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Neurologic status, cough, secretions and extubation outcomes

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Abstract *Objective:* To determine the degree to which neurologic function, cough peak flows and quantity of endotracheal secretions affected the extubation outcomes of patients who had passed a trial of spontaneous breathing (SBT). *Design:* Prospective observational study. *Setting:* The medical intensive care unit of a 325-bed teaching hospital. *Measurements and main results:* Cough peak flow (CPF), endotracheal secretions and ability to complete four simple tasks were measured just before extubation in patients who had passed a SBT. Eighty-eight patients were studied; 14 failed their first trials of extubation. The CPF of patients who failed was lower than that of those who had a successful extubation (58.1± 4.6 l/min vs 79.7±4.1 l/min, p=0.03) and those with CPF 60 l/min or less were nearly five times as likely to fail extubation compared to those with CPF higher than 60 l/min (risk ratio [RR]=4.8; 95% CI=1.4–16.2). Patients with secretions of more than 2.5 ml/h were three times as likely to fail (RR=3.0; 95% CI=1.0–8.8) as those with fewer secretions. Patients who were unable to complete four simple tasks (i.e. open eyes, follow with eyes, grasp hand, stick out tongue) were more than four times as likely to fail as those who completed the four commands (RR=4.3; 95% CI=1.8–10.4). There was synergistic interaction between these risk factors. The failure rate was 100% for patients with all three risk factors compared to 3% for those with no risk factors (RR=23.2; 95% CI=3.2–167.2). The presence of any two of the above risk factors had a sensitivity of 71 and specificity of 81% in predicting extubation failure. Patients who failed a trial of extubation were 3.8 times as likely to have any two risk factors compared to those who were successful. *Conclusions:* These simple, reproducible methods may provide a clinically useful approach to guiding the extubation of patients who have passed a SBT.

Keywords Extubation · Neurologic status · Outcomes · Mechanical ventilation · Weaning · Cough

Introduction

Removal of the artificial airway, endotracheal extubation, is the final step in the liberation of a patient from invasive positive pressure ventilation. While numerous studies have examined factors that predict combined liberation/extubation outcomes, few have focussed exclusively on the process of endotracheal extubation of patients who are otherwise able to breathe without the ventilator (i.e. who have passed a trial of spontaneous breathing; SBT). Traditional weaning indices, including the respiratory rate:tidal volume (f/Vt), are poor predictors of extubation outcome in patients who have passed a SBT [1].

In two previous studies, we demonstrated that the magnitude of endotracheal secretions and the strength of patients' coughs were predictive of extubation outcomes

[2, 3]. Patients with neurologic diagnoses were more likely to fail extubation [3], but we did not quantify neurologic dysfunction at the time of extubation. Coplin and colleagues found previously that the presence of spontaneous cough and the frequency of endotracheal suctioning were predictors of extubation outcomes, but that gross neurologic function was not associated with outcome [4].

In the current study we assess, using quantitative methods, the impact of neurologic status, cough strength and volume of endotracheal secretions on the extubation outcomes of patients who have passed a SBT.

Methods

The investigational review board of our hospital approved the study protocol. All patients in our medical-cardiac intensive care units (ICU) who were receiving mechanical ventilation via an endotracheal tube between July 2002 and May 2003 were eligible for the study. Patients were studied when they had successfully completed SBTs and when their caregivers were about to extubate them. In our ICU, weaning is guided by a non-mandatory protocol that is performed by bedside nurses, respiratory therapists and resident trainees who are supervised by five board-certified intensivists. Patients who are hemodynamically stable without vasoactive medications *and* whose PaO_2:FIO_2 ratio is 120 or more (on PEEP $\leq$5cmH_2O) are assessed daily with SBTs (T-piece or pressure support $\leq$7 cmH_2O). The SBT is terminated if patients develop: distress despite attempts of the bedside personnel to relieve anxiety, increments of heart rate of more than 20 beats/min or systolic blood pressure more than 20 mmHg, respiratory rate more than 35 breaths/min, tidal volumes less than 0.3 l or sustained pulse oximetry desaturation requiring more than 50% inspired oxygen. Patients who successfully complete a SBT of 30–60 min are considered for a trial of extubation. Patients were excluded from this study if the extubation was performed to withdraw life-sustaining therapies or if they had a tracheostomy.

