicted and observed outcomes. The prediction model showed accurate discrimination in the development and validation cohorts, with area under the receiver operating characteristic curve values of 0.828 (95% CI: 0.812 to 0.844) and 0.833 (95% CI: 0.809 to 0.857), respectively. Decision curve analysis indicated that the predictive model was clinically beneficial.

Conclusion The MP-oriented model of weaning failure accurately predicts the risk of weaning failure in mechanical ventilation patients and provides valuable information for clinicians making decisions on weaning.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Multiple imputation was used to impute variables with <15% missing data to minimise the bias caused by missing values.
⇒ Continuous predictors with non-linear trends were transformed into categorical variables based on their distribution and clinical significance, increasing the utility of this prediction model.
⇒ The nomogram was constructed using the multivariable logistic regression analysis with the R package 'rms'.
⇒ The area under the receiver operating characteristic curve, calibration curves and decision curve analysis were enrolled to evaluate the performance of the prediction model in the development and validation cohort.
⇒ We could not compare the performance of the mechanical power-oriented model with the existing model (eg, the modified Burns Wean Assessment Program scores).

INTRODUCTION

Mechanical ventilation is an advanced respiratory support technique widely used in the intensive care unit (ICU).[1] Both prolonged ventilation and premature weaning are associated with poor patient outcomes, resulting in an increased risk of ventilator-associatedpneumonia, longer hospital stays and higher mortality.[2] Therefore, it is important to accurately predict the risk of weaning failure in mechanically ventilated patients and optimise the weaning time.[3] The reasons for weaning failure are complicated, with airway and pulmonary dysfunction, and the imbalance of respiratory load and respiratory muscle function as main influencing factors.[4–6] Traditional weaning evaluation methods include Rapid Shallow Breathing Index (RSBI) and spontaneous breathing test (SBT). However, the specificity of RSBI is affected by various factors such as ventilator settings, health state and body position.[7] In addition, between 3% and 19% of the patients who passed the SBT were reintubated due to weaning failure,[7 8] which may be related to the inaccuracy of short-term

SBTs in reflecting airway and lung function, and the lack of objectivity in assessing the endurance of respiratory muscles to spontaneous breathing load.

Mechanical power (MP) is the energy delivered by the ventilator to the entire respiratory system per unit time.[9] MP can be used as a dynamic and objective measure of the energy load on the respiratory muscles before weaning, and accurately reflects the airway and lung function status. Based on multiple studies, Ghiani *et al*[10 11] concluded that MP can be used to assess the workload of the respiratory muscles before SBT and to guide the weaning of patients with long-term mechanical ventilation. In this study, we aimed to further develop and validate an MP-oriented weaning failure prediction model through a retrospective analysis of the Medical Information Mart for Intensive Care-IV (MIMIC-IV) database and use nomograms to visualise the model for evaluation of weaning failure to assist clinicians in making decisions about weaning.

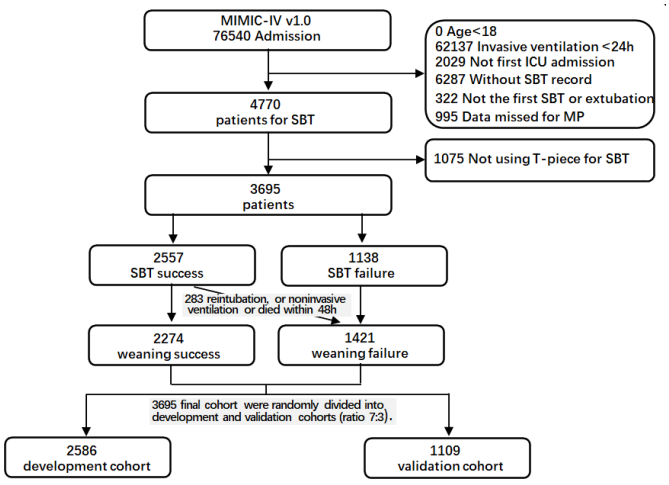

Figure 1 Flow chart of the study. ICU, intensive care unit; MIMIC-IV, Medical Information Mart for Intensive Care-IV; MP, mechanical power; SBT, spontaneous breathing test.

METHODS

Data source

We performed a retrospective analysis of data from the large US MIMIC-IV V.1.0, which integrates comprehensive clinical data from 76 540 intensive care unit (ICU) admissions at Beth Israel Deaconess Medical Center in Boston, Massachusetts, USA, from 2008 to 2019. Since all patient identification information was de-identified, the requirement for informed consent was waived.[12] The researcher (YY) completed the National Institutes of Health (NIH) 'Protecting Human Research Participants' online course and obtained access to the database (Certification Number: 41699414).

Study cohort

After screening the MIMIC-IV database, a total of 3695 patients with invasive mechanical ventilation (IMV) for more than 24 hours and weaned with T-tube ventilation strategies were included in this study. The research cohort was randomly divided into development and validation cohorts at a ratio of 7:3. The development cohort was used to build the predictive model, and the validation cohort was used for validation. Each cohort was further divided into weaning success and weaning failure groups according to the weaning outcome (figure 1).

Data extraction

Data extraction was performed using structured query language with the following analysis variables: (1) basic demographic data (age, sex, body mass index (BMI), smoking history and Sequential Organ Failure Score (SOFA)); (2) time-related data, time to first intubation, the start and end time of mechanical ventilation, the start time of the first SBT, the successful and aborted time of SBT, the time of the first extubation, the time of the second intubation, the time of the first non-invasive ventilation after extubation, the length of ICU stay and the duration of IMV before SBT; (3) combined symptoms, extracting comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, congestive heart failure, chronic kidney disease, stroke) according to the International Classification Of Diseases (ICD)-9 codes recorded in the MIMIC-IV database; (4) the average value of respiratory mechanics parameters (tidal volume (V_T), respiratory rate (RR), peak inspiratory pressure (P_{peak}), plateau pressure (P_{plat}), end-expiration positive pressure (PEEP), minute ventilation, inspired oxygen concentration (FiO_2)) 4 hours before the first SBT; (5) laboratory indicators (white blood cell count (WBC), serum creatinine (SCr)) before SBT, and hourly urine output before SBT (urine output rate (Uorate)); and (6) vital signs (heart rate (HR), respiration (breathing frequency (BF)), mean arterial pressure, blood oxygen saturation (SPO_2); arterial blood gas analysis during SBT, including PH, arterial oxygen partial pressure (PO_2), arterial partial pressure of carbon dioxide (PCO_2), oxygenation index (PO_2/FiO_2, PF)) during SBT.

