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# Predictors of Re-intubation in Critically Ill Patients

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**Running head:** Prediction of extubation failure

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## Disclosures of potential conflicts of interest

Dr. Miu has no actual or potential conflict of interest to disclose
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## Abstract

**BACKGROUND:** Assessment of patient's readiness for removal of the endotracheal tube in the Intensive Care Unit (ICU) is based on respiratory, airway and neurological measures. However, nearly 20% of patients require reintubation. We aimed to generate a prediction model for the need of reintubation that incorporates variables importantly contributing to extubation failure.

**METHODS:** Cohort study of 2,007 endotracheally intubated patients who required ICU admission at a single tertiary care center. Data collection included: demographic, hemodynamic, respiratory and neurological variables preceding extubation. Data were compared between patients extubated successfully and those who required reintubation using bivariate logistic regression models with the binary outcome reintubation and the baseline characteristics as predictors. Multivariable logistic regression analysis with robust variance was used to build the prediction model.

**RESULTS:** Of 2,007 patients analyzed, 376 (19%) required reintubation. In bivariate analysis, admission SAPS-II, minute ventilation, respiratory rate, oxygenation, number of prior SBTs, rapid-shallow breathing index, secretion frequency and quantity, heart rate, and diastolic blood pressure differed significantly between the extubation success and failure groups. In multivariable analysis, higher SAPS-II and suction frequency, were associated with failed extubation. The areas under the receiving operator curve were 0.68 for failure at any time and 0.71 for failure within 24 hours model. However, prior failed SBTs, minute ventilation and diastolic blood pressure were additional independent predictors of failure at any time, while oxygenation predicted extubation failure within 24 hours.

**CONCLUSIONS:** A small number of independent variables explained a substantial portion of variability of extubation failure and can help identify with accuracy patients at high risk of

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needing reintubation. These characteristics should be incorporated in the decision-making process of ICU extubation.

**Key words**: Extubation, Mechanical Ventilation, Intensive Care Unit, Cohort Study, Airway Management, Clinical Prediction Model, Human

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## Introduction

The decision to liberate a patient from invasive mechanical ventilation is a two-component process, which requires clinicians to assess the continued need for positive pressure ventilation as well as assess the need for the artificial airway. Typically, assessment of gas exchange and pulmonary mechanics occurs with the performance of spontaneous breathing trial (SBT)[1]. Single point-in-time examination of ratios of respiratory frequency to tidal volume, integration of thoracic compliance, respiratory rate, arterial oxygenation, and maximum occlusion pressure, or dynamic changes in these indices over the course of the SBT differentiate between successes and failures of this trial [2-4]. Nonetheless, even after a passing their SBT, nearly one in five will require reintubation at some time during the hospital stay with half of these patients requiring reintubation within the first 24 hours [3, 5]. Salam et al. [6] reported the ability to maintain a patent upper airway and clear secretions, indicated by a cough peak flow >60 l/min, tracheal secretions <2.5 ml/min, and the ability to follow 4 simple tasks (i.e. open eyes, track with eyes, grasp with hands, and stick out tongue) increased the odds of successful extubation. Mokhlesi and colleagues [7] reported on 122 patients who were followed after extubation to identify those who were reintubated within 48 hours. Of the 13% of patients who required early reintubation, moderate to copious tracheal secretions, Glasgow Coma Scale (GCS) <10, and a $PaCO_2$ >44 mm Hg during the SBT all independently predicted failure. Unfortunately, the ability to generalize these results to larger and more diverse patient groups is limited by the small numbers of observations included in these reports. Despite a wealth of literature reporting the associations between a variety of individual indices and success or failure of extubation, few studies have reported on clinical decision rules that could better predict what patients are at risk for extubation failure after the successful completion of a SBT.

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Thus, the aim of the present study was to build a model with high precision to predict extubation failure early (reintubation within the first 24 hours) or at any time during the hospitalization using commonly available bedside pre-extubation variables in a large population of critically ill adults.

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## Methods

*Study Setting*

The University of Washington Institutional Review Board approved this study with a waiver of informed consent. The study site was Harborview Medical Center, a 413-bed Level 1 trauma hospital in Seattle, Washington, affiliated with the University of Washington and serving as a tertiary referral center for critically ill patients in a four-state region (Washington, Alaska, Montana, and Idaho). There are 88 ICU beds distributed among medical/cardiac (18 beds), trauma/surgical (24 beds), cardiac, neurology/neurosurgical ICUs (28 beds), and pediatric/burn ICU (18 beds). The ICUs admit approximately 3,500 patients per year, and over half of them are mechanically ventilated for any duration of time during their hospital stay. These ICUs are covered 24 hours a day by an intensivist-led team consisting of an attending physician, critical care fellow, senior resident, and junior resident. The departments of surgery, anesthesiology, internal medicine, neurology, and emergency medicine provide physician coverage, attendings, and trainees. A dedicated ICU team rounds at least once a day and writes orders. Respiratory therapists help to manage all ventilated patients, including performance of spontaneous breathing trials (SBTs). Elements of airway assessment and management are done by the ICU team.

