Original

Crit Care Shock (2017) 20:90-101

Decision making of tracheostomy and extubation outcomes in mechanically ventilated patients evaluated by logistic regression and decision tree analyses

Susumu Hirosako, Hirotsugu Kohrogi, Katsuyuki Sagishima, Keisuke Sakai, Yohei Migiyama, Hidenobu Kamohara, Hiroaki Kawano, Yoshihiro Kinoshita

Abstract

***Background*: Most studies determining the predictors of extubation outcomes in patients with mechanical ventilation have not included high-risk populations who avoid extubation and undergo tracheostomy.**

***Objective*: To evaluate predictors of extubation intolerance by analyzing patients regardless of whether extubation was attempted or not.**

***Design*: Retrospective cohort study.**

***Settings*: Mixed intensive care unit (ICU) of Kumamoto University Hospital.**

***Patients and participants:* Medical data of 288 consecutive mechanically ventilated adults were collected. Initial outcomes of endotracheal tube treatment were classified as 1) successful extubation, 2) extubation failure, and 3) tracheostomy without attempting extubation. Clinical variables responsible for those outcomes were determined by logistic regression and decision tree analyses. We defined combined outcome of extubation failure and tracheostomy as extubation intolerance in the present study.**

***Results*: Of 288 patients, 17 failed extubation and 37 opted for tracheostomy without extubation. Logistic regression analysis revealed that the significant predictors of extubation failure were weak cough strength, poor consciousness, and excessive airway secretion. The propensity score of extubation failure calculated by logistic regression analysis in the tracheostomy group was as high as that of extubation failure group. A decision tree to predict the outcomes was described by branching with consciousness, style of ICU admission, and volume of airway secretion.**

***Conclusions*: The principle predictors of extubation intolerance were related to instability of airway patency, and the decision making of tracheostomy was shown to be appropriate. These statistical methods could reduce the selection bias of study subjects.**

Key words: Mechanical ventilation, extubation, tracheostomy, logistic regression analysis, propensity score, decision tree.

Introduction

Appropriate weaning and extubation are critical matters for patients with invasive mechanical ventilation. “Weaning” is the process in which mechanical ventilation is gradually withdrawn and the patient resumes spontaneous breathing, (1) while “extubation” is defined the process in which the patient is liberated from an endotracheal tube.

Extubation failure is generally defined as the need for re-intubation within 48-72 h after planned extubation. (2,3) Such failure can lengthen ventilatory support (4) and increase the incidence of nosocomial pneumonia. (5,6) Further, it is associated with mortality. (7) Early extubation when the patient’s condition is not adequately recovered causes failure; however, prolonged invasive mechanical ventilation increases patient discomfort, the incidence of ventilator-associated pneumonia, (8) and medical expense. (9) Thus, it is necessary to analyze the pathophysiology of extubation failure to determine the appropriate timing for extubation.

Numerous predictors of extubation outcome, such as advanced age, (5,7) cough strength, (10,11) respiratory frequency (f) divided by tidal volume (Vt),

From Division of Emergency and Critical Care Medicine, Kumamoto University Hospital, Kumamoto University, Kumamoto, Japan (Susumu Hirosako, Katsuyuki Sagishima, Keisuke Sakai, Yohei Migiyama, Hidenobu Kamohara, Hiroaki Kawano, Yoshihiro Kinoshita), Department of Respiratory Medicine, Kumamoto University Hospital, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan (Susumu Hirosako, Hirotsugu Kohrogi, Yohei Migiyama), Department of Dermatology and Plastic Surgery, Kumamoto University Hospital, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan (Keisuke Sakai), and Department of Clinical Nursing, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan (Hiroaki Kawano).

Address for correspondence:
Susumu Hirosako, MD
Department of Respiratory Medicine, Kumamoto University Hospital, Faculty of Life Sciences, Kumamoto University
1-1-1, Honjo, Chuo-ku, Kumamoto 860-8556, Japan
Tel: +81-96-373-5012
Fax: +81-96-373-5007
Email: hirosako@kumamoto-u.ac.jp

(3,12) amount of endotracheal secretion, (10,11) level of consciousness, (10,12) and levels of B-type natriuretic peptide during a spontaneous breathing trial (SBT) (13) have been indicated. In almost all studies, the predictors of extubation outcome, such as sensitivity, specificity, predictive value, and likelihood ratio, have been calculated on the basis of the data of successful or failed extubation. However, these evaluations have targeted only selected patients who underwent extubation and have not included patients who were deemed intolerant of extubation and therefore underwent tracheostomy. Recently, the pre-test probability of extubation failure has been found to be relatively low (10%-16%), (14-16) in part, because clinicians likely avoided extubation in high-risk patients. Therefore, the risk of extubation failure tends to be obscured and difficult to study. To determine the precise predictors of extubation outcome, all mechanically ventilated patients would need extubation without considering tracheostomy. If this occurred, many of them would likely require re-intubation, making this approach unethical.