Calculation of MP

After excluding patients with missing variables required to calculate MP, including patients with missing P_{plat} (ie, all patients in the study had P_{plat} measurements in volume control mode before SBT), we extracted data according to the simplified MP equation in the volume-controlled model proposed by Gattinoni *et al*[9] as follows:

$$MP\ (J/min)=0.098\times V_T\times RR\times(P_{peak}-0.5\times\Delta P).$$

Where V_T represents tidal volume, RR represents respiratory rate, P_{peak} represents peak inspiratory pressure and ΔP represents driving pressure.

Driving pressure (ΔP) in the ventilation mode was calculated using P_{plat} and PEEP:

$$\Delta P\ (cmH_2O)=P_{plat}-PEEP.$$

Where P_{plat} represents plateau pressure, and PEEP represents end-expiration positive pressure.

Dynamic lung compliance (C_{dyn}) refers to the change in lung volume caused by a unit pressure change, reflecting

the compliance of the overall respiratory system[11] and is calculated as follows:

C_{dyn} (mL/cmH_2O)=V_T/(P_{peak}–PEEP).

Where V_T represents tidal volume, P_{peak} represents peak inspiratory pressure and PEEP represents end-expiration positive pressure.

Definition of weaning failure

Weaning failure was defined as failure of SBT (ie, premature termination of SBT), or the need for reintubation or non-invasive ventilation within 48 hours of cessation of mechanical ventilation, or death within 48 hours of extubation.[13] Early termination of SBT in the MIMIC-IV database was assigned as follows: RR >35 beats/min >5 min; heart rate >140 beats/min; blood pressure >180 or <90 mm Hg; new-onset arrhythmia; pulse oximetry (SpO_2) <90% >2 min; with use of accessory respiratory muscles. SBT was discontinued when the clinicians at the bedside observed that the patient's vital signs exceeded the above indicators. Only patients on T-tube ventilation during weaning were included in this study to reduce the influence and bias of different SBT modalities on weaning outcomes.[14]

Statistical analysis

Variables with >15% missing data in the study were excluded, and multiple imputation was used to impute variables with <15% missing data to minimise the bias caused by missing values.[15] A linear trend test was performed on continuous predictors.[16] Variables with non-linear trends in predictors and weaning outcomes were transformed into categorical variables based on the distribution of the independent variables and their clinical significance. Normally distributed measurement data were expressed as the mean±SD, and t-test was used for comparisons between groups. Non-normally distributed measurement data were expressed as the median and IQR and compared using the Mann-Whitney U test or the Kruskal-Wallis H test. Enumeration data were expressed as numbers (percentages), and the χ^2 test was used for comparison between groups.

A logistic risk regression model was used to screen important predictors of weaning outcome, and the results were expressed as OR with 95% CI. To limit the variables and increase the practicability of the final model, variables with p<0.05 in the univariate analysis were included in the multivariate regression model for variable screening using the backward method. A nomogram was constructed based on the results of the multivariate analysis, and the discrimination and accuracy of the model were evaluated by receiver operating characteristic curve (ROC) and calibration curve.[17] The accuracy of the nomogram, MP and C_{dyn} in predicting the outcome of weaning failure was further compared by area under the ROC (AUC). Decision curve analysis (DCA) was used to evaluate the clinical validity of the predictive model.

All tests were two-tailed, and p<0.05 was set as the threshold for statistical significance. Data analysis was performed using Stata V.16.0 (StataCorp, Texas, USA) software and R software V.4.1.2 (2021-11-01).[18] Graphs were drawn with the R package 'ggplot 2' V.3.3.5.[19]

Patient and public involvement

Patients and/or the public were not directly involved in this study.

RESULTS

Baseline characteristics of the development cohort and validation cohort

By screening data in the MIMIC-IV from 2008 to 2019, we identified 3695 patients with IMV for more than 24 hours who were weaned by T-tube ventilation strategy. This cohort comprised 2274 patients (61.5%) who were successfully weaned and 1421 patients who failed weaning (38.5%) (figure 1). Weaning failure patients included 1138 patients (80.1%) who failed SBT, and 283 patients (19.9%) who were reintubated, received non-invasive ventilation or died 48 hours after weaning. Eligible patients were randomised into a development cohort (n=2586, 70%) and a validation cohort (n=1109, 30%). Table 1 summarises the demographic and clinical baseline characteristics of the different weaning outcome groups in the development and validation cohorts. See detailed comparison of continuous variables between groups in supplementary materials (online supplemental tablea S1 and S2). The baseline characteristics of the development and validation cohorts were balanced.

