Tracheostomy timing and weaning outcomes following prolonged mechanical ventilation

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Definitions of ventilatory variables and indexes

Ventilatory ratio (VR)	Ventilatory ratio (VR) is a surrogate of pulmonary dead space fraction and a simple bedside index of impaired efficiency of ventilation[1-2]: $\mathbf{VR = VE_{measured} * P_aCO_{2\text{-}measured} / VE_{predicted} * P_aCO_{2\text{-}ideal}}$ $VE_{measured}$ is the measured minute ventilation (mL/min), $P_aCO_{2\text{-}measured}$ is the measured arterial pressure of carbon dioxide (mmHg), $VE_{predicted}$ is the predicted minute ventilation calculated as predicted bodyweight x 100 (mL/min), and P_aCO2_{ideal} is the expected arterial pressure of carbon dioxide in normal lungs if ventilated with the predicted minute ventilation. $P_aCO_{2\text{-}ideal}$ is set at 37.5 mmHg (5 kPa) for all patients.
Mechanical power (MP)	Mechanical power (MP)[4] provided by the ventilator in the pressure-controlled mode was calculated using a simplified formula, including respiratory rate (RR), tidal volume (VT), and peak airway pressure (P_{max})[3-4]: $\mathbf{MP\ (Joule/min) = 0.098 * RR * VT * P_{max}}$ $\mathbf{MP\ (Joule/min) = 0.098 * VE * P_{max}}$
Mechanical power normalized to dynamic respiratory system compliance (C_{dyn}-MP), referred to as "power density."	MP normalized to dynamic lung-thorax compliance (C_{dyn}-MP) was calculated using MP and dynamic respiratory compliance (C_{dyn})[5]: $\mathbf{C_{dyn}\text{-}MP\ (J/min * cmH_2O/mL) = MP / C_{dyn}}$ $\mathbf{C_{dyn}\text{-}MP\ (J/min * cmH_2O/mL) = (0.098 * RR * VT * P_{max}) * (\Delta P_{aw} / VT)}$ ↓ $\mathbf{C_{dyn}\text{-}MP\ (cmH_2O^2/min) = RR * P_{max} * \Delta P_{aw}}$ $\mathbf{C_{dyn}\text{-}MP\ (cmH_2O^2/min) = RR * P_{max} * (P_{max} – PEEP)}$ This formula accounts for different effects of changes in respiratory rate, inflation pressure (P_{max}), and PEEP (and thus changes in ΔP_{aw}) on delivered energy. This index measures the intensity of mechanical stress placed on the respiratory system, determined by peak airway pressure, dynamic driving pressure, and the frequency of their application. In physical terms, this normalization equals mechanical "*power density*". Power density is related to tidal "*strain energy density*", which represents the stored energy per unit of volume resulting from a body's linear elastic deformation (resistive-elastic unicompartmental model). Concerning mechanical ventilation, causing the lungs and thorax to expand elastically, SED is the stored energy per unit of tidal volume displaced, ultimately driving expiration[6-7].

Propensity score matching – Specification of covariates and results

Variable selection

Propensity scores (PS) were calculated using demographics, baseline clinical characteristics, and comorbidities to ensure that baseline patient-related factors were balanced among the matched groups, including those who underwent an early (≤ 14 days) and late tracheostomy.

The following variables were included in the binary logistic regression model to calculate the propensity score, which measures the likelihood of an early tracheostomy after intubation: **Age**, **female gender**, **obesity** (body mass index ≥ 30 kg/m^2), **APACHE-II**, provision of **extracorporeal lung support** during acute respiratory failure, **percutaneous tracheostomy**, **COVID-19** pneumonia as the main reason for mechanical ventilation, **surgery**, **Charlson comorbidity index**, **renal insufficiency**, **hemodialysis** on weaning center admission, **COPD**, **chronic heart failure**, and diagnosis of **interstitial lung diseases**. Subjects were matched 1:1 without replacement using the nearest-neighbor method, with a caliper distance of 0.1 SD of the propensity score logit.

Results

PS matching resulted in 220 patients within each group, categorized by early (≤ 14 days) and late tracheostomies. Based on a standard mean difference (SMD) of -0.34 * 10^{-3} ([95%CI -0.34 * 10^{-2} – 0.27 * 10^{-2}]; *P* = 0.828) of the PS scores, both groups exhibited a good balance of baseline characteristics (Table 1).

PS matching in sensitivity analysis was performed using identical variables for the logistic regression model, yielding a standard mean difference (SMD) of -0.17 * 10^{-2} ([95%CI -0.53 * 10^{-2} – 0.18 * 10^{-2}]; *P* = 0.340) of the PS score between the early and late tracheostomy groups.

Table S1. Clinical characteristics on admission to the weaning center – Comparison of patients with early (≤ 14 days) and late tracheostomy (> 14 days)

Clinical characteristics	**All patients** (n = 738)	**Early tracheostomy** (n = 507)	**Late tracheostomy** (n = 231)	***P* value[a]**
Age (years)	70 (62–76)	71 (62–77)	69 (59–77)	0.054[b]
Female gender	268 (36)	180 (36)	88 (38)	0.497[c]
Predicted body weight (kg)	66 (60–75)	66 (61–75)	66 (57–73)	0.355[b]
Body mass index (kg/m^2)	25.5 (22.9–30.5)	25.4 (23.0 – 30.2)	25.8 (22.7 – 30.8)	0.891[b]
Obesity (BMI ≥ 30 kg/m^2)	191 (26)	129 (25)	62 (27)	0.688[c]
Smoking history	292 (40)	209 (41)	83 (36)	0.173[c]
APACHE-II (points)	16 (12–19)	16 (12–20)	15 (12–18)	**0.043[b]**
Pre-existing domiciliary NIV	36 (5)	27 (5)	9 (4)	0.404[c]
Extracorporeal lung support	63 (9)	30 (6)	33 (14)	**< 0.01[c]**
Percutaneous tracheostomy	538 (73)	368 (73)	170 (74)	0.775[c]
Intubation to tracheostomy (days)	11 (7–16)	9 (6–12)	19 (17–22)	–
Ventilator days on center admission	23 (15–33)	18 (13–27)	31 (25–42)	**< 0.01[b]**
Reason for intubation				
Pneumonia	262 (36)	182 (36)	80 (35)	0.739[c]
SARS-CoV-2 infection	79 (11)	51 (10)	28 (12)	0.401[c]
Surgery	206 (28)	133 (26)	73 (32)	0.132[c]
Cardiopulmonary resuscitation	69 (9)	46 (9)	23 (10)	0.702[c]
Sepsis (extrapulmonary)	57 (8)	43 (9)	14 (6)	0.254[c]
Acute exacerbation of COPD	60 (8)	47 (9)	13 (6)	0.093[c]
Acute heart failure	16 (2)	9 (2)	7 (3)	0.278[d]
Other	68 (9)	47 (9)	21 (9)	0.938[c]
Comorbidities				
Charlson index (points)	5 (4–7)	6 (4–7)	5 (4–7)	0.086[b]
Renal insufficiency	200 (27)	127 (25)	73 (32)	0.064[c]
Hemodialysis on admission	126 (17)	77 (15)	49 (21)	**0.044[c]**
Diabetes mellitus	183 (25)	131 (26)	52 (23)	0.332[c]
Coronary artery disease	207 (28)	146 (29)	61 (26)	0.503[c]
COPD	155 (21)	110 (22)	45 (20)	0.494[c]
Chronic heart failure	112 (15)	74 (15)	38 (17)	0.515[c]
Malignancy	65 (9)	47 (9)	18 (8)	0.512[c]
Hepatopathy	37 (5)	24 (5)	13 (6)	0.606[c]
Interstitial lung diseases	33 (5)	25 (5)	8 (4)	0.371[c]
Neuromuscular disease	24 (3)	17 (3)	7 (3)	0.819[c]

Legend

Continuous variables are presented as median (– interquartile range [IQR]); categorical variables are presented as numbers (%). Significant values ($P < 0.05$) are in bold.

a: P value for differences between patients with early (≤ 14 days) and late (> 14 days) tracheostomy
b: Mann-Whitney *U*-test
c: Chi-squared test
d: Fisher's exact test

Abbreviations: BMI, body mass index; APACHE-II, Acute Physiology and Chronic Health Evaluation II score; NIV, non-invasive ventilation; COPD, chronic obstructive pulmonary disease.

Table S2. Variables independently associated with prolonged weaning failure – Results of univariable and multivariable binary logistic regression analysis – Tracheostomy timing as a categorical variable (N = 738)

Variables	Univariable analysis		Multivariable analysis	
	OR (95%CI)	***P value***	**OR (95%CI)**	***P value***
Tracheostomy timing				
Early tracheostomy < 14 days	1.29 (0.93–1.80)	0.132	–	n.s.
Early tracheostomy < 10 days	1.57 (1.16–2.13)	**< 0.01**	–	n.s.
Clinical characteristics				
Age (years)	1.01 (1.00–1.02)	0.132	–	n.s.
Female gender	2.03 (1.49–2.77)	**< 0.01**	1.77 (1.23–2.56)	**< 0.01**
Obesity *(BMI ≥ 30 kg/m^2)*	1.62 (1.16–2.27)	**< 0.01**	2.06 (1.37–3.08)	**< 0.01**
APACHE-II (points)	1.02 (0.99–1.05)	0.242	–	n.s.
Extracorporeal lung support	0.14 (0.06–0.36)	**< 0.01**	0.27 (0.10–0.71)	**< 0.01**
Percutaneous tracheostomy	0.65 (0.46–0.90)	**0.010**	–	n.s.
Reason for intubation				
SARS-CoV-2 pneumonia	0.21 (0.10–0.43)	**< 0.01**	0.30 (0.14–0.65)	**< 0.01**
Surgery	0.57 (0.40–0.81)	**< 0.01**	0.64 (0.42–0.96)	**0.031**
Comorbidities				
Charlson index (points)	1.09 (1.02–1.16)	**< 0.01**	1.10 (1.02–1.19)	**0.015**
Renal insufficiency	0.58 (0.41–0.83)	**< 0.01**	–	n.s.
Hemodialysis on admission	0.70 (0.46–1.06)	0.093	–	n.s.
Coronary artery disease	0.92 (0.66–1.30)	0.650	–	n.s.
COPD	10.6 (6.88–15.9)	**< 0.01**	9.60 (6.17–14.9)	**< 0.01**
Chronic heart failure	0.86 (0.56–1.31)	0.478	–	n.s.
Interstitial lung diseases	0.48 (0.21–1.13)	0.094	–	n.s.

Legend
Variables deemed clinically relevant a priori and those with *P* values less than 0.2 were used as input variables in the multivariable binary regression analysis.

Abbreviations: OR, odds ratio; 95%CI, 95% confidence interval; n.s., not significant; APACHE-II, Acute Physiology and Chronic Health Evaluation II score; COPD, chronic obstructive pulmonary disease.

Table S3. Multivariable binary logistic regression model of variables predicting prolonged weaning failure – Tracheostomy timing as a categorical variable (N = 738)

Logit(p)	L = – 1.80496 + (0.57311 * female gender) + (0.72027 * Obesity) + (-1.30334 * ECLS) + (-1.20221 * SARS-CoV-2 pneumonia) + (-0.45208 * surgery) + (0.094573 * Charlson index) + (2.26154 * COPD)			
OR (95%CI); *P* value	Female gender	1.77 (1.23–2.56)		< 0.01
	Obesity	2.06 (1.37–3.08)		< 0.01
	ECLS	0.27 (0.10–0.71)		< 0.01
	SARS-CoV-2 pneumonia	0.30 (0.14–0.65)		< 0.01
	Surgery	0.64 (0.42–0.96)		0.031
	Charlson index	1.10 (1.02–1.19)		0.015
	COPD	9.60 (6.17–14.9)		< 0.01
Hosmer & Lemeshow	0.787			
Nagelkerke R^2	0.337			
AUROC (95%CI)	0.80 (0.77 – 0.83)			
2 x 2 table	**TP** 128		**FP** 41	
	FN 131		**TN** 438	
Metrics from 2 x 2 table (95%CI)	**Sensitivity**	49% (43–56)	**PLR**	5.77
	Specificity	91% (89–94)	**NLR**	0.55
	PPV	76% (69–81)	**DOR**	10.5
	NPV	77% (75–79)	**F_1 score**	0.60
	Accuracy	77% (73–80)	**MCC**	0.46

Legend

Variables independently associated with prolonged weaning failure after adjustment for tracheostomy timing (early tracheostomy < 14 days/10 days *vs.* late tracheostomy), age, gender, obesity, APACHE-II, ECLS, tracheostomy technique (percutaneous *vs.* surgical), SARS-CoV-2 pneumonia and surgery (as the reason for intubation), Charlson index, and renal insufficiency, hemodialysis on admission, coronary artery disease, COPD, chronic heart failure, and interstitial lung disease (as comorbidities).

Abbreviations: L, log-odds/Logit(p); ECLS, extracorporeal lung support; COPD, chronic obstructive pulmonary disease; OR, odds ratio; 95%CI, 95% confidence interval; AUROC, area under the receiver operating characteristic curve; TP, true positive; FP, false positive; FN, false negative; TN, true positive; PPV, positive predictive value; NPV, negative predictive value; PLR, positive likelihood ratio; NLR, negative likelihood ratio; DOR, diagnostic odds ratio; MCC, Matthews correlations coefficient.

Table S4. Variables independently associated with prolonged weaning failure – Results of univariable and multivariable binary logistic regression analysis – Tracheostomy timing as a continuous variable (N = 738)

Variables	Univariable analysis		Multivariable analysis	
	OR (95%CI)	***P value***	**OR (95%CI)**	***P value***
Tracheostomy timing				
Intubation to tracheostomy (days)	0.97 (0.95–0.99)	**< 0.01**	0.97 (0.95–0.99)	**0.011**
Clinical characteristics				
Age (years)	1.01 (1.00–1.02)	0.132	–	n.s.
Female gender	2.03 (1.49–2.77)	**< 0.01**	1.79 (1.24–2.58)	**< 0.01**
Obesity *(BMI ≥ 30 kg/m^2)*	1.62 (1.16–2.27)	**< 0.01**	2.11 (1.40–3.16)	**< 0.01**
APACHE-II (points)	1.02 (0.99–1.05)	0.242	–	n.s.
Extracorporeal lung support	0.14 (0.06–0.36)	**< 0.01**	0.30 (0.11–0.80)	**0.016**
Percutaneous tracheostomy	0.65 (0.46–0.90)	**0.010**	–	n.s.
Reason for intubation				
SARS-CoV-2 pneumonia	0.21 (0.10–0.43)	**< 0.01**	0.31 (0.14–0.68)	**< 0.01**
Surgery	0.57 (0.40–0.81)	**< 0.01**	0.65 (0.43–0.99)	**0.044**
Comorbidities				
Charlson index (points)	1.09 (1.02–1.16)	**< 0.01**	1.09 (1.01–1.18)	**0.022**
Renal insufficiency	0.58 (0.41–0.83)	**< 0.01**	–	n.s.
Hemodialysis on admission	0.70 (0.46–1.06)	0.093	–	n.s.
Coronary artery disease	0.92 (0.66–1.30)	0.650	–	n.s.
COPD	10.6 (6.88–15.9)	**< 0.01**	9.97 (6.38–15.6)	**< 0.01**
Chronic heart failure	0.86 (0.56–1.31)	0.478	–	n.s.
Interstitial lung diseases	0.48 (0.21–1.13)	0.094	–	n.s.

Legend
Variables deemed clinically relevant a priori and those with *P* values less than 0.2 were used as input variables in the multivariable binary regression analysis.

Abbreviations: OR, odds ratio; 95%CI, 95% confidence interval; n.s., not significant; APACHE-II, Acute Physiology and Chronic Health Evaluation II score; COPD, chronic obstructive pulmonary disease.

Table S5. Multivariable binary logistic regression model of variables predicting prolonged weaning failure – Tracheostomy timing as a continuous variable (N = 738)

Logit(p)	L = – 1.43477 + (0.58013 * female gender) + (0.74515 * Obesity) + (-1.19581 * ECLS) + (-1.16199 * SARS-CoV-2 pneumonia) + (-0.42431 * surgery) + (0.089617 * Charlson index) + (2.29967 * COPD) + (-0.031424 * Intubation to tracheostomy)			
OR (95%CI); *P* value	Female gender	1.79 (1.24–2.58)		< 0.01
	Obesity	2.11 (1.40–3.16)		< 0.01
	ECLS	0.30 (0.11–0.80)		0.016
	SARS-CoV-2 pneumonia	0.31 (0.14–0.68)		< 0.01
	Surgery	0.65 (0.43–0.99)		0.044
	Charlson index	1.09 (1.01–1.18)		0.022
	COPD	9.97 (6.38–15.6)		< 0.01
	Intubation to tracheostomy	0.97 (0.95–0.99)		0.011
Hosmer & Lemeshow	0.885			
Nagelkerke R^2	0.347			
AUROC (95%CI)	0.80 (0.77 – 0.83)			
2 x 2 table	**TP** 137		**FP** 46	
	FN 122		**TN** 433	
Metrics from 2 x 2 table (95%CI)	**Sensitivity**	53% (47–59)	**PLR**	5.51
	Specificity	90% (87–93)	**NLR**	0.52
	PPV	75% (69–80)	**DOR**	10.6
	NPV	78% (76–80)	**F_1 score**	0.62
	Accuracy	77% (74–80)	**MCC**	0.48

Legend

Variables independently associated with prolonged weaning failure after adjustment for tracheostomy timing (early tracheostomy < 14 days/10 days *vs.* late tracheostomy), age, gender, obesity, APACHE-II, ECLS, tracheostomy technique (percutaneous *vs.* surgical), SARS-CoV-2 pneumonia and surgery (as the reason for intubation), Charlson index, and renal insufficiency, hemodialysis on admission, coronary artery disease, COPD, chronic heart failure, and interstitial lung disease (as comorbidities).

Abbreviations: L, log-odds/Logit(p); ECLS, extracorporeal lung support; COPD, chronic obstructive pulmonary disease; OR, odds ratio; 95%CI, 95% confidence interval; AUROC, area under the receiver operating characteristic curve; TP, true positive; FP, false positive; FN, false negative; TN, true positive; PPV, positive predictive value; NPV, negative predictive value; PLR, positive likelihood ratio; NLR, negative likelihood ratio; DOR, diagnostic odds ratio; MCC, Matthews correlations coefficient.

Table S6. Clinical characteristics on admission to the weaning center – Comparison of patients with early (≤ 10 days) and late tracheostomy (> 10 days)

Clinical characteristics	**All patients** (n = 738)	**Early tracheostomy** (n = 342)	**Late tracheostomy** (n = 396)	***P* value[a]**
Age (years)	70 (62–76)	71 (62–77)	69 (61–76)	0.100[b]
Female gender	268 (36)	124 (36)	144 (36)	0.976[c]
Predicted body weight (kg)	66 (60–75)	66 (61–75)	66 (58–75)	0.988[b]
Body mass index (kg/m^2)	25.5 (22.9–30.5)	25.1 (23.0–29.4)	26.0 (22.9–30.9)	0.345[b]
Obesity (BMI ≥ 30 kg/m^2)	191 (26)	79 (23)	112 (28)	0.109[c]
Smoking history	292 (40)	145 (42)	147 (37)	0.144[c]
APACHE-II (points)	16 (12–19)	16 (13–20)	15 (12–19)	0.061[b]
Pre-existing domiciliary NIV	36 (5)	22 (6)	14 (4)	0.069[c]
Extracorporeal lung support	63 (9)	16 (5)	47 (12)	**< 0.01[c]**
Percutaneous tracheostomy	538 (73)	248 (73)	290 (73)	0.827[c]
Intubation to tracheostomy (days)	11 (7–16)	7 (5–9)	16 (13–20)	–
Ventilator days on center admission	23 (15–33)	16 (11–25)	27 (20–39)	**< 0.01[b]**
Reason for intubation				
Pneumonia	262 (36)	122 (36)	140 (35)	0.928[c]
SARS-CoV-2 infection	79 (11)	28 (8)	51 (13)	**0.040[c]**
Surgery	206 (28)	86 (25)	120 (30)	0.120[c]
Cardiopulmonary resuscitation	69 (9)	29 (9)	40 (10)	0.451[c]
Sepsis (extrapulmonary)	57 (8)	26 (8)	31 (8)	0.909[c]
Acute exacerbation of COPD	60 (8)	40 (12)	20 (5)	**< 0.01[c]**
Acute heart failure	16 (2)	6 (2)	10 (3)	0.474[d]
Other	68 (9)	33 (10)	35 (9)	0.704[c]
Comorbidities				
Charlson index (points)	5 (4–7)	6 (4–7)	5 (4–7)	**0.026[b]**
Renal insufficiency	200 (27)	82 (24)	118 (30)	0.076[c]
Hemodialysis on admission	126 (17)	42 (12)	84 (21)	**< 0.01[c]**
Diabetes mellitus	183 (25)	92 (27)	91 (23)	0.291[c]
Coronary artery disease	207 (28)	111 (33)	96 (24)	**0.013[c]**
COPD	155 (21)	82 (24)	73 (18)	0.067[c]
Chronic heart failure	112 (15)	56 (16)	56 (14)	0.400[c]
Malignancy	65 (9)	32 (9)	33 (8)	0.625[c]
Hepatopathy	37 (5)	16 (5)	21 (5)	0.698[c]
Interstitial lung diseases	33 (5)	20 (6)	13 (3)	0.093[c]
Neuromuscular disease	24 (3)	12 (4)	12 (3)	0.715[c]

Legend

Continuous variables are presented as median (– interquartile range [IQR]); categorical variables are presented as numbers (%). Significant values (*P* < 0.05) are in bold.

a: P value for differences between patients with early (≤ 10 days) and late (> 10 days) tracheostomy
b: Mann-Whitney *U*-test
c: Chi-squared test
d: Fisher's exact test

Abbreviations: BMI, body mass index; APACHE-II, Acute Physiology and Chronic Health Evaluation II score; NIV, non-invasive ventilation; COPD, chronic obstructive pulmonary disease.

Table S7. Clinical characteristics on admission to the weaning center – Comparison of propensity score-matched cohorts with early (≤ 10 days) and late tracheostomy (> 10 days)

Clinical characteristics	**All patients** (n = 578)	**Early tracheostomy** (n = 289)	**Late tracheostomy** (n = 289)	***P* value[a]**
Age (years)	71 (62–76)	70 (62–77)	71 (62–76)	0.791[b]
Female gender	217 (38)	110 (38)	107 (37)	0.797[c]
Predicted body weight (kg)	66 (60–73)	66 (60–74)	66 (59–73)	0.989[b]
Body mass index (kg/m^2)	25.3 (22.9–30.4)	25.4 (23.0–29.6)	25.2 (22.5 – 30.6)	0.728[b]
Obesity (BMI ≥ 30 kg/m^2)	148 (26)	71 (25)	77 (27)	0.568[c]
Smoking history	247 (43)	120 (42)	127 (44)	0.557[c]
APACHE-II (points)	16 (13–19)	16 (12–19)	16 (13–19)	0.553[b]
Pre-existing domiciliary NIV	31 (5)	18 (6)	13 (5)	0.356[c]
Extracorporeal lung support	32 (6)	15 (5)	17 (6)	0.716[c]
Percutaneous tracheostomy	414 (72)	209 (72)	205 (71)	0.712[c]
Intubation to tracheostomy (days)	11 (7–15)	7 (5–9)	15 (13–20)	–
Ventilator days on center admission	23 (15–32)	17 (12–26)	27 (20–38)	**< 0.01[b]**
Reason for intubation				
Pneumonia	197 (34)	103 (36)	94 (33)	0.430[c]
SARS-CoV-2 infection	56 (10)	27 (9)	29 (10)	0.779[c]
Surgery	157 (27)	78 (27)	79 (27)	0.926[c]
Cardiopulmonary resuscitation	52 (9)	20 (7)	32 (11)	0.081[c]
Sepsis (extrapulmonary)	49 (9)	23 (8)	26 (9)	0.654[c]
Acute exacerbation of COPD	51 (9)	32 (11)	19 (7)	0.057[c]
Acute heart failure	15 (3)	6 (2)	9 (3)	0.433[d]
Other	57 (10)	27 (9)	30 (10)	0.676[c]
Comorbidities				
Charlson index (points)	6 (4–7)	5 (4–7)	6 (4–7)	0.855[b]
Coronary artery disease	157 (27)	76 (26)	81 (28)	0.640[c]
Renal insufficiency	143 (25)	72 (25)	71 (25)	0.923[c]
Hemodialysis on admission	78 (14)	38 (13)	40 (14)	0.808[c]
Diabetes mellitus	145 (25)	73 (25)	72 (25)	0.924[c]
COPD	137 (24)	70 (24)	67 (23)	0.769[c]
Chronic heart failure	85 (15)	40 (14)	45 (16)	0.557[c]
Malignancy	52 (9)	26 (9)	26 (9)	0.999[c]
Hepatopathy	27 (5)	14 (5)	13 (5)	0.844[c]
Interstitial lung diseases	21 (4)	9 (3)	12 (4)	0.505[c]
Neuromuscular disease	19 (3)	10 (4)	9 (3)	0.816[c]

Legend

Continuous variables are presented as median (– interquartile range [IQR]); categorical variables are presented as numbers (%). Significant values ($P < 0.05$) are in bold.

a: P value for differences between matched patients with early (≤ 10 days) and late (> 10 days) tracheostomy
b: Mann-Whitney *U*-test
c: Chi-squared test
d: Fisher's exact test

Abbreviations: BMI, body mass index; APACHE-II, Acute Physiology and Chronic Health Evaluation II score; NIV, non-invasive ventilation; COPD, chronic obstructive pulmonary disease.

Table S8. Results of prolonged weaning – Comparison of propensity score-matched cohorts with early (≤ 10 days) and late tracheostomy (> 10 days)

Primary outcome	**All patients** (n = 578)	**Early tracheostomy** (n = 289)	**Late tracheostomy** (n = 289)	***P* value**[a]
Prolonged weaning failure	219 (38)	120 (42)	99 (34)	0.072[c]
HMV-NIV	82 (14)	42 (15)	40 (14)	0.812[c]
HMV-IMV	137 (24)	78 (27)	59 (20)	0.063[c]
Secondary outcomes				
Weaning duration from first SBT (days)	14 (11–21)	14 (11–21)	14 (11–21)	0.396[b]
Duration of mechanical ventilation (days)[§]	43 (33–59)	36 (28–51)	48 (39–66)	**< 0.01**[b]
VFD-90 (days)	47 (31–57)	54 (39–62)	42 (24–51)	**< 0.01**[b]
Decannulation failure	254 (44)	130 (45)	124 (43)	0.615[c]
SB at weaning completion (hours per day)[$]	24 (15–24)	24 (14–24)	24 (16–24)	0.298[b]
LTOT at hospital discharge*	378 (71)	196 (73)	182 (69)	0.256[c]
Weaning unit-LOS (days)	33 (24–49)	32 (24–50)	34 (25–49)	0.803[c]
Death during weaning	18 (3)	8 (3)	10 (4)	0.632[c]
Hospital mortality	47 (8)	22 (8)	25 (9)	0.648[c]

Legend

Continuous variables are presented as median (– interquartile range [IQR]); categorical variables are presented as numbers (%). Significant values ($P < 0.05$) are in bold.

§: The total duration of mechanical ventilation, the period from intubation in the referring ICU until the completion of weaning at the weaning center.
$: The values of 18 patients who died during weaning were set at 0 hours per day.
*: Excluding 47 patients who died during their hospital stay.

a: P value for differences between matched patients with early (≤ 10 days) and late (> 10 days) tracheostomy
b: Mann-Whitney *U*-test
c: Chi-squared test

Abbreviations: HMV-NIV, Home mechanical ventilation – Non-invasive ventilation; HMV-IMV, Home mechanical ventilation – Invasive mechanical ventilation; SBT, spontaneous breathing trial; VFD-90, ventilator-free days within 90 days following endotracheal intubation; SB, spontaneous breathing; LTOT, long-term oxygen therapy; LOS, length of stay.

Table S9. Respiratory system evaluation at first SBT following center admission – Comparison of propensity score-matched cohorts with early (≤ 10 days) and late tracheostomy (> 10 days)

Ventilatory variables and indexes (pre-SBT)	**All patients** (n = 578)	**Early tracheostomy** (n = 289)	**Late tracheostomy** (n = 289)	***P* value**[a]
P/F ratio (mmHg)	276 (220–331)	272 (217–329)	278 (222–331)	0.646[b]
P/F ratio < 250 mmHg	217 (38)	109 (38)	108 (37)	0.932[c]
VT/PBW (mL/kg)	8.3 (7.3–9.6)	8.3 (7.5–9.4)	8.3 (7.3–9.7)	0.874[b]
Dynamic driving pressure (cmH_2O)	16 (15–19)	16 (15–20)	16 (15–18)	0.051[b]
Ventilatory ratio	1.85 (1.56–2.28)	1.85 (1.54–2.20)	1.86 (1.57–2.37)	0.354[b]
C_{dyn} (mL/cmH_2O)	32 (27–41)	32 (26–40)	33 (28–41)	0.143[b]
Mechanical power (Joule/min)	20.7 (17.3–25.0)	20.6 (17.4–24.9)	20.9 (17.3–25.0)	0.925[b]
C_{dyn}-MP (cmH_2O^2/min)	6624 (4800–8320)	6840 (4797–8664)	6300 (5040–8123)	0.227[b]
Arterial blood gas analysis (pre-SBT)				
P_aO_2 (mmHg)	79 (71–91)	79 (71–92)	80 (71–89)	0.924[b]
P_aCO_2 (mmHg)	36 (32–40)	36 (32–40)	35 (31–39)	0.138[b]
pH	7.48 (7.45–7.51)	7.48 (7.45–7.51)	7.48 (7.45–7.52)	0.132[b]

