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Extubation failure in the elderly ☆

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Summary To determine the causes, risk factors and complications of planned extubation failure of critically ill elderly patients, we conducted a prospective study of 175 consecutive patients ($\geqslant$70 years old) admitted with respiratory failure. Thirty-six (21%) failed extubation within 72 h after planned extubation. Compared to a younger age group (<70 years old) matched for severity of illness, inability to handle secretions (20%) was the most common reason of airway causes leading to extubation failure in the elderly while upper airway obstruction (22%) was the predominant cause in the control group. As for nonairway causes, COPD related hypercapnic respiratory failure accounted for the majority of cases in both groups. After adjusting for severity of illness, elderly patients who required reintubation had a higher risk of developing nosocomial pneumonia. The presence of underlying pulmonary disease (odds ratio (OR), 2.9; 95% confidence interval (CI) 1.2–6.9), length of intubation >4 days (OR, 4.3; 95% CI 1.8–10.2), and albumin levels <2.5 g/dl (OR, 2.7; 95% CI 1.2–6.7) were independently associated with extubation failure in the old. Objective measurements of cough strength and secretion volume are needed to reduce the morbidity of elderly patients at risk for extubation failure.

Introduction

The incidence of extubation failure in the general population ranges from 3% to 19% and may be high as 33% in patients with mental status changes and neurologic impairment.[1] Extubation failure carries an estimated eight-fold higher odds ratio (OR) for nosocomial pneumonia[2] and a 6–12-fold increased mortality risk.[3,4] Among the reasons advanced for increased mortality include old age, the presence of significant comorbid conditions, and the act of reintubation itself resulting in serious complications.

The process of discontinuing mechanical ventilatory support begins with recognition of adequate recovery from acute respiratory failure. Patients may fail to wean as a result of impaired respiratory center drive, or more frequently as a result of neuromuscular abnormalities including respiratory muscle fatigue, impaired lung mechanics, or impaired gas exchange. A series of investigations have identified various factors predisposing for extubation failure. These factors included age above 70 years,[5,6] higher severity of illness at weaning onset,[7] anemia,[8] and possibly a longer duration of mechanical ventilation prior to extubation.[9] None of these investigations has examined the reasons for the increased risk of extubation failure in the elderly nor compared them with those of matched controls. To address this problem, we

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sought to determine prospectively the causes, risk factors and outcome of extubation failure in those 70 years of age and older compared to a younger group of subjects (<70 years of age) matched for severity of illness.

Methods

Patient Population

The study was conducted prospectively between June 1999 and December 2001 at a 12-bed medical intensive care unit within a university-affiliated tertiary care hospital. The Institutional Review Board of the University at Buffalo approved the study. An informed consent was obtained from all participants or their next of kin. Patients with unplanned extubation (i.e. self-extubation, or endotracheal tube malfunction) were not included in the study. Patients who were extubated because of prior advance directives, or limitation of treatment were also excluded. A control group less than 70 years of age who failed extubation was matched for severity of illness (age adjusted APACHE II score) to the next critically ill patients >70 years of age who failed extubation over the same time period.

Criteria for extubation and reintubation

A protocol-directed weaning of mechanical ventilation was instituted during the study period. Patients were extubated only if they tolerated at least 0.5–2 h of minimal ventilatory support via pressure support $\leqslant 8$ cm water, and positive end-expiratory pressure level $\leqslant 5$ cm water, and passed the weaning trial by satisfying the following criteria: arterial oxygen saturation $\geqslant 90\%$ or arterial pressure of oxygen (PaO_2)$\geqslant 60$ mmHg while receiving fractional inspired of oxygen (FIO_2)$\leqslant 0.4$; spontaneous rapid shallow breathing index (f/v_T) less than 100;[10] need for infrequent suctioning of airway secretions; alert mental status; stable hemodynamic profile; stable cardiac rhythm; increase in arterial pressure of carbon dioxide ($PaCO_2$) <10 mmHg; and decrease in pH <0.10. In general, isolated criteria such as tachypnea, tachycardia, diaphoresis, agitation or anxiety were considered inadequate for deeming the patient a weaning failure. After extubation all patients received supplemental oxygen. The use of bronchodilators and expectorant was administered when clinically indicated. Criteria for considering reintubation included an absolute increase in $PaCO_2 \geqslant 10$ mmHg and decrease in pH$\geqslant 0.10$; PaO_2 <60 mmHg or SaO_2 $<90\%$ while receiving FIO_2 greater than 0.50–1.0; signs of increased work (tachypnea, use of accessory respiratory muscles, thoracoabdominal paradox); inability to protect the airway because of upper airway obstruction or inability to clear pulmonary secretions.

