# Comparing Extubation Outcomes in Patients with Primary Brain Injury and Patients without Primary Brain Injury

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### Abstract

**Object:** Patients intubated for primarily neurological reasons represent a unique critically-ill population. Extubation failure rates in Primary Brain Injury (PBI) patients are 18%-38% compared to 13%-18% in the general critical care population. These populations have never been directly compared. We hypothesized that intubated PBI patients would have higher rates of extubation failure compared to non-PBI patients.

**Methods:** A retrospective cohort of intubated patients with and without PBI admitted between October 1, 2008 and September 30, 2010 who had a planned non-terminal trial of extubation in either the Medical Intensive Care Unit and Neurocritical Care Unit in a tertiary-care university hospital.

Results: Of the 1684 patient charts reviewed, 349 were included; 107 patients had PBI, and 242 did not have PBI. Combined extubation failure rates before 48 hours, 72 hours and 1 week were 13.7%, 17.5%, and 22.9%, respectively. Comparing PBI patients with non-PBI patients, extubation failure rates at the same time points were 19% vs. 12% (p=0.091), 24% vs. 14% (p=0.032) and 29% vs. 20% (p=0.097). PBI patients had a significant increased relative risk of failing before 72 hours (OR 1.90 (95% CI 1.07-3.35), p=0.027). PBI patients had fewer ventilator days prior to their extubation attempt than non-PBI patients 4 days (3 days-6 days) vs. 5 days (3 days-8 days), p=0.007). There was no difference in rates of extubation failure in PBI patients admitted to the NeuroICU (24.4%) vs. the MICU (24.1%). PBI patients were more likely to develop Ventilator-Associated Pneumonia (VAP) [OR 5.58 (1.41-22.00), p=0.014]. Failing extubation at 72 hours did not put patients at increased odds for VAP. PBI patients who failed at 72 hours did not have a significant increase in ventilator days, intensive care unit days or mortality; however, none of these patients were discharged to home.

Keywords: Endotracheal extubation • Mechanical ventilation • Brain injury

## Introduction

Almost one-third of critically-ill patients will require intubation for respiratory failure or airway protection. Although this intervention can be life-saving, it can be associated with severe complications, including infection, acid-base disturbances, and organ failure [1]. Premature extubation has been associated with increased mortality and morbidity, including an increased number of ventilator days, longer Intensive Care Unit (ICU) and hospital stays, and decreased likelihood of being discharged home [2]. However, delaying extubation is associated with an increased incidence of pneumonia and prolonged ICU and hospital stays [3]. Determining the appropriate time to extubate a patient is paramount in avoiding unintended adverse effects.

When to extubate a patient is not always clear. Extubation failure rates in the general critical care population are 12%-18% [1, 4], while extubation failure rates in patients with primary neurologic injury have been reported to be as high as 38% [5]. To our knowledge, extubation failure rates in Primary Brain Injury (PBI) patients and non-PBI patients have never been directly compared. We hypothesized that intubated PBI patients would have higher rates of extubation failure compared to non-PBI patients.

## **Materials and Methods**

A retrospective cohort of intubated patients admitted to the 18-bed medical intensive care unit or the 12-bed neurological intensive care unit at a tertiarycare university hospital from October 1, 2008 to September 30, 2010 were studied. The Institutional Review Board (IRB) approved the study prior to data collection. Patient characteristics and outcomes were identified by chart review. All patients with a planned non-terminal extubation attempt were included. PBI was defined as ischemic stroke. Intracerebral Haemorrhage (ICH), Subarachnoid Haemorrhage (SAH), Traumatic Brain Injury (TBI), Primary Central Nervous Systems (CNS) infection, or cerebral neoplasm. Patients were excluded if they met any of the following criteria: prior history of dementia, ischemic or haemorrhagic stroke, or TBI; elective intubation for surgery or procedure; extubation within 24 hours of intubation; terminal extubation; intubation secondary to sedation from medication effect or for toxic or metabolic encephalopathy; intubation secondary to neuromuscular weakness or traumatic spinal cord injury; death prior to extubation attempt; self-extubation; direct tracheostomy without prior extubation attempt or prior tracheostomy still in place; or member of a vulnerable population as defined by the IRB.

The decision to extubate was at the discretion of the primary team. Per respiratory protocol in both ICUs, patients were trialed on minimal pressure support ventilation or T-piece and 40% fraction of inspired oxygen before a planned extubation attempt. Extubation failure, defined as the need for reintubation, was recorded at three time points (48 hours, 72 hours, and one week). For patients with multiple extubations during the same admission, only the first attempt was analyzed. Patients who would have required reintubation but whose code status was advanced to comfort measures after a planned non-terminal extubation attempt were counted as extubation failures. Ventilator-Associated Pneumonia (VAP) was documented by the Department of Epidemiology and Infection Control using the Centres for Disease Control/National Healthcare Safety Network definition [6]. For each included patient, lengths of ICU and hospital stays were determined. The total number of intubations need for tracheostomy, discharge disposition, and in-hospital mortality also were recorded.

All data were analyzed using Stata SE 10 (College Station, TX). Categorical variables were analyzed using Fisher's exact test. Non-normally distributed continuous variables were analyzed using the Wilcoxon sum rank test. Significance was defined as p<0.05 [7].

# Results

A total of 1684 intubated patients were identified; 1335 patients were excluded, mostly due to the short duration of intubation, elective intubation for surgery or procedure, or terminal extubation. Of the 349 patients included, 107 patients were admitted with PBI (42 patients had TBI, 25 ICH, 18 SAH, 11 ischemic strokes, 10 CNS infection, and 1 CNS neoplasm) and 242 patients were admitted without PBI. The median age was similar between PBI and non-PBI patients [57 years (IQR 46-70) vs. 60 years (49-71), p=0.34]. There were more men with PBI than without PBI (64% vs. 52%, p=0.046).

Comparing PBI patients to non-PBI patients, PBI patients were significantly more likely to fail extubation before 72 hours (24.3% vs. 14.5%, p=0.032)

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with a trend toward increased odds for extubation failure before 48 hours and before one week (Table 1, Figure 1). Total ventilator days were similar between PBI and non-PBI patients, but PBI patients had their first planned extubation attempt sooner compared to those without PBI (Table 2). ICU days were similar between PBI and non-PBI patients, but PBI patients had longer hospital stays (Table 2). Patients who failed before 72 hours were no differences in a number of ventilator days until the first extubation attempt compared to those whose extubations were successful; however, they had significantly more total ventilator, ICU, and hospital days.

Seventy-eight PBI patients (72.9%) were admitted to the neuro ICU and 29 patients (27.1%) were admitted to the MICU. There was no difference in rates of extubation failure in PBI patients admitted to the neuro ICU (24.4%) vs. the MICU (24.1%). PBI patients were more likely to develop VAP OR 5.58 (1.41-22.00), p=0.014; adjusted for age and gender, OR 5.02 (1.25-20.18), p=0.0023). Failing extubation before 72 hours did not put patients at

increased odds for VAP OR 2.08 (0.52-8.27), p=0.30; adjusted for age and gender, OR 2.42 (0.59-9.93), p=0.22.

Patients who failed before 72 hours were more likely to receive a tracheostomy [OR 39.31 (14.16-109.10), p<0.0001]; adjusted for age and gender, OR 41.97 (14.86-118.50), p<0.0001), but PBI patients who failed before 72 hours did not have a higher incidence of tracheostomy than non-PBI patients who failed before 72 hours (42% vs. 40%, p=NS).

PBI patients and patients who failed before 72 hours were discharged home less frequently when compared to those who do not have PBI and those who successfully extubated, respectively (Table 2). Of note, none of the PBI patients who failed before 72 hours were discharged to home. Patients who failed extubation before 72 hours were more likely to die in the hospital [OR 3.59 (1.81-7.10), p<0.0001]; adjusted for age and gender, (OR 3.56) (1.70-7.45), p=0.001. There was no difference in mortality between those patients with PBI and those without PBI who failed before 72 hours (Table 2).

	All patients	PBI	Non-PBI patients	р	Unadjusted odds ratio (95% CI)	р	Adjusted odds ratio (95% CI)	р
	(n=349)	patients	(n=242)					
-		(n=107)			(95% CI)			
Failed before 48 hours	48 (13.8%)	20 (18.7%)	28 (11.6%)	0.09	1.76	0.08 -	1.79	0.07
					(0.94-3.28)		(0.95-3.37)	
Failed before 72 hours	61 (17.5%)	26 (24.3%)	35 (14.5%)	0.03	1.9	0.03 -	1.95	0.02
					(1.07-3.35)	0.03	(1.10-3.47)	
Failed before one week	80 (22.9%)	31 (29.0%)	49 (20.3%)	0.1	1.61	0.08	1.69	0.05
					(0.95-2.71)		(0.99-2.89)	

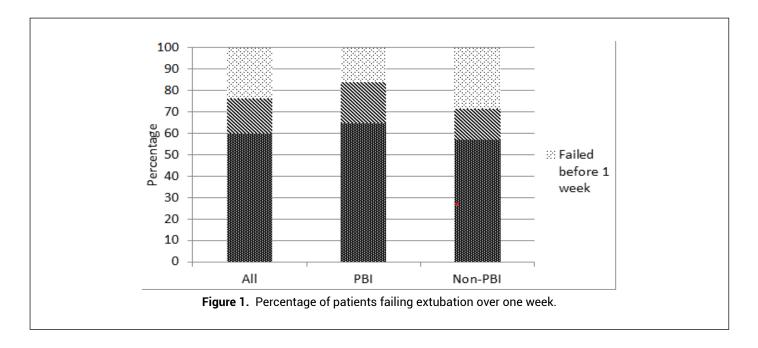


Table 2. Outcomes in primary brain injured patients and patients failing extubation.

	PBI patients (n=107)	Non-PBI patients (n=242)	р	Patient who failed extubation before 72 hours (n=61)	Patients who had successful extubations before 72 hours (n=288)	р	PBI patients who failed before 72 Hours (n=26)	Non-PBI patients who failed before 72 Hours (n=35)	р
Ventilator days to first extubation, median (IQR)	t 4 (3-6)	5 (3-8)	0.007	5 (3-8)	4 (3-7)	0.26	4 (3-8)	5 (4-9)	0.27
Total ventilator days	5 (3-10)	6(3-10)	0.12	15 (8-19)	4 (3-8)	<0.0001	13 (7-19)	16 (9-28)	0.14
ICU Days	12 (7-20)	11 (7-17)	0.13	22 (14-37)	10 (6-15)	<0.0001	22 (11-30)	22 (16-40)	0.23
Hospital length of stay	22 (11-30)	16 (11-25)	0.046	31 (17-45)	16 (11-25)	<0.0001	27(16-45)	34 (17-48)	0.58
Discharge to home, %(n)	8% (9)	43% (104)	<0.0001	13% (8)	36% (105)	<0.0001	0% (0)	23% (8)	0.016
In-hospital mortality	11% (12)	11% (27)	1	28% (17)	10% (28)	<0.0001	27% (7)	29% (10)	1

### Discussion

This study demonstrates that patients with PBI are more likely to fail extubation before 72 hours than patients who do not have PBI. To our knowledge, this is the first study that directly compares extubation outcomes in patients with PBI and those without PBI. Comparing extubation failure rates in the literature is difficult given the varying time intervals for defining extubation failure and the heterogeneity of neurological patients. Studies involving the medical and surgical ICU populations have used both 48 hours and 72 hours to define extubation failure. Similarly, extubation failure in neurologic patients has also been defined at 48 hours, 72 hours [8], and at any point during hospitalization [5]. Given a lack of consensus of when to define extubation failure, we studied extubation failure at three predetermined time points: 48 hours, 72 hours, and one week. Our data revealed a trend toward PBI patients failing extubation more frequently than non-PBI patients before 48 hours and one week and a statistically significant increase in extubation failure in PBI patients before 72 hours. A larger sample size might demonstrate PBI patients are at increased odds of extubation failure at all-time points. Our study found a similar rate of extubation failure (14.5%) in non-PBI patients as compared to the general critical care population (12%-18%) [1,4], but a higher rate in PBI patients (24.3%). PBI patients were cared for in both the Neurointensive Care Unit (NeuroICU) and Medical Intensive Care Unit (MICU). The same respiratory protocol is used in both ICUs. While the treating physicians were different and clinical decision-making to extubate might vary between the NeuroICU and MICU, no difference was found in the extubation rate of PBI patients.

Predicting extubation success in PBI patients has proven difficult. PBI patients often meet traditional pulmonary weaning parameters for extubation. However, these criteria have not been shown to be predictive of extubation success in patients with neurologic injury [7]. Additionally, evaluation of mental status as a predictor of extubation success in neurological patients has resulted in conflicting data regarding extubation outcomes. Some studies associate a Glasgow Coma Scale (GCS) score of  $\geq$  8 [5] and the ability to follow simple commands [8] with successful extubation, but other studies demonstrate that the GCS score [3] and the Four Score [7] are not predictive of successful extubation. The lack of specific respiratory or mental status criteria for extubation readiness in neurologic patients might account for the increased rate of extubation failure in PBI patients.

In addition, of those who failed, a higher percentage of PBI patients when compared to non-PBI patients failed before 72 hours. A patient's mental status and inability to protect the airway might account for earlier extubation failure. PBI patients meet traditional pulmonary weaning parameters that might contribute to the shorter number of days to first extubation attempt. The study also highlights that extubation failure before 72 hours is associated with serious adverse outcomes [9]. Patients who failed extubation had more ventilator days, longer ICU and total lengths of stay, increased rates of tracheostomy, increased risk of in-hospital mortality, and decreased likelihood of discharge to home. Specifically, none of the PBI patients who failed before 72 hours were discharged to home. Interestingly, once defined as an extubation failure, patients were at increased odds for tracheostomy and mortality regardless of whether they had PBI or not.

Neurologic injury can occur by a variety of mechanisms, resulting in a heterogeneous patient population. We sought to minimize the diversity of patients by focusing on patients with structural brain injury and excluding those with neuromuscular or spinal cord diseases, encephalopathies, and previous brain injuries [10]. An opportunity for further study would be to evaluate each mechanism and location of brain injury separately. Attempting to create a more homogenous population did limit the sample size for this study [11]. Other limiting factors in our study include that this is a retrospective study and that the data was collected from a single centre.

## Conclusions

Patients with PBI are more likely to fail extubation before 72 hours. Identifying predictors of extubation failure in future studies would be helpful in identifying those PBI patients most at risk for extubation failure and in preventing the adverse outcomes associated with extubation failure.

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## **Disclosures**

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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