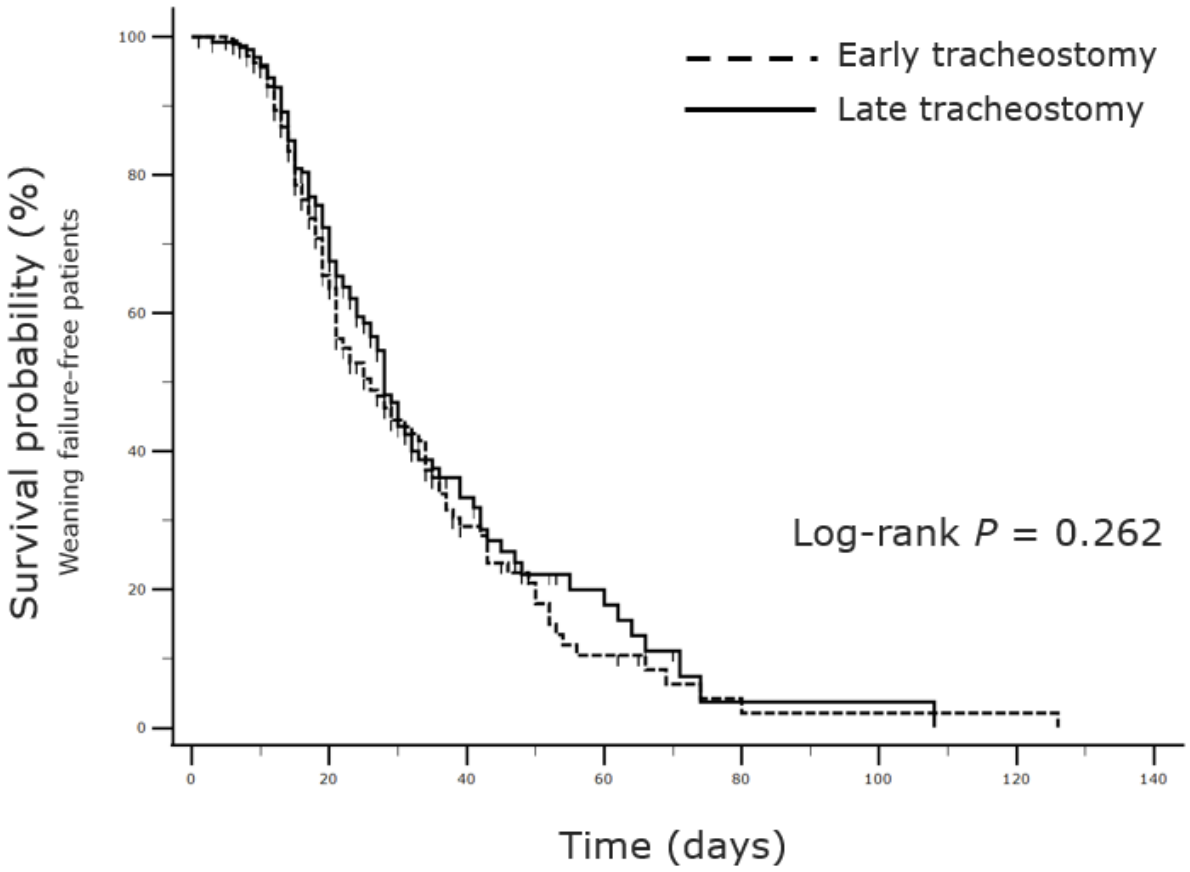
Legend

Continuous variables are presented as median (– interquartile range [IQR]). Significant values ($P < 0.05$) are in bold.

a: P value for differences between matched patients with early (≤ 10 days) and late (> 10 days) tracheostomy
b: Mann-Whitney *U*-test
c: Chi-squared test

Abbreviations: SBT, spontaneous breathing trial; P/F ratio, the ratio of partial pressure of oxygen to fraction of inspired oxygen; VT/PBW, tidal volume normalized to the predicted body weight; C_{dyn}, dynamic respiratory system compliance; C_{dyn}-MP, mechanical power normalized to dynamic respiratory system compliance.

Figure S1. Kaplan-Meier curves comparing patients with early and late tracheostomy



Legend
Comparison of prolonged weaning outcomes between patients with early (≤ 10 days) and late tracheostomy (N = 738).

E-References

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