*Study Eligibility Criteria*

All patients who were admitted to the one of the ICUs and required invasive mechanical ventilation via an endotracheal tube placed in the pre-hospital or hospital setting, in the period between July 1, 2008 and August 31, 2009 were eligible for inclusion. Patients less than 18 years of age, those extubated in the context of comfort care, after tracheostomy placement, or who died prior to extubation were excluded. Patients who had airway management for elective or emergency procedure in the operating room were not considered as ICU extubation failures.

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All patients underwent a daily protocolized ventilator weaning assessment, as follows. Patients were considered for a spontaneous breathing trial (SBT) if they met the following criteria: evidence of resolution or improvement of the underlying cause of respiratory failure, a minute ventilation ($V_E$) <15 L/min, positive end-expiratory pressure ≤8 $cmH_20$, $FiO_2$ <0.5, $PaO_2/FiO_2$ ≥150, pH ≥7.25 with intact respiratory drive, intracranial pressure (ICP) <20 $cmH_2O$, and hemodynamic stability without cardiovascular support. Sedation for mechanical ventilation was provided per standardized ICU protocol targeting a goal of 0 to -1 on the Richmond Agitation and Sedation Scale. Unless contraindicated, a spontaneous awakening trial was performed daily followed by a SBT [8]. Per routine protocol, all SBTs are performed with a continuous positive pressure of 5 $cmH_2O$ without additional pressure support. Failure of the SBT was defined as: respiratory rate >35 breaths/min, oxygen saturation < 90% for >30 seconds, reduction in $V_E$ <75% of baseline during mechanical ventilation, a heart rate >140 bpm or a change >20% from baseline, a systolic blood pressure >180 or <90 mmHg, sustained increase in anxiety, diaphoresis or other clinical sign of respiratory distress, an increase ICP >20 $cmH_2O$ for >2 minutes, arrhythmia, pH ≤7.25 or a $PaCO_2$ increase ≥10 mm Hg [9]. Additional factors considered prior to extubation after the patient has passed the SBT included the requirement for tracheal suctioning more than every 4 hours, presence of an effective spontaneous cough, presence of a leak around the deflated tracheal tube cuff with a sustained manual inspiratory pressure of <30 cm $H_2O$, and absence of airway reflexes. These criteria applied to all intubated patients through a hospital protocol, unless extubation was unplanned.

*Data Collection*

Data were abstracted via automated search from the electronic medical record. Manual review of the electronic medical record was conducted as needed for variables not retrievable

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through the automated search and for data verification. Demographic variables collected included age, sex, ethnicity, height, weight, hospital and ICU length of stay, and severity of illness measured by the Simplified Acute Physiology Score II (SAPS II). Admission services included medical, general surgery, neurological surgery, orthopedic surgery, vascular surgery and otolaryngology.

Clinical variables which were recorded included ventilatory variables (inspired fraction of oxygen, positive end expiratory pressure, amount of pressure support, tidal volume, minute ventilation, and respiratory rate), the number of attempted SBTs prior to actual extubation, arterial blood gas values at the end of the SBT (pH, partial pressures of carbon dioxide and oxygen), cumulative 24-hour frequency and quantity of secretions (graded copious [3 points], moderate [2 points], or mild [1 point]), the need for oral suctioning, and presence or absence of endotracheal tube cuff leak. Hemodynamic and continuously monitored variables included systolic, mean, and diastolic blood pressure, heart rate, and $SpO_2$. Neurological variables included: GCS and the numeric score for each response (eyes, verbal, motor), presence or absence of a gag reflex, pupillary light reflex measurements, and ICP when monitoring available. The value that was used in our study was obtained either during the last successful SBT, or during the SBT itself.

Decisions regarding extubation and the need for reintubation, if applicable, were made as part of routine clinical care by the primary ICU service caring for the patient. For patients requiring reintubation, the time to reintubation in hours was abstracted from the record.

*Study endpoints and definitions*

Patients were classified in two groups based on the requirement for reintubation, i.e., "never reintubated" versus "one or more reintubations" during the hospital stay, not including

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intubations for operating room procedures. The primary endpoint was success of extubation, defined as reaching hospital discharge without requiring out-of-operating room reintubation. Secondary endpoints were vital signs, respiratory and ventilator variables, and neurologic exam findings during SBT or immediately prior to extubation.

Extubation failure was defined as the requirement for reinstitution of mechanical ventilation any time after initial extubation, and requiring out-of-operating room tracheal intubation during the hospital stay. Early extubation failure was defined as extubation failure ≤24 hours after extubation. Reintubation events in the operating room for elective or emergency procedures did not count toward the study defined out-of-operating room reintubation.

*Statistical Analysis*

Baseline characteristics were compared between the groups of patients never reintubated *versus* those who were reintubated outside the operating room at least once, using bivariate logistic regression models with the binary outcome reintubation and the baseline characteristics as predictors. Patterns of missing values were explored in descriptive analyses and missingness for each variable is reported in the tables. For the primary analysis, multivariable logistic regression was used to estimate the adjusted odds ratio of reintubation to account for important predictors, explanatory variables and potential confounders. We included predictors that are potential confounders and known risk factors: age, gender, body mass index (BMI), and SAPS II. Variable thought to be collinear were not included simultaneously in the model if their correlation coefficient was >0.6. Robust (sandwich) variance estimates were used in all regression models to compute the confidence intervals. We planned *a priori* a secondary analysis that was restricted to reintubation events that occurred within 24 hours of extubation. A two-sided alpha level of .05 was considered statistically significant. The statistical software STATA,

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version 11.0 (Stata Corp., College Station, TX) was used for the analyses. Data are presented as mean ± SD unless otherwise noted.

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## Results

Data from 2,007 patients were analyzed, of whom 379 (19%) failed extubation at any time during the hospital stay and required out-of-operating room reintubation. The most common reason for reintubation was respiratory failure (n=287, 76%), followed by airway obstruction (n=65, 17%). Early reintubation (within 24 hours) was observed in 155 (7.7%) patients. Details of the study population have been previously reported [5]. Overall, patients in the study population were 49.5 ± 17.9 years of age, 66% male, and with a mean SAPS II score of 39.4 ± 15.2. Patients who required reintubation any time during their ICU or hospital stay tended to be of older age and have a higher mean SAPS II scores. Type of admission or admitting service (general surgery, orthopedics, vascular, neurosurgery, head & neck, medicine; $p = 0.64$), presence of traumatic injury ($p = 0.87$), and BMI were not associated with failed extubation. The prevalence of ALI or ARDS at any time during hospitalization was similar between groups.

Respiratory, airway, cardiovascular and neurological variables measured prior to initiating the SBT are displayed in Table 1, stratified by extubation failure at any time. Some respiratory and cardiovascular variables and measures of secretion burden differed between the two patient populations. None of the neurological system exam, such as GCS scores, pupil diameter and reactivity, or presence of a cough/gag reflex differed significantly between groups.

Respiratory and cardiovascular variables during the SBT are shown in Table 2. Predictors of extubation failure during the SBT were largely respiratory variables (Table 2). Variables measured within one hour of extubation are shown in Table 3, with lower oxygenation on pulse oxymeter being associated with extubation failure.

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Independent predictors associated with the need for reintubation at any time during hospitalization by multivariate analyses were higher admission SAPS II score, higher secretion burden (either secretion frequency or cumulative amount of secretion in 24 hours), higher minute ventilation (either immediately prior or during the SBT), higher number of daily SBTs performed prior to extubation, and lower diastolic blood pressure prior to the SBT (Table 4). Independent predictors of the need for reintubation within 24 hours were higher admission SAPS II score, lower oxygenation (either the $PaO_2/FiO_2$ ratio or the $PaO_2$ from the SBT arterial blood gas, or the $SpO_2$ during the SBT), and higher secretion burden (either secretion frequency or cumulative amount of secretion in 24 hours, Table 4). When determining sensitivity and specificity, both multivariate models showed approximately 70% accuracy in correctly predicting whether an individual patient would fail extubation during the pre-specified time period. The area under the receiver-operator curves for each model are shown in Figures 1 and 2.

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## Discussion

The decision to discontinue invasive mechanical ventilation involves weighing the benefits of decreased morbidity associated with prolonged mechanical ventilation with the possibility of increased airway-attributable morbidity in the event that extubation is premature and the patient requires reintubation [10]. Individual risk factors associated with extubation failure have been previously reported [11], but studies reporting clinically useful decision tools are sparse. Herein, we report the generation of two prediction models for extubation failure (one for failure at any time during hospitalization and another for failure in the first 24 hours after extubation) in patients who have already passed a traditional SBT. The models only retained four (early failure) and five (failure at any time) clinically accessible variables, respectively, that were highly contributory to predict extubation failure. It is noteworthy that despite some overlap (disease severity, minute ventilation and secretion burden), variables predicting early failure were not the same as those predicting failure at any time, with oxygenation being an important component of early failure while lower diastolic pressure and repeatedly failed SBT being significant contributors to failure at any time.

Both models were found to have an area under the receiver operating curve of approximately 70% indicating fairly good accuracy [12]. Although this accuracy might be increased by the addition of more variables, this would be at the expense of including covariates with minor contribution to explain the model variability and adding complexity to the data gathering by the clinician. Adding variables with small contribution to overall variability could also affect the model performance due to overfitting resulting in reduced generalizability to other settings.

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In both models, severity of illness, as indicated by SAPS II score in our study, independently predicted extubation failure and is consistent with two prior publications [9, 13]. Similar to previous reports [7], we also found that increased secretion burden was a significant contributor to extubation failure in both models. It seems intuitive that patients who cannot adequately perform pulmonary toilet are at greater risk for upper airway obstruction, inspissated secretions with resultant dependent post-obstructive atelectasis, increased elastic and resistive work of breathing, and elevated intrapulmonary shunt fraction. Indeed, the $PaO_2/F_iO_2$ ratio, a rough approximation of shunt fraction [14], was also a significant predictor in the early extubation failure model. Further, a number of other investigators have reported that the absolute amount of tracheal secretions and the ability (or lack thereof) to clear them by generating an adequate cough response increases the risk of extubation failure in patients who no longer appear to need positive pressure ventilation [6, 15, 16]. Consistent with a previous report [11], another risk factor for extubation failure was the number of previously failed SBTs, suggesting that despite a pattern of improvement over time, some patients with more difficult weaning may not have yet returned to complete resolution of acute respiratory failure and may be more likely to require reintubation [17]. Frutos-Vivar et al. also reported that positive fluid balance in the previous 24 hours was a significant predictor of extubation failure [11]. However, the predictive ability of this variable even when combined with RSBI was weak. This finding might be related to the variability of fluid balance over the ICU course and the accuracy of recording balance in the medical record. A recent study at our institution examined fluid balance in patients with subarachnoid hemorrhage, and suggested extensive day-to-day variability in the response to fluid administration [18].

We chose to define early extubation failure as reintubation within 24 hours, as the median time to reintubation was 22 hours [5], therefore capturing more than half of extubation failures

within this window. Furthermore, 24 hours is an important post-extubation milestone for decision to transfer patients out of the ICU after liberation from mechanical ventilation.

For extubation failure at any time, we found lower diastolic blood pressure to be a significant risk factor of extubation failure. This has not been reported previously. Different explanations to interpret this finding can be proposed including cardiac-related weaning failure or autonomic dysfunction. Recently, transthoracic echocardiography performed during the SBTs has documented impaired ventricular relaxation and diastolic dysfunction leading to cardiac-related weaning failure [19]. Spontaneous inspiratory efforts can precipitate left ventricular dilatation and cardiogenic shock in patients without coronary artery disease [20], and lower arterial diastolic pressure may reflect spontaneous-ventilation induced decrease in intra-thoracic pressure [21]. However, lower diastolic blood pressure could also be a surrogate of autonomic nervous system dysfunction and reflect increased efferent sympathetic nerve activity.

Neurologic function as assessed by GCS was not associated with extubation failure in either model. In a cohort of 122 patients mechanically ventilated for $\geq$48 hours, Mokhlesi and colleagues reported a GCS <10 to confer a 13-fold increase in risk of extubation failure [7]. In a randomized controlled trial comparing a non-physician directed ventilator weaning protocol to routine care in a neurosurgical intensive care unit, Namen et al reported a GCS $\geq$8 to be strongly associated with extubation success in neurosurgical patients [22]. Salam and colleagues reported that patients unable to complete four tasks commands (open eyes, follow with eyes, grasp hand, and stick out tongue) prior to extubation were four times more likely to require re-intubation [6]. However, the study by Coplin et al reported similar extubation failure among brain injured patients regardless of their GCS [23]. In addition, using the Full Outline of UnResponsiveness (FOUR) score, which combines assessment of eyes, brainstem, reflexes, and respiration, to

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assess mental status in 62 patients with a primary neurologic injury, Ko and colleagues reported similar scores among those who were successfully extubated and those that failed [24]. In all likelihood, it is the combination of mental status and the ability to clear the upper and lower airways which determines successful extubation in patients who have passed an SBT. The SBT reflects the patient ability to maintain adequate oxygenation and ventilation without or with minimal support. It is that crucial second aspect of successful extubation, the complete removal of positive pressure and the necessity of the artificial airway, which remains in question [17]. Our data support the increased importance of respiratory secretions over mentation.

The present cohort represents one of the largest studies to date, both from the number of patients included in the study and the number of detailed variables examined, on determining predictors of extubation failure in the ICU population. Because we captured data over a 15-month period, historical trend should not influence the results. Due to the large sample of this study, the absolute differences in some variables were statistically significant, however, were not necessarily clinically relevant. Small absolute differences in continuous variables were contributory when jointly combined with other variables in the model and weighted based on their regression coefficient. The joint effect of all weighted variables included in the model yielded the individual predicted probabilities of extubation failure.

Several limitations of our study are worth noting. The data collection was retrospective in nature and therefore, data not recorded during the patient's hospital stay were not available. Subjective measurements, such as grading the quality and quantity of secretions, were not standardized. Lastly, as the ultimate decision of whether or not to extubate rested with the primary critical care service, primary specialty, level of training, and practice patterns may have differed among physicians. Given that we only had patients from one single medical center, the

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generalizability of our results to patients in other regions and to hospitals with different practice styles may be limited.

**Conclusion.** In summary, we have identified few important risk factors for extubation failure at any time during hospitalization and within the first 24 hours of extubation. These independent variables explained a substantial portion of the variability in extubation failure and can help identify with accuracy patients at high risk of failure. Under both models, disease severity, secretion burden and minute ventilation were significant predictors of extubation failure. Additionally, lower oxygenation was a risk factor for failure within 24 hours, while the number of previously failed SBTs and lower diastolic pressure were risk factors for failure at any time.

These data imply that, once a patient is deemed ready for extubation, the clinician can identify patients who may require increased post-extubation vigilance and devise a back-up plan that might include continuation of high intensity monitoring, prompt availability of airway and drug supplies for possible reintubation, or request an immediate consultation by respiratory therapists to initiate aggressive bronchial hygiene protocols. Future studies are needed to prospectively validate and optimize this prediction model by capturing additional potentially important variables that may play a role in extubation failure, such as response to fluid administration or biomarkers of disease (troponin, brain natriuretic peptide, and pro-brain natriuretic peptide).

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## References

1. Ely EW, Baker AM, Dunagan DP, Burke HL, Smith AC, Kelly PT, et al. Effect on the duration of mechanical ventilation of identifying patients capable of breathing spontaneously. N Engl J Med 1996;335(25):1864-1869.
2. Yang KL, Tobin MJ. A prospective study of indexes predicting the outcome of trials of weaning from mechanical ventilation. N Engl J Med 1991;324(21):1445-1450.
3. 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(5):1211-1218.
4. Su WL, Chen YH, Chen CW, Yang SH, Su CL, Perng WC, et al. Involuntary cough strength and extubation outcomes for patients in an ICU. Chest 2010;137(4):777-782.
5. Menon N, Joffe AM, Deem S, Yanez ND, Grabinsky A, Dagal AH, et al. Occurrence and complications of tracheal reintubation in critically ill adults. Respir Care 2012;57(10):1555-1563.
6. Salam A, Tilluckdharry L, Amoateng-Adjepong Y, Manthous CA. Neurologic status, cough, secretions and extubation outcomes. Intensive Care Med 2004;30(7):1334-1339.
7. 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(12):1710-1717.
8. Girard TD, Kress JP, Fuchs BD, Thomason JW, Schweickert WD, Pun BT, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial. Lancet 2008;371(9607):126-134.

9. Esteban A, Alia I, Gordo F, Fernandez R, Solsona JF, Vallverdu 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(2 Pt 1):459-465.

10. 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(12):2612-2618.

11. Frutos-Vivar F, Ferguson ND, Esteban A, Epstein SK, Arabi Y, Apezteguia C, et al. Risk factors for extubation failure in patients following a successful spontaneous breathing trial. Chest 2006;130(6):1664-1671.

12. Mandrekar JN. Receiver operating characteristic curve in diagnostic test assessment. J Thorac Oncol 2010;5(9):1315-1316.

13. Epstein SK, Ciubotaru RL, Wong JB. Effect of failed extubation on the outcome of mechanical ventilation. Chest 1997;112(1):186-192.

14. Covelli HD, Nessan VJ, Tuttle WK, 3rd. Oxygen derived variables in acute respiratory failure. Crit Care Med 1983;11(8):646-649.

15. Smina M, Salam A, Khamiees M, Gada P, Amoateng-Adjepong Y, Manthous CA. Cough peak flows and extubation outcomes. Chest 2003;124(1):262-268.

16. 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(4):1262-1270.

17. Tobin MJ. Extubation and the myth of "minimal ventilator settings". Am J Respir Crit Care Med 2012;185(4):349-350.

18. Martini RP, Deem S, Brown M, Souter MJ, Yanez ND, Daniel S, et al. The association between fluid balance and outcomes after subarachnoid hemorrhage. Neurocrit Care 2012;17(2):191-198.

19. Caille V, Amiel JB, Charron C, Belliard G, Vieillard-Baron A, Vignon P. Echocardiography: a help in the weaning process. Crit Care 2010;14(3):R120.

20. Buda AJ, Pinsky MR, Ingels NB, Jr., Daughters GT, 2nd, Stinson EB, Alderman EL. Effect of intrathoracic pressure on left ventricular performance. N Engl J Med 1979;301(9):453-459.

21. Pinsky MR. Breathing as exercise: the cardiovascular response to weaning from mechanical ventilation. Intensive Care Med 2000;26(9):1164-1166.

22. 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(3 Pt 1):658-664.

23. Coplin WM, Pierson DJ, Cooley KD, Newell DW, Rubenfeld GD. Implications of extubation delay in brain-injured patients meeting standard weaning criteria. Am J Respir Crit Care Med 2000;161(5):1530-1536.

24. Ko R, Ramos L, Chalela JA. Conventional weaning parameters do not predict extubation failure in neurocritical care patients. Neurocrit Care 2009;10(3):269-273.

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**Legend to Figures**

***Figure 1.*** Area under the receiver operator curve of the multivariable logistic regression model with robust variance estimation for the prediction of extubation failure at any time during the hospital stay. The variables included in the model are: Simplified Acute Physiology Score (SAPS) II, number of spontaneous breathing trials (SBTs) prior to extubation, diastolic blood pressure (DBP) prior to SBT, frequency of tracheal suctioning in the previous 24 hours, and minute ventilation during the SBT.

Equation: Logit [Y|X] = -2.24 + 0.019*SAPS II +0.113*number of prior SBTs – 0.012*DBP + 0.049*suction frequency + 0.034*minute ventilation.

Probability of extubation failure at any time = Expit (logit[Y|X]), where expit (x) = $e^x/(1+e^x)$

***Figure 2.*** Area under the receiver operator curve of the multivariable logistic regression model with robust variance estimation for the prediction of extubation failure within 24 hours of extubation. The variables included in the model are: Simplified Acute Physiology Score (SAPS) II, oxygenation on pulse oximeter during the SBT, frequency of tracheal suctioning in the previous 24 hours, and minute ventilation during the SBT.

Equation: Logit [Y|X] = 10.07 + 0.015*SAPS II - 0.140*oxygenation + 0.108*suction frequency + 0.035*minute ventilation.

Probability of extubation failure within 24 hours = Expit (logit[Y|X]), where expit (x) = $e^x/(1+e^x)$

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Table 1. Respiratory, airway, cardiovascular and neurological characteristics prior to the last successful spontaneous breathing trial. Data are presented as mean ± SD (number of observations) unless otherwise noted

| Characteristics | All Patients (n=2007) | Not Reintubated (n=1628) | Reintubated (n=379) | AUC* | p-value† |
|---|---|---|---|---|---|
| Respiratory Variables | | | | | |
| Tidal volume, mL | 534 ± 94 (1720) | 534 ± 94 (1400) | 525 ± 98 (320) | .524 | .18 |
| Resp. rate, breaths/min | 18 ± 6 (1811) | 18 ± 6 (1466) | 20 ± 6 (345) | .596 | <.01 |
| Min. ventilation, L/min | 7.6 ± 2.9 (898) | 7.4 ± 2.9 (711) | 8.5 ± 2.9 (187) | .615 | <.01 |
| PEEP, $cmH_2O$ | 5 ± 1 (1804) | 5 ± 1 (1459) | 5 ± 1 (345) | .503 | .53 |
| $FiO_2$, % | 40 ± 10 (1809) | 41 ± 11 (1464) | 40 ± 8 (345) | .498 | .18 |
| $SpO_2$, % | 98.8 ± 1.8 (1813) | 98.9 ± 1.8 (1468) | 98.6 ± 1.9 (345) | .557 | <.01 |
| Airway Variables | | | | | |
| Suction frequency | 6.9 ± 4.2 (1771) | 6.6 ± 4.1 (1428) | 8.4 ± 4.0 (343) | .629 | <.01 |
| Secretion quantity | 9.6 ± 7.3 (1769) | 9.0 ± 7.0 (1425) | 12.2 ± 8.0 (344) | .633 | <.01 |
| Positive cuff leak, n (%) | 138 (86) | 109 (86) | 29 (85) | .503 | .94 |
| Cardiovascular Variables | | | | | |
| Heart rate, beats/min | 90 ± 19 (1810) | 90 ± 19 (1465) | 92 ± 18 (345) | .535 | .05 |
| SBP, mmHg | 130 ± 22 (1810) | 130 ± 22 (1465) | 128 ± 24 (345) | .528 | .23 |
| DBP, mmHg | 75 ± 15 (1810) | 75 ± 14 (1465) | 72 ± 16 (348) | .556 | <.01 |
| MAP, mmHg | 92 ± 16 (1789) | 93 ± 16 (1450) | 91 ± 17 (342) | .540 | .06 |
| Neurological Variables | | | | | |
| GCS | 9.7 ± 1.9 (1733) | 9.8 ± 1.9 (1404) | 9.6 ± 1.7 (329) | .521 | .17 |
| GCS-E | 3.1 ± 1.0 (1738) | 3.1 ± 1.0 (1408) | 3.1 ± 1.0 (330) | .507 | .71 |
| GCS-V | 1.1 ± 0.7 (1738) | 1.2 ± 0.8 (1408) | 1.1 ± 0.6 (330) | .509 | .13 |
| GCS-M | 5.6 ± 0.9 (1735) | 5.6 ± 0.9 (1405) | 5.5 ± 09 (330) | .522 | .13 |
| Positive cough, n (%) | 1132 (99) | 911 (99) | 228 (98) | .504 | .32 |
| Positive gag, n (%) | 806 (93) | 654 (94) | 152 (89) | .521 | .06 |
| Positive corneal, n (%) | 889 (97) | 722 (98) | 167 (97) | .503 | .55 |
| Pupil size, mm | 2.8 ± 0.8 (1683) | 2.8 ± 0.8 (1359) | 2.8 ± 0.7 (324) | .508 | .96 |
| Pupil reaction, n (%) | 1440 (85) | 1165 (85) | 275 (85) | .508 | .51 |
| Admission SAPS II | 39 ± 15 (2007) | 38 ± 15 (1631) | 44 ± 16 (376) | .615 | <.01 |

AUC, area under curve; $SpO_2$ , oxygen saturation on pulse oximetry; PEEP, positive end expiratory pressure; $FiO_2$ , fraction of inspired oxygen; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; GCS, Glasgow Coma Scale [E = eye, V = verbal, M = motor]; ICP, intracranial pressure; SAPS II, Simplified Acute Physiology Score.

* Area under ROC curve from bivariate logistic regression.

† Logistic regression p-values, with robust standard errors.

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Table 2. Respiratory, arterial blood gas and cardiovascular characteristics during the spontaneous breathing trial. Data are presented as mean ± SD (number of observations) unless otherwise noted

| Characteristics | All Patients (n=2007) | Not Reintubated (n=1628) | Reintubated (n=379) | AUC* | p-value† |
|---|---|---|---|---|---|
| Number of prior SBTs | 2.6 ± 2.3 (1706) | 2.4 ± 2.0 (1374) | 3.5 ± 3.0 (332) | .636 | <.01 |
| Respiratory Variables | | | | | |
| Tidal volume, mL | 533 ± 99 (1793) | 534 ± 97 (1477) | 526 ± 108 (316) | .523 | .15 |
| Resp. rate, breaths/min | 18 ± 6 (1971) | 18 ± 6 (1597) | 20 ± 7 (374) | .605 | <.01 |
| Min ventilation, L/min | 7.7 ± 3.8 (1890) | 7.5 ± 3.7 (1539) | 8.4 ± 4.1 (351) | .563 | <.01 |
| RSBI | 36 ± 29 (1785) | 35 ± 24 (1471) | 41 ± 45 (314) | .597 | .31 |
| PEEP, mm Hg | 5.1 ± 0.8 (1825) | 5.1 ± 0.8 (1479) | 5.1 ± 0.7 (346) | .502 | .59 |
| $FiO_2$, % | 41 ± 11 (1894) | 41 ± 11 (1540) | 41 ± 10 (354) | .496 | .67 |
| $SpO_2$, % | 99 ± 2 (1971) | 99 ± 2 (1600) | 98 ± 2 (374) | .563 | <.01 |
| Arterial blood gas | | | | | |
| pH | 7.41 ± .05 (1842) | 7.41 ± .05 (1496) | 7.41 ± .05 (346) | .499 | .47 |
| $PaCO_2$, mm Hg | 41 ± 7 (1842) | 41 ± 7 (1496) | 41 ± 7 (346) | .511 | .64 |
| $PaO_2$, mm Hg | 141 ± 55 (1842) | 144 ± 56 (1496) | 126 ± 45 (346) | .600 | <.01 |
| $PaO_2/FiO_2$ | 357 ± 796 (1783) | 371 ± 882 (1447) | 300 ± 110 (340) | .599 | <.01 |
| Cardiovascular Variables | | | | | |
| Hear rate, beats/min | 93 ± 19 (1971) | 93 ± 19 (1600) | 94 ± 20 (371) | .514 | .39 |
| SBP, mm Hg | 132 ± 22 (1971) | 133 ± 22 (1600) | 131 ± 24 (371) | .524 | .26 |
| ICP during SBT, cm $H_2O$ | 9.8 ± 6.4 (190) | 10.2 ± 6.3 (141) | 8.6 ± 6.9 (49) | .556 | .10 |

RSBI, rapid shallow breathing index; PEEP, positive end expiratory pressure; $FiO_2$, fraction of inspired oxygen; $PaCO_2$, arterial partial pressure of carbon dioxide; $PaO_2$, arterial partial pressure of oxygen; $SpO_2$, oxygen saturation on pulse oximetry; SBT, spontaneous breathing trial; SBP, systolic blood pressure.

* Area under ROC curve from bivariate logistic regression.

† Logistic regression p-values, with robust standard errors.

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Table 3. Recorded clinical variable during the first 60 minutes after extubation. Data are presented as mean ± SD (number of observations)

| | All Patients (n=2007) | Not Reintubated (n=1628) | Reintubated (n=379) | AUC[a] | p-value[b] |
|---|---|---|---|---|---|
| $SpO_2$, % | 98 ± 3 (1971) | 98 ± 3 (1600) | 97 ± 5 (371) | .557 | <.01 |
| Heart rate, beats/min | 96 ± 19 (1971) | 96 ± 19 (1600) | 98 ± 20 (371) | .525 | .07 |
| SBP, mmHg | 134 ± 23 (1969) | 134 ± 22 (1599) | 136 ± 25 (371) | .520 | .19 |
| ICP, $cmH_2O$ | 9.2 ± 6.2 (164) | 9.3 ± 6.6 (120) | 9.0 ± 4.7 (44) | .487 | .77 |

$SpO_2$ , oxygen saturation on pulse oximetry; SBP, systolic blood pressure; ICP, intracranial pressure.
[a] Area under ROC curve from bivariate logistic regression.
[b] Logistic regression p-values, with robust standard errors.

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Table 4. Multivariable logistic regression model – Patients who failed extubation any time during hospital stay or early (within 24 hours)

| Variable | Odds Ratio (95% Confidence Interval) | AUC* (95% Confidence Interval) | P-value |
|---|---|---|---|
| Failure at any time | | 0.68 (0.65, 0.72) | |
| SAPS II | 1.02 (1.01, 1.03) | | <.01 |
| Suction Frequency | 1.05 (1.02, 1.09) | | <.01 |
| Number of prior SBTs | 1.12 (1.06, 1.19) | | <.01 |
| DBP, mmHg | 0.99 (0.978,0.997) | | .01 |
| Minute ventilation (SBT), L/min | 1.03 (0998, 1.071) | | .06 |
| Early failure | | 0.72 (0.68, 0.75) | |
| SAPS II | 1.01 (1.00, 1.02) | | <.01 |
| Suction Frequency | 1.10 (1.06, 1.14) | | <.01 |
| $SpO_2$, % | 0.91 (0.84, 0.98) | | .01 |
| Minute ventilation (SBT), L/min | 1.04 (099, 1.08) | | .10 |

SAPS II, Simplified Acute Physiology Score, version II; $PaO_2$, arterial partial pressure of oxygen; DBP, diastolic blood pressure; $SpO_2$ ,oxygen saturation on pulse oximetry; SBT, spontaneous breathing trial.
* Area under ROC curve from multivariable logistic regression.

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**Figure 1**

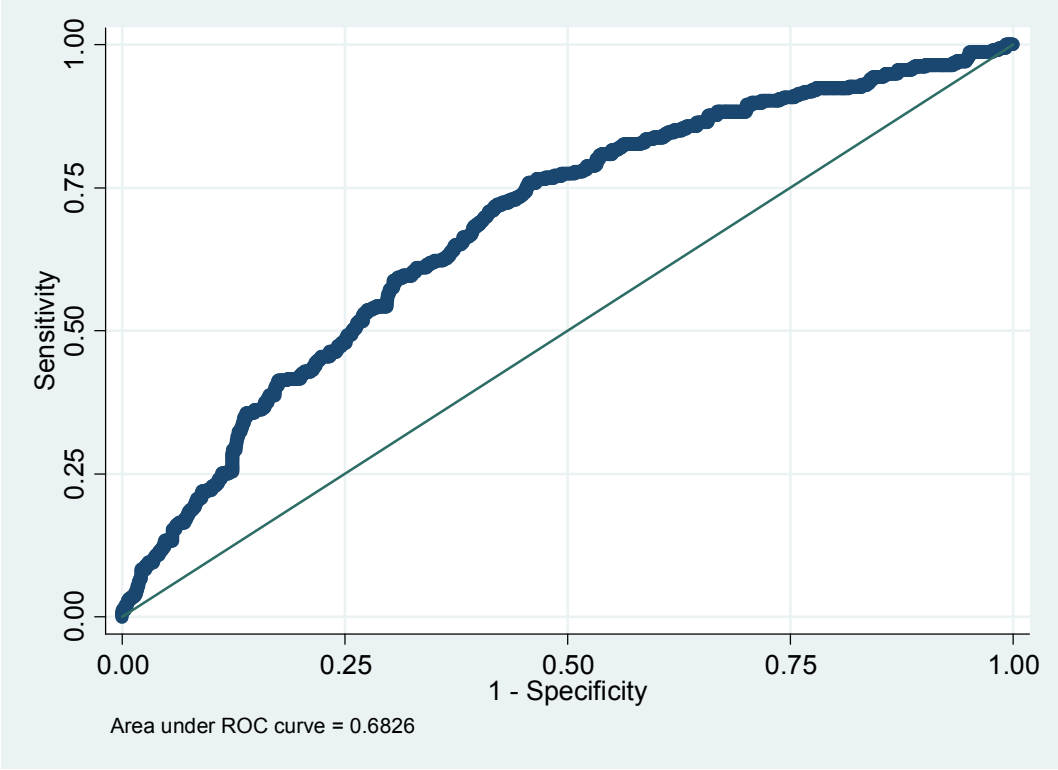

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**Figure 2**