The following data were gathered for each patient: age, ICU admission APACHE (Acute Physiology And Chronic Health Evaluation) II score, duration of endotracheal intubation/mechanical ventilation, endotracheal tube size, hemoglobin on the morning of extubation, arterial blood gas levels on full ventilatory support and during the SBT, and cardiorespiratory variables after 30 min of spontaneous breathing.

When patients had passed an SBT and extubation was being considered, they were asked to cough into a pneumotachograph-calibrated [3] Aztech peak flow meter placed in series with the endotracheal tube via Hudson RCI Bacterial/Viral filters. Patients were positioned with the head of the bed at 30–45° and coached to "cough" maximally; the best of three attempts was recorded as the patient's cough peak flow (CPF). Patients were also asked to cough through the open-ended endotracheal tube while a white file card was placed 1–2 cm from its end. Any moisture present on the card following 2–3 coughs was considered a positive white card test. During the study period, inspired gases were actively humidified during both ventilation and T-piece trials. Endotracheal secretions were collected in a suction trap starting 2–3 h before an anticipated extubation. Nurses and respiratory therapists were asked to suction the patients at least once an hour. If saline was used to lavage the airways, the quantity instilled was subtracted from the total of retrieved secretions. The volume of suctioned endotracheal secretions per hour over this period was recorded. Neurologic function was assessed by asking the patient to complete four simple tasks: open eyes, follow observer with eyes, grasp hand and stick out tongue [5]. Caregivers were *not* made aware of the CPF, volume of secretions or number of completed tasks.

Patients were extubated as per the instructions of their attending physicians. Patients who remained extubated at 72 h were classified as successful extubations. Patients were classified as extubation failures if they required re-intubation within 72 h. Patients were followed for this study until discharge from the hospital or death. For purposes of analysis, CPF, volume of suctioned secretions, f/Vt, hemoglobin, admission APACHE II scores and age were categorized using threshold values defined a priori when conventional thresholds existed and using means/medians when no such threshold existed.

The main outcome of interest was extubation failure or success. Risk ratios (RRs) were computed as the preferred measure of the strength of association between the predictive variables and the binary outcomes of interest. To guide clinical decisions, sensitivity, specificity and likelihood ratios for predicting extubation failure were computed. The likelihood ratio was presented in preference to the positive and negative predictive values because of its relative stability across varying prevalences of extubation outcomes. Mean values of the continuous outcome variables were compared across categories of potential predictors using analysis of variance. Comparisons of median values were made using non-parametric methods (Kruskal-Wallis and Mann-Whitney tests). For grouped data, chi-square and/or Fisher's exact test were used in comparing differences in proportions between the two groups and in deriving p values. Logistic regression analyses were performed to ascertain the independent predictive potential of cough strength, volume of secretions and cognitive status for extubation failure. In addition, the Rothman Synergy Index (S) was calculated to determine the presence of interaction of these variables [6]. The Synergy Index is equal to one (S=1) in the absence of a synergistic interaction. In such a case, the joint effect of two predictive variables is equal to the sum of their independent effects (i.e. is additive). A Synergy Index greater than one (S>1) suggests the presence of synergistic interaction; the observed joint effect is greater than that expected from the sum of the independent effects of the component variables (i.e. is synergistic). Conversely, a Synergy Index less than 1 (S<1) suggests "antagonistic" effect or negative interaction. Analyses were facilitated by the use of Epi Info 2000. A p value less than 0.05 was used to signify statistical significance.

Results

Eighty-eight patients met eligibility criteria during the study period. These patients contributed a total of 100 separate extubations. Their ages ranged from 20 to 87, with a mean of 62.3±1.8 (mean ± SE) and median of 62 years. Fifty-three (60.2%) were men. The acuity of illness ranged from APACHE II scores of 9 to 42 (mean 23.8±0.8) and the median duration of intubation was 4 days. The primary reasons for their ICU admissions and intubation were airway protection for a variety of medical conditions (33), pneumonia (27), congestive heart failure (9), COPD exacerbations (14), asthma (4), sepsis (5) and other or mixed etiologies in the remainder (8). Patients were intubated for 1–25 days with a median of 3.5 days.