For the purpose of this study, the amount of secretions was assessed as scant (requiring endotracheal suctioning every 4 h or more), moderate (requiring suctioning every 2–4 h) or abundant (requiring suctioning every 2 h or less). The nurse assigned to the project was asked to rate the amount of secretions independently of the extubation decision.

Data collection and definitions

For all patients, clinical and laboratory data were collected at the onset of mechanical ventilation, at the onset of weaning trial, and prior to extubation. The data collected were of two categories: demographic and intensive care unit (ICU) related. Demographic data included age, gender, weight, ICU admitting diagnosis, comorbid conditions and Charlson Index.[11] The Charlson Index provides a prognostic taxonomy for comorbid conditions which singly or in combination assesses the risk of 1 year mortality. Each comorbid condition is assigned a weight ranging from 1 to 6 based on the number and seriousness of comorbid diseases. The index severity score is calculated by totaling the assigned weight for each of the patient's comorbidities.

Comorbidities were classified as follows: a *cardiac comorbidity* is considered present if a treatment is being provided for coronary artery disease, congestive heart failure, arrhythmias, or valvular heart disease; *pulmonary comorbidity*: treatment for chronic obstructive lung disease, or interstitial lung disease; *renal comorbidity*: preexisting renal disease with documented abnormal creatinine level prior to hospitalization; *hepatic*: preexisting chronic hepatitis or liver cirrhosis; *endocrine*: treatment for diabetes mellitus; *central nervous system*: presence of symptomatic acute or chronic vascular or nonvascular encephalopathy; *neoplastic disease*: presence of active malignancy (solid tumor or hematologic malignancy) at the time of presentation; *immunosuppression*: the use of steroids at a dose greater than 20 mg/day for more than 2 months, HIV infection with CD4 count less than 200 cells/mm^3, neutropenia with absolute neutrophil count less than 1000/mm^3, or the use of cytotoxic drugs.[12]

ICU related data included date of admission to the ICU, vital signs (temperature, heart rate, respiratory rate, and blood pressure), laboratory data (arterial blood gas, serum sodium, potassium, chloride, bicarbonate, creatinine, bilirubin, albumin, CBC, PT and PTT), mode (continuous and intermittent) and type of sedatives agents (benzodiazepines, propofol), complications post extubation, length of mechanical ventilation, length of ICU stay, and outcome. Generalized severity of illness was determined using the acute physiology and chronic health evaluation (APACHE) II score.[13]

Etiologies for respiratory failure necessitating mechanical ventilation were classified into four types.[14] Type I or acute hypoxic respiratory failure referred to any alveolar-filling pathology present on chest radiography associated with impaired gas exchange (e.g., pulmonary edema, acute respiratory distress syndrome (ARDS), pneumonia). Type II or hypercapnic respiratory failure referred to any process associated with excessive respiratory load, impaired neuromuscular function, or a decreased ventilatory drive (e.g., obstructive lung disease, obesity hypoventilation, muscle weakness). Type III or metabolic respiratory failure referred to any state of severely deranged acid–base disorder leading to the need for mechanical ventilation. Type IV indicated a respiratory failure related to airway protection and was not considered evidence of organ dysfunction. If the cause of respiratory failure was multi-factorial, the patient was classified by the primary reason for intubation and mechanical ventilation as discerned from the ICU progress notes.

The time to reintubation was measured in hours from extubation rounded off to the nearest hour. Causes for extubation failure were assigned using the following definitions: (1) *airway etiology:* upper airway obstruction (stridor with resolution upon reintubation) and/or aspiration or excess pulmonary secretions (witnessed aspiration or an inability to maintain airway patency because of pulmonary secretions); (2) *non-airway etiology:* hypoxic or hypercapnic respiratory failure (signs of increased work of breathing associated with hypoxemia ($PaO_2 < 60$ mmHg or $SaO_2 < 90\%$ while administering $FIO_2 > 0.5$–1.0) or hypercapnia (increase in $PaCO_2 \geqslant 10$ mmHg and decrease in pH$\geqslant$0.1)) in the absence of upper airway obstruction or excessive pulmonary secretions.

Statistical analysis

Results are expressed as mean$\pm$SD. Continuous variables were analyzed using a two-tailed student's-*t*-test for normally distributed variables and the Mann–Whitney test for non-normally distributed variables. Proportions were compared using the Chi-square test with Yates correction or Fisher's exact test when necessary. A logistic regression analysis was performed to ascertain which factors among the elderly group contributed independently to extubation failure. Variables that were significant at the 0.1 level in univariate analysis were considered for inclusion in the logistic regression model. Interactions among variables were tested for possible association. *P*-Value equal or less than 0.05 was considered significant. All statistical analysis was performed using software (SPSS, Version 10.0; Chicago, IL).

Results

Characteristics of study population

One hundred seventy five consecutive critically ill elderly patients (mean age 77.9$\pm$6.3 years) ventilated for a minimum of 6 h were enrolled. They included 83 patients (47.4%) admitted from home, 58 patients (33.1%) from nursing homes, 25 patients (14.2%) transferred from medical wards and 9 patients (5.1%) referred from other hospitals. Thirty-six elderly patients (21%) required reintubation within 72 h of extubation. Comparing those who were successfully extubated and those who failed extubation, there were no significant differences in terms of age, gender, or residence prior to admission between the two groups (Table 1). Although chronic obstructive pulmonary disease (COPD) was the only comorbidity reported more frequently in those subjects who failed extubation, the Charlson index was essentially the same in two groups. The control group who failed extubation was more likely to be admitted from the community and less likely to have underlying chronic neurologic impairment (Table 1).

COPD and pneumonia were the main underlying reasons for ICU admission for both the elderly and the control population (Table 2). Twenty-eight patients in the elderly group required vasopressors for more than 24 h. Septic shock was the predominant indication for the use of inotropic agents in these cases. Table 3 displays the types of respiratory failure in the elderly cohort. Only, hypoxic respiratory failure (Type I) was more commonly observed in the extubation failure group compared to those in the extubation success group ($P = 0.03$). However there were no differences in the types of respiratory failure between the elderly and the control group who failed extubation.

Table 1 Demographic characteristics of the study population.

	Extubation success ($\geqslant$70 years) (n = 139)	Extubation failure ($\geqslant$70 years) (n = 36)	Extubation failure (<70 years) (n = 36)
Age, years	78.0±2.3	77.4±1.6	52±6.1[a]
Gender, Male/Female	67/72	15/21	26/10
Home/Nursing home	82/57	23/13	33/3[a]
Age adjusted APACHE II score	20.2±2.3	22.4±0.8	21.9±1.7
Comorbid illness, n (%)			
Cardiac	16 (12)	7 (19)	5 (14)
Pulmonary	47 (34)	20 (56)[b]	18 (50)
Renal	22 (16)	3 (8)	4 (11)
Neurologic	29(21)	16(44)	6 (17)[a]
Charlson Index	3.2±0.5	2.9±0.4	2.4±0.5

[a]Comparing the difference between extubation failure group $\geqslant$70 years and extubation failure group $\leqslant$70 years; $P \leqslant 0.05$.
[b]Comparing the difference between extubation failure group and extubation success group in those $\geqslant$70 years; $P \leqslant 0.05$.

Table 2 Admission diagnosis.

Diagnosis, *n* (%)	Extubation success ($\geqslant$70 years) (n = 139)	Extubation failure ($\geqslant$70 years) (n = 36)	Extubation failure (<70 years) (n = 36)
Pneumonia	33 (24)	7 (19)	6 (17)
COPD	31 (22)	16 (44)[a]	14 (39)
Septic shock	24 (17)	6 (17)	5 (11)
Pulmonary edema	10 (7)	3 (9)	1 (3)
Cerebrovascular accident	11 (8)	4 (11)	1 (3)
Renal failure	12 (9)	0	2 (6)
Status epilepticus	6 (4)	0	1 (3)
Status asthmaticus	0	0	1 (3)
Hepatic cirrhosis	0	0	3 (9)
Others	12 (9)	0	2 (6)

[a]Comparing the difference between extubation failure group and extubation success group in those $\geqslant$70 years; $P \leqslant 0.05$.

Table 3 Comparison of the types of respiratory failure between elderly patients with extubation success and extubation failure.

	Extubation failure (n = 36)	Extubation success (n = 139)	*P*-value
Hypoxic respiratory failure	8 (24%)	11 (8%)	0.03
Hypercapnic respiratory failure	23 (64%)	109 (78%)	0.11
Metabolic related respiratory failure	4 (11%)	11 (8%)	0.8
Airway protection related respiratory failure	1 (3%)	8 (6%)	0.7

Extubation failure

Assist control was the mode of ventilation used in all participants at the time of initiation of weaning. Elderly patients who failed extubation had longer duration of mechanical ventilation prior to weaning trials compared to those who were liberated successfully from mechanical ventilation (6.1±7.5 days and 3.5±5.5 days; respectively; $P = 0.002$). Neither the type of sedative agents nor the mode of delivery of sedation was significantly different between those who failed extubation and those

Table 4 Parameters at the time of extubation.

	Extubation success ($\geqslant$70 years) ($n = 139$)	Extubation failure ($\geqslant$70 years) ($n = 36$)	Extubation failure (<70 years) ($n = 36$)
PaO_2/FIO_2	283.3±67.1	269.2±80.6	275.6±45.6
$PaCO_2$ (mm Hg)	42.9±7.3	45.8±4.7	39.6±5.4
Frequency/tidal volume (min/l)	66.2±4.6	73.8±6.5	67.6±7.1
Frequency endotracheal suctioning, n (%)			
Scant	116 (83)	27 (75)	31 (86)
Moderate	23 (17)	9 (25)	5 (14)
Abundant	0	0	0
Minute ventilation (l/min)	10.1±0.8	9.7±0.7	11.2±0.4
Glasgow coma scale	12.7±5.4	11.4±3.9	14.3±2.1[a]
Age adjusted APACHE II score	16.2±2.3	15.4±1.6	14.5±0.8

[a]Comparing the difference between extubation failure group $\geqslant$70 years and extubation failure group $\leqslant$70 years; $P\leqslant 0.05$.

Table 5 Causes of extubation failure.

	Extubation failure ($\geqslant$70 years) ($n = 36$)	Extubation failure (<70 years) ($n = 36$)
Airway causes		
Excess secretion	7 (20%)	4 (11%)
Upper airway obstruction	3 (8%)	8 (22%)
Non-airway causes		
COPD related hypercapnia	18 (50%)	12 (34%)
Encephalopathy	3 (8%)	4 (11%)
Aspiration	3 (8%)	2 (6%)
Pulmonary edema	2 (6%)	5 (13%)
Seizure	0	1 (3%)

who were extubated successfully. In addition, none of participants of either the elderly or the control group received neuromuscular blocking agents during their hospitalization. Clinical and laboratory values including weaning parameters, the amount of secretions, and age adjusted APACHE II scores at the time of extubation are shown in Table 4. There were no significant differences among the groups in term of severity of hypoxemia, the minute ventilation, the spontaneous shallow breathing index, or the frequency of endotracheal suction. Only the Glasgow coma scale was significantly higher in the control group compared to the elderly who failed extubation.

Causes of extubation failure in the elderly and the control group are shown in Table 5. Inability to handle secretions was the most common reason of airway causes leading to extubation failure in the elderly group while upper airway obstruction was the predominant cause in the control group. As for nonairway causes, COPD related hypercapnic respiratory failure accounted for the majority of cases of extubation failure in both groups.

The median time to reintubation was 21 h (range 1–72 h; mean (SD) 21.9 (25.7)) for the elderly cohort. Patients who failed extubation because of upper airway obstruction or excess secretions needed to be reintubated earlier (0–24 h) compared to those of nonairway causes. Notably, none of the participants had noninvasive positive pressure ventilation in the period post extubation.