Prognostic factors in the development cohort

Variables such as basic demographics, and respiratory mechanics, laboratory and clinical parameters in the development cohort were further tested by univariate regression analysis (table 2). BMI, SOFA, RR, PEEP, P_{plat}, P_{peak}, MP, C_{dyn}, FiO_2, WBC, SCr, Uorate, HR, BF, MBP, SPO_2, PH, PF, the length of ICU stay and duration of IMV at the first SBT were identified as potential predictors of weaning failure (p<0.05). Incorporating these predictors into a multivariate logistic regression equation showed that PEEP, MP, C_{dyn}, FiO_2, the length of ICU stay and duration of IMV before the first SBT were independent predictors of weaning failure (table 2). Analyses showed that higher PEEP is associated with an increased risk of weaning failure (<5 vs 5–8, ≥8, OR=1.34, 3.52, both p<0.05), and patients with high MP had the highest risk of weaning failure (≤5 vs 5–10, 10–15, ≥15, OR=2.52, 3.90, 4.55, all p<0.001), followed by patients with low C_{dyn} (≥50 vs 40–50, 30–40, ≤30, OR=3.02, 3.42, 4.44, all p<0.001). The risk of weaning failure in patients with high FiO_2 was higher than that in patients with low FiO_2 (OR=1.37, p=0.002). Additionally, longer ICU days (<7 vs ≥7, OR=2.43, p<0.001) and IMV duration (<3 vs ≥3, OR=2.33, p<0.001) were associated with a higher risk of higher weaning failure.

A prognostic nomogram of weaning failure

A predictive model of weaning failure in patients with IMV was constructed based on the six independent predictors

Table 1 Baseline characteristics of the development and validation cohorts

Variables	Development cohort				Validation cohort			
	Weaning failure (n=995)	Weaning success (n=1591)	Total (n=2586)	P value	Total (n=1109)	Weaning success (n=683)	Weaning failure (n=426)	P value
Age (years)				0.474				0.417
≤65	1170 (45.2)	711 (44.7)	459 (46.1)		514 (46.3)	310 (45.4)	204 (47.9)	
>65	1416 (54.8)	880 (55.3)	536 (53.9)		595 (53.7)	373 (54.6)	222 (52.1)	
Gender				0.664				0.097
Female	1121 (43.3)	695 (43.7)	426 (42.8)		472 (42.6)	304 (44.5)	168 (39.4)	
Male	1465 (56.7)	896 (56.3)	569 (57.2)		637 (57.4)	379 (55.5)	258 (60.6)	
BMI (kg/m^2)	27.9 (24.5–32.4)	27.6 (24.4–31.6)	28.4 (24.7–34.0)	0.001	27.9 (24.3–32.7)	27.8 (24.2–32.3)	28.4 (24.6–33.2)	0.194
Smoking history				0.740				0.288
No	2353 (91.0)	1450 (91.1)	903 (90.8)		1027 (92.6)	637 (93.3)	390 (91.5)	
Yes	233 (9.0)	141 (8.9)	92 (9.2)		82 (7.4)	46 (6.7)	36 (8.5)	
SOFA	7 (4–10)	6 (4–9)	8 (5–11)	<0.001	7 (5–10)	7 (4–9)	8 (5–11)	<0.001
Hypertension				0.543				0.917
No	1537 (59.4)	953 (59.9)	584 (58.7)		679 (61.2)	419 (61.3)	260 (61.0)	
Yes	1049 (40.6)	638 (40.1)	411 (41.3)		430 (38.8)	264 (38.7)	166 (39.0)	
Diabetes mellitus				0.108				0.702
No	1807 (69.9)	1130 (71.0)	677 (68.0)		750 (67.6)	459 (67.2)	291 (68.3)	
Yes	779 (30.1)	461 (29.0)	318 (32.0)		359 (32.4)	224 (32.8)	135 (31.7)	
COPD				0.839				0.888
No	2428 (93.9)	1495 (94.0)	933 (93.8)		1011 (91.2)	622 (91.1)	389 (91.3)	
Yes	158 (6.1)	96 (6.0)	62 (6.2)		98 (8.8)	61 (8.9)	37 (8.7)	
Congestive heart failure				0.286				0.455
No	1840 (71.2)	1144 (71.9)	696 (69.9)		748 (67.4)	455 (66.6)	293 (68.8)	
Yes	746 (28.8)	447 (28.1)	299 (30.1)		361 (32.6)	228 (33.4)	133 (31.2)	
Chronic kidney disease				0.336				0.308
No	2019 (78.1)	1252 (78.7)	767 (77.1)		838 (75.6)	509 (74.5)	329 (77.2)	
Yes	567 (21.9)	339 (21.3)	228 (22.9)		271 (24.4)	174 (25.5)	97 (22.8)	
Stroke				0.766				0.159
No	2079 (80.4)	1282 (80.6)	797 (80.1)		883 (79.6)	553 (81.0)	330 (77.5)	
Yes	507 (19.6)	309 (19.4)	198 (19.9)		226 (20.4)	130 (19.0)	96 (22.5)	
V_T (mL)	451 (394–510)	452 (392–519)	449 (397–505)	0.272	452 (396–515)	451 (391–520)	454 (401–512)	0.681
RR (bpm)				<0.001				<0.001
≤20	1621 (62.7)	1091 (68.6)	530 (53.3)		689 (62.1)	454 (66.5)	235 (55.2)	
>20	965 (37.3)	500 (31.4)	465 (46.7)		420 (37.9)	229 (33.5)	191 (44.8)	
PEEP (cmH_2O)				<0.001				<0.001
<5	312 (12.1)	268 (16.8)	44 (4.4)		146 (13.2)	122 (17.9)	24 (5.6)	
5–8	1575 (60.9)	1071 (67.3)	504 (50.7)		674 (60.8)	460 (67.3)	214 (50.2)	
≥8	699 (27.0)	252 (15.8)	447 (44.9)		289 (26.1)	101 (14.8)	188 (44.1)	
P_{plat} (cmH_2O)	17.5 (15.0–20.4)	17.0 (14.0–20.0)	19.0 (16.0–22.0)	<0.001	17.5 (15.0–21.0)	17.0 (14.0–20.0)	19.0 (15.5–22.0)	<0.001
P_{peak} (cmH_2O)				<0.001				<0.001
≤20	1325 (51.2)	1035 (65.1)	290 (29.1)		585 (52.8)	452 (66.2)	133 (31.2)	
20–25	699 (27.0)	362 (22.8)	337 (33.9)		283 (25.5)	142 (20.8)	141 (33.1)	
≥25	562 (21.7)	194 (12.2)	368 (37.0)		241 (21.7)	89 (13.0)	152 (35.7)	
MP (J/min)				<0.001				<0.001

Continued

Table 1 Continued

Variables	Development cohort				Validation cohort			
	Weaning failure (n=995)	Weaning success (n=1591)	Total (n=2586)	P value	Total (n=1109)	Weaning success (n=683)	Weaning failure (n=426)	P value
≤5	303 (11.7)	285 (17.9)	18 (1.8)		144 (13.0)	136 (19.9)	8 (1.9)	
5–10	781 (30.2)	597 (37.5)	184 (18.5)		336 (30.3)	246 (36.0)	90 (21.1)	
10–15	743 (28.7)	418 (26.3)	325 (32.7)		307 (27.7)	181 (26.5)	126 (29.6)	
≥15	759 (29.4)	291 (18.3)	468 (47.0)		322 (29.0)	120 (17.6)	202 (47.4)	
C_{dyn} (mL/cmH_2O)				<0.001				<0.001
≥50	618 (23.9)	545 (34.3)	73 (7.3)		279 (25.2)	248 (36.3)	31 (7.3)	
40–50	321 (12.4)	214 (13.5)	107 (10.8)		141 (12.7)	89 (13.0)	52 (12.2)	
30–40	669 (25.9)	373 (23.4)	296 (29.7)		279 (25.2)	145 (21.2)	134 (31.5)	
≤30	978 (37.8)	459 (28.8)	519 (52.2)		410 (37.0)	210 (29.4)	209 (49.1)	
FiO_2 (%)				<0.001				<0.001
≤40	1552 (60.0)	1075 (67.6)	477 (47.9)		687 (61.9)	479 (70.1)	208 (48.8)	
>40	1034 (40.0)	516 (32.4)	518 (52.1)		422 (38.1)	204 (29.9)	218 (51.2)	
WBC (×10^9/L)	11.8 (8.8–15.8)	11.4 (8.5–15.3)	12.6 (9.3–16.8)	<0.001	11.8 (9.0–15.2)	11.5 (8.9–14.7)	12.4 (9.3–15.8)	0.014
SCr (mg/dL)				<0.001				0.276
≤1.1	1235 (47.8)	818 (51.4)	417 (41.9)		528 (47.6)	334 (48.9)	194 (45.5)	
>1.1	1351 (52.2)	773 (48.6)	578 (58.1)		581 (52.4)	349 (51.1)	232 (54.5)	
Uorate (mL/kg/h)				0.001				0.037
≤0.63	1281 (49.5)	747 (47.0)	534 (53.7)		521 (47.0)	304 (44.5)	217 (50.9)	
>0.63	1305 (50.5)	844 (53.0)	461 (46.3)		588 (53.0)	379 (55.5)	209 (49.1)	
HR (bpm)				0.036				0.001
≤90	1658 (64.1)	1045 (65.7)	613 (61.6)		729 (65.7)	474 (69.4)	255 (59.9)	
>90	928 (35.9)	546 (34.3)	382 (38.4)		380 (34.3)	209 (30.6)	171 (40.1)	
BF (bpm)	18.5 (16.0–22.0)	18.0 (15.0–21.0)	20.0 (16.5–24.0)	<0.001	18.5 (15.5–22.0)	18.0 (15.0–21.5)	20.0 (16.0–23.8)	<0.001
MBP (mm Hg)	75 (68–84)	76 (68–86)	74 (67–82)	<0.001	75 (68–84)	75 (68–85)	74 (68–84)	0.189
SPO_2 (%)	98 (97–100)	99 (97–100)	98 (96–100)	<0.001	98 (96–100)	99 (97–100)	98 (96–100)	0.001
PH	7.39 (7.34–7.44)	7.40 (7.35–7.44)	7.38 (7.33–7.43)	0.003	7.40 (7.34–7.44)	7.40 (7.36–7.44)	7.38 (7.32–7.44)	0.006
PO_2 (mm Hg)	106 (85–130)	108 (86–132)	104 (84–128)	0.336	105 (84–131)	104 (87–132)	107 (81–130)	0.755
PCO_2 (mm Hg)	39 (34–44)	39 (34–44)	39 (34–45)	0.856	39 (34–45)	38 (34–44)	39 (34–46)	0.636
PF (mm Hg)	242 (182–320)	254 (195–333)	228 (166–305)	<0.001	238 (174–325)	248 (189–338)	226 (160–310)	0.012
ICU days				<0.001				<0.001
<7	1341 (51.9)	1047 (65.8)	294 (29.5)		564 (50.9)	447 (65.4)	117 (27.5)	
≥7	1245 (48.1)	544 (34.2)	701 (70.5)		545 (49.1)	236 (34.6)	309 (72.5)	
IMV duration				<0.001				<0.001
<3	1344 (52.0)	1057 (66.4)	287 (28.8)		570 (51.4)	453 (66.3)	117 (27.5)	
≥3	1242 (48.0)	534 (90.4)	708 (71.2)		539 (48.6)	230 (33.7)	309 (72.5)	

Data are median (IQR) or n/total (%).
BF, breathing frequency; BMI, body mass index; C_{dyn}, dynamic lung compliance; COPD, chronic obstructive pulmonary disease; FiO_2, inspired oxygen concentration; ICU, intensive care unit; IMV, invasive mechanical ventilation; MBP, mean blood pressure; MP, mechanical power; PEEP, positive end-expiratory pressure; PF, arterial partial pressure of oxygen (PaO_2) divided by the inspired oxygen concentration (FiO_2); P_{peak}, peak inspiratory pressure; P_{plat}, plateau pressure; RR, respiratory rate; SCr, serum creatinine; SOFA, Sequential Organ Failure Assessment; SPO_2, pulse oximetry; Uorate, urine output rate; V_T, tidal volume; WBC, white blood cell.

identified in the multivariate logistic regression model, and presented as a nomogram (figure 2). As shown in the nomogram, corresponding scores were assigned on the scale according to the OR value of each factor in these variables, with higher OR values corresponding to higher risk scores. The probability of weaning failure is predicted by summing the scores calculated for each prognostic factor in the nomogram. For instance, one patient with

Table 2 Univariate and multivariable analyses for the relationship between weaning success and weaning failure in the development cohort

	Univariate model			Multivariable model		
Variables	**OR**	**95% CI**	**P value**	**OR**	**95% CI**	**P value**
BMI (kg/m^2)	1.02	1.01 to 1.04	<0.001			
SOFA	1.07	1.05 to 1.09	<0.001			
RR (bpm)						
≤20	1 (reference)					
>20	1.91	1.63 to 2.25	<0.001			
PEEP (cmH_2O)						
<5	1 (reference)			1 (reference)		
5–8	1.15	0.82 to 1.48	<0.001	1.34	1.07 to 1.69	0.012
≥8	2.97	2.58 to 3.36	<0.001	3.52	2.56 to 4.86	<0.001
P_{plat} (cmH_2O)	1.14	1.12 to 1.16	<0.001			
P_{peak} (cmH_2O)						
≤20	1 (reference)					
20–25	1.20	1.00 to 1.40	<0.001			
≥25	1.91	1.70 to 2.13	<0.001			
MP (J/min)			<0.001			
≤5	1 (reference)			1 (reference)		
5–10	1.59	1.08 to 2.09	<0.001	2.52	1.51 to 4.41	<0.001
10–15	2.51	2.01 to 3.01	<0.001	3.90	2.33 to 6.87	<0.001
≥15	3.24	2.74 to 3.74	<0.001	4.55	2.66 to 8.17	<0.001
C_{dyn} (mL/cmH_2O)						
≥50	1 (reference)			1 (reference)		
40–50	1.32	0.98 to 1.65	<0.001	3.02	2.07 to 4.43	<0.001
30–40	1.78	1.49 to 2.07	<0.001	3.42	2.47 to 4.78	<0.001
≤30	2.13	1.86 to 2.41	<0.001	4.44	3.25 to 6.13	<0.001
FiO_2 (%)						
≤40	1 (reference)			1 (reference)		
>40	2.26	1.92 to 2.66	<0.001	1.37	1.12 to 1.68	0.002
WBC (×10^9/L)	1.04	1.02 to 1.05	<0.001			
SCr (mg/dL)						
≤1.1	1 (reference)					
>1.1	1.47	1.25 to 1.72	<0.001			
Uorate (mL/kg/h)						
≤0.63	1 (reference)					
>0.63	0.76	0.65 to 0.90	0.001			
HR (bpm)						
≤90	1 (reference)					
>90	1.19	1.01 to 1.41	0.036			
BF (bpm)	1.08	1.07 to 1.10	<0.001			
MBP (mm Hg)	0.99	0.98 to 0.99	<0.001			
SPO_2 (%)	0.91	0.88 to 0.94	<0.001			
PH, per 10^{-1}	0.77	0.65 to 0.90	0.001			
PF, per 10 mm Hg	0.97	0.96 to 0.98	<0.001			
ICU days						

Continued

Table 2 Continued

	Univariate model			Multivariable model		
Variables	**OR**	**95% CI**	**P value**	**OR**	**95% CI**	**P value**
<7	1 (reference)			1 (reference)		
≥7	4.59	3.87 to 5.45	<0.001	2.43	1.96 to 3.02	<0.001
IMV duration				1 (reference)		
<3	1 (reference)			2.33	1.87 to 2.90	<0.001
≥3	4.88	4.11 to 5.80	<0.001			

BF, breathing frequency; BMI, body mass index; C_{dyn}, dynamic lung compliance; FiO_2, inspired oxygen concentration; HR, heart rate; ICU, intensive care unit; IMV, invasive mechanical ventilation; MBP, mean blood pressure; MP, mechanical power; PEEP, positive end-expiratory pressure; PF, arterial partial pressure of oxygen (PaO_2) divided by the inspired oxygen concentration (FiO_2); P_{peak}, peak inspiratory pressure; P_{plat}, plateau pressure; RR, respiratory rate; SAPS II, simplified acute physiology score II; SCr, serum creatinine; SOFA, Sequential Organ Failure Assessment; SPO_2, pulse oximetry; Uorate, urine output rate; WBC, white blood cell.

IMV with a PEEP of 8 cmH_2O (83 points), an MP of 12 J/min (89 points), a C_{dyn} of 35 mL/cmH_2O (81 points), an FiO_2 of 45% (24 points), an ICU length of 7 days (59 points) and an IMV duration of 3 days (56 points) had a total score of 392 points, which corresponded to a weaning failure probability of approximately 86% in the nomogram.

Evaluation of the prognostic nomogram performance

Internal cross-validation of nomograms using the bootstrap method (bootstrap=1000 resampling) in the development cohort. As shown in figure 3A, the calibration plot yielded a straight line with a slope close to 1, indicating that the nomogram was well calibrated for predicting weaning failure. Using ROC curves, we evaluated the effectiveness of the nomogram in predicting weaning failure in both the development and validation cohorts, with an AUC of 0.828 (95% CI: 0.812 to 0.844) for the development cohort and 0.833 (95% CI: 0.809 to 0.857) for the validation cohort (figure 3C and D). In addition, by comparison, the accuracy of the nomogram in the development cohort and the validation cohort in the prediction of weaning failure was significantly higher than that of the single indexes MP and C_{dyn} (development cohort AUC, 0.828 vs 0.746, 0.692, both p<0.001; validation cohort AUC, 0.833 vs 0.743, 0.682, both p<0.001) (figure 3C and D). Based on DCA, we concluded that the nomogram was clinically valid in the validation cohort (figure 3B).