Fourteen (15.9%) of the 88 patients failed their first extubation. Fifty-six patients were extubated after trials of pressure support or continuous positive airway pressure, six after flow-by trials (without pressure support) and 26 after T-piece trials. Seventy-five (85%) could execute all

Table 1 Selected patient characteristics of the cohort stratified by extubation outcome. Values are presented as means ± SE; median; range

Variable	Total cohort	Extubation successes	Extubation failures	*p* value*
Sex	88	74	14	0.1
Males	53	47	6	
Females	35	27	8	
Age (years)	62.3±1.8 (62; 20–87)	62.4±1.9 (62; 22–87)	62.0±4.7 (58; 20–83)	0.9
APACHE II score	23.8±0.8 (24; 9–42)	23.1±0.9 (23; 9–42)	27.5±1.6 (28; 18–39)	0.04
Duration of intubation (days)	5.7±0.6 (4; 1–25)	5.6±0.6 (3; 1–25)	6.3±1.9 (3.5; 1–23)	0.7
RSBI (breaths/min per l)	61.1±3.4 (54.5; 16–166)	58.6±3.4 (56; 16–162)	74.4±11.8 (61; 30–166)	0.09
Hemoglobin (g/dl)	10.7±0.2 (10.5; 8.1–16.2)	10.8±0.2 (10.5; 8.1–16.2)	10.1±0.3 (10.1; 8.4–12.8)	0.2
Peak cough flow (l/min) (*n*=83)	76.3±3.6 (70; 10–200)	79.7±4.1 (75; 10–200)	58.1±4.6 (60; 40–130)	0.03
Secretions (ml/h)	2.3±0.2 (2; 0–8)	2.3±0.4 (2; 0–8)	2.5±0.9 (2.8; 0–6)	0.7
Neurologic status (number of tasks completed)	3.6±0.1 (4, 0–4)	3.8±0.1 (4, 0–4)	2.9±0.5 (4, 0–4)	0.0008
ICU stay (days)	8.3±0.6 (5; 1–50)	7.3±0.8 (5; 1–30)	13.9±3.7 (10; 1–50)	0.006
Hospital stay (days)	26.0±3.4 (14; 3–239)	22.1±2.4 (14; 3–110)	47.0±17.3 (25; 3–239)	0.006

RSBI rapid shallow breathing index (=f/V_t)

four commands prior to their first extubation; two could execute three of four, eight could perform two of four, and four could perform none of the commands. CPFs could be measured in all but five patients who were unable to comprehend the instruction to or could not attempt a cough. For the remaining 83 patients who attempted to cough, the CPFs ranged from 10 to 200 l/min; 41% of the measurements were 60 l/min or less. There was an association between ability to execute the four commands and CPF (regression coefficient =9.3, p=0.04). Sixty-seven percent of patients who could not execute all four commands had CPFs of 60 l/min or less, compared to 38% of patients who could execute all four commands (p=0.09). There were no statistically significant differences in age, admission APACHE II score or endotracheal tube size among patients with CPF 60 or less versus more than 60 l/min. The volume of endotracheal secretions ranged from 0 to 8 ml/h, with a median of 2 ml/h (mean 2.3±0.2 ml/h). Fifty patients had a positive white card test, i.e. were able to propel secretions to a white card held 1–2 cm from the end of the open endotracheal tube.

Table 1 describes characteristics of the 14 patients who failed their first extubation. Reasons for failure were hypoxia (12), respiratory distress/increased work of breathing (5), mental status changes (4), excessive endotracheal secretions (1) and anxiety (1). Twenty-three percent of extubations in women were unsuccessful compared to 11% among the men (p=0.1). There were no differences in age or duration of intubation between those who were successfully and those who were unsuccessfully extubated. The mean CPF was lower in extubation failures (58.1±4.6 l/min vs 79.7±4.1 l/min, p=0.03). The mean volume of secretions retrieved prior to extubation was not significantly different between first-time extubation successes and failures (2.5±0.9 ml/h vs 2.3±0.4 ml/h, p=0.7).

