Implications of Extubation Delay in Brain-Injured Patients Meeting Standard Weaning Criteria

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We hypothesized that variation in extubating brain injured patients would affect the incidence of nosocomial pneumonia, length of stay, and hospital charges. In a prospective cohort of consecutive, intubated brain-injured patients, we evaluated daily: intubation status, spontaneous ventilatory parameters, gas exchange, neurologic status, and specific outcomes listed above. Of 136 patients, 99 (73%) were extubated within 48 h of meeting defined readiness criteria. The other 37 patients (27%) remained intubated for a median 3 d (range, 2 to 19). Patients with delayed extubation developed more pneumonias (38 versus 21%, $p < 0.05$) and had longer intensive care unit (median, 8.6 versus 3.8 d; $p < 0.001$) and hospital (median, 19.9 versus 13.2 d; $p = 0.009$) stays. Practice variation existed after stratifying for differences in Glasgow Coma Scale scores (10 versus 7, $p < 0.001$) at time of meeting readiness criteria, particularly for comatose patients. There was a similar reintubation rate. Median hospital charges were $29,057.00 higher for extubation delay patients ($p < 0.001$). This study does not support delaying extubating patients when impaired neurologic status is the only concern prolonging intubation. A randomized trial of extubation at the time brain-injured patients fulfill standard weaning criteria is justifiable.

Despite numerous studies during the last quarter century (1), weaning (2, 3), or liberation (4), of patients from mechanical ventilation is still an area of clinical practice that generates controversy. In part this is because discontinuation of ventilatory support and removal of the endotracheal tube (extubation) are often lumped together under the umbrella term “weaning.” However, the need for ventilatory support is distinct from the need for an artificial airway as recent studies of noninvasive positive-pressure ventilation demonstrate (5–7). Clinical syndromes such as acute epiglottitis and other upper airway diseases indicate that the need for an artificial airway does not necessarily mean that ventilatory support is required (8).

Commonly used predictors of successful weaning such as the traditional “weaning parameters” of vital capacity, minute ventilation ($\dot{V}_E$), and maximum inspiratory pressure (MIP) (9), and the “rapid shallow breathing index” (RSBI; spontaneous respiratory rate divided by spontaneous tidal volume) (10), were designed to measure a patient’s ability to breathe without assistance. These measures do not examine a patient’s ability to clear respiratory tract secretions or to protect their lower airways from aspiration and therefore do not provide clinicians with information about the patient’s need for an artificial airway.

Patients with acute brain injury and impaired consciousness but no other indication for mechanical ventilation constitute a group in whom the needs for ventilatory support and for an artificial airway might be separate. Clinicians frequently face the dilemma of whether to extubate a brain-injured patient with satisfactory weaning parameters when there are concerns about the patient’s level of consciousness and ability to maintain an airway. These patients might benefit from continued intubation through the prevention of aspiration and the ability to suction secretions. On the other hand, a retrospective study of patients admitted to our institution found a high incidence of pneumonia in patients with traumatic brain injury (TBI) who had prolonged intubation (11), and endotracheal tubes are a known conduit for lower airway contamination that predisposes to the development of pneumonia.

Although there are no studies establishing predictive indices for successful extubation in patients with impaired mental status, clinical experience tells us that many patients with profoundly abnormal mental status appear to do well without an artificial airway. In the absence of clear guidelines, clinicians will show substantial variability in their practice. We hypothesized that clinicians would vary considerably in the timing the extubation of brain-injured patients once these patients were capable of spontaneous breathing. Further, we hypothesized that many patients could be extubated promptly and safely despite such ostensibly poor predictive factors as coma, absence of a gag reflex, and the presence of respiratory tract secretions, and that patients in whom extubation was delayed would have worse outcomes in terms of pneumonia, length of stay, or costs.

METHODS

Study Population

We performed a prospective observational cohort study of consecutive patients with acute brain injury who were admitted intubated to our intensive care units (ICUs) during a 7-mo period. Harborview Medical Center (HMC) is the Seattle/King County public hospital and the level-one trauma center for a five-state referral region. All acutely ill intubated patients are managed in one of the ICUs. Using daily screening of ICU admissions, we prospectively identified all patients with TBI, aneurysmal subarachnoid hemorrhage (SAH), stroke, global cerebral ischemia (for example, after cardiac arrest), status epilepticus, and encephalitis who were intubated and mechanically ventilated.

Patients were excluded if they were admitted to the ICU intubated because of unexplained metabolic or toxic coma, after elective unruptured cerebral aneurysm clipping, or if they met all the criteria for extubation readiness on the day of admission. To create a homogeneous population of patients with isolated cerebral injury, patients with any of the conditions listed in Table 1 either on admission or at any time prior to the extubation readiness date were excluded from the study. Patients extubated without reasonable hope for survival in anticipation of their deaths were excluded from analysis. Patients did not meet extubation readiness criteria until spinal precautions (i.e., hard cervical collar, log-rolling) were safely discontinued and spinal cord injury ruled out. The University of Washington Human Subjects Review Committee approved the study.