In the present study, we targeted all mechanically ventilated high-risk patients, including those who underwent tracheostomy without extubation, and analyzed the risk factors of extubation intolerance by logistic regression analysis, calculation of propensity score, and decision tree analyses.

Methods

Patients

We enrolled 288 consecutive patients aged 18 years and above who were treated with invasive mechanical ventilation via an endotracheal tube in the mixed intensive care unit (ICU) of Kumamoto University Hospital during a 20-month period. The ICU has 11 beds and admits approximately 400 patients per year. Specialized clinicians and intensivists affiliated with the ICU discussed in-patient treatments twice daily in conferences. Patients who either died or were discharged from the ICU before extubation or tracheostomy were excluded from the study.

Data collection

This was a retrospective cohort study. All clinical data up to the time when the enrolled patients either underwent extubation or underwent tracheostomy as well as extubation outcomes were collected from medical records.

The criteria for SBT initiation were as follows: 1) improvement in the pathology requiring mechanical ventilation, 2) $PaO_2/FiO_2 \geq 200$ mmHg, 3) PEEP≤5 cmH_2O, 4) no excessive airway secretion, 5) adequate cough reflex, 6) low risk of myocardial ischemia, 7) low catecholamine dosage, 8) no increase in intracranial pressure, and 9) adequate level of consciousness. SBT was performed when all criteria were satisfied or when the attending clinician judged that a patient could perform SBT without adverse events, even if some criteria were not satisfied. At the beginning of SBT, the mode of the ventilator was changed to continuous positive airway pressure (CPAP), and after 30-60 min, competence was assessed by the following criteria: 1) SpO_2>90%, 2) increase in $PaCO_2 \leq 10$ mmHg, 3) f/Vt≤100 breaths/min/L, 4) systolic blood pressure of 90-180 mmHg with increases ≤30 mmHg, 5) heart rate <140/min with increases ≤20%, 6) no sweating, and 7) stable mental status (no delirium, agitation, or restlessness). Clinicians carefully observed the patient, and if the patient complained of severe distress or deviated from the abovementioned criteria prior to 60 min or at the end of SBT, he/she was again provided ventilatory support until the next SBT. SBT findings were discussed, and extubation decisions were made by attending clinicians, including intensivists.

Most patients underwent SBT once, and some underwent it twice. Rarely, three procedures were required. For this study, we collected data relevant to the last SBT. Five patients in the tracheostomy group did not undergo SBT, while three did not breathe spontaneously or showed very low ventilatory function and two others were hemodynamically unstable. In these cases, ventilatory modes were not changed and clinical findings 1-2 days before tracheostomy (other than f/Vt) were collected. These data did not constitute SBT but were recorded for convenience.

Although there is no stipulated protocol for the decision to perform tracheostomy, there is a consensus among clinicians that if the patients cannot satisfy the SBT/extubation criteria after 2 weeks of invasive mechanical ventilation or if the patients are not expected to satisfy that criteria by 2 weeks, they are judged to be candidates for tracheostomy.

The extubation failure group consisted of cases requiring re-intubation or emergency support with non-invasive positive airway pressure (NPPV) within 48 h of extubation, while the tracheostomy group consisted of cases that had undergone tracheostomy without undergoing extubation based on the clinician's decision. A combined group including extubation failure and tracheostomy patients was designated as extubation intolerant in this study. The practice of re-extubation or tracheostomy after the first extubation failure was not included in this analysis.

The following determinants were collected: age, sex, body surface area (BSA), body mass index (BMI), style of ICU admission, blood examination data, f during SBT, Vt during SBT, P/F ratio during SBT, systolic blood pressure during SBT, cough strength, volume of airway secretion, and level of consciousness.

Nursing staff assessed cough strength based on responses when a suction tube was inserted into the trachea through the endotracheal tube, and responses were scored as four grades. The grade "none" indicated no cough reflex, "weak" indicated the degree of cough in which one could not spit secretions, "moderate" indicated that one could occasionally spit secretions, and "adequate" indicated a level at which one could always spit secretions. Nursing staff also assessed the airway secretion volume when they suctioned secretions through the endotracheal tube, and responses were classified as follows: "little" indicated that the collected secretion was <1 cm3, "moderate" indicated that the collected secretion was 1-3 cm3, and "large" indicated that the collected secretion was >3 cm3 based on visual observation. Consciousness was classified into three levels: "good" was defined as waking spontaneously (equivalent to E4 and M6 in the Glasgow coma scale [GCS]), "moderate" was defined as waking in response to stimuli equivalent to E2-3 or M4-5 in GCS, and "poor" was defined as not waking to stimuli equivalent to E1 or M1-3 in GCS.

The study was approved by the Ethical Committee of the Faculty of Life Science at Kumamoto University (approval number 647) and performed in accordance with the principles laid down in the 1964 Declaration of Helsinki.