Patients who were unable to complete all four tasks were more than four times as likely to fail their first extubation compared to those who completed the four tasks (RR=4.3; 95% CI=1.8–10.4; see Table 2). Similar elevated RRs for extubation failure were seen among patients with CPF 60 l/min or less (RR=4.8; 95% CI=1.4–16.2) and with secretions of greater than 2.5 ml/h (RR=3.0; 95% CI=1.01–8.8). Twenty-two percent of patients with negative white card tests failed extubation compared to 10% of those with positive tests (RR=2.3; 95% CI=0.8–6.7; p=0.1). There were no statistically significant differences in extubation outcome across categories of hemoglobin concentration (>10 vs $\leq$10 mg/dl), age (>65 vs $\leq$65 years), admission APACHE II score (>24 vs $\leq$24) or f/V_t (>100 vs $\leq$100 breath/min per l). Whereas failure to perform any of the four simple tasks was highly specific in predicting extubation failure (specificity 90.5%), it was insensitive in identifying most of the extubation failures (sensitivity 42.8%). On the other hand, CPF 60 l/min or less and secretions of 2.5 ml/h or more were moderately sensitive but less specific in identifying extubation failures. The presence of any two of the above three risk factors (CPF $\leq$60 l/min, secretions $\geq$2.5 ml/h and/or inability to perform any one of the four tasks)

Table 2 Predictive characteristics of various parameters in predicting extubation failure

Variable	Sensitivity (%)	Specificity (%)	Likelihood ratio	Risk ratio (95% CI)
CPF ≤60 l/min	76.9	65.7	2.2	4.8 (1.4–16.2)
Secretions ≥2.5 ml/h	71.4	62.0	1.9	3.0 (1.01–8.8)
<4 tasks	42.8	90.5	4.5	4.3 (1.8–10.4)
Any 2 risks	71.4	81.1	3.8	6.7 (2.3–19.3)
Negative WCT	71.4	51.4	1.5	2.3 (0.8–6.7)
RSBI >100/min per l	14.3	93.2	2.1	1.9 (0.5–6.9)

CPF cough peak flow, *<4 tasks* inability to perform any one command, *Any 2 risks* of CPF ≤60 l/min, secretions ≥2.5 ml/h or <4 tasks, *WCT* white card test, *RSBI* rapid shallow breathing index (=f/V_t)

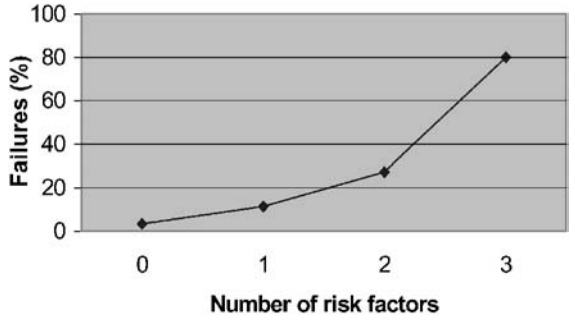

Fig. 1 Cumulative modifiable risks and risk of extubation failure. Risk factors included: inability to perform all four simple tasks, cough peak flow of 60 l/min or less and secretions of 2.5 ml/h or more. The accumulation of risks was additive

provided the best test characteristics, with a sensitivity of 71.4%, specificity of 81.1% and likelihood ratio of 3.8.

The results from both the stratified and logistic regression analyses confirmed the independent predictive potential for neurologic status, categorized as the ability to perform all four tasks versus inability to complete all four, in predicting extubation failure. This relationship remained significant even after simultaneous adjustment for CPF and secretions (adjusted OR=8.0; 95% CI=1.6–39.4, p=0.01; adjusted RR=3.2; 1.6–6.1, p=0.01), and was independent of the duration of mechanical ventilation. There were statistically significant differences in the association of neurologic status, as determined by the ability to perform four simple tasks, with extubation failure among men and women and across categories of CPF. For instance, among men, those unable to complete all four tasks were 24 times as likely to fail extubation as compared to those who completed all four tasks. Among women, those unable to complete all four tasks were only 1.1 times as likely to fail. However, there was a consistency in the association of neurologic status with extubation outcome within categories of volume of secretions, age, hemoglobin level and APACHE II scores.