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TABLE 1

PATIENTS MEETING INCLUSION AND EXCLUSION CRITERIA

Inclusion Criteria (*n* = *136*)	Patients (*n*)	Exclusion Criteria (*n* = *106*)*	Patients (*n*)
Traumatic brain injury	78	Chest trauma	30
Aneurysmal hemorrhage	26	Adbominal injury or laparotomy	17
Stroke	24	Traction or external fixators	16
Global cerebral ischemia	4	Parameters not met before extubation or death	15
Status epilepticus	3	Children < 6 yr or cuffless endotracheal tube	15
Encephalitis	1	Impending brain death	12
		Parameters met, but died or tracheotomy before extubation	10
		Pelvic or long bone fracture	6
		Preexisting lung disease	4
		Spinal cord injury	2
		Withdrawal of support	2
		Acute lung injury	2
		Tracheostomy at admission	1
		Surgery requiring general anesthesia planned within 72 h	1
		Multiple organ dysfunction syndrome	1

* 106 patients met a total of 134 exclsuion criteria; some patients had more than one reason for exclusion.

Definitions and Data Collection

One of the investigators screened all patients admitted to one of the ICUs for potential inclusion in the study. All patients who met the study's inclusion criteria were seen daily by one of the investigators and evaluated for the criteria in Table 2. We identified three sentinel dates during the hospitalization: (*1*) admission day, (*2*) the day the patient met all of the extubation readiness criteria in Table 2, and (*3*) the day the patient was extubated. We will refer to these as admission day, extubation readiness day, and extubation day, respectively. Successful extubation was specifically defined as removal of the endotracheal tube without subsequent reintubation or tracheostomy for pulmonary or airway reasons.

The following spontaneous ventilatory parameters (SVPs) were measured every morning on all patients: respiratory rate (f), tidal volume (V_T), RSBI, MIP, and $\dot{V}_E$. Our respiratory therapists employed a standardized method for measuring SVPs. Frequency was observed as the raw number of breaths after disconnection of the ventilator. Tidal volume was measured by assessing the average or most common volume seen using an in-line meter attached to the endotracheal tube. The RSBI was calculated as the observed frequency divided by the recorded Vt (10). We measured MIP by occluding the airway with a metered one-way valve and measuring the observed inspiratory force, usually after several efforts.

Patients did not have SVPs measured on a given morning if one or more of the following were present: inspired oxygen fraction ($F_{I_{O_2}}$) $>$ 0.7, positive end-expiratory pressure (PEEP) $>$ 10 cm H_2O, $\dot{V}_E > 12$ L/min while receiving ventilation, sustained intracranial pressure (ICP) $>$ 20 mm Hg, or use of neuromuscular blocking agents. Patients were required to satisfy all the factors in Table 2 to meet the extubation readiness criteria.

In addition, staff respiratory therapists who were unaware of the purpose of the assessment evaluated the need for airway care each day using the six-part semiquantitative scheme shown in Table 3. Results of daily SVPs were continuously available to the physicians managing the patients; results of the airway care assessment, which was not part of routine care, were not. Managing physicians were unaware of the nature and purpose of the study. Managing physicians were in control of all aspects of the care of these patients. In general, these patients were ventilated with intermittent mandatory ventilation (IMV) with or without additional pressure support.

Neurologic assessment included daily determination of the Glasgow Coma Scale (GCS) score (12), either by one of the investigators (WMC) or by a nurse who had been specially trained for this purpose. We arbitrarily designated the verbal component of the GCS as 1 for intubated patients. Intracranial pressure monitoring was performed at the discretion of the treating physician, but it is the practice in our institution to use ICP monitoring in all comatose patients with acute brain trauma or hemorrhage.

Extubation delay was defined as the number of days that elapsed between extubation readiness day and extubation day minus 48 h. We subtracted this 48-h "grace period" to allow for communication among the team members managing the patient. After they were extubated we followed the patients as long as they remained in the hospital for the need for reintubation or tracheotomy, development of pneumonia, or death. We defined pneumonia as a temperature $> 38.5°$ C, blood leukocyte count $>$ 12,000/ml, purulent tracheobronchial secretions, new or progressive localized opacity on chest radiograph, and, when obtainable, positive sputum and/or blood culture for a likely pathogen (13, 14).

Data on hospital charges came from Hospital Decision and Research Support. The numbers include total gross hospital charges per patient stay, including both billed and unbilled charges; however, this number excludes Association of University Physicians (University of Washington) billed professional fees, but does include billed professional fees for HMC hospital-paid physicians.