Complications related to reintubation occurred in 15 (42%) elderly patients who failed extubation and in 10 (28%) of the younger age group (Table 6). The development of pneumonia after reintubation was unrelated to time to reintubation (pneumonia 36±8 h versus no pneumonia 29±6 h, $P = 0.3$). Twenty-six patients who failed extubation had a

Table 6 Complications associated with reintubation.

Variables, *n* (%)	Extubation success ($\geqslant$70 years) ($n = 139$)	Extubation failure ($\geqslant$70 years) ($n = 36$)	Extubation failure ($<$70 years) ($n = 36$)
Pneumonia	7 (5%)	9 (25%)[a]	6 (17%)
Myocardial infarction	8 (6%)	1 (3%)	0
Arrhythmia	25 (18%)	4 (17%)	1 (3%)
Pneumothorax	2 (1%)	0	1 (3%)
Others	4 (3%)	1 (3%)	2 (6%)

[a]Comparing the difference between extubation failure group and extubation success group in those $\geqslant$70 years; $P \leqslant 0.05$.

tracheostomy performed after intubation; 14 of those were in the elderly and 12 in the control group.

Outcome

The mean lengths of ICU and hospital stay were significantly longer for elderly patients who failed extubation (17.2 ± 18.1 days and 26.8 ± 22.2 days, respectively) compared to those who were successfully extubated (7.3 ± 11.1 days and 15.9 ± 15.1; respectively; $P = 0.003$). In addition, those elderly patients who failed extubation spent an additional 9.1 ± 8.5 days receiving mechanical ventilation. Using multiple logistic regression analysis, the presence of underlying pulmonary disease (OR 2.9; 95% confidence interval (CI) 1.2–6.9), length of intubation greater than 4 days (OR 4.3; 95% CI 1.8–10.2), and albumin levels less than 2.5 g/dl (OR 2.7; 95% CI 1.2–6.7) were found to be independently associated with extubation failure.

The in-hospital mortality was 47% for the elderly with extubation failure and 41% for the control group compared to 20% for the extubation success group ($P < 0.002$ and < 0.01, respectively). Those who survived hospitalization were more likely to require reintubation for airway causes (8 out of 19 survivors) whereas nonsurvivors were reintubated predominantly for nonairway causes (14 out of the 17 nonsurvivors) ($P = 0.03$). The immediate causes of death in the elderly group requiring reintubation included ARDS in 10 patients; sepsis with multiple organ failure in 3 patients; ventricular arrhythmia in 3 patients and pulmonary embolism in one patient.

Discussion

The principal findings of this study are that: (1) both COPD related hypercapnic respiratory failure and inability to clear secretions were the most common causes of extubation failure in the elderly; (2) the presence of underlying pulmonary disease, the need for mechanical ventilation for more than 4 days, and severe hypoalbuminemia are associated with increased risk of extubation failure in the elderly; and (3) extubation failure carries a higher morbidity and mortality.

The ability to predict successful extubation remains a daunting task to health care providers more so in the elderly population than any other age group. Traditional weaning parameters obtained prior to and during the weaning might not reflect who will fail extubation.[15] Many classical predictors as the frequency tidal volume ratio, negative inspiratory force, and minute ventilation are advocated in the evaluation of patients prior to possible extubation, but none of these parameters were found to be predictive of extubation failure in our elderly population. Structural changes in the respiratory muscles[16] and in the chest wall of the elderly were not accounted for in these equations. Moreover, numerous factors have been delineated as potential elements that may affect extubation failure. The severity of illness at weaning onset, the mode of ventilator support prior to extubation, the duration of spontaneous breathing trials prior to extubation, and the mode of intravenous sedation were linked to extubation failure. Our data did not show any of these parameters to be significantly different between those elderly who were extubated successfully and those who failed extubation. Despite the high percentage of COPD patients in our study population, the rate of extubation failure (21%) was comparable to previously published studies (15–20%).[17,18]

Two recent studies pointed to an association between anemia and extubation failure. In a retrospective study of 395 patients (abstract), Epstein and coworkers[19] reported elevated risk of reintubation in those with hematocrit $< 30\%$. Similarly, in prospective study of 91 adult patients, Khamiees and colleagues noted that those with hemoglobin levels $\leqslant 10$ g/dl were more than five times as likely to fail extubation as compared to those with higher values.[8] We have been unable to identify such a relationship in our study population. One of the likely explanations for differences in our findings and those of Khamiees is the high percentage of patients with underlying cardiac comorbidities included in the latter study. In a retrospective study of 78,974 Medicare beneficiaries hospitalized with acute myocardial infarction, patients with lower hematocrit values on admission had higher 30 days mortality rates.[20] Our study excluded all patients admitted to the coronary care unit and those diagnosed with acute myocardial infarction.

The risk of extubation failure is known to increase when patients are incapable of adequately protecting their airways and effectively clearing their secretions. Traditional evaluation of airways clearance hinged on demonstrating an adequate and effective cough reflex, yet the definition of and criteria used to identify effective cough remains elusive. Using an innovative approach, Khamiees and coworkers applied a semi-objective assessment to assess cough strength using a white card held 1–2 cm from the endotracheal tube.[8] Those patients who were unable to propel their secretions into the card were three times as likely to fail extubation as those who could. The use of such technique however has not been validated in an elderly cohort and it may be difficult to implement in those with cognitive impairment or severely impaired mental status.

We found that the proportion of patients who could not be extubated successfully was more likely to have poor nutritional indices. Malnutrition has been suggested to impair the patients' ability to be weaned off ventilatory support through several mechanisms: weakness of inspiratory muscles,[21] decrease of ventilatory drive,[22,23] and alteration of immune lung defenses resulting in an increased risk of nosocomial infections.[24] Hence, every attempt should be made to avoid withholding nutrition during ICU stay in order to improve outcome of extubation.

Various studies[7,25] related to extubation failure concluded that patients who require reintubation have an increased risk of major physiologic complications and death. Several reasons have been cited in the past regarding the association of extubation failure with an adverse outcome. Reintubation has been shown to be linked to ventilator-associated pneumonia.[2] This finding reflects the increased risk of aspiration of colonized oropharyngeal secretions into the lower airways by patients with acquired subglottic dysfunction or impaired consciousness after several days of sedation. A recent case-control study of 135 patients following heart surgery found reintubation to be a major risk factor for VAP since pneumonia occurred in 92% of the reintubated patients versus 12% of the control subjects.[26] Another reason could be that clinical deterioration may occur between the time of extubation and reintubation, by causing new or worsening organ dysfunction. Patients with extubation failure receive mechanical ventilation for an additional time period, thereby increasing the likelihood of ventilator-related complications will occur. An increased duration of mechanical ventilation increases the likelihood that the patients will require long-term rehabilitation because of associated prolonged inactivity and consequent increase in debility and deconditioning. Data from our report support this conclusion. Elderly patients with extubation failure had prolonged duration of mechanical ventilation, ICU stay, hospital stay and higher mortality.

We acknowledge that the study has several limitations, and care must be taken in generalizing our findings to other groups. First of all, our study population represents a highly selective population of elderly patients admitted to the ICU for mechanical ventilation. The potential of a selection bias in the population under investigation cannot be ignored particularly if physicians elected to refer patients who they thought would benefit from ICU care whereas others restricted such an access for patients who they considered too debilitated to benefit from aggressive ICU management. Second, our study population comprised of elderly patients admitted to medical intensive care units, therefore our findings may not pertain to subjects who failed extubation post surgical procedures. Third, we have not investigated the role of non-invasive ventilation on the outcome of patients with extubation failure. Finally, there were many confounding variables we were unable to control such as the treating physicians, hospital discharge, and in-puts from the patients families.

In conclusion, we have presented a report on the causes of extubation failure in the critically ill elderly patients. We have observed a substantially higher mortality in these patients and have identified several variables independently associated with extubation failure. With the rising prevalence of elderly population in the US, future research should focus on implementing strategies designed to reduce the incidence of extubation failure and long-term complications during ICU stay.

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