Overall, there were synergistic interactions between the quantity of secretions and neurologic status (S=5.2), with about a seven-fold relative excess risk of extubation failure due to the synergistic interaction between secretions and CPF in predicting extubation failure. There was no synergy between CPF and neurologic status (S=0.5). Fig. 1 demonstrates extubation failure rates as a function of cumulative risk factors.

The data were reanalyzed to include repeat extubations in first-time failures. There were no substantial differences in any of the relationships when data from subsequent extubations were considered.

Discussion

The current study identifies neurologic status, as measured by the ability to complete four simple tasks, as another potent independent predictor of extubation outcome and confirms, as previously published, the importance of increased secretions and cough strength. There is synergistic interaction between increased secretions and cough strength, and between increased secretions and neurologic status, in predicting extubation failure. Overall, patients who were unable to complete all four tasks of cognitive function, had secretions of more than 2.5 ml/h and whose CPF was 60 l/min or less had a 100% rate of extubation failure, compared to a failure rate of 4.2% of those with none of these risks. The presence of any two of the three risk factors had 71.4% sensitivity and 81.1% specificity in predicting extubation failure. Patients who failed a trial of extubation were 3.8 times as likely to have any two risk factors compared to those who were successful. These simple quantitative measures of neurologic status, cough strength and amount of endotracheal secretions may provide a clinically useful approach to predicting extubation outcomes of patients who have passed.

The potent association of neurologic status and extubation failure found in this study differs from the findings of Coplin and colleagues [4]. These investigators examined extubation outcomes of brain-injured patients who met a number of clinical criteria including stable neurologic status and intracranial pressure less than 20 mmHg. The article did not state whether successful SBTs were required before a trial of extubation, so it is not clear whether the study examined purely extubation (as opposed to combined liberation/extubation) outcomes. Respiratory therapists assessed "airway care" using a number of subjective parameters (cough: vigorous, moderate,

weak, none; gag: vigorous, moderate, weak, none; sputum: none, 1 pass, 2 passes, ≥3 passes; viscosity: watery, frothy, thick, tenacious; suctioning: frequency; sputum: clear, tan, yellow, green). Glasgow coma (GCS) and other scales were used to grade neurologic impairment. These investigators determined that more severe neurologic dysfunction was associated with longer delays of extubation. However, patients who met their "standard" weaning criteria and whose neurologic function was *stable* were safely extubated. Neither the absolute Glasgow score nor the aggregate airway score predicted extubation outcomes. However, a study by Namen and colleagues [7] examined predictors of successful extubation of patients with neurosurgical problems. Of the 98 patients who underwent at least one trial of extubation, the GCS score, f/Vt, PaO_2:FIO_2 ratio and minute ventilation were independent predictors of extubation outcomes.

Notwithstanding this discordance of results using the GCS, we postulate that the difference in our study findings from those of Coplin et al. is due largely to the differing methods used to measure neurologic status. The GCS, a widely used measure of consciousness, does not explicitly address a patient's ability to perform tasks even if "alert" and may be too crude a measure of a patient's ability to react to airway irritants and secretions. The method we used to assess cognitive function has heretofore only been used to assess "level of sedation [5]", but the four simple tasks test abilities: (1) to understand simple commands (i.e. require integrity of receptive and integrative neurologic pathways) and (2) to perform motor skills as commanded (i.e. require integrity of descending, including cranial, motor pathways). After endotracheal extubation patients are asked to participate in their pulmonary toilet, which includes coughing, deep-breathing and expectorating. Perhaps, ability to perform the four tasks reflects more sensitively the level of neurologic function required to maintain a "competent airway." Accordingly, it was not entirely unexpected that inability to follow commands correlated with poor cough strength. A strong voluntary cough requires intact cognitive function *and* strong respiratory muscles, which is independent of cognitive function (and independently predictive of outcomes as well). Irrespective, until further studies are performed to confirm our results, the four simple tasks should not be used exclusively, in lieu of other more validated measures of neurologic function, to make extubation decisions.

In several studies [2, 3, 4] there is a consistent association of cough and extubation outcomes, irrespective of the method used to measure cough strength. We suggest that the CPF provides a much more reproducible measure of cough strength (than subjective methods of quantification). While the endotracheal tube is in place, patients cannot close their glottis to complete a true cough. Accordingly, we must emphasize that, technically, we measured "glottis-free cough." Thus the CPF might be considered a "huff" or, perhaps, a peak expiratory flow maneuver—which explains why values of CPF were significantly lower than expected for extubated coughs. Our current study confirms that the threshold value of 60 l/min or less is reasonably discriminative in predicting extubation failure.

In a previous study [2], the "white card test," which integrates cough strength and secretions, was predictive of extubation outcomes. However, even in that study bedside observers' subjective estimates of cough strength were superior. We recognized that the white card test has inherent limitations. For example, the white card test is often negative in patients with strong cough but little/no endotracheal secretions—a population expected to do well following extubation. The current study suggests that quantitative measurement of cough strength is superior to the white card test in predicting outcomes.

The quantity of endotracheal secretions also re-emerged as an independent predictor of extubation outcomes that synergistically interacted with both CPF and cognitive function. In our first study, secretions were measured subjectively (i.e. "large, moderate, small") and semi-quantitatively (by frequency of endotracheal suctioning), both of which were associated with extubation outcomes. Coplin [4] likewise demonstrated that extubation failure was associated with more frequent endotracheal suctioning. In our second study [3] we sought to quantify secretions by connecting suction traps to the ventilator circuits of patients in the hours prior to extubation, but we did not ask respiratory therapists to follow a minimal frequency of endotracheal suctioning. In the current study, respiratory therapists were asked to suction at a minimal frequency of every hour and more frequently, if they felt it was needed, in the 2 h prior to extubation. Using this method, the quantity of suctioned secretions was predictive of extubation outcomes. There have heretofore been no published methods to standardize quantification of endotracheal secretions. Nonetheless, we were very surprised by the relatively small amount of secretions (i.e. 2.5 ml/h) that demarcated extubation success and failure. Insofar as the quantity of retrieved secretions is dependent upon the suctioning techniques of bedside personnel, this element of our extubation screen is most vulnerable to inter-operator variability and, therefore, these results should be generalized cautiously. Future studies may be helpful in creating more "standardized" methods of endotracheal suctioning and in determining whether the threshold of 2.5 ml/h is valid.

The presence of synergistic interaction between increased secretions and neurologic status or CPF in predicting extubation failure suggests one must be cautious in attempting extubation of patients with these risk factors. Moreover, patients with any two risk factors had a likelihood ratio (LR) of 3.8 for failing extubation. Unlike positive and negative predictive values, which are prevalence-dependent, the LR does not change with the

prevalence of disease (in this case the frequency of extubation failure). The LR also aids in combining results from multiple screening tests and in calculating post-test odds/probabilities. For example, if the estimated probability (P) of extubation failure is 20% for a typical ICU patient, the pre-test odds of failure for that patient (P/1-P) are 0.25. If the patient has two risk factors for extubation failure, the post-test odds of failure (i.e. pre-test odds*LR) are 0.95. This converts to a post-test probability of failure (i.e. odds/1+odds) of 48.7%. In this case, the clinician should be wary of immediate extubation. A reasonable strategy might be to prolong the weaning process, treat remediable causes of cough weakness and excessive secretions, and re-assess daily the chances of extubation failure until the predictors become more favorable. If the current results are replicated in other centers and with larger study populations, it will be prudent, at a minimum, to caution against extubation of patients with all three risk factors.

The current study is unique in integrating simple reproducible measures of neurologic status, cough strength and secretions in predicting the extubation outcomes of patients who have passed a SBT. In spite of its overall positive findings, the study is limited by its relatively small sample size. This led to rather imprecise parameter estimates (with wide confidence intervals) in the subgroup analyses, especially of patients failing multiple tasks. Also, the volume of secretions measured was generally small and may not necessarily be reflective of patients in other centers who have passed SBTs. Furthermore, the cohort had very few patients with neuromuscular disease. CPFs in such patients may differ from general populations of critically ill patients [8] and thus these findings may not be generalizable to that population.

In conclusion, this study demonstrates that neurologic function, voluntary CPF and magnitude of endotracheal secretions contribute to extubation outcomes. This study also offers a simple bedside test of neurologic function that predicts extubation outcomes. If these findings are replicated at other centers, these tools may provide clinicians with an inexpensive, objective method of assessing extubation readiness of such patients.

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