Statistical Analyses

University of Washington computer resources were used to analyze the data. The p values for categorical variables were calculated by the chi-square test and Fisher's exact test (two-sided). Continuous vari-

TABLE 2

CRITERIA USED TO DETERMINE READINESS FOR DISCONTINUATION OF VENTILATORY SUPPORT*

Category	Criteria
Neurologic status	Physical examination not deteriorating ICP $<$ 20 mm Hg (when ICP measured) CPP $\geqslant$ 60 mm Hg (when ICP measured)
Cardiovascular status	Systolic BP $>$ 90 and $<$ 160 mm Hg HR $>$ 60 and $<$ 125 beats/min No acute dysrhythmia
Arterial oxygenation	$Pa_{O_2}/F_{I_{O_2}} \geqslant 200$ mm Hg $Pa_{O_2} \geqslant 80$ mm Hg on $F_{I_{O_2}} \leqslant 0.50$ (on $\leqslant$ 5 cm H_2O PEEP)
Spontaneous ventilatory mechanics	MIP $>$ 20 cm H_2O RSBI (f/V_T) $<$ 105 Spontaneous $\dot{V}_E \leqslant 12$ L/min Spontaneous $\dot{V}_E \geqslant 80\%$ of ventilator spontaneous $\dot{V}_E$
Absence of specific indication for mechanical ventilation	Surgery requiring general anesthesia not planned within 72 h No deliberate hyperventilation Cervical-spine status cleared

Definition of abbreviations: CPP = cerebral perfusion pressure (mean arterial pressure minus ICP); ICP = intracranial pressure; MIP = maximum inspiratory pressure; RSBI = rapid shallow breathing index. For definitions of other terms, *see text*.

* Patients had to meet all criteria.

TABLE 3

SEMIQUANTITATIVE ASSESSMENT OF NEED FOR AIRWAY CARE

Spontaneous Cough		Gag		Sputum Quantity	
0	Vigorous	0	Vigorous	0	None
1	Moderate	1	Moderate	1	1 pass
2	Weak	2	Weak	2	2 passes
3	None	3	None	3	$\geq$ 3 passes
Sputum Viscosity		**Suctioning Frequency (*per last 8 h*)**		**Sputum Character**	
0	Watery	0	$>$ 3 h	0	Clear
1	Frothy	1	q2–3 h	1	Tan
2	Thick	2	q1–2 h	2	Yellow
3	Tenacious	3	$<$ q1 h	3	Green

ables were compared using Wilcoxon's nonparametric rank sum; however, to convey the magnitude of the difference between groups both medians and means are presented. A logistic regression model, controlling for possible confounding variables, was used to assess the association, if any, between extubation delay and mortality. The criterion for statistical significance was a $p < 0.05$.

RESULTS

Patient Characteristics

There were 242 consecutive intubated ICU patients with the inclusion diagnoses who were screened for study entry. Ninety-six patients were initially excluded using the criteria in Table 1. The 146 remaining patients were followed daily for data collection. All 146 patients eventually met extubation readiness criteria. Ten of the 146 patients died or received a tracheotomy before extubation and were excluded from further analysis. Characteristics of the remaining 136 patients are shown in Table 4.

Extubation Delay, Neurologic Status, and Airway Function

Of the 136 patients, 99 (73%) were extubated without delay (within 48 h of meeting the readiness criteria in Table 2). In the 37 patients (27%) with extubation delay, extubation occurred a median of 3 d (range, 2 to 19) after the extubation readiness date. Nine of these patients (25% of the extubation delay population) were extubated 6 d or more after the extubation readiness date. As a group the 37 patients with extubation delay experienced a total of 165 d of mechanical ventilation between extubation readiness date and extubation, including the 2-d grace period.

Patients with extubation delay were intubated for a longer time prior to meeting readiness criteria, had lower GCS scores, and required more airway care, as shown in Tables 4 and 5, than patients who were extubated without delay. Despite these differences, there was considerable variability in extubation practices. Although patients who were intubated longer prior to readiness date had delayed extubation (*see* Table 5), seven of 12 patients (58%) who required intubation for at least 5 d prior to meeting extubation readiness criteria were extubated without delay, and 23 of 103 patients (22%) who were intubated for less than 3 d prior to meeting extubation readiness criteria had delayed extubation. Patients with TBI and stroke were more likely to be extubated without delay, and the number of patients with vasospasm after SAH was equally split between the delayed and timely extubation groups.

Neurologic function, as measured by GCS, was associated with extubation delay: 29 of 60 patients (48.3%) who were comatose (GCS $\leq$ 8) on extubation readiness day had delayed extubation, and eight of 76 patients (10.5%) who were not comatose when they met readiness criteria had delayed extubation ($p < 0.001$). Despite this association, there was considerable overlap between the groups. Thirty-one of the 60 patients (51.7%) with a GCS $\leq$ 8 on extubation readiness day were extubated without delay; 4 of 10 patients (40.0%) with a GCS $\leq$ 4 on extubation readiness day were extubated without delay, and eight of 76 patients (10.5%) with a GCS $\geq$ 9 on extubation readiness day had delayed extubation. To explore the possibility that clinicians delayed extubation pending an improvement in neurologic status, we looked at the changes in GCS scores between extