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ORIGINAL ARTICLE

# Association of Extubation Failure and Functional Outcomes in Patients with Acute Neurologic Illness

**Muhammad Adeel Rishi[1] · Rahul Kashyap[1] · Gregory Wilson[1] · Louis Schenck[2] · Sara Hocker[3]**

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**Abstract**
*Background* An association between extubation failure and neurologic and functional outcomes in patients with primary neurologic illness has not been investigated rigorously. We plan to conduct a retrospective chart review to study this association.
*Methods* A total of 949 unique patients intubated and ventilated for at least 48 h in Neuro ICU (NICU) were obtained. Extubation failure was defined as need for reintubation within 48 h of initial extubation. Independent and dependent association between extubation failure and clinical parameters was assessed.
*Results* The patients had a median age [interquartile range (IQR)] of 58.5 (23.0) years. 60.5 % were male and 81.9 % were Caucasian. Extubation failure occurred in 108 (12.8 %) patients. There was no difference in age, APACHE 3 score, FOUR score, or GCS score of patients at ICU admission between those who experienced extubation failure and those who did not. Extubation failure was associated with longer NICU and hospital LOS [median (IQR); 13.7 (11.3) vs. 9.1(8.2) days, $P < 0.01$ and 24.5 (20.0) vs. 16.8 (16.7) days, $P < 0.01$]. Patients with extubation failure had worse functional outcomes at 6 months as measured by the modified Rankin score [MRS; median (IQR), 5.0 (2.0) vs. 4.0 (3.0), $P < 0.01$]. After adjusting for confounders, extubation failure was associated with longer hospital and ICU LOS and worse functional outcomes.
*Conclusions* In patients with acute neurological illness, extubation failure is associated with longer ICU and hospital stays but does not impact hospital mortality. Patients with extubation failure may experience a worsening of their functional status over time.

**Keywords** Extubation failure · Reintubation · Mechanical ventilation · Neurological ICU · Respiratory failure

## Introduction

Patients with acute neurological illness (ANI) sometimes require endotracheal intubation and mechanical ventilation (MV) in order to achieve adequate oxygenation, ventilation, and airway protection; however, there are known risks associated with the use of MV [1, 2]. After recovery from the initial insult, patients may meet respiratory criteria for extubation, but there is often uncertainty as to whether a patient will be able to protect his or her airway, in the setting of impaired level of consciousness or bulbar dysfunction [3]. As such, the rate of extubation failure, defined

✉ Muhammad Adeel Rishi
rishi.muhammad@mayo.edu

Rahul Kashyap
kashyap.rahul@mayo.edu

Gregory Wilson
wilson.gregory@mayo.edu

Louis Schenck
schenck.louis@mayo.edu

Sara Hocker
hocker.sarah@mayo.edu

1 Multidisciplinary Epidemiological and Translational Research in Critical Care Medicine (METRIC), Mayo Clinic, 200 First St SW, Rochester, MN 55905, USA

2 Division of Biomedical Statistics and Informatics, Mayo Clinic, Rochester, MN, USA

3 Division of Critical Care Neurology, Mayo Clinic, Rochester, MN, USA

as a need for reintubation within 24–72 h after extubation, is considerably higher in this patient population [4]. Additionally, respiratory weaning parameters outlined in currently available guidelines are not predictive of extubation failure in patients with ANI intubated solely for neurologic reasons [5].

Despite reports of worse outcomes in patients with extubation failure, [6–8] the impact of extubation failure on the functional outcomes of patients with ANI remains unknown and is possibly underestimated [3]. We conducted a retrospective study in a neuroscience intensive care unit (NICU) of a large quaternary care medical center. The primary aim of our study was to investigate the association between extubation failure and functional outcomes. The secondary aim of our study was to examine the association between extubation failure and NICU or hospital length of stay (LOS) and mortality in patients with ANI.

## Materials and Methods

The study was approved by the Mayo Clinic Institutional Review Board for the use of existing medical records of patients who gave prior research authorization.

### Patient Population

We performed a retrospective review of patients with ANI admitted from January 1, 2002, through December 31, 2011 to the NICU at Mayo Clinic, Rochester, Minnesota. During the study period, 18,572 consecutive patient records admitted to the NICU were reviewed for inclusion and exclusion criteria. 2848 adult patients required MV during the study period. Adult patients (≥18 years of age) who had been diagnosed with ANI, who had been on MV via an endotracheal tube (ETT) for at least 48 h in the NICU were included in the study. After excluding patients (1) without research authorization, (2) ≤18 years of age, and (3) those who required no MV or MV <48 h, 949 patients were included in the analysis (Fig. 1). For patients with multiple hospital admissions, only the first hospital admission was used in this analysis. Patients who received MV for <48 h were not included to exclude patients who are intubated for completely reversible reason without ANI for short duration of time (for procedures, overdose or for a post-ictal state after a single seizure etc.).

### Classification and Definitions

Planned extubation (elective) was defined as extubation after a successful spontaneous breathing trial in a patient fulfilling all weaning criteria. Self extubation was defined as the deliberate removal of the ETT by the patient and accidental extubation was defined as the accidental or unplanned removal of an ETT during nursing care or transportation. If any of the extubation episodes for a patient were self or accidental extubation during their hospital visit, then the patient was considered as having a self or accidental extubation for the analysis.

In accordance with standardized practices in our NICU, sedation was turned off at least 30 min prior to initiation of SBT. The decision to conduct SBT was made by the attending physician based on (1) control of cause of respiratory failure, (2) adequate gas exchange on $FiO_2$ ≤40 %, and (3) hemodynamic stability. What constituted the control of cause of respiratory failure and hemodynamic stability was based on physician's clinical judgement. The SBT was performed by respiratory therapists and was protocol based. The patient was placed on either T-piece or pressure support of 5 cm $H_2O$ for 30 min. SBT was terminated at any time if patient develops tachypnea (respiratory rate ≥35), hypoxia ($O_2$ saturation ≤88 %), or hemodynamic instability. At the end of the 30 min, a rapid shallow breathing index [9] [RSBI; Respiratory rate/Tidal volume (L)] was calculated. If patient passed the SBT (RSBI ≤100), the attending physician was alerted. The decision to extubate patients was based on clinical judgement and made by the attending physician and takes into account the RSBI, as well as other factors such as ICP and blood pressure etc. Extubation failure was defined as the need for reintubation within 72 h after extubation [10]. Patients were reintubated for the following reasons: severe hemodynamic instability without response to fluids and vasoactive drugs, $SpO_2$ persistently <85 %, worsening of pH and $PaCO_2$ values with depressed mental status, loss of consciousness, persistent inability to remove copious airway secretions, and respiratory or cardiac arrest. The cause for reintubation was deciphered manually from the procedure note written by the attending physician at the time of reintubation.

### Automated Electronic Strategy for Identifying Extubation Failure

Extubation failure was identified from the electronic medical records using an automated search strategy. Details of this search strategy have been described elsewhere [11]. Briefly, data from the Mayo Clinic Life Sciences System [12], an exhaustive database of patient information which has been validated [13, 14], was accessed using a Web-based commercial software tool set [Data Discovery and Query Builder (DDQB); International Business Machines Corp] [15]. Extubation failure data were extracted through a query that accesses flow sheet data using DDQB, returning the flow sheet row data equal

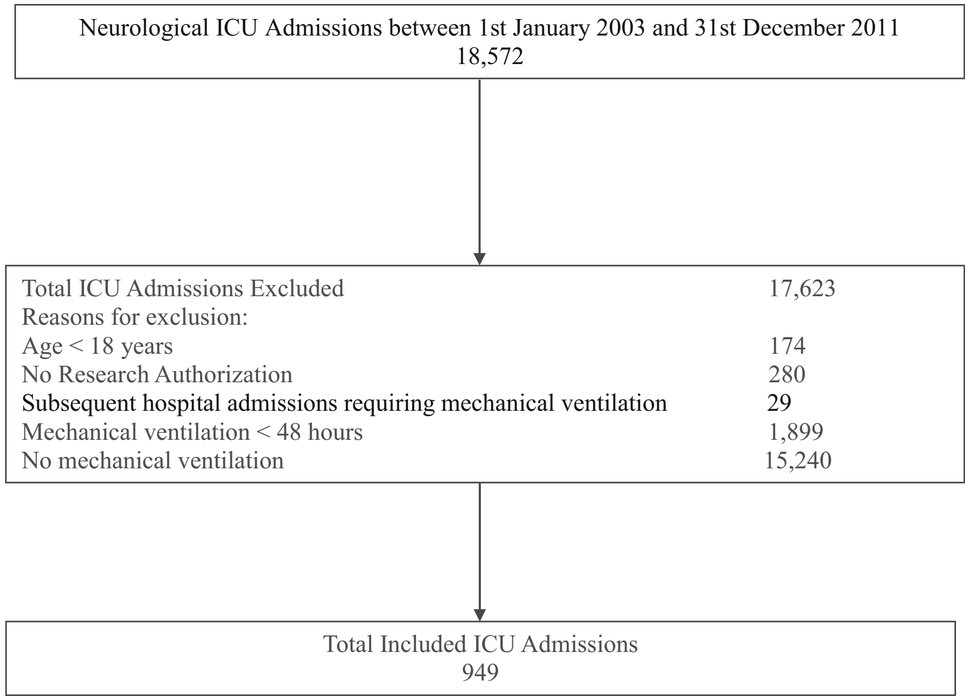


**Fig. 1** Electronic search flow diagram of patients admitted to the Neurological Intensive Care Unit from January 2002 through December 2011. ICU indicates intensive care unit

to "Airway Tube Status" where patient's nurses chart the intubation/extubation status of the patient.

A subset of 100 randomly selected patients was used for derivation. The automated search algorithm was further validated against another set of 100 randomly selected patients from the cohort. A manual search strategy was used as a comparative gold standard. The medical records of the derivation and validation groups were reviewed manually and independently by two critical care clinicians (M.R. and S.H.). The selection of 100 patients in both subsets was chosen to limit manual annotation burden, while ensuring a robust sample size for the two subsets.

Patients with multiple ICU admissions during their hospitalization were classified as having extubation failure if the episode occurred during any of the ICU admissions. Patients having multiple episodes of extubation failure during their hospitalization were included in the analysis only once.

## Data Collection

All extubated patients were categorized as having elective, self, or accidental extubation. For all of the patients who were reintubated, we collected the date, time, and reason for reintubation. The time to reintubation was measured in hours. Reasons for reintubation were classified as airway-related problems (e.g., upper airway obstruction, aspiration/excess pulmonary secretions, and bronchospasm) and non-airway-related problems (e.g., excessive respiratory distress, reduced level of consciousness, procedures, and others).

The level of consciousness was assessed by the Glasgow Coma Scale (GCS) score [16] and the Full Outline of Unresponsiveness (FOUR) score [17]. Progression of illness was assessed using Sequential Organ Failure Assessment (SOFA) score. This score has been previously described to predict outcomes in patients admitted to NICU [18].

We analyzed the following clinical outcomes: ICU mortality, hospital mortality, need for tracheostomy, ICU LOS, hospital LOS, change of goals of care, and functional outcomes at hospital discharge and at 6 months following hospital discharge.

A "change in goals of care" in our ICU is defined as change of "code status" of patient to "do not intubate (DNI)," "do not resuscitate (DNR)," "DNR/DNI" or "comfort care," when the goal of care is to provide comfort, and not to prolong life. Change in code status was treated as a bivariate variable (those who had any change in code status and those who did not). Although DNI or DNR/DNI status is different from comfort care, treating it as a stratified variable did not change regression models and patients changed to "DNI status" or "DNR/DNI status" after initial extubation, had hospital mortality and ICU and hospital LOS no different from patients who were made 'comfort care."

The Modified Rankin Score [19] (MRS) has been widely used for evaluating functional outcomes in patients with neurological disease [20]. We used the extended MRS in order to determine functional outcomes. The MRS consists of seven categories ranging from complete recovery (MRS 0) to death (MRS 6) [19, 20]. Patients were graded on the extended MRS at hospital discharge and again at 6 months after hospital discharge. Change in MRS for patients alive at hospital discharge was classified by an increase, decrease, or no change. Each category was mutually exclusive. Subjects without an MRS score at the end of 6 months were excluded when analyzing changes in MRS. The MRS variable was also dichotomized into good functional status (MRS 0–3) and poor functional status (MRS 4–6) categories. This categorization enables distinction of patients able to walk independently (MRS $\leq$3) from those who cannot.

We used APACHE III score to characterize severity of illness. Predictive accuracy of APACHE score is high for assessments made within 24 h of ICU admission for hospital mortality and ICU LOS [21]. The APACHE III score has also been shown to be effective in predicting patient outcomes in the NICU [22].

The patients who failed extubation were compared with those who were successfully extubated in terms of the length of ICU stay, the length of hospital stay, need for tracheostomy, ICU mortality, in-hospital mortality, and functional outcome.

### Statistical Analysis

Descriptive statistics [medians with interquartile range (IQR), mean ±standard deviation (SD), proportions, etc.,] were used to summarize sample. Wilcoxon rank sum test and Chi-square test were used to assess differences in baseline characteristics between the patients successfully extubated and those who failed. Changes in MRS between the successful extubation and extubation failure groups were analyzed using odds ratios estimated by multinomial logistic regression. Differences in-hospital mortality and ICU mortality were assessed using a logistic regression. A negative binomial regression model was used to assess differences in-hospital LOS and ICU LOS. To handle possible confounders, baseline characteristics determined to have statistically significant differences between successful extubation and failed extubation groups were used as adjustors. Age and APACHE 3 scores were modeled with smoothing splines to allow non-linear effects.

Analysis was performed using EpiInfo [23] (Centers for Disease Control and Prevention, Atlanta, GA) and SAS 9.3 (SAS Institute Inc., Cary, NC). All hypothesis tests were two-tailed with $P \leq 0.05$ being considered statistically significant.

## Results

Patient characteristics and reasons for NICU admission are included in Table 1. Median age was 57.0 (26.0) years and 60.6 % were male. The most common diagnoses were traumatic brain injury (15.4 %), subarachnoid hemorrhage (13.6 %), and intraparenchymal hemorrhage (10.6 %). Admission APACHE 3, GCS, and FOUR scores were 51.0 (43.0), 8.0 (6.0), and 9.0 (6.0), respectively.

Extubation failure occurred in 108 (11.4 %) patients, including 9 (8 %) with self extubation. Thirty-seven patients (3.8 %) required reintubation after 72 h and were not included in the extubation failure group. There was no difference between groups with and without extubation failure in terms of age, FOUR score, and GCS score at admission or APACHE 3 score 24 h after admission (Table 2). More patients in the extubation failure group were male (70.4 vs. 59.2 %, $P < 0.01$). The cause for extubation failure was identified as an airway-related problem in 58.7 % of the patients and non-airway-related problem in 30.3 % of the patients. Cause of extubation failure remained unclear in the rest.

Mean time to reintubation was 19.3 ± 20.1 h. Patients with extubation failure were reintubated: (1) from 0 to 12 h of extubation (54; 50 %), (2) 12–24 h of extubation (16; 14.8 %), (3) 24–48 h from extubation (29; 26.4 %), and (4) 48–72 h from extubation (9; 8.1 %). Regarding the evolution of the patients with extubation failure, 22 (20 %) underwent extubation again; of those, 10/22 (45.4 %) failed extubation a second time. Of the patients who failed extubation a second time, 3/22 (13.6 %) were extubated a third time, and one of these remained ventilator free permanently. Outcomes of 108 patients with extubation failure are shown in Fig. 2.

Extubation failure resulted in longer NICU and hospital length of stays [13.7 (11.3) vs. 9.1(8.2) days, $P < 0.01$] and [24.5 (20.0) vs. 16.8 (16.7) days, $P < 0.01$], respectively, (Table 2). This difference is consistent with the percentage decrease in the NICU and hospital LOS for extubation success. This decrease persisted when after adjusting for age, gender, APACHE 3 score, and change in goals of care (Table 3). Unadjusted hospital mortality was lower in patients with extubation failure. This observation is likely a result of confounding. In regression models adjusting for age, gender, APACHE III score, and change in goals of care, there was no difference in the ICU and hospital mortality between those who had extubation failure and those who did not (Table 4). Extubation failure also resulted in higher rates of tracheostomy procedures (OR 2.8, $P < 0.01$).

Extubation failure was associated with worse functional outcomes defined by MRS [5.0 (2.0) vs. 4.0 (3.0),

**Table 1** Patients' characteristics and reasons for Neurological ICU admission

| Characteristics | Cohort ($n = 949$) |
|---|---|
| Age [years; (median (IQR[d])] | 57.0 (26.0) |
| Sex (Male %) | 60.5 |
| Race (Caucasian %) | 81.9 |
| APACHE III[e] score [median (IQR)] | 51.0 (43.0) |
| GCS[f] score [median (IQR)] | 8.0 (6.0) |
| FOUR[g] score [median (IQR)] | 9.0 (6.0) |
| Primary diagnosis (%) | |
| Traumatic brain injury | 15.4 |
| Subarachnoid hemorrhage | 13.6 |
| Intracerebral hemorrhage | 10.6 |
| Anterior circulation stroke | 9.7 |
| CNS neoplasm | 9.6 |
| Seizures | 7.6 |
| Subdural hemorrhage | 3.7 |
| Cervical spondylosis | 2.9 |
| Cervical spine fracture | 2.7 |
| Myasthenia exacerbation | 2.1 |
| Inflammatory demyelinating polyneuropathy | 1.8 |
| Posterior circulation stroke | 1.5 |
| Meningitis | 1.4 |
| Encephalitis | 1.2 |
| Intracranial vascular malformation | 1.1 |
| Amyotrophic lateral sclerosis | 1.1 |
| Others | 14 |
| NICU[a] LOS[b] [days, median (IQR)] | 9.5 (8.8) |
| Hospital LOS [days, median (IQR)] | 17.5 (17.9) |
| NICU mortality (%) | 13.3 |
| Hospital mortality (%) | 22.8 |
| MRS[c] at hospital discharge [median (IQR)] | 4.0 (2.0) |

[a] Neurological

[b] Length of stay

[c] Modified Rankin Score

[d] Interquartile range

[e] Acute physiology and chronic health evaluation III

[f] Glasgow Coma Scale

[g] Full outline of unresponsiveness ICU

$P < 0.01$] at 6 months and a higher 6 month mortality among those who survived to hospital discharge (22.0 vs. 9.8 %, $P < 0.01$) (Table 2). The odds of poor functional outcome (MRS 4–6) at hospital discharge and at 6 months were significantly higher in the extubation failure group (OR 1.9, $P < 0.01$, and OR 3.2, $P < 0.01$, respectively).

In regression models that included age, gender, APACHE 3 scores and change in goals of care, extubation failure was associated with worsening of functional status as defined by an increase in MRS at 6 months (OR 2.2, $P = 0.02$) and a significant proportion of patients died within 6 months of hospital discharge (OR 2.7, $P = 0.03$; Table 5).

## Discussion

We examined the association of extubation failure with outcomes in a NICU patient population. We found that the patients who failed extubation had longer ICU and hospital

**Table 2** Comparison of study groups

| Characteristics | Extubation failure (*n* = 108) | Extubation success (*n* = 841) | *P* value |
|---|---|---|---|
| Age [years, median (IQR[d])] | 58.5 (23.0) | 57 (25.0) | 0.2 |
| Sex (Male %) | 70.4 | 59.2 | *0.02* |
| Race (Caucasian %) | 82.0 | 81.8 | 0.9 |
| APACHE III[e] score [median (IQR)] at admission | 56.0 (42.0) | 51.0 (42.0) | 0.5 |
| GCS[f] score [median (IQR)] at admission | 9.0 (5.0) | 8.0 (6.0) | 0.2 |
| FOUR[g] score [median (IQR)] at admission | 11.0 (5.0) | 9.0 (6.0) | 0.4 |
| Unadjusted NICU[a] LOS[b] [days, median (IQR)] | 13.7 (11.3) | 9.1 (8.2) | *<0.01* |
| Unadjusted hospital LOS [days, median (IQR)] | 24.5 (20.0) | 16.8 (16.7) | *<0.01* |
| Change in goals of care (%) | 13.9 | 23.9 | *0.02* |
| Unadjusted NICU mortality (%) | 7.4 | 14 | *0.05* |
| Unadjusted Hospital mortality (%) | 13.9 | 23.9 | *0.02* |
| MRS[c] at discharge [median (IQR)] | 4.0 (1.0) | 4.0 (2.0) | 0.4 |
| MRS at 6 months [median (IQR)] | 5.0 (2.0) | 4.0 (3.0) | *<0.01* |

Values given in italics are significant ($P > 0.05$)

[a] Neurologic ICU

[b] Length of stay

[c] Modified Raskin Score

[d] Interquartile range

[e] Acute physiology and chronic health evaluation III

[f] Glasgow Coma Scale

[g] Full outline of unresponsiveness

stays, greater need for tracheostomy, and had worse functional outcomes persisting to 6 months after hospital discharge.

In our study, the incidence of extubation failure in patients in NICU was found to be 11.4 %. The reported incidence of extubation failure varies widely, ranging from 2 to 25 % [24]. Because of the different definitions of extubation failure across studies, it can be difficult to compare the reported incidences of extubation failure. In addition, this variation can be partially explained by the heterogeneity of the studied populations [25, 26]. We also found a significant number of patients (3.8 %) who required reintubation beyond the 72 h, a cutoff traditionally used to define extubation failure. This is similar to findings of Karanjia et al. [26].

Extubation failure rates have been reported to be higher in patients with neurological involvement [4]. A recent study suggested that the "optimal" extubation failure rate is 5–10 % [27]. It is not easy to determine the ideal extubation failure rate; however, it has been suggested that rates close to 0 % indicate that patients may have remained on MV for an unnecessarily long time and that extremely high rates are suggestive of premature withdrawal of MV [28].

The common reasons for reintubation in the present study were respiratory failure, secretions, and altered mental status, findings that are consistent with those reported in previous studies [29, 30]. We found no association between the reason for reintubation and in-hospital mortality, a finding that corroborates those of Menon et al. [31].

ICU mortality rates have been reported to be higher in patients who failed extubation than in those who were successfully extubated [3, 32]. However, patients who fail extubation may be more likely to have their goals of care changed, leading to increased ICU mortality. Similarly, depending on local practices, patients with the most severe neurologic insult may have their goals of care changed before a trial of extubation is attempted and are subsequently extubated without any intention to reintubate. Although the unadjusted hospital mortality was lower in patients with extubation failure (Table 4), this was likely confounded by change in goals of care, as described previously. After adjusting for 'change in goals of care,' we did not find extubation failure to be associated with increased ICU or hospital mortality. Lack of a similar adjustment may have resulted in dissimilar results in previous studies. In addition, we found that the patients who failed extubation had longer ICU and hospital stays, a finding that corroborates previous findings [3, 7].

The number of patients requiring tracheostomy was substantially higher in the extubation failure group. This finding is similar to that reported by one group of authors [33].

Another important finding of our study was the association between extubation failure and functional outcome.

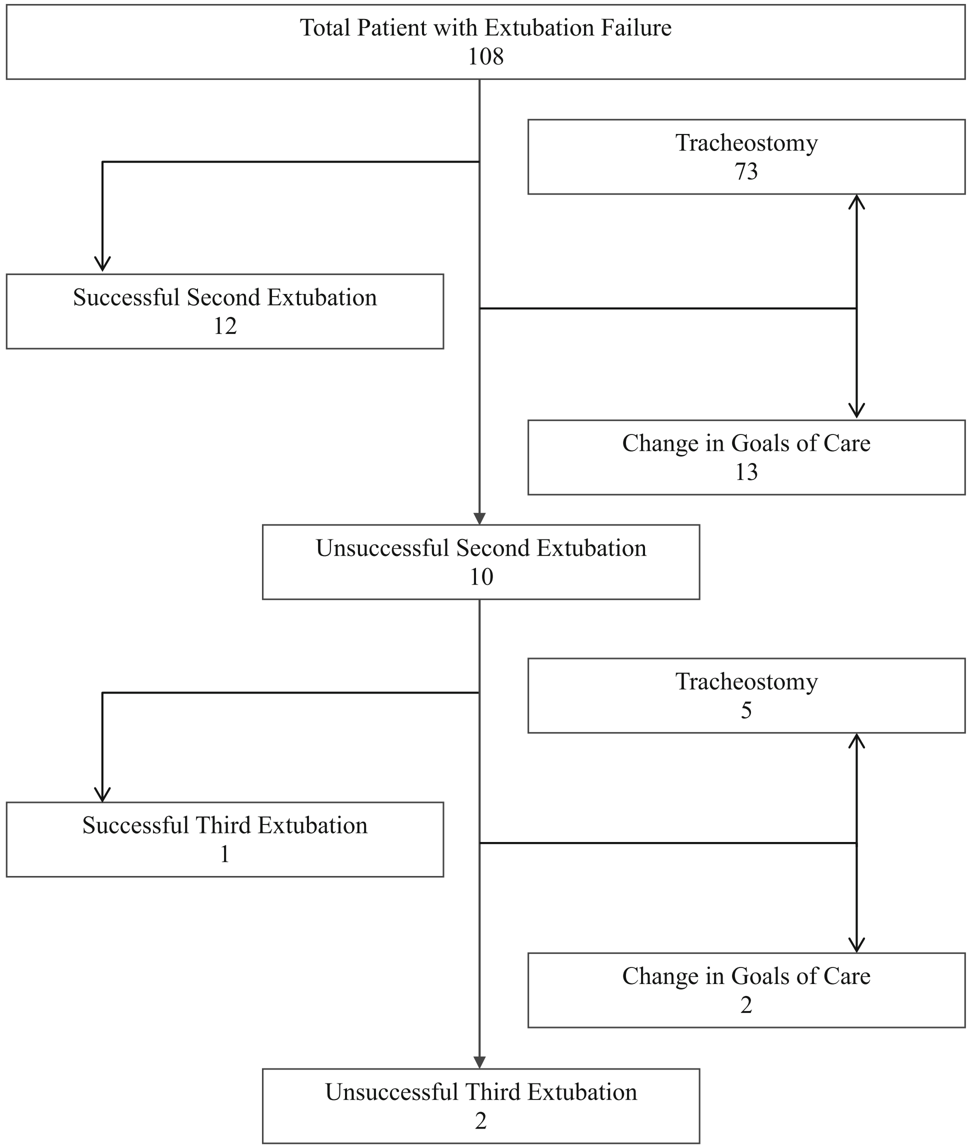


**Fig. 2** Outcomes of patients with extubation failure

**Table 3** Effect of extubation success on unadjusted and adjusted ICU and hospital length of stay

| Outcomes | Percentage decreased LOS | *P* value |
|---|---|---|
| ICU LOS[a] unadjusted | 32.9 (16.1–52.1) | <0.01 |
| ICU LOS adjusted[b] | 32.9 (15.8–50.5) | <0.01 |
| Hospital LOS unadjusted | 36.3 (18.2–57.2) | <0.01 |
| Hospital LOS adjusted | 30.1 (13.7–48.8) | <0.01 |

All data presented as percentage (95 % CI)

[a] Length of stay

[b] Adjusted for age, change in goals of care, APACHE III and gender

While the association between extubation failure, mortality and length of hospital stay has been studied, [7, 8, 34] data on the association between extubation failure and subsequent functional status are scarce. One previous study associated extubation failure in patients with traumatic brain injury with poor functional outcomes at hospital discharge [3]. Regardless, this is the first study of patients with ANI associating extubation failure with poor long-

**Table 4** Odds ratios for mortality in patients with extubation failure

| Outcomes | OR[a] (95 % CI) | P value |
|---|---|---|
| ICU mortality—unadjusted | 0.49 (0.23–1.03) | 0.06 |
| ICU mortality—adjusted[b] | 0.81 (0.31–2.14) | 0.67 |
| Hospital mortality—unadjusted | 0.51 (0.29–0.91) | 0.02 |
| Hospital mortality—adjusted | 0.80 (0.25–2.56) | 0.71 |

[a] Odds ratio

[b] Adjusted for change in age, goals of care, APACHE III and gender

**Table 5** Odds (OR) of change in MRS from discharge to 6 months in patients with extubation failure

| Outcomes | Un adjusted OR | Adjusted OR |
|---|---|---|
| Decrease in MRS[a] | 0.96 (0.39–2.37) | 1.03 (0.41–2.61) |
| | *P* value = 0.93 | *P* value = 0.94 |
| MRS unchanged | 1.00 (Ref) | 1.00 (Ref) |
| Increase in MRS (excluding patient who died by 6 months) | 2.43 (0.82–7.19) | 2.23 (0.76–7.38) |
| | *P* value = 0.11 | *P* value = 0.14 |
| Death by 6 months | 2.39 (1.13–4.87) | 2.48 (1.06–5.62) |
| | *P* value = 0.02 | *P* value = 0.04 |
| MRS increasing (including death by 6 months) | 2.36 (1.17–4.77) | 2.42 (1.11–5.28) |
| | *P* value = 0.02 | *P* value = 0.03 |

[a] Modified Rankin Score

term functional outcomes. We also found that extubation failure is associated with worsening functional status at 6 months when compared to functional status at hospital discharge. It is possible that under these circumstances, extubation failure may be a marker of the severity of underlying neurological illness.

Our study had several limitations. Even though this is an retrospective observational study, it is reasonable to assume that the results obtained are representative of our current clinical practice in the NICU. Another potential limitation is the fact that the study was conducted in a single center. Nevertheless, the incidence of extubation failure was found to be consistent with incidence reported in the literature. We excluded patients who required MV for $<48$ h. This lends the study to potential selection bias. However, patient intubated for short duration are at minimal risk for extubation failure [25], and previous studies investigating extubation failure have used different cutoffs (12–48 h) to exclude patients who are placed on MV for completely reversible causes [11, 35]. Additionally, our study did not control for the type of acute neurologic illness which almost certainly impacts extubation rates and prognosis. It has also been suggested that different adjustments may be more appropriate for each diagnostic category. However, the most common diagnosis, traumatic brain injury, made up only 15 % of the cohort. Attempts at adjustments for individual diagnoses [NIH stroke scale (NIHSS) for stroke, head injury score (HIS) for TBI etc.,] resulted in loss of statistical significance. Secondly, our data are spread over 10 years. Review of patient charts revealed that various scoring systems (NIHSS, HIS etc.,) were not consistently recorded over the years. Similarly, the breakdown of neurologic pathologies in our NICU may differ from that of others, limiting generalizability.

## Conclusions

In patients with acute neurologic illness, extubation failure appears to be associated with longer hospital stays and impaired functional outcomes. Extubation failure may be a useful marker of severity of disease in this patient population that should perhaps be considered when discussing expected prognosis and goals of care with patients and their families. Any such discussion would have to take into account the other clinical and social variables including the type of neurologic disease which is the primary determinant of prognosis and was not controlled for in this analysis.

**Conflict of interest** Muhammad Rishi, Rahul Kashyap, Gregory Wilson, Louis Schenck, and Sara Hocker declare that they have no conflicts of interests.

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