Original Article Development and validation of an online nomogram for predicting the outcome of open tracheotomy decannulation: a two-center retrospective analysis

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Received July 4, 2022; Accepted November 7, 2022; Epub November 15, 2022; Published November 30, 2022

Abstract: Background: Tracheotomy decannulation is critical for patients in the intensive care unit (ICU) to recover. In this study, we developed and validated an intuitive nomogram to predict the success rate of tracheotomy decannulation. Methods: We collected the data of 627 ICU patients before open tracheotomy decannulation from two medical institutions, including 466 patients (135 success and 331 failure) from the First Affiliated Hospital of Anhui Medical University as a training cohort, and 161 patients (57 success and 104 failure) from the Second Affiliated Hospital of Anhui Medical University as an external validation cohort. A least absolute shrinkage and multivariate logistic regression analysis were performed to determine the independent risk factors and construct the nomogram. The area under the receiver operating characteristic curve (AUC) was used to assess discrimination and the calibration plots were used to assess consistency. The clinical application was assessed using decision curve analysis and the clinical impact curve. Results: 7 independent risk factors were 0.932, 0.926, and 0.915, showing good discrimination. The model performed well in terms of calibration, decision curve analysis, and clinical impact curves. The superior performance of the model was also confirmed by external validation. Conclusion: This nomogram can help ICU physicians identify high-risk patients for decannulation and plan their pre-decannulation treatment accordingly.

Keywords: Decannulation, tracheotomy, intensive care unit, dynamic nomogram, lasso regression

Introduction

Tracheotomy is a common method for establishing an artificial airway in the intensive care unit (ICU). It is an invasive operation that opens the airway by incising the anterior wall of the cervical trachea and placing a metal cannula or a silicone cannula. Traditionally a tracheotomy is performed as an open surgical operation with good cost-effectiveness [1]. Although percutaneous dilational tracheotomy (PDT) has been relatively advanced in recent years, it can lead to longer apnea and exposure to generated aerosols [2]. There is a large body of literature comparing the techniques, and generally such studies do not show superiority of one technique over the other [3]. Up to 10% of patients requiring mechanical ventilation (MV) for at least three days will eventually undergo tracheotomy to prolong MV or airway support time [4]. Tracheotomy has many advantages over direct tracheal intubation, including reduced throat injury, lower risk of sinusitis, decreased need for sedation, and easy reinsertion in accidental decannulation [4]. It can be used to relieve dyspnea in critically ill patients due to retention of laryngeal, lower respiratory tract secretions, or reduced respiratory capacity [4].

The existence of tracheotomy tube can cause a series of complications such as tracheal stenosis, bleeding infection, and aspiration pneumonia. Therefore, tracheotomy decannulation is critical for ICU patients to recover and is usually performed after removing the fundamental reasons for tracheotomy [5]. However, about 2-32.4% of the cases failed in planned decannulation according to the relevant literature [6. 7]. Failure to tracheotomy decannulation is usually defined as the need for reinserting an artificial airway within 48 to 96 hours of planned decannulation [8]. Failure of decannulation and subsequent reinsertion may lead to increased duration of mechanical ventilation, prolonged length of ICU stay, increased nosocomial infections, and greater medical expenditures [9]. These negative effects require clinicians to manage the decannulation process carefully and develop a decannulation plan in advance.

In clinical practice, whether a patient is ready for decannulation is only judged based on the complicated indications for decannulation and clinician experience, which may result in decannulation failure owing to misjudgment and, ultimately, detrimental consequences to patients. Notably, several advantages have been observed for online dynamic nomograms in predicting event outcomes, including visualization, digitization, and user-friendliness. However, no predictive model for the success rate of tracheotomy decannulation has been devised. Therefore, this analysis aimed to develop and validate a simple and clinically effective online dynamic nomogram to assist ICU physicians in assessing the success rate of decannulation of patients following tracheotomy.

Methods

Patient data

This is an auxiliary analysis of a dual-center observational study conducted by the First Affiliated Hospital and the Second Affiliated Hospital of Anhui Medical University. The data of patients undergoing open tracheotomy decannulation in 13 ICUs of 2 medical centers within 36 months from December 1, 2017 to December 1, 2020 were retrospectively analyzed. All critical adult patients who underwent tracheotomy for the first time during hospitalization in ICU were screened after leaving me-

chanical ventilation. Exclusion criteria are contraindications of random decannulation (unconsciousness, severe swallowing dysfunction, airway patency or tracheotomy with airway control), age less than 18 years, or death expected to occur before discharge (according to Sabadell score, which is a measure of mortality risk). Patients who received PDT, had an emergency tracheotomy in the ICU for sudden dyspnea, a history of laryngeal cancer or radiotherapy to the head and neck, or a history of laryngeal fractures were also excluded. In our study, decannulation success was defined as a patient surviving 48 to 96 hours after decannulation without reintubation. Decannulation failure was defined as: 1. Failure to block the catheter: 2. Re-establishment of the artificial airway within 48 to 96 hours after decannulation, regardless of cause; 3. Death occurring within 48 to 96 hours after decannulation. A total of 667 eligible patients were included in the First Affiliated Hospital of Anhui Medical University through retrospective consultation, case retrieval and telephone follow-up. Among them, 35 patients were lost to follow-up or with incomplete information and 166 patients did not meet the indications and died without attempting decannulation, who were excluded. Similarly, a total of 275 eligible patients were included in the Second Affiliated Hospital of Anhui Medical University, of which 33 patients with incomplete information and 81 patients who died without attempting decannulation were excluded, and finally 161 patients were included in the external validation cohort. All relevant contents of this study were in strict accordance with the declaration of Helsinki and have been approved by the clinical medical research ethics committee of the First Affiliated Hospital of Anhui Medical University (ethics approval No.: Quick-PJ 2022-01-32). In this study, the written informed consent of the subjects and their families was obtained, and all data were guaranteed to be anonymous.

Data collection

Basic information such as subject gender, age, height and weight were collected, as well as clinical data such as etiology, indication for surgery, number of endotracheal intubation days (ETID), length of ICU stay (ICULOS), infection control, state of consciousness (conscious or comatose), endotracheal tube size (ETT. size), and days of ventilator away underwent tracheotomy (DVAUT). The occurrence of complications was recorded categorically, including injury to posterior trachea wall, clogged casing, tracheal stenosis, tracheoesophageal fistula, mediastinal emphysema, swallowing dysfunction, incision infection, incision bleeding, cardiovascular disease (CVD, such as acute or chronic heart failure, coronary artery disease and cardiac respiratory arrest), respiratory system disease (RSD, such as pneumothorax, interstitial lung disease, pulmonary infection, ventilator associated pneumonia and chronic obstructive pulmonary disease), neuromuscular disease (NMD, diseases involving respiratory muscles, such as amyotrophic lateral sclerosis, severe Guillain-Barre syndrome and myasthenia gravis crisis), renal insufficiency (RI), diabetes, hepatopathy, malignancy. The cough reflex (CR, good or poor), coagulopathy, serum albumin (ALB), hemoglobin (HB) levels, partial pressure of oxygen (PaO₂), and partial pressure of CO₂ (PCO₂) data were collected three days before decannulation.

The Glasgow Coma Scale was used to assess the patient's level of consciousness, with a score of 8 indicating severe impairment of consciousness and a score of less than 6 consistently indicating a poor prognosis.

The Acute Physiology and Chronic Health Evaluation II (APACHE II) score was obtained within the first 24 hours of admission to evaluate the severity of the pathogenetic condition and death risk of ICU/high-dependency unit patients, and the score increased with the aggravation of the disease. Furthermore, all subjects' 1-month and 3-month prognostic survival was collected.