Statistical analysis

Representative numerical values of patient characteristics with non-normal distribution were presented by the median and interquartile range, and the values of the three patient groups were compared by Kruskal Wallis analysis and Steel-Dwass post hoc tests where appropriate. Values with normal distribution were presented as means and standard deviations, and the three patient groups were compared by one-way analysis of variance (ANOVA) and Tukey HSD post hoc tests where appropriate. Categorical data were presented as the number of patients and percentage of total patients in the same group, and the three groups were compared by chi-square analysis or Fisher's exact test.

Logistic regression analysis was used to adjust for confounders and identify variables that independently predict extubation failure and extubation intolerance. The method of variable selection in the logistic regression models was forward selection (likelihood ratio). Patients in whom extubation was attempted (n=251) were analyzed for predictors of extubation failure, and all the patients (n=288) were analyzed for predictors of extubation intolerance (**Figure 1**). The propensity score of extubation failure was calculated by a logistic regression model including significant explanatory variables relevant to the outcome of extubation failure. The algorithm used in the decision tree model was chi-squared automatic interaction detection (CHAID).

The level of significance chosen for all analyses was $p<0.05$. Analyses were performed using SPSS software version 24 (SPSS Inc., Chicago, IL, USA).

Results

Patient characteristics

Among 288 patients mechanically ventilated in the ICU during the study period, 234 were successfully extubated, 17 failed extubation, and 37 underwent tracheostomy without extubation based on the clinician's decision. Thus, 54 were determined intolerant for extubation (by combining the last two groups) in the present study (**Figure 1**). By Bayes' theorem, the pre-test probability of extubation failure was 0.068, that of tracheostomy was 0.128, and that of extubation intolerance was 0.188.

Table 1 shows patient characteristics and clinical data. Univariate analysis showed that the common findings significantly responsible for both extubation failure and the decision to perform tracheostomy compared with successful extubation were as follows: 1) emergent admission to the ICU, 2) larger number of days from the initiation of mechanical ventilation to SBT, 3) lower level of consciousness, 4) larger volume of airway secretion, and 5) longer stay in the ICU. There was no variable that was significant only in extubation failure and not in tracheostomy.

Logistic regression analysis for predictors of extubation outcomes

Table 2 shows the results of logistic regression analyses to define significant predictors of extubation failure (A) and extubation intolerance (B).

Significant predictors of extubation failure were determined to be as follows: 1) insufficient cough strength (odds ratio [OR] 0.370, p=0.003), 2) low level of consciousness (OR 4.106, p=0.003), and 3) excessive airway secretion (OR 4.929, p< 0.001).

Significant predictors of extubation intolerance were as follows: 1) insufficient cough strength (OR 0.423, p=0.001), 2) low level of consciousness

(OR 8.520, p<0.001), 3) excessive airway secretion (OR 2.409, p=0.002), 4) emergent admission to the ICU (OR 4.982, p=0.002), and 5) low PaO2/FiO2 ratio (OR 0.993, p=0.009).

Propensity scores of extubation failure among outcome groups

Propensity scores of extubation failure were calculated in all patients by logistic regression models containing the significant variables of cough strength, consciousness, and volume of airway secretion. A higher score, close to 1, indicated "likely to fail extubation," while a lower score, close to 0, indicated "likely to extubate successfully." The distribution of propensity score in the group of tracheostomy without extubation was as high as that in the extubation failure group (**Figure 2**).

Decision tree model to predict extubation outcomes and decision to perform tracheostomy

The variables of consciousness, style of ICU admission, and volume of airway secretion were selected by decision tree analysis as significant predictors of the outcomes (**Figure 3**). Twelve total nodes were described by the branching structure. In total, 99.2% of patients grouped with "good consciousness," "planned ICU admission," and "little volume of airway secretion" were successfully extubated. Further, 26.7% of patients with "good consciousness," "emergent ICU admission," and "moderate/large volume of airway secretion" failed extubation. All the patients with "poor level of consciousness" avoided extubation and underwent tracheostomy (**Figure 3**).

Discussion

In the present study, we analyzed mechanically ventilated patients in the ICU, including the high-risk population who avoided extubation and selected tracheostomy, by multivariate analysis. We determined several significant predictors of extubation failure and evaluated the accuracy of decision making for performing tracheostomy. Furthermore, we established a decision tree that clearly described the outcomes of endotracheal tube management.

It has been shown in many past studies that protocol-directed weaning and extubation in mechanically ventilated patients increase successful extubation. (17,18) The rate of re-intubation after extubation is now low, (14-16) likely due to advancements in the understanding of endotracheal tube management and the decreased number of extubations performed on high-risk patients in many hospitals. These circumstances create difficulty in evaluating accurate predictors of extubation failure. If extubation criteria were strictly followed and only extubated patients were studied, potential extubation predictors would not be detected. However, our unique analysis is essential because the study design included patients who underwent tracheostomy without attempted extubation and thus permitted the detection of insidious risk factors.

Before analyzing our data, we had assumed that the factors responsible for extubation failure and tracheostomy would be similar because the decision to perform tracheostomy appeared to be predicated by the inability to perform successful extubation. Consistent with our assumption, the predictors of these two outcomes were similar (**Table 2**). The three common predictors, i.e., weak cough strength, poor consciousness, and excessive airway secretion, are important for maintaining airway patency, and their significance was shown in past studies. (10,11) In addition, the neurological status has previously been associated with extubation outcome. (10,12) and our findings confirm these collective observations.

Logistic regression analysis revealed that emergent ICU admission and low PaO2/FiO2 ratio were also significant predictors of extubation intolerance (combined outcome of extubation failure and tracheostomy [**Table 2**]). These two variables demonstrate a stronger relationship with tracheostomy than extubation failure (**Table 1**). Patients with emergent ICU admission have a generally unfavorable systemic condition compared with patients with planned admission. For example, in patients with emergent ICU admission, the number of days from ICU admission to SBT was longer (median [interquartile range]: 6 [3-11] vs. 1 [1-1], p<0.001), APACHE 2 score in ICU admission was higher (21 [15-27] vs. 18 [16-20], p=0.001), and RSBI at the end of SBT was higher (47.6 [32.5-69.3] vs. 36.9 [24.8-48.3], p<0.001) than those in patients with planned admission. Emergent admission may be determined as a significant predictor that is representative of the factors mentioned above. These inconspicuous variables in patients with emergent ICU admission may cause physicians to avoid extubation and to decide on performing tracheostomy. Namen et al showed that low oxygenation was associated with an increased risk of extubation failure in neurosurgical patients; (12) however, other studies have revealed that low oxygenation does not predict extubation outcome. (3,19,20) In the present study, a low PaO2/FiO2 ratio was significant in comparison of tracheostomy and successful extubation (**Table 1**) and logistic regression (**Table 2B**) but did not be selected

as a significant variable in the decision tree model (**Figure 3**).

The propensity score is often used in non-randomized studies when study subjects are selected by matching the subjects of another group. (21) In the present study, the propensity score was used to evaluate whether the decision to perform tracheostomy without extubation was appropriate, and we identified that the propensity score of extubation failure in the tracheostomy group was as high as that in the extubation failure group.

Decision tree analysis for outcomes of endotracheal tube management in mechanically ventilated adult patients has been used in some previous studies; (22-24) however, no study has evaluated simultaneously the three outcomes: successful extubation, extubation failure, and decision making of tracheostomy. The results of the decision tree model in the present study could be visually recognized and easily understood by a wide variety of medical staff.

Two studies have analyzed the risk factors of extubation failure in populations including patients who have undergone tracheostomy. (25,26) Both have indicated that the greatest common risk factor of extubation failure is atelectasis. These studies targeted patients with myasthenic crisis, and multivariate analysis was not performed because of the small sample size. Further, they mainly evaluated treatments and complications. In contrast, in the present study, we mainly evaluated physiological parameters.

A limitation of our study was that the design was retrospective and observational without any intervention. However, we feel that there was minimal bias in the clinician's decision with regard to extubation because the staff did not know at that time that extubation practices were targets of the research. Although our results should be confirmed in large prospective studies, it may be difficult to evaluate precise predictors of extubation failure as the rate of extubation failure is decreased, as described above. Therefore, we suggest that the methods used in the present study are a superior way to detect insidious predictors. Another limitation of our study was that the research was conducted at a single center. Although all the patients were treated in the ICU, they were assigned to respective specialties, and decisions regarding extubation were made not only by a limited number of experts in intensive care but also by specialists in various departments.

Conclusion

We analyzed mechanically ventilated patients in the ICU, including those at a high risk of extubation failure who underwent tracheostomy, by multivariate analysis and determined the significant predictors of extubation failure that were related to instability of airway patency. The accuracy of the decision to perform tracheostomy was evaluated by propensity scoring of extubation failure as well as decision tree analysis that distinguished the outcomes of endotracheal tube management. These statistical methods could exclude the selection bias of study subjects.

Acknowledgments

This work was supported by Grant-in-Aid for Scientific Research ([C] JSPS KAKENHI Grant Number 15K09176). The authors would like to thank Enago (www.enago.jp) for the English language review.

Table 1. Patient characteristics and clinical data

	Successful extubation (n=234)	Extubation failure (n=17)	Tracheostomy without extubation (n=37)	p value
Age (year)	64.0 (54.0-73.3)	65.0 (60.0-74.0)	73.0 (64.0-78.0)*	0.008
Gender (n) - Male - Female	 148 (63.2) 86 (36.8)	 14 (82.4) 3 (17.6)	 27 (73.0) 10 (27.0)	0.167
BMI (kg/m2)	22.2 (19.7-24.5)	19.6 (18.5-23.9)	21.2 (17.2-22.9)	0.019
Style of ICU admission (n) - planned - emergent	 160 (68.4) 74 (31.6)	* 7 (41.2) 10 (58.8)	* 1 (0.0) 36 (100.0)	<0.001
Sodium (mEq/L)	139 (137-141)	136 (134-139)	139 (136-142)	0.049
Total bilirubin (mg/dL)	1.0 (0.6-1.5)	1.0 (0.6-2.0)	0.8 (0.6-1.9)	0.837
Creatinine (mg/dL)	0.8 (0.6-1.1)	0.8 (0.7-1.2)	0.8 (0.6-1.6)	0.700
Hematocrit (%)	31.0 (28.0-36.0)	29.0 (26.5-36.5)	33.0 (26.5-38.5)	0.635
White blood cells (×1000/mm3)	9.5 (7.0-13.0)	8.0 (7.0-11.5)	11.0 (7.8-16.0)	0.248
Day from admission to SBT (day)	1.0 (1.0-3.0)	6.0 (1.0-8.0)*	9.0 (4.0-15.0)*	0.003
Respiratory frequency (f) in SBT (breaths/min)	18.0 (15.0-22.0)	25.0 (13.0-28.5)	22.0 (15.5-26.0)*	0.004
Tidal volume (Vt) in SBT (L)	0.45 (0.37-0.51)	0.48 (0.34-0.59)	0.39 (0.30-0.48)	0.017
f/Vt in SBT (breaths/min/L)	38.6 (30.0-58.0)	40.0 (26.6-88.8)	64.8 (35.8-82.4)*	0.003
P/F ratio in SBT (mmHg)	341.5±74.4	327.8±89.0	266.8±104.8*	<0.001
PEEP in SBT (cmH2O)	3.0 (3.0-4.0)	3.0 (3.0-4.0)	5.0 (4.0-5.5)*	<0.001
Systolic blood pressure in SBT (mmHg)	120 (106-135)	119 (101-126)	120 (95-130)	0.389
Heart rate in SBT (/min)	79 (70-90)	80 (73-95)	90 (78-110)*	0.017
Cough strength (n) - non - weak - moderate - adequate	 5 (2.1) 40 (17.1) 86 (36.8) 103 (44.0)	 2 (11.8) 5 (29.4) 5 (29.4) 5 (29.4)	* 4 (10.8) 13 (35.1) 10 (27.0) 10 (27.0)	0.003
Consciousness (n) - good - moderate - poor	 210 (89.7) 24 (10.3) 0 (0.0)	* 11 (64.7) 6 (35.3) 0 (0.0)	* 8 (21.6) 19 (51.4) 10 (27.0)	<0.001
Volume of airway secretion (n) - little - moderate - large	 170 (72.6) 45 (19.2) 9 (8.1)	* 3 (17.6) 6 (35.3) 8 (47.1)	* 13 (35.1) 11 (29.7) 13 (35.1)	<0.001

Legend: Numerical data are shown as the median (interquartile range) or the mean (standard deviation), and categorical data are shown as the number of patients (percentage of total patients in the same group). p values provided in the table are calculated by multiple comparison for numerical data and by chi-square analysis or Fisher's exact test for categorical data. *=p<0.05 compared with the successful extubation group by post hoc analysis after multiple comparisons; BMI=body mass index; SBT=spontaneous breathing trial; f/Vt=respiratory frequency/tidal volume; P/F=PaO2/FiO2; PEEP=positive end-expiratory pressure.

Table 2. Significant predictors of extubation failure and extubation intolerance (combined outcome of extubation failure and tracheostomy decision) by logistic regression analyses

A. Extubation failure

Variable	Coefficient	Odds ratio (95% CI)	p value
Cough strength	-0.993	0.370 (0.191-0.719)	0.003
Consciousness	1.412	4.106 (1.113-15.141)	0.003
Volume of airway secretion	1.595	4.929 (2.434-9.982)	<0.001

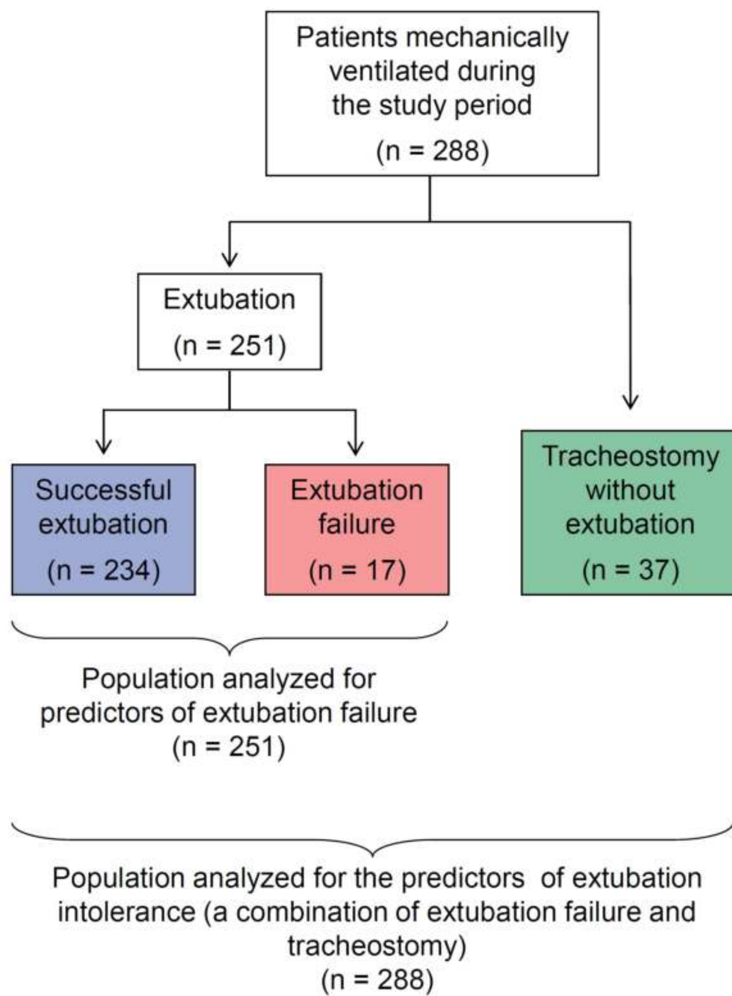
Legend: CI=confidence interval.

B. Extubation intolerance (combined outcome of extubation failure and tracheostomy)

Variable	Coefficient	Odds ratio (95% CI)	p value
Cough strength	-0.860	0.423 (0.249-0.718)	0.001
Consciousness	2.142	8.520 (3.582-20.269)	<0.001
Volume of airway secretion	0.879	2.409 (1.399-4.149)	0.002
Emergent ICU admission	1.606	4.982 (1.773-13.994)	0.002
PaO2/FiO2 ratio	-0.007	0.993 (0.988-0.998)	0.009

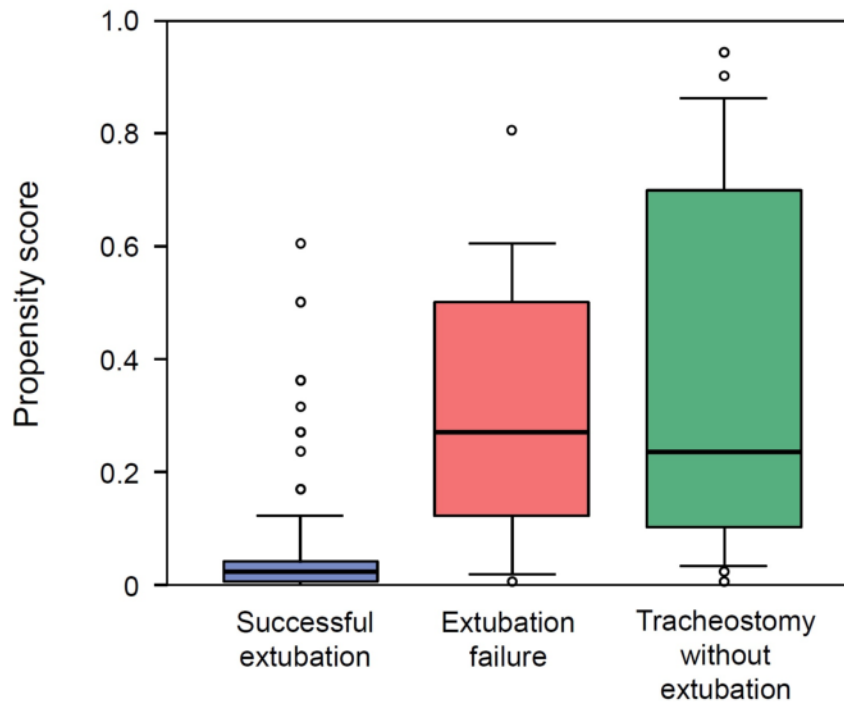
Legend: CI=confidence interval.

Figure 1. Study populations grouped by treatments and extubation outcomes



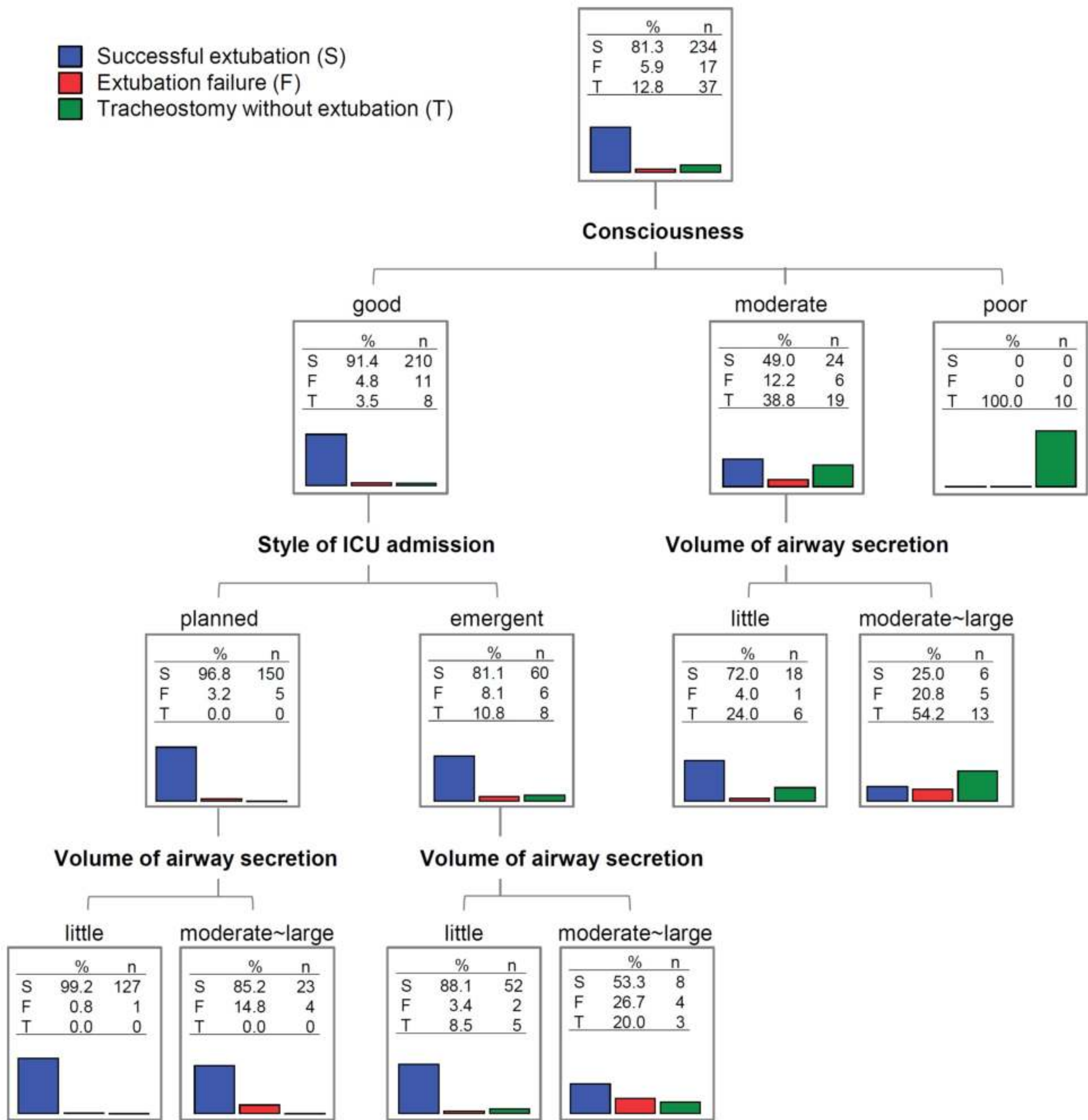
Legend: Three study groups were classified by treatments and extubation outcomes: successful extubation, extubation failure, and performance of tracheostomy without extubation. Patients who underwent extubation were analyzed for predictors of extubation failure, and all the patients were analyzed for predictors of extubation intolerance (a combined outcome of extubation failure and tracheostomy) by logistic regression models.

Figure 2. Comparison of propensity scores of extubation failure calculated by logistic regression model among the outcomes



Legend: The distribution of propensity scores for extubation failure in three outcome groups calculated by logistic regression models using the significant variables cough strength, consciousness, and volume of airway secretion. Box plots display the median, interquartile range, 10th and 90th percentile, as well as outlying data points.

Figure 3. Decision tree of extubation outcomes and decision making to perform tracheostomy



Legend: The decision tree describes 12 nodes branched by significant variables responsible for the outcomes, and the percentage and frequency of outcomes are shown.

References

1. Slutsky AS. Mechanical ventilation. American College of Chest Physicians' Consensus Conference. Chest 1993;104:1833-59.
2. Esteban A, Alía I, Gordo F, Fernández R, Solsona JF, Vallverdú I, et al. Extubation outcome after spontaneous breathing trials with T-tube or pressure support ventilation. The Spanish Lung Failure Collaborative Group. Am J Respir Crit Care Med 1997;156:459-65.
3. Frutos-Vivar F, Ferguson ND, Esteban A, Epstein SK, Arabi Y, Apezteguía C, et al. Risk factors for extubation failure in patients following a successful spontaneous breathing trial. Chest 2006;130:1664-71.
4. Esteban A, Anzueto A, Frutos F, Alía I, Brochard L, Stewart TE, et al. Characteristics and outcomes in adult patients receiving mechanical ventilation: a 28-day international study. JAMA 2002;287:345-55.
5. Thille AW, Harrois A, Schortgen F, Brun-Buisson C, Brochard L. Outcomes of extubation failure in medical intensive care unit patients. Crit Care Med 2011;39:2612-8.
6. Torres A, Gatell JM, Aznar E, el-Ebiary M, Puig de la Bellacasa J, González J, et al. Re-intubation increases the risk of nosocomial pneumonia in patients needing mechanical ventilation. Am J Respir Crit Care Med 1995; 152:137-41.
7. Epstein SK, Ciubotaru RL, Wong JB. Effect of failed extubation on the outcome of mechanical ventilation. Chest 1997;112:186-92.
8. Tobin MJ. Mechanical ventilation. N Engl J Med 1994;330:1056-61.
9. Cooper LM, Linde-Zwirble WT. Medicare intensive care unit use: analysis of incidence, cost, and payment. Crit Care Med 2004;32: 2247-53.
10. Salam A, Tilluckdharry L, Amoateng-Adjepong Y, Manthous CA. Neurologic status, cough, secretions and extubation outcomes. Intensive Care Med 2004;30:1334-9.
11. Khamiees M, Raju P, DeGirolamo A, Amoateng-Adjepong Y, Manthous CA. Predictors of extubation outcome in patients who have successfully completed a spontaneous breathing trial. Chest 2001;120:1262-70.
12. Namen AM, Ely EW, Tatter SB, Case LD, Lucia MA, Smith A, et al. Predictors of successful extubation in neurosurgical patients. Am J Respir Crit Care Med 2001;163:658-64.
13. Chien JY, Lin MS, Huang YC, Chien YF, Yu CJ, Yang PC. Changes in B-type natriuretic peptide improve weaning outcome predicted by spontaneous breathing trial. Crit Care Med 2008;36:1421-6.
14. Frutos-Vivar F, Esteban A, Apezteguia C, González M, Arabi Y, Restrepo MI, et al. Outcome of reintubated patients after scheduled extubation. J Crit Care 2011;26:502-9.
15. Peñuelas O, Frutos-Vivar F, Fernández C, Anzueto A, Epstein SK, Apezteguía C, et al. Characteristics and outcomes of ventilated patients according to time to liberation from mechanical ventilation. Am J Respir Crit Care Med 2011;184:430-7.
16. Funk GC, Anders S, Breyer MK, Burghuber OC, Edelmann G, Heindl W, et al. Incidence and outcome of weaning from mechanical ventilation according to new categories. Eur Respir J 2010;35:88-94.
17. Kollef MH, Shapiro SD, Silver P, St John RE, Prentice D, Sauer S, et al. A randomized, controlled trial of protocol-directed versus physician-directed weaning from mechanical ventilation. Crit Care Med 1997;25:567-74.
18. Dries DJ, McGonigal MD, Malian MS, Bor BJ, Sullivan C. Protocol-driven ventilator weaning reduces use of mechanical ventilation, rate of early reintubation, and ventilator-associated pneumonia. J Trauma 2004;56:943-51.
19. Savi A, Teixeira C, Silva JM, Borges LG, Pereira PA, Pinto KB, et al. Weaning predictors do not predict extubation failure in simple-to-wean patients. J Crit Care 2012;27:221.e1-8.
20. Mokhlesi B, Tulaimat A, Gluckman TJ, Wang Y, Evans AT, Corbridge TC. Predicting extubation failure after successful completion of a spontaneous breathing trial. Respir Care 2007; 52:1710-7.
21. Stukel TA, Fisher ES, Wennberg DE, Alter DA, Gottlieb DJ, Vermeulen MJ. Analysis of observational studies in the presence of treatment selection bias: effects of invasive cardiac management on AMI survival using propensity score and instrumental variable methods. JAMA 2007;297:278-85.
22. Liu Y, Wei LQ, Li GQ, Lv FY, Wang H, Zhang YH, et al. A decision-tree model for predicting extubation outcome in elderly patients after a successful spontaneous breathing trial. Anesth Analg 2010;111:1211-8.
23. Liu Y, Mu YU, Li GQ, Yu X, Li PJ, Shen ZQ, et al. Extubation outcome after a successful spontaneous breathing trial: A multicenter validation of a 3-factor prediction model. Exp

Ther Med 2015;10:1591-601.
25. Berney SC, Gordon IR, Opdam HI, Denehy L. A classification and regression tree to assist clinical decision making in airway management for patients with cervical spinal cord injury. Spinal Cord 2011;49:244-50.
26. Rabinstein AA, Mueller-Kronast N. Risk of extubation failure in patients with myasthenic crisis. Neurocrit Care 2005;3:213-5.
24. Seneviratne J, Mandrekar J, Wijdicks EF, Rabinstein AA. Predictors of extubation failure in myasthenic crisis. Arch Neurol 2008;65:929-33.