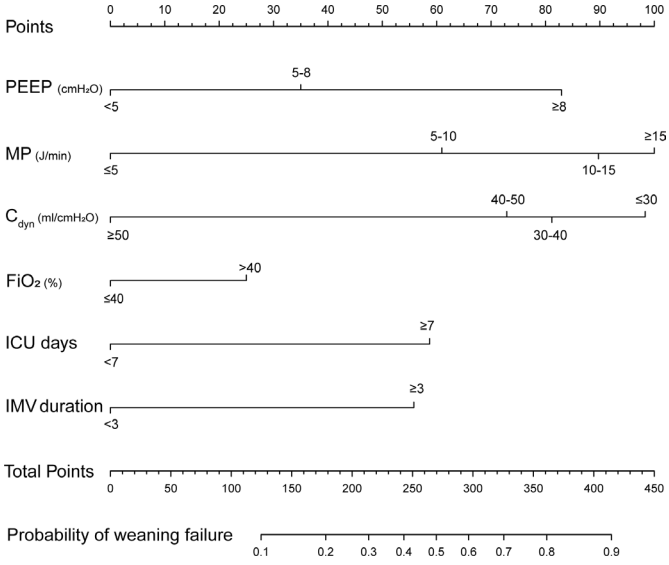

Figure 2 Nomogram predicting the probability of weaning failure. C_{dyn}, dynamic lung compliance; FiO_2, inspired oxygen concentration; ICU, intensive care unit; IMV, invasive mechanical ventilation; MP, mechanical power; PEEP, positive end expiratory pressure.

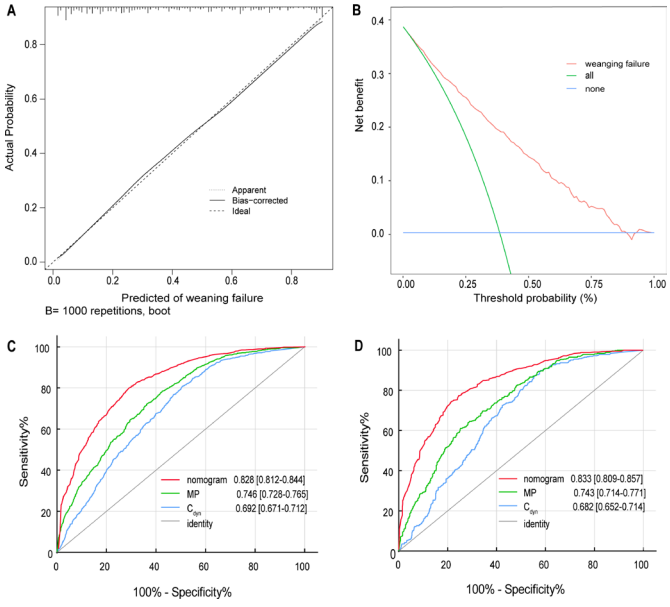

Figure 3 Evaluation of the prognostic nomogram performance in the development and validation cohort. Calibration plot of the nomogram for the probalility of weaning failure within development (A). Decision curve for treatment failure within validation cohort (B). Area under the receiver operating characteristic curve (95% CI) for nomogram, MP and C_{dyn} within development (C) and validation cohort (D). C_{dyn}, dynamic lung compliance; MP, mechanical power.

DISCUSSION

This study is the first to establish and validate a mechanical power-oriented prediction model for weaning outcomes based on a large database. The model visualises six simple and easily obtained variables through a nomogram, and can be used to evaluate the risk of weaning failure before the SBT, thereby assisting clinicians in making decisions related to weaning in critically ill mechanically ventilated patients.

Increased respiratory load and respiratory muscle work resulting from increased airway resistance combined with decreased respiratory system compliance are major causes of weaning failure.[5 6] MP integrates multiple factors of mechanical ventilation, and the total energy delivered by the ventilator to the lung parenchyma can be calculated by combining parameters such as V_T, PEEP, P_{plat}, P_{peak} and RR.[9 20] The measurement of MP is simple and non-invasive, and the workload required to maintain optimal alveolar ventilation acting on the respiratory muscles per unit time can be obtained without disconnecting the ventilator at the bedside; consequently, MP has recently become a new guideline for clinical weaning.[10 11 21] The MP-oriented weaning outcome prediction model has certain advantages in the assessment of respiratory load before weaning and provides a comprehensive judgement of weaning decisions combined with clinical feasibility.

Among the 3695 mechanically ventilated patients in this study, 38.5% (1421/3695) failed weaning after the first SBT. Furthermore, 11.07% (283/2557) of patients required reintubation, non-invasive ventilation or died 48 hours after successful SBT weaning, which was consistent with the multicentre observational study by Jaber *et al*.[22] Among a total of 32 variables were assessed in the study, the following 20 key variables related to weaning outcomes were identified through screening: BMI, SOFA score, respiratory mechanics indicators (RR, PEEP, P_{plat}, P_{peak}, MP, C_{dyn}, FiO_2), inflammatory markers (WBC), organ function status (SCr), fluid management (Uorate), physiological status at weaning (HR, BF, MBP, SPO_2, PH, PF), the length of ICU stay and duration of IMV (table 2). Our study and previous research shows that higher BMI[23] and SOFA score,[24] abnormal vital signs,[25] acid-base balance,[26] degree of infection control,[27] organ function and fluid levels and management[23] are important predictors of weaning failure risk. However, after incorporating these potential predictors into a multivariate logistic regression model, only six predictors (PEEP, MP, C_{dyn}, FiO_2, the length of ICU stay and duration of IMV) were found to be independently associated with weaning failure. Four of these were respiratory mechanics-related indicators (table 2). These findings suggest that respiratory factors have greater weight in the prediction of weaning outcomes, which is consistent with the results reported by Heunks and van der Hoeven.[4] Although reversible factors leading to weaning failure are treated aggressively, objective assessment of airway and lung function is still an important aspect of avoiding weaning failure.