Statistical analysis

The study followed Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) guidelines, and The TRIPOD checklist is shown in <u>Table S1</u>. Data from the First Affiliated Hospital served as the training cohort, while data from the Second Affiliated Hospital served as the external validation cohort. Differences in baseline characteristics and clinical data between the training cohort and the external validation cohort were compared. The patients were divided into two groups for variable comparisons based on whether the tracheotomy tube was successfully removed later. Differences in clinical characteristics between the two groups of patients in each cohort were compared separately. For continuous variables, the normal distribution data were described by mean ± standard deviation (SD), and the skewed distribution data were expressed by median (interguartile range, IQR). The Student t-test was used to compare the normal distribution data between groups, and the Wilcoxon rank-sum test was used to compare the skewed distribution. Categorical variables were presented as frequencies and respective percentages and analyzed by chisquare test.

The receiver operating characteristic (ROC) curve was used to assess the diagnostic value of tracheotomy decannulation-related variables. The least absolute shrinkage and selection operator (LASSO) was used and the best prediction factor was chosen through crossvalidation [10]. The two dashed lines represent two unique values: λ_{min} on the left and λ_{1se} on the right. In order to improve the accuracy of the model, we chose $\lambda_{_{min}}$ to build the model. The values between these two values were deemed appropriate. Since some ICU hospitalized patients were severely ill and stayed longer than a year, to avoid extreme values, we obtained the optimal cut-off value for the mean ICULOS by the ROC curve and converted it into a dichotomous variable. Following that, a multivariate logical analysis was performed to identify true independent risk factors. To investigate the internal correlation between the variables, correlation heatmaps were created. With an optimal model, a nomogram predicting the outcome of tracheotomy decannulation was finally established. The discrimination and calibration curves were used to evaluate the nomogram's performance.

The area under the receiver operating characteristic curve (AUC), which ranges from 0.5 (no discrimination) to 1 (perfect discrimination), was used to determine the model's discriminative ability [11]. An internal validation method of 10-fold cross-validation was also applied to calculate a corrected AUC. To determine the net benefit prediction thresholds, decision curve



Figure 1. Flow chart of this study. ROC: Receiver Operating Characteristic; LASSO: Least Absolute Shrinkage and Selection Operator.

analysis and clinical impact curves were established [12]. Shiny, version 0.13.2.26, was used to create an interactive web-based dynamic nomogram application to facilitate its application in clinical practice.

All the calculations were carried out under the R software (Version 4.1.1) and various packages. Results with a p-value < 0.05 were considered statistically significant.

Results

Overall characteristics of patients and correlation between clinicopathological variables and decannulation outcome

Figure 1 showed the whole process of this study. From December 1, 2017 to December 1, 2020, 942 patients underwent open tracheotomy decannulation in 13 ICUs of 2 medical cen-

ters. During the study, 68 patients with missing or incomplete data and 247 patients who died without attempting decannulation due to ineligibility were excluded. Finally, 466 and 161 subjects were included in the training cohort and the external validation cohort, respectively. Among the ICU patients enrolled in this study who underwent tracheotomy, 30.6% (192/627) were successfully decannulated. Through extensive literature review, we finally determined the clinical cut-off values of relevant variables, which were age ≥ 60 years and < 60 years, ETID \geq 7 days and < 7 days, ETT. Size \geq 7.5 millimeters (mm) and < 7.5 mm, DVAUT \geq 30 days and < 30 days, $PaO_2 \le 75$ millimeters of mercury (mmHg) and > 75mmHg, PCO₂ \geq 45 mmHg and < 45 mmHg, Hb \geq 90 grams per liter (g/I) and < 90 g/I, Alb ≥ 35 g/l and < 35 g/l, respectively [13-23]. The comparison of clinical characteristics between the two cohorts were shown in Table 1, and no significant differences were observed. Table

2 showed the differences in clinical characteristics between the different decannulation outcome groups in the two cohorts, respectively. According to the results of the univariate analysis for the training cohort and external validation cohort, the variables that were significantly associated with the outcome of decannulation included ETID (P < 0.001, P < 0.001), ICULOS (P < 0.001, P < 0.001), APACHE II (P < 0.001, P < 0.001), DVAUT (P=0.039, P=0.262), PaO, (P < 0.001, P < 0.001), PCO₂ (P < 0.001, P < 0.001), Hb (P=0.016, P=0.006), ALB (P < 0.001, P=0.015), CS (P=0.009, P=0.015), CR (P < 0.001, P < 0.001), NMD (P=0.038, P=0.423), CVD (P=0.013, P=0.022) and RSD (P=0.033, P=0.010).

At one-month follow-up after tracheotomy in the training cohort, there were 0 deaths (0%), 135 survivors (100%), and 0 lost to follow-up

Characteristics	The First Affiliated Hospital (Training Cohort)	The Second Affiliated Hospital (External Test Cohort)	P value
Ν	466	161	
Age n (%)			0.792
< 60 years	224 (48.1%)	80 (49.7%)	
≥ 60 years	242 (51.9%)	81 (50.3%)	
Gender n (%)			1
Female	159 (34.1%)	55 (34.2%)	
Male	307 (65.9%)	106 (65.8%)	
Height (Mean (SD))	166.9 (9.78)	166.86 (11.7)	0.608
Weight (Mean (SD))	66.53 (11.74)	67.94 (13.73)	0.143
BMI (Mean (SD))	23.63 (3.23)	23.85 (3.19)	0.347
Etiology n (%)			0.874
Non-nervous System	176 (37.8%)	59 (36.6%)	
Nervous System	290 (62.2%)	102 (63.4%)	
COT n (%)			0.053
Hard to offline	415 (89.1%)	134 (83.2%)	
Retention	51 (10.9%)	27 (16.8%)	
ETID n (%)			0.485
< 7	209 (44.8%)	78 (48.4%)	
≥ 7	257 (55.2%)	83 (51.6%)	
ICULOS (Mean (SD))	29.27 (49.88)	30.09 (32.56)	0.280
APACHE II (Mean (SD))	20.69 (4.85)	20.2 (5.33)	0.158
ETT. size n (%)			0.981
≥ 7.5	445 (95.5%)	153 (95%)	
< 7.5	21 (4.5%)	8 (5%)	
DVAUT n (%)	, , , , , , , , , , , , , , , , , , ,		0.111
≥ 30	11 (2.4%)	8 (5%)	
< 30	455 (97.6%)	153 (95%)	
PaO, n (%)			0.542
≤ 75	153 (32.8%)	48 (29.8%)	
> 75	313 (67.2%)	113 (70.2%)	
PCO. n (%)		(,,	0.908
≥ 45	288 (61.8%)	98 (60.9%)	
< 45	178 (38.2%)	63 (39.1%)	
Hb n (%)			0.191
< 90	222 (47.6%)	87 (54%)	
≥90	244 (52.4%)	74 (46%)	
ALB n (%)	(0 ,		0.317
≥ 35	64 (13.7%)	28 (17.4%)	3. 0 ±1
< 35	402 (86.3%)	133 (82.6%)	
PT. APTT. INR n (%)			0.907
Yes	105 (22 5%)	37 (23.0%)	0.001
No	361 (7.5%)	124 (77 0%)	
CS n (%)			0.678
Coma	273 (58 6%)	98 (60 9%)	0.070
Awake	193 (11 1%)	63 (39 1%)	1
Awane	100 (+1.+/0)	00 (00.1/0)	-

Table 1. Baseline characteristics and clinical data before decannulation

CR n (%)			
Poor	245 (52.6%)	84 (52.2%)	
Good	221 (47.4%)	77 (47.8%)	
Injury to Posterior Trachea Wall n (%)			0.338
Yes	1 (0.2%)	2 (1.2%)	
No	465 (99.8%)	159 (98.8%)	
The Position of the Casing n (%)			0.982
Yes	1 (0.2%)	1 (0.6%)	
No	465 (99.8%)	160 (99.4%)	
Incision Bleeding n (%)			0.487
Yes	38 (8.2%)	16 (10.0%)	
No	428 (91.8%)	145 (90.0%)	
Offline n (%)			0.982
Yes	1 (0.2%)	1 (0.6%)	
No	465 (99.8%)	160 (99.4%)	
Incision Infection n (%)			0.966
Yes	5 (1.1%)	1 (0.6%)	
No	461 (98.9%)	160 (99.4%)	
Tracheoesophageal Fistula n (%)			0.587
Yes	2 (0.4%)	2 (1.2%)	
No	464 (99.6%)	159 (98.8%)	
Clogged Casing n (%)			0.368
Yes	3 (0.6%)	3 (1.9%)	
No	463 (99.4%)	158 (98.1%)	
Mediastinal Emphysema n (%)			0.982
Yes	1 (0.2%)	1 (0.6%)	
No	465 (99.8%)	160 (99.4%)	
Swallowing Dysfunction n (%)			0.587
Yes	2 (0.4%)	2 (1.2%)	
No	464 (99.6%)	159 (98.8%)	
Tracheal Stenosis n (%)			0.587
Yes	3 (0.6%)	1 (0.6%)	
No	463 (99.4%)	160 (99.4%)	
NMD n (%)			0.493
Yes	29 (6.2%)	7 (4.3%)	
No	437 (93.8%)	154 (95.7%)	
Hepatopathy n (%)			0.758
Yes	94 (20.2%)	30 (18.6%)	
No	372 (79.8%)	131 (81.4%)	
CVD n (%)			0.340
Yes	271 (58.2%)	86 (53.4%)	
No	195 (41.8%)	75 (46.6%)	
RSD n (%)			0.887
Yes	140 (30%)	50 (31.1%)	
No	326 (70%)	111 (68.9%)	
Diabetes n (%)			0.511
Yes	91 (19.5%)	36 (22.4%)	
No	375 (80.5%)	125 (77.6%)	

RI n (%)			0.892
Yes	143 (30.7%)	51 (31.7%)	
No	323 (69.3%)	110 (68.3%)	
Malignancy n (%)			1
Yes	49 (10.5%)	17 (10.6%)	
No	417 (89.5%)	144 (89.4%)	
1-month follow-up n (%)			0.823
Death	13 (2.8%)	4 (2.5%)	
Survive	452 (97.0%)	157 (97.5%)	
Lost	1 (0.2%)	O (0%)	
3-month follow-up n (%)			0.635
Death	26 (5.6%)	6 (3.7%)	
Survive	430 (92.3%)	152 (94.4%)	
Lost	10 (2.1%)	3 (1.9%)	

SD: Standard Deviation; BMI: Body Mass Index; COT: Cause of Tracheotomy; ETID: Endotracheal Intubation Days; ICULOS: Intensive Care Unit Length of Stay; APACHE II: Acute Physiology and Chronic Health Evaluation II; ETT. Size: Endotracheal Tube Size; DVAUT: Days of Ventilator Away Underwent Tracheotomy; PaO₂: Partial Pressure of Oxygen; PCO₂: Partial Pressure of CO₂; Hb: Hemoglobin; ALB: Serum Albumin; PT: Prothrombin Time; APTT: Activated Partial Thromboplastin Time; INR: International Normalized Ratio; CS: Conscious State; CR: Cough Reflex; NMD: Neuromuscular Disease; CVD: Cardiovascular Disease; RSD: Respiratory System Disease; RI: Renal Insufficiency.

	The First Affil	iated Hospital (The Second Affiliated Hospital			
Variables		Cohort)	(External Test Cohort)			
variables	Decannula-	Decannula-	P	Decannula-	Decannula-	P
	tion Success	tion Failure	Р	tion Success	tion Failure	Р
Ν	135	331		57	104	
Age n (%)			1			0.208
< 60 years	65 (48.1%)	159 (48%)		24 (42.1%)	56 (53.8%)	
≥ 60 years	70 (51.9%)	172 (52%)		33 (57.9%)	48 (46.2%)	
Gender n (%)			0.925			0.481
Female	47 (34.8%)	112 (33.8%)		22 (38.6%)	33 (31.7%)	
Male	88 (65.2%)	219 (66.2%)		35 (61.4%)	71 (68.3%)	
Height (Mean (SD))	166.45 (6.82)	167.08 (10.76)	0.085	166.39 (7.23)	167.12 (13.56)	0.106
Weight (Mean (SD))	66.08 (11.91)	66.71 (11.68)	0.422	65.55 (12.56)	69.25 (14.22)	0.077
BMI (Mean (SD))	23.77 (3.57)	23.58 (3.08)	0.942	23.54 (3.57)	24.01 (2.97)	0.393
Etiology n (%)			0.246			0.894
Non-nervous System	57 (42.2%)	119 (36%)		20 (35.1%)	39 (37.5%)	
Nervous System	78 (57.8%)	212 (64%)		37 (64.9%)	65 (62.5%)	
COT n (%)			0.284			0.492
Hard to offline	124 (91.9%)	291 (87.9%)		49 (87.7%)	85 (81.7%)	
Retention	11 (8.1%)	40 (12.1%)		8 (12.3%)	19 (18.3%)	
ETID n (%)			< 0.001			< 0.001
< 7	96 (71.1%)	113 (34.1%)		39 (68.4%)	39 (37.5%)	
≥7	39 (28.9%)	218 (65.9%)		18 (31.6%)	65 (62.5%)	
ICULOS (Mean (SD))	23.53 (32.25)	31.6 (55.36)	< 0.001	27.51 (42.55)	31.5 (25.63)	< 0.001
APACHE II (Mean (SD))	18.57 (3.99)	21.56 (4.91)	< 0.001	17.89 (4.59)	21.46 (5.31)	< 0.001
ETT. size n (%)			0.486			1
≥ 7.5	127 (94.1%)	318 (96.1%)		54 (94.7%)	99 (95.2%)	
< 7.5	8 (5.9%)	13 (3.9%)		3 (5.3%)	5 (4.8%)	
DVAUT n (%)			0.039			0.262
≥ 30	0 (0%)	11 (3.3%)		1 (1.8%)	7 (6.7%)	
< 30	135 (100%)	320 (96.7%)		56 (98.2%)	97 (93.3%)	

Table 2. Comparison of variables between successful and failed decannulation groups

PaO ₂ n (%)			< 0.001			< 0.001
≤ 75	4 (3%)	149 (45%)		1 (1.8%)	47 (45.2%)	
> 75	131 (97%)	182 (55%)		56 (98.2%)	57 (54.8%)	
PCO ₂ n (%)			< 0.001			< 0.001
≥45	37 (27.4%)	251 (75.8%)		18 (31.6%)	80 (76.9%)	
< 45	98 (72.6%)	80 (24.2%)		39 (68.4%)	24 (23.1%)	
Hb n (%)			0.016			0.006
< 90	52 (38.5%)	170 (51.4%)		22 (38.6%)	65 (62.5%)	
≥90	83 (61.5%)	161 (48.6%)		35 (61.4%)	39 (37.5%)	
ALB n (%)			< 0.001			0.015
≥35	35 (25.9%)	29 (8.8%)		16 (28.1%)	12 (11.5%)	
< 35	100 (74.1%)	302 (91.2%)		41 (71.9%)	92 (88.5%)	
PT, APTT, INR n (%)			0.381			0.667
Yes	34 (25.2%)	71 (21.5%)		12 (21.1%)	25 (24.0%)	
No	101 (74.8%)	260 (78.5%)		45 (78.9%)	79 (76.0%)	
CS n (%)			0.009	- ()		0.015
Coma	66 (48,9%)	207 (62.5%)		27 (47,4%)	71 (68.3%)	
Awake	69 (51.1%)	124 (37.5%)		30 (52.6%)	33 (31.7%)	
CB n (%)	00 (0111/0)	121 (01.07.6)	< 0.001	00 (02.070)	00 (01.176)	< 0.001
Poor	37 (27.4%)	208 (62 8%)	0.001	19 (33.3%)	65 (62 5%)	0.001
Good	98 (72 6%)	123 (37.2%)		38 (66 7%)	39 (37 5%)	
Injury to Posterior Trachea Wall n (%)	30 (12.070)	120 (01.270)	0.643	00 (00.170)	00 (01.070)	0 757
Vee	0 (0%)	1 (0 3%)	0.040	0 (0%)	2 (1 9%)	0.101
No	135 (100%)	330 (00 7%)		57 (100%)	102 (98 1%)	
The Position of the Casing n (%)	133 (100%)	550 (55.170)	0.643	57 (100%)	102 (98.170)	0 750
Voc	0 (0%)	1 (0.2%)	0.045	0 (0%)	1 (0 0%)	0.155
No	125 (100%)	I (0.3%)		0 (0%)	102 (00 1%)	
Incipion Blooding p (%)	133 (100%)	330 (99.7%)	0.004	57 (100%)	103 (99.1%)	0.460
Voo	16 (11 00/)	22 (6 7%)	0.094	7 (10 20/)	0 (8 70/)	0.402
No	110 (11.970)	22(0.7%)		7 (12.370) 50 (97.7%)	9 (0.7 %)	
Offling n (%)	119 (88.170)	303 (33.370)	0.642	50 (81.170)	95 (91.5%)	0.750
Voc	0 (0%)	1 (0.2%)	0.045	O(O%)	1 (0 0%)	0.759
No	125 (100%)	I (0.3%)		0 (0%)	102 (00 1%)	
(0/1)	133 (100%)	330 (99.7%)	0.050	57 (100%)	103 (99.1%)	0.750
	1 (0 70()	4 (4 00()	0.959	0 (00()	1 (0 0%)	0.759
tes	1 (0.7%)	4 (1.2%)		0 (0%)	1 (0.9%)	
	134 (99.3%)	327 (98.8%)	0.001	57 (100%)	103 (99.1%)	0 757
Tracheoesophageal Fistula n (%)	0 (00()		0.901	0 (00()	0 (4 0%)	0.757
Yes	0 (0%)	2 (0.6%)		0 (0%)	2 (1.9%)	
	135 (100%)	329 (99.4%)	0.007	57 (100%)	102 (98.1%)	0 5 0 0
Clogged Casing n (%)	0 (00()		0.637	4 (4 70()	0 (4 0%)	0.593
Yes	0 (0%)	3 (0.9%)		1 (1.7%)	2 (1.9%)	
No	135 (100%)	328 (99.1%)		56 (98.3%)	102 (98.1%)	
Mediastinal Emphysema n (%)			0.215			0.759
Yes	0 (0%)	1 (0.3%)		0 (0%)	1 (0.9%)	
No	135 (100%)	330 (99.7%)		57 (100%)	103 (99.1%)	
Swallowing Dysfunction n (%)			0.901			0.757
Yes	0 (0%)	2 (0.6%)		0 (0%)	2 (1.9%)	
No	135 (100%)	329 (99.4%)		57 (100%)	102 (98.1%)	
Tracheal Stenosis n (%)			0.637			0.759
Yes	1 (0.7%)	2 (0.6%)		0 (0%)	1 (0.9%)	
No	134 (99.3%)	329 (99.4%)		57 (100%)	103 (99.1%)	
NMD n (%)			0.038			0.423
Yes	3 (2.2%)	26 (7.9%)		1 (1.8%)	6 (5.8%)	
No	132 (97.8%)	305 (92.1%)		56 (98.2%)	98 (94.2%)	

Hepatopathy n (%)			0.852			1
Yes	26 (19.3%)	68 (20.5%)		11 (19.3%)	19 (18.3%)	
No	109 (80.7%)	263 (79.5%)		46 (80.7%)	85 (81.7%)	
CVD n (n%)			0.013			0.022
Yes	66 (48.9%)	205 (61.9%)		23 (40.4%)	63 (60.6%)	
No	69 (51.1%)	126 (38.1%)		34 (59.6%)	41 (39.4%)	
RSD n (%)			0.033			0.010
Yes	31 (23.0%)	109 (32.9%)		10 (17.5%)	40 (38.5%)	
No	104 (77.0%)	222 (67.1%)		47 (82.5%)	64 (61.5%)	
Diabetes n (%)			0.287			0.765
Yes	31 (23%)	60 (18.1%)		14 (24.6%)	22 (21.2%)	
No	104 (77%)	271 (81.9%)		43 (75.4%)	82 (78.8%)	
RI n (%)			0.837			1
Yes	40 (29.6%)	103 (31.1%)		18 (31.6%)	33 (31.7%)	
No	95 (70.4%)	228 (68.9%)		39 (68.4%)	71 (68.3%)	
Malignancy n (%)			0.664			0.427
Yes	16 (11.9%)	33 (10%)		8 (14%)	9 (8.7%)	
No	119 (88.1%)	298 (90%)		49 (86%)	95 (91.3%)	
1-month follow-up n (%)			0.080			0.929
Death	0 (0%)	13 (3.9%)		2 (3.5%)	2 (1.9%)	
Survive	135 (100%)	317 (95.8%)		55 (96.5%)	102 (98.1%)	
Lost	0 (0%)	1 (0.3%)		0 (0%)	0 (0%)	
3-month follow-up n (%)			< 0.001			0.771
Death	0 (0%)	26 (7.9%)		2 (3.5%)	4 (3.8%)	
Survive	135 (100%)	295 (89.1%)		55 (96.5%)	97 (93.3%)	
Lost	0 (0%)	10 (3.0%)		0 (0%)	3 (2.9%)	

SD: Standard Deviation; BMI: Body Mass Index; COT: Cause of Tracheotomy; ETID: Endotracheal Intubation Days; ICULOS: Intensive Care Unit Length of Stay; APACHE II: Acute Physiology and Chronic Health Evaluation II; ETT. Size: Endotracheal Tube Size; DVAUT: Days of Ventilator Away Underwent Tracheotomy; Pa0₂: Partial Pressure of Oxygen; PCO₂: Partial Pressure of CO₂; Hb: Hemoglobin; ALB: Serum Albumin; PT: Prothrombin Time; APTT: Activated Partial Thromboplastin Time; INR: International Normalized Ratio; CS: Conscious State; CR: Cough Reflex; NMD: Neuromuscular Disease; CVD: Cardiovascular Disease; RSD: Respiratory System Disease; RI: Renal Insufficiency.

(0%) in the successful decannulation group, while 13 deaths (3.9%), 317 survivors (95.8%), and 1 lost to follow-up (0.3%) in the failed decannulation group. There was no significant difference between the two groups (P=0.080). At the three-month follow-up, there were 0 deaths (0%), 135 survivors (100%) and 0 lost to follow-up (0%) in the successful decannulation group, while 26 deaths (7.9%), 295 survivors (89.1%) and 10 lost to follow-up (3.0%) in the failed decannulation group. The difference between the two groups was statistically significant (P < 0.001). In the external validation cohort, there were 2 deaths (3.5%), 55 survivors (96.5%), and 0 lost to follow-up (0%) in the successful decannulation group, while 2 deaths (1.9%), 102 survivors (98.1%), and 0 lost to follow-up (0%) in the failed decannulation group at the one-month follow-up, with no significant difference between the two groups (P=0.929). At the three-month follow-up, there

were 2 deaths (3.5%), 55 survival (96.5%) and 0 lost to follow-up (0%) in the successful decannulation group, while 4 deaths (3.8%), 97 survival (93.3%) and 3 lost to follow-up (2.9%) in the failed decannulation group. The difference between the two groups was not significant (P=0.771).

ROC analysis was conducted on the above statistically significant variables. ICULOS (AUC= 0.618), ETID (AUC=0.685), APACHE II (AUC= 0.688), CS (AUC=0.568), CR (AUC=0.677), PaO₂ (AUC=0.710), PCO₂ (AUC=0.742), HB (AUC=0.564), ALB (AUC=0.586) and CVD (AUC=0.565) were greater than 0.55, while DVAUT (AUC=0.517), NMD (AUC=0.528) and RSD (AUC=0.550) were excluded (Figure 2). The results of the ROC curve analysis were shown in Table 3, and the optimal cut-off value of 28 days for the mean length of ICU stay was obtained.



Figure 2. ROC curve analysis of 13 candidate diagnostic indexes. ROC: Receiver Operating Characteristic; AUC: Area Under the ROC Curve; ICULOS: Intensive Care Unit Length of Stay; ETID: Endotracheal Intubation Days; DVAUT: Days of Ventilator Away Underwent Tracheotomy; APACHE II: Acute Physiology and Chronic Health Evaluation II; CS: Conscious State; CR: Cough Reflex; PaO₂: Partial Pressure of Oxygen; PCOi: Partial Pressure of COa; Hb: Hemoglobin; ALB: Serum Albumin; NMD: Neuromuscular Disease; CVD: Cardiovascular Disease; RSD: Respiratory System Disease.

Factor selection for the predictive model, calibration and validation of the nomogram

The original model included ten variables, and all of them were later retained as potential predictors using the LASSO regression analysis. Then, a coefficient profile plot (**Figure 3A**) was constructed, and the coefficients were shown in <u>Figure S1</u>. **Figure 3B** depicted a cross-validated error plot of the LASSO regression model. The vertical dashed line in **Figure 3B** depicted the most regularized and parsimonious model, which included ten variables and had a cross-validated error within 1 standard error of the minimum.

Further multivariate logistic analysis was performed to determine whether the ten variables listed above were independent risk factors for decannulation outcomes. The results showed that ETID (adjusted odds ratio [adjusted OR] =0.25, P < 0.001), ICULOS (adjusted OR=0.32, P < 0.01), APACHE II (adjusted OR=0.86, P < 0.001), PCO₂ (adjusted OR=0.15, P < 0.001) were significantly negative related to decannulation outcome, while CR (adjusted OR= 3.87, P < 0.001), PaO, (adjusted OR=35.40, P < 0.001), ALB (adjusted OR=4.49, P < 0.001) showed a significant positive correlation (Figure 4A). Internal correlation analysis was performed among the seven variables chosen, Figure 4B showed the correlation heatmap among variables.

The final logistic model incorporated seven independent predictors (ETID, ICULOS, APA-CHE II, PCO₂, CR, PaO₂, and ALB) and was developed as a simple-to-use nomogram represented in **Figure 5A**, which was available online (https://hanchenchen.shinyapps.io/Dy-nNomapp/) as screenshotted in **Figure 5B**.

Figure 6A and 6B revealed that the AUCs of the nomogram

and external validation were 0.932 and 0.915, indicating that the model has high prediction performance. Moreover, the relatively corrected AUC value through 10-fold cross-validation was 0.926 (Figure S2A-J). Figure 6C and 6D showed that the calibration curves, respectively based on the apparent prediction results of the original model and after 1000 resampling to correct the deviation, both basically coincide with the ideal curve (The mean and absolute error of sampling were 0.008 and 0.011), indicating that the accuracy of the model is great.

Decision curve analysis and clinical impact curve

Figure 6E-H respectively depicted the decision curves and the clinical impact curves for the nomogram and external validation. As can be seen in **Figure 6E**, the net return using this model was above all patients with or without intervention when the threshold probability of

	-		-				
Variables	AUC	Cut-off value	Youden index	Sensitivity	Specificity	95% CI	P-Value
ICULOS	0.618	28.00	0.218	0.889	0.329	0.564-0.672	< 0.001
ETID	0.685	-	0.370	0.711	0.659	0.639-0.731	< 0.001
DVAUT	0.517	-	0.033	1.000	0.033	0.426-0.540	0.573
APACHE II	0.688	18.50	0.300	0.737	0.466	0.638-0.738	< 0.001
CS	0.568	-	0.136	0.625	0.358	0.511-0.626	0.021
CR	0.677	-	0.354	0.628	0.443	0.624-0.730	< 0.001
PaO ₂	0.710	-	0.421	0.450	0.419	0.664-0.757	< 0.001
PCO ₂	0.742	-	0.484	0.758	0.551	0.698-0.786	< 0.001
HB	0.564	-	0.128	0.615	0.514	0.507-0.621	0.030
ALB	0.586	-	0.172	0.259	0.912	0.526-0.646	0.004
NMD	0.528	-	0.056	0.978	0.079	0.472-0.585	0.340
CVD	0.565	-	0.130	0.511	0.619	0.508-0.623	0.027
RSD	0.550	-	0.100	0.770	0.329	0.493-0.606	0.091

Table 3. ROC analysis results of 13 candidate diagnostic indicators

ROC: Receiver Operating Characteristic; AUC: Area Under the ROC Curve; CI: Confidence Interval; ICULOS: Intensive Care Unit Length of Stay; ETID: Endotracheal Intubation Days; DVAUT: Days of Ventilator Away Underwent Tracheotomy; APACHE II: Acute Physiology and Chronic Health Evaluation II; CS: Conscious State; CR: Cough Reflex; PaO₂: Partial Pressure of Oxygen; PCO₂: Partial Pressure of CO₂; Hb: Hemoglobin; ALB: Serum Albumin; NMD: Neuromuscular Disease; CVD: Cardiovascular Disease; RSD: Respiratory System Disease.



Figure 3. A. The LASSO coefficients profiles plot. B. Tuning parameter (λ) selection cross-validation error curve. LASSO: Least Absolute Shrinkage and Selection Operator; ICULOS: Intensive Care Unit Length of Stay; ETID: Endotracheal Intubation Days; APACHE II: Acute Physiology and Chronic Health Evaluation II; CS: Conscious State; CR: Cough Reflex; PaO₂: Partial Pressure of Oxygen; PCOe: Partial Pressure of COa; Hb: Hemoglobin; ALB: Serum Albumin; CVD: Cardiovascular Disease.

0-0.9, while **Figure 6G** demonstrated that the net return from using this model in the external validation cohort was consistently above all patients with or without intervention. All figures above visually indicated that the nomogram in this study has a high clinical net benefit and clinical value.

Discussion

Between 1993 and 2012, 1,352,432 adult patients (9.1% of MV patients) received tracheotomy in the United States, and more than 110,000 tracheotomy cases are still recorded each year [24, 25]. Failure to decannulate in



Figure 4. A. Forest maps of Logistic regression analysis of different decannulation outcome cohorts. *P < 0.05, **P < 0.01, ***P < 0.001. B. Heat map of correlation among 7 indicators (ETID, ICULOS, APACHE II, PCO₂, CR, PaO₂, and ALB). ETID: Endotracheal Intubation Days; ICULOS: Intensive Care Unit Length of Stay; APACHE II: Acute Physiology and Chronic Health Evaluation II; CS: Conscious State; CR: Cough Reflex; PaO₂: Partial Pressure of Oxygen; PCOe: Partial Pressure of COP; CVD: Cardiovascular Disease; Hb: Hemoglobin; ALB: Serum Albumin.

the short term can delay a patient's recovery, increase their psychological burden and medical costs. Respiratory and neurological dysfunctions are generally considered to be common risk factors for decannulation failure [26, 27]. In 2003, Ceriana et al. developed a flow chart for decannulation. The criteria for decannulation include (1) stable arterial blood gases; (2) stable clinical condition; (3) normal endoscopic examination or revealing stenotic lesions occupying 30% of the airway; (4) absence of delirium or psychiatric disorders; (5) adequate swallowing evaluated by gag reflex, blue dye, and video fluoroscopy; (6) patient able to expectorate on request; (7) maximum expiratory pressure \geq 40 cm H₂O [28]. In 2014, Vinciya et al. described a new tracheotomy capping and decannulation protocol that helps predict success or failure of decannulation [29]. Prospective studies have shown that the above criteria can reduce the reintubation rate of decannulation to a certain extent, but it lacks the ability of quantitative prediction. The protocol stipulated modifications of care for patients who previously did not meet the capping criteria that enabled successful decannulation. However, Gonzalo et al.'s study in 2020 showed that according to suction frequency plus continuous high flow oxygen therapy could further reduce decannulation time compared to 24 hours capping experiment plus intermittent high flow oxygen therapy, and there was no difference in the incidence of decannulation failure between the two groups [30]. Despite significant advances in pre-decannulation assessment in recent years, a comprehensive evaluation system for the success rate of decannulation has yet to be devised owing to the complexity of post-decannulation respiratory mechanisms and pathology. Establishing a prospective quantitative predictive nomogram will help address this issue and help ICU physicians prepare for individualized decannulation.

This is the first study to use a newly developed nomogram to predict the success rate of decannulation in ICU patients undergoing open tracheotomy. In the present study, ETID, ICULOS, APACHE II, PCO₂, CR, PaO₂, and ALB were identified as significant predictors, which together influence clinical outcomes and prognosis of open tracheotomy decannulated patients. Based on these 7 variables, we constructed a nomogram for predicting the success rate of tracheotomy decannulation. The nomogram has good distinguishing ability and clinical application value. Considering the convenience of clinical application, we constructed an online version based on a traditional nomogram, which can be easily accessed through mobile devices such as smartphones or tablets, more effectively providing digital and personalized prognostic outcome prediction for ICU tracheotomy patients requiring decannulation.



In this study, ETID and ICULOS were found to be significant predictors of decannulation results in ICU patients. The period between endotracheal intubation and tracheotomy, as well as

the time of admission to the ICU, may be used to classify tracheotomies as early or late. Most studies have shown that early tracheotomy has a higher survival benefit for ICU patients than



Figure 6. Evaluation and validation of the model. A. ROC curve of training cohort. B. External validation cohort. C. Calibration diagram of training cohort. D. External validation cohort. E, F. Decision curve analysis and clinical impact curve of training cohort. G, H. Decision curve analysis, and clinical impact curve of external cohort. ROC: Receiver Operating Characteristic; AUC: Area Under the ROC Curve.

late tracheotomy, which supports our findings [31, 32]. Additionally, O'Connor et al. demonstrated that individuals who failed decannulation had a significantly shorter time of tracheotomy tube placement [33]. Similarly, the possible correlation between ICULOS and decannulation outcomes has been described in some researches [34]. We suspect that when the ETID and ICULOS are extended, patients are more likely to suffer from infection, malnutrition, and organ failure, resulting in poor decannulation outcomes [35].

The APACHE II score is an authoritative assessment system widely used in ICU, which can comprehensively evaluate the severity of patients and the risk of death, so as to objectively formulate and modify medical plans [36, 37]. APACHE II score has an excellent ability to predict the prognosis of ICU patients [38]. The scoring system includes 12 acute physiological parameters, chronic health assessment, and age adjustment score [39]. The weight of each variable is 0-4, and the total score interval is 0-71. The higher the score, the more serious the disease, and the higher the risk of death. Our LASSO regression and multivariate logic analysis findings indicated that the APACHE II score was a significant factor in predicting the outcome of tracheotomy decannulation.

Malnutrition is considered to be the most powerful predictor of poor postoperative outcomes. At the same time, ALB is the most abundant plasma protein and also the most studied protein for diagnosing malnutrition [40]. The reduction of ALB concentration in ICU patients is mainly due to reassignment from intravascular compartments to extracellular space or loss due to massive bleeding [41]. The serum ALB value of the patient can be determined to reflect the patient's systemic status and, as a result, to help judge the results of the decannulation procedure. In this study, we found that ALB level was significantly reduced in patients with decannulation failure and was an independent risk factor for predicting the results of decannulation. The possible pathophysiological explanation is that ALB correlates with the biochemical and biophysical status of surfactants in the airway, which are thought to be catalysts for successful decannulation and clinical improvement in patients [42, 43].

A prospective, descriptive analysis of ICU patients after tracheotomy found that sputum retention and ineffective cough were the primary causes of decannulation failure [26]. Moreover, Bishnoi et al. and Perin et al. have confirmed that objective measurement of cough intensity is a common predictor of decannulation success, which is consistent with the results of our study [44, 45]. This finding can be attributed to the high-speed expiratory airflow generated by cough reflex can effectively expel airway foreign bodies or secretions, ensuring that the airway is open and avoiding aspiration and infection after decannulation [46, 47].

Arterial blood gas analysis is used in clinical practice to determine whether patients can remove their tracheotomy tubes. A normal test result indicates that the patient is getting the recommended amount of oxygen for his or her body [48]. Decannulation failure is linked to $PCO_2 > 45$ mmHg and $PaO_2 < 75$ mmHg. This conclusion is supported by Pasqua et al.' findings [49].

Although age and sex have been reported to be linked to decannulation results in some studies, they were not statistically significant in our study [13, 50, 51]. This could be due to the deviation caused by regional differences or differences in sample size.

The use of LASSO regression facilitates the selection of important independent variables that influence decannulation outcomes while taking into account significant correlations between dependent variables, which is one of the study's advantages. Another benefit of this research is the simultaneous use of internal and external validation, which ensures model stability and high validation efficiency.

However, the study has some limitations: (1) There were other possible factors associated with outcomes that may optimize the model, but our medical institution did not record. (2) The selection of each variable index and the construction of the model in this study all rely on relatively simple statistical methods. The clinical application value of nomogram in tracheotomy decannulation needs further practice verification.

Conclusion

Based on LASSO and multivariate logistic analysis, seven independent predictors of success or failure of tracheotomy decannulation were screened in this study, including ETID, ICULOS, APACHE II, PCO₂, CR, PaO₂, and ALB, and an online dynamic nomogram predictive map was constructed. This model demonstrated superior performance and differential ability in both training and external validation cohorts, which may help ICU physicians select the most appropriate time for decannulation in tracheotomy patients. Considering that tracheotomy decannulation is a high-risk procedure, future studies need to clarify the role of timing in optimizing the effect of tracheotomy decannulation and minimizing the risk of poor prognosis for patients.

Acknowledgements

We thank all the patients who consented to donate their data for analysis. This project was supported by National Natural Science Fundation (82171127). The data collection was approved by the Medical Ethics Committee of The First Affiliated Hospital of Anhui Medical University (Reference number: Quick-PJ 2022-01-32).

Written informed consent was obtained for each participant according to federal and institutional guidelines.

Disclosure of conflict of interest

None.

Abbreviations

ICU, Intensive Care Unit; AUC, Area Under The Receiver Operating Characteristic Curve; PDT, Percutaneous Dilational Tracheotomy; MV, Mechanical Ventilation: ETID. Endotracheal Intubation Days; ICULOS, Length of ICU Stay; ETT. Size, Endotracheal Tube Size; DVAUT, Days of Ventilator Away Underwent Tracheotomy; CVD, Cardiovascular Disease; RSD, Respiratory System Disease; NMD, Neuromuscular Disease; RI, Renal Insufficiency; CR, Cough Reflex; ALB, Serum Albumin; HB, Hemoglobin; PaO₂, Partial Pressure of Oxygen; PCO₂, Partial Pressure of CO₂; APACHE II, Acute Physiology and Chronic Health Evaluation II; TRIPOD, Transparent Reporting of A Multivariable Prediction Model for Individual Prognosis or Diagnosis; SD, Standard Deviation; IQR, Interquartile Range; ROC, Receiver Operating Characteristic; LASSO, Least Absolute Shrinkage and Selection Operator; Mm, Millimeters; MmHg, Millimeters of Mercury; g/l, Grams per Liter; Adjusted OR, Adjusted Odds Ratio.

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References

- Grover A, Robbins J, Bendick P, Gibson M and Villalba M. Open versus percutaneous dilatational tracheostomy: efficacy and cost analysis. Am Surg 2001; 67: 297-301; discussion 301-2.
- [2] Botti C, Lusetti F, Neri T, Peroni S, Castellucci A, Salsi P and Ghidini A. Comparison of percutaneous dilatational tracheotomy versus open surgical technique in severe COVID-19: complication rates, relative risks and benefits. Auris Nasus Larynx 2021; 48: 511-517.
- [3] McGrath BA, Brenner MJ, Warrillow SJ, Pandian V, Arora A, Cameron TS, Añon JM, Hernández Martínez G, Truog RD, Block SD, Lui GCY, McDonald C, Rassekh CH, Atkins J, Qiang L, Vergez S, Dulguerov P, Zenk J, Antonelli M, Pelosi P, Walsh BK, Ward E, Shang Y, Gasparini S, Donati A, Singer M, Openshaw PJM, Tolley N, Markel H and Feller-Kopman DJ. Tracheostomy in the COVID-19 era: global and multidisciplinary guidance. Lancet Respir Med 2020; 8: 717-725.
- [4] Durbin CG Jr. Tracheostomy: why, when, and how? Respir Care 2010; 55: 1056-1068.
- [5] O'Connor HH and White AC. Tracheostomy decannulation. Respir Care 2010; 55: 1076-1081.
- [6] Bach JR and Saporito LR. Criteria for extubation and tracheostomy tube removal for patients with ventilatory failure. A different approach to weaning. Chest 1996; 110: 1566-1571.
- [7] Denison S. Decannulation of patients with long-term tracheostomies. Nurs Times 2004; 100: 58-59.
- [8] Stelfox HT, Crimi C, Berra L, Noto A, Schmidt U, Bigatello LM and Hess D. Determinants of tracheostomy decannulation: an international survey. Crit Care 2008; 12: R26.
- [9] Singh RK, Saran S and Baronia AK. The practice of tracheostomy decannulation-a systematic review. J Intensive Care 2017; 5: 38.
- [10] Friedman J, Hastie T and Tibshirani R. Regularization paths for generalized linear models via coordinate descent. J Stat Softw 2010; 33: 1-22.
- [11] Zhou ZR, Wang WW, Li Y, Jin KR, Wang XY, Wang ZW, Chen YS, Wang SJ, Hu J, Zhang HN, Huang P, Zhao GZ, Chen XX, Li B and Zhang TS. In-depth mining of clinical data: the construc-

tion of clinical prediction model with R. Ann Transl Med 2019; 7: 796.

- [12] Zhang Z, Rousson V, Lee WC, Ferdynus C, Chen M, Qian X and Guo Y; written on behalf of AME Big-Data Clinical Trial Collaborative Group. Decision curve analysis: a technical note. Ann Transl Med 2018; 6: 308.
- [13] Hernández G, Ortiz R, Pedrosa A, Cuena R, Vaquero Collado C, González Arenas P, García Plaza S, Canabal Berlanga A and Fernández R. The indication of tracheotomy conditions the predictors of time to decannulation in critical patients. Med Intensiva 2012; 36: 531-539.
- [14] Chorath K, Hoang A, Rajasekaran K and Moreira A. Association of early vs late tracheostomy placement with pneumonia and ventilator days in critically ill patients: a meta-analysis. JAMA Otolaryngol Head Neck Surg 2021; 147: 450-459.
- [15] Halum SL, Ting JY, Plowman EK, Belafsky PC, Harbarger CF, Postma GN, Pitman MJ, LaMonica D, Moscatello A, Khosla S, Cauley CE, Maronian NC, Melki S, Wick C, Sinacori JT, White Z, Younes A, Ekbom DC, Sardesai MG and Merati AL. A multi-institutional analysis of tracheotomy complications. Laryngoscope 2012; 122: 38-45.
- [16] Panuganti BA, Pang J, Francis DO, Klebaner D, Asturias A, Alattar A, Wood S, Terry M, Bryson PC, Tipton CB, Zhao EE, O'Rourke A, Maria CS, Grimm DR, Sung CK, Lao WP, Thompson JM, Crawley BK, Rosen S, Berezovsky A, Kupfer R, Hennesy TB, Clary M, Joseph IT, Sarhadi K, Kuhn M, Abdel-Aty Y, Kennedy MM, Lott DG and Weissbrod PA. Clinicodemographic predictors of tracheotomy tube size and decannulation: a multiinstitutional retrospective cohort study on tracheotomy. Ann Surg 2022; [Epub ahead of print].
- [17] Malkar MB, Gardner W, Welty SE and Jadcherla SR. Antecedent predictors of feeding outcomes in premature infants with protracted mechanical ventilation. J Pediatr Gastroenterol Nutr 2015; 61: 591-5.
- [18] de Graaff AE, Dongelmans DA, Binnekade JM and de Jonge E. Clinicians' response to hyperoxia in ventilated patients in a Dutch ICU depends on the level of FiO₂. Intensive Care Med 2011; 37: 46-51.
- [19] Almanza-Hurtado A, Polanco Guerra C, Martínez-Ávila MC, Borré-Naranjo D, Rodríguez-Yanez T and Dueñas-Castell C. Hypercapnia from physiology to practice. Int J Clin Pract 2022; 2022: 2635616.
- [20] Desai M, Gutman J, Taylor SM, Wiegand RE, Khairallah C, Kayentao K, Ouma P, Coulibaly SO, Kalilani L, Mace KE, Arinaitwe E, Mathanga DP, Doumbo O, Otieno K, Edgar D, Chaluluka E, Kamuliwo M, Ades V, Skarbinski J, Shi YP, Mag-

nussen P, Meshnick S and Ter Kuile FO. Impact of sulfadoxine-pyrimethamine resistance on effectiveness of intermittent preventive therapy for malaria in pregnancy at clearing infections and preventing low birth weight. Clin Infect Dis 2016; 62: 323-333.

- [21] He BB, Wei L, Gu YJ, Han JF, Li M, Liu YX, Bao YQ and Jia WP. Factors associated with diabetic retinopathy in Chinese patients with type 2 diabetes mellitus. Int J Endocrinol 2012; 2012: 157940.
- [22] Gatta A, Verardo A and Bolognesi M. Hypoalbuminemia. Intern Emerg Med 2012; 7 Suppl 3: S193-9.
- [23] Ge J and Xu Y. Internal medicine. Beijing: People's Sanitary Publishing Press; 2019.
- [24] Mehta AB, Syeda SN, Bajpayee L, Cooke CR, Walkey AJ and Wiener RS. Trends in tracheostomy for mechanically ventilated patients in the United States, 1993-2012. Am J Respir Crit Care Med 2015; 192: 446-454.
- [25] Shah RK, Lander L, Berry JG, Nussenbaum B, Merati A and Roberson DW. Tracheotomy outcomes and complications: a national perspective. Laryngoscope 2012; 122: 25-29.
- [26] Choate K, Barbetti J and Currey J. Tracheostomy decannulation failure rate following critical illness: a prospective descriptive study. Aust Crit Care 2009; 22: 8-15.
- [27] Chia AZH, Ng ZM, Pang YX, Ang AHC, Chow CCT, Teoh OH and Lee JH. Epidemiology of pediatric tracheostomy and risk factors for poor outcomes: an 11-year single-center experience. Otolaryngol Head Neck Surg 2020; 162: 121-128.
- [28] Ceriana P, Carlucci A, Navalesi P, Rampulla C, Delmastro M, Piaggi G, De Mattia E and Nava S. Weaning from tracheotomy in long-term mechanically ventilated patients: feasibility of a decisional flowchart and clinical outcome. Intensive Care Med 2003; 29: 845-848.
- [29] Pandian V, Miller CR, Schiavi AJ, Yarmus L, Contractor A, Haut ER, Feller-Kopman DJ, Mirski MA, Morad AH, Carey JP, Hillel AT, Maragos CS and Bhatti NI. Utilization of a standardized tracheostomy capping and decannulation protocol to improve patient safety. Laryngoscope 2014; 124: 1794-1800.
- [30] Hernández Martínez G, Rodriguez ML, Vaquero MC, Ortiz R, Masclans JR, Roca O, Colinas L, de Pablo R, Espinosa MD, Garcia-de-Acilu M, Climent C and Cuena-Boy R. High-flow oxygen with capping or suctioning for tracheostomy decannulation. N Engl J Med 2020; 383: 1009-1017.
- [31] Shan L, Zhang R and Li LD. Effect of timing of tracheotomy on clinical outcomes: an update meta-analysis including 11 trials. Chin Med Sci J 2013; 28: 159-166.

- [32] Liu X, Wang HC, Xing YW, He YL, Zhang ZF and Wang T. The effect of early and late tracheotomy on outcomes in patients: a systematic review and cumulative meta-analysis. Otolaryngol Head Neck Surg 2014; 151: 916-922.
- [33] O'Connor HH, Kirby KJ, Terrin N, Hill NS and White AC. Decannulation following tracheostomy for prolonged mechanical ventilation. J Intensive Care Med 2009; 24: 187-194.
- [34] Tobin AE and Santamaria JD. An intensivist-led tracheostomy review team is associated with shorter decannulation time and length of stay: a prospective cohort study. Crit Care 2008; 12: R48.
- [35] Gillespie M, Kuijpers M, Van Rossem M, Ravishankar C, Gaynor JW, Spray T and Clark B 3rd. Determinants of intensive care unit length of stay for infants undergoing cardiac surgery. Congenit Heart Dis 2006; 1: 152-160.
- [36] Moreno RP and Nassar AP Jr. Is APACHE II a useful tool for clinical research? Rev Bras Ter Intensiva 2017; 29: 264-267.
- [37] Godinjak A, Iglica A, Rama A, Tančica I, Jusufović S, Ajanović A and Kukuljac A. Predictive value of SAPS II and APACHE II scoring systems for patient outcome in a medical intensive care unit. Acta Med Acad 2016; 45: 97-103.
- [38] Tian Y, Yao Y, Zhou J, Diao X, Chen H, Cai K, Ma X and Wang S. Dynamic APACHE II score to predict the outcome of intensive care unit patients. Front Med (Lausanne) 2021; 8: 744907.
- [39] Niewiński G, Starczewska M and Kański A. Prognostic scoring systems for mortality in intensive care units-the APACHE model. Anaesthesiol Intensive Ther 2014; 46: 46-49.
- [40] Zhang Z, Pereira SL, Luo M and Matheson EM. Evaluation of blood biomarkers associated with risk of malnutrition in older adults: a systematic review and meta-analysis. Nutrients 2017; 9: 829.
- [41] Vincent JL, Russell JA, Jacob M, Martin G, Guidet B, Wernerman J, Ferrer R, McCluskey SA and Gattinoni L. Albumin administration in the acutely ill: what is new and where next? Crit Care 2014; 18: 231.
- [42] Chida S, Fujiwara T, Konishi M, Shimada S and Takahashi A. Surfactant proteins and stable microbubbles in tracheal aspirates of infants with respiratory distress syndrome: relation to the degree of respiratory failure and response to exogenous surfactant. Eur J Pediatr 1997; 156: 131-138.
- [43] Heching M, Lev S, Shitenberg D, Dicker D and Kramer MR. Surfactant for the treatment of ARDS in a patient with COVID-19. Chest 2021; 160: e9-e12.
- [44] Bishnoi T, Sahu PK and Arjun AP. Evaluation of factors determining tracheostomy decannula-

tion failure rate in adults: an Indian Perspective Descriptive Study. Indian J Otolaryngol Head Neck Surg 2020; 1-6.

- [45] Perin C, Meroni R, Rega V, Braghetto G and Cerri CG. Parameters influencing tracheostomy decannulation in patients undergoing rehabilitation after severe acquired brain injury (sABI). Int Arch Otorhinolaryngol 2017; 21: 382-389.
- [46] Andrani F, Aiello M, Bertorelli G, Crisafulli E and Chetta A. Cough, a vital reflex. Mechanisms, determinants and measurements. Acta Biomed 2019; 89: 477-480.
- [47] Amin SN, Rodney JP and Gelbard A. Open airway surgery in a paraplegic: the importance of an adequate cough. Ann Otol Rhinol Laryngol 2019; 128: 1194-1197.
- [48] Larkin BG and Zimmanck RJ. Interpreting arterial blood gases successfully. AORN J 2015; 102: 343-354; quiz 355-7.

- [49] Pasqua F, Nardi I, Provenzano A and Mari A; Lazio Regional Section, Italian Association of Hospital Pulmonologists (AIPO). Weaning from tracheostomy in subjects undergoing pulmonary rehabilitation. Multidiscip Respir Med 2015; 10: 35.
- [50] Mathur NN and Sohliya LM. Pre-decannulation peristomal findings in tracheostomized cases and their effect on the success of decannulation. Indian J Otolaryngol Head Neck Surg 2015; 67: 91-97.
- [51] Bach JR and Saporito LR. Indications and criteria for decannulation and transition from invasive to noninvasive long-term ventilatory support. Respir Care 1994; 39: 515-528; discussion 529-531.

Section /Tonic	ltom		Checklist Itom	Para
Title and abstract	nem			rage
	4	D.11	Identify the study on developing and (as well-deting a multi-sub-black of the study	Davia 4
litle	1	D;v	identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	Page 1
Abstract	2	D;V	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	Page 3-4
Introduction				
Background and objectives	3a	D;V	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	Page 5-6
	Зb	D;V	Specify the objectives, including whether the study describes the develop- ment or validation of the model or both.	Page 6
Methods				
Source of data	4a	D;V	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	Page 6-7
	4b	D;V	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	Page 7
Participants	5a	D;V	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	Page 6-7
	5b	D;V	Describe eligibility criteria for participants.	Page 7
	5c	D;V	Give details of treatments received, if relevant.	/
Outcome	6a	D;V	Clearly define the outcome that is predicted by the prediction model, includ- ing how and when assessed.	Page 7
	6b	D;V	Report any actions to blind assessment of the outcome to be predicted.	Page 7-8
Predictors	7a	D;V	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	Page 8-9
	7b	D;V	Report any actions to blind assessment of predictors for the outcome and other predictors.	Page 8-9
Sample size	8	D;V	Explain how the study size was arrived at.	Page 9
Missing data	9	D;V	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	Page 9-10
Statistical analysis methods	10a	D	Describe how predictors were handled in the analyses.	Page 9-10
	10b	D	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	Page 10
	10c	V	For validation, describe how the predictions were calculated.	Page 10-11
	10d	D;V	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	Page 10-11
	10e	V	Describe any model updating (e.g., recalibration) arising from the validation, if done.	/
Risk groups	11	D;V	Provide details on how risk groups were created, if done.	Page 10-11
Development vs. validation	12	V	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	Page 10-11
Results		_		_
Participants	13a	D;V	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	Page 11; Figure 1
	13b	D;V	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	Page 11-12; Table 1
	13c	V	For validation, show a comparison with the development data of the distribu- tion of important variables (demographics, predictors and outcome).	Table 2
Model development	14a	D	Specify the number of participants and outcome events in each analysis.	Table 2
	14b	D	If done, report the unadjusted association between each candidate predictor and outcome.	Figure 4
Model specification	15a	D	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	Page 14; Figure 5
	15b	D	Explain how to the use the prediction model.	Page 14-15
Model performance	16	D;V	Report performance measures (with Cls) for the prediction model.	Page 14-15
Model-updating	17	V	If done, report the results from any model updating (i.e., model specification, model performance).	/

Table S1. The TRIPOD (

Discussion				
Limitations	18	D;V	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	Page 19
Interpretation	19a	V	For validation, discuss the results with reference to performance in the devel- opment data, and any other validation data.	Page 16
	19b	D;V	Give an overall interpretation of the results, considering objectives, limita- tions, results from similar studies, and other relevant evidence.	Page 19
Implications	20	D;V	Discuss the potential clinical use of the model and implications for future research.	Page 17
Other information				
Supplementary information	21	D;V	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	Supplementary file
Funding	22	D;V	Give the source of funding and the role of the funders for the present study.	Page 22
Implications Other information Supplementary information Funding	19b 20 21 22	D;V D;V D;V D;V	Give an overall interpretation of the results, considering objectives, limita- tions, results from similar studies, and other relevant evidence. Discuss the potential clinical use of the model and implications for future research. Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets. Give the source of funding and the role of the funders for the present study.	Page 19 Page 17 Supplementary fil Page 22

TRIPOD: Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis; Items relevant only to the development of a prediction model are denoted by D, items relating solely to a validation of a prediction model are denoted by V, and items relating to both are denoted D;V. Some of the items were not applicable (/) to the current study.



Figure S1. The coefficient of seven indicators used to establish the model. PCO_2 : Partial Pressure of CO_2 ; ETID: Endotracheal Intubation Days; ICULOS: Intensive Care Unit Length of Stay; APACHE II: Acute Physiology and Chronic Health Evaluation II; CR: Cough Reflex; ALB: Serum Albumin; PaO₂: Partial Pressure of Oxygen.



Figure S2. A-J. 10-fold cross validation for internal validation process. AUC: Area Under the Receiver Operating Characteristic Curve.