PEEP can prevent lung collapse and reduce intrapulmonary shunting, thereby maintaining alveolar recruitment and increasing arterial oxygenation.[28] The lower the level of PEEP required to achieve the therapeutic goal before weaning reflects a lower number of collapsed alveoli and better uniformity of lung ventilation.[28] Zhao *et al*[8] also used PEEP as an independent risk indicator for predicting weaning failure. FiO_2 levels before weaning reflect the severity of hypoxia, as well as the state of circulatory function and oxygen transport capacity.[29] Our results are consistent with those of Yan Jia *et al*,[30] but differ from the findings of Savi *et al*,[31] showing that FiO_2 is a better predictor of the risk of weaning failure than PO_2/FiO_2. This discrepancy may be related to significant influence of FiO_2 and PEEP levels on PO_2/FiO_2.[32] PEEP and FiO_2 are also important indicators for weaning screening tests.[26] In accordance with the findings of Baptistella *et al*,[3] our research supported the conclusion that dynamic lung compliance is a respiratory mechanics parameter that can be used as a predictor of weaning outcome. C_{dyn} represents the pressure required to generate an appropriate volume to meet physiological needs, reflecting the ease with which the lung undergoes volume change under the action of external force.[33] C_{dyn} is affected by both lung tissue elasticity and airway resistance, with greater lung compliance during weaning associated with lower risk of weaning failure.[3] As a comprehensive respiratory mechanics index, MP is a quantitative measure of the energy required to overcome pulmonary resistance and maintain alveolar opening and optimal oxygenation during mechanical ventilation, and can reflect the severity of lung lesions.[34] In this study, we found that larger MP values before weaning were associated with a greater energy load that must be overcome by the respiratory muscles during spontaneous breathing, and a higher the risk of weaning failure, which is consistent with the findings of Ghiani *et al*.[11]

In accordance with previous studies,[3 35] the length of ICU stay and duration of IMV were also independent predictors of weaning failure. With a length of stay in ICU >7 days and duration of IMV >3 days, the OR values of the risk of weaning failure increased to 2.43 (95% CI: 1.96 to 3.02) and 2.33 (95% CI: 1.87 to 2.90), respectively, (both p<0.001) (table 2). This may be related to the increased risk of weaning failure due to prolonged mechanical ventilation and prolonged ICU stays leading to increased risk of diaphragmatic dysfunction, ventilator-related morbidity and mortality.[2 36] Although a single index such as MP and C_{dyn} can predict the weaning outcome to a certain extent, our ROC analysis provided evidence that the nomogram (AUC=0.828) constructed using a combination of parameters is more accurate in predicting weaning failure than a single index, which is consistent with the conclusions reported by Torrini *et al*.[37] In clinical practice, the MP-oriented prediction model constructed by combining the respiratory system parameters and the overall condition of the patient can be used to improve the prediction of weaning failure. Given that there are no

identified risk factors with the need for laboratory parameters and all variables in the final model are available at the bedside, the prediction model has better generalisability and simplicity than previous predictive scoring tools (eg, Extubation Predictive Score).[3]

Several limitations of this study should be pointed out. First, we mainly extracted the data for patients with complete P_{plat} measurements and MP calculated in volume control mode before SBT. Since this study is a secondary analysis of the data set in the MIMIC-IV for clinical purposes, there is no guarantee that the parameters analysed were collected under standard conditions without spontaneous breathing and adequate levels of sedation. Second, due to database limitations and missing data for some variables, we cannot rule out the possibility that other variables that were not included in our study, such as serological markers B-type natriuretic peptide[38] and central veins pressure,[39] may also have predictive value for weaning outcomes. In addition, we could not compare the performance of the MP-oriented model with the existing model (eg, the modified Burns Wean Assessment Program scores).[40] Finally, although we randomly assigned a validation cohort of 30% of the total sample size to verify the superiority of our model, analysis of a large external cohort will further enhance the credibility and validity of our model.

In conclusion, this study is the first to establish and validate an MP-oriented prediction model for weaning failure based on a database and provides an intuitive and visualisation of the model with a nomogram that predicts weaning failure with good accuracy and clinical validity. The model is simple to use and can be used with ease to provide information with clinical practicability. Moreover, this model can be used by clinicians as a decision support tool in the weaning process.

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REFERENCES

1 Fadila M, Rajasurya V, Regunath H. Ventilator Weaning. In: *StatPearls [Internet]*. Treasure Island (FL): StatPearls Publishing, 2021.
2 Fernandez-Zamora MD, Gordillo-Brenes A, Banderas-Bravo E, *et al*. Prolonged mechanical ventilation as a predictor of mortality after cardiac surgery. *Respir Care* 2018;63:550–7.
3 Baptistella AR, Mantelli LM, Matte L, *et al*. Prediction of extubation outcome in mechanically ventilated patients: development and validation of the extubation predictive score (ExPreS). *PLoS One* 2021;16:e0248868.
4 Heunks LM, van der Hoeven JG. Clinical review: the ABC of weaning failure--a structured approach. *Crit Care* 2010;14:245.
5 Vassilakopoulos T, Roussos C, Zakynthinos S. Weaning from mechanical ventilation. *J Crit Care* 1999;14:39–62.
6 Gong J, Zhang B, Huang X, *et al*. Product of driving pressure and respiratory rate for predicting weaning outcomes. *J Int Med Res* 2021;49:1–8.
7 Teixeira C, Zimermann Teixeira PJ, Hohër JA, *et al*. Serial measurements of f/VT can predict extubation failure in patients with f/VT < or = 105? *J Crit Care* 2008;23:572–6.
8 Zhao Q-Y, Wang H, Luo J-C, *et al*. Development and validation of a Machine-Learning model for prediction of extubation failure in intensive care units. *Front Med* 2021;8:676343.
9 Gattinoni L, Tonetti T, Cressoni M, *et al*. Ventilator-related causes of lung injury: the mechanical power. *Intensive Care Med* 2016;42:1567–75.
10 Ghiani A, Paderewska J, Walcher S, *et al*. Mechanical power normalized to lung-thorax compliance predicts prolonged ventilation weaning failure: a prospective study. *BMC Pulm Med* 2021;21:202.
11 Ghiani A, Paderewska J, Walcher S, *et al*. Mechanical power normalized to lung-thorax compliance indicates weaning readiness in prolonged ventilated patients. *Sci Rep* 2022;12:6.
12 Johnson A, Bulgarelli L, Pollard T, *et al*. *MIMIC-IV (version 1.0). PhysioNet*, 2021.
13 Ruan S-Y, Teng N-C, Wu H-D, *et al*. Durability of weaning success for liberation from invasive mechanical ventilation: an analysis of a nationwide database. *Am J Respir Crit Care Med* 2017;196:792–5.
14 Subirà C, Hernández G, Vázquez A, *et al*. Effect of pressure support vs T-piece ventilation strategies during spontaneous breathing trials on successful extubation among patients receiving mechanical ventilation: a randomized clinical trial. *JAMA* 2019;321:2175–82.
15 Zhang Z. Multiple imputation with multivariate imputation by chained equation (mice) package. *Ann Transl Med* 2016;4:30.
16 Bouwmeester W, Zuithoff NPA, Mallett S, *et al*. Reporting and methods in clinical prediction research: a systematic review. *PLoS Med* 2012;9:1–12.

17 Alba AC, Agoritsas T, Walsh M, *et al*. Discrimination and calibration of clinical prediction models: users' guides to the medical literature. *JAMA* 2017;318:1377–84.
18 Team, R. C. *R: a language and environment for statistical computing*. R Foundation for Statistical Computing, 2021.
19 Wickham H. *ggplot2: elegant graphics for data analysis*. Springer-Verlag, 2016.
20 Serpa Neto A, Deliberato RO, Johnson AEW, *et al*. Mechanical power of ventilation is associated with mortality in critically ill patients: an analysis of patients in two observational cohorts. *Intensive Care Med* 2018;44:1914–22.
21 Ghiani A, Paderewska J, Sainis A, *et al*. Variables predicting weaning outcome in prolonged mechanically ventilated tracheotomized patients: a retrospective study. *J Intensive Care* 2020;8:19.
22 Jaber S, Quintard H, Cinotti R, *et al*. Risk factors and outcomes for airway failure versus non-airway failure in the intensive care unit: a multicenter observational study of 1514 extubation procedures. *Crit Care* 2018;22:236.
23 Maezawa S, Kudo D, Miyagawa N, *et al*. Association of body weight change and fluid balance with extubation failure in intensive care unit patients: a single-center observational study. *J Intensive Care Med* 2021;36:175–81.
24 Fabregat A, Magret M, Ferré JA, *et al*. A machine learning decision-making tool for extubation in intensive care unit patients. *Comput Methods Programs Biomed* 2021;200:105869.
25 Xie J, Cheng G, Zheng Z, *et al*. To extubate or not to extubate: risk factors for extubation failure and deterioration with further mechanical ventilation. *J Card Surg* 2019;34:1004–11.
26 Mallat J, Baghdadi FA, Mohammad U, *et al*. Central Venous-to-Arterial PCO2 difference and central venous oxygen saturation in the detection of extubation failure in critically ill patients. *Crit Care Med* 2020;48:1454–61.
27 Upadya A, Tilluckdharry L, Muralidharan V, *et al*. Fluid balance and weaning outcomes. *Intensive Care Med* 2005;31:1643–7.
28 Collino F, Rapetti F, Vasques F, *et al*. Positive end-expiratory pressure and mechanical power. *Anesthesiology* 2019;130:119–30.
29 Telias I, Brochard LJ, Gattarello S, *et al*. The physiological underpinnings of life-saving respiratory support. *Intensive Care Med* 2022;48:1–13.
30 Jia Y, Kaul C, Lawton T, *et al*. Prediction of weaning from mechanical ventilation using Convolutional neural networks. *Artif Intell Med* 2021;117:102087.
31 Savi A, Teixeira C, Silva JM, *et al*. Weaning predictors do not predict extubation failure in simple-to-wean patients. *J Crit Care* 2012;27:221.e1–8.
32 Hou JJ, YJ X, Zhu DM, *et al*. Effects of oxygen indexes on the diagnosis of acute lung injury. *Chin J Emerg Med* 2006;15:971–4.
33 Edwards Z, Annamaraju P. Physiology, Lung Compliance. In: *StatPearls [Internet]*. Treasure Island (FL): StatPearls Publishing, 2022.
34 Xie Y, Qian Y, Liu K, *et al*. [Correlation analysis between mechanical power and lung ultrasound score and their evaluation of prognosis in patients with acute respiratory distress syndrome]. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue* 2019;31:704–8.
35 Liu W, Tao G, Zhang Y, *et al*. A simple weaning model based on interpretable machine learning algorithm for patients with sepsis: a research of MIMIC-IV and eICU databases. *Front Med* 2021;8:814566.
36 Mayo P, Volpicelli G, Lerolle N, *et al*. Ultrasonography evaluation during the weaning process: the heart, the diaphragm, the pleura and the lung. *Intensive Care Med* 2016;42:1107–17.
37 Torrini F, Gendreau S, Morel J, *et al*. Prediction of extubation outcome in critically ill patients: a systematic review and meta-analysis. *Crit Care* 2021;25:391.
38 Farghaly S, Galal M, Hasan AA, *et al*. Brain natriuretic peptide as a predictor of weaning from mechanical ventilation in patients with respiratory illness. *Aust Crit Care* 2015;28:116–21.
39 Chen H, Zhu Z, Zhao C, *et al*. Central venous pressure measurement is associated with improved outcomes in septic patients: an analysis of the MIMIC-III database. *Crit Care* 2020;24:433.
40 Jiang J-R, Yen S-Y, Chien J-Y, *et al*. Predicting weaning and extubation outcomes in long-term mechanically ventilated patients using the modified burns Wean assessment program scores. *Respirology* 2014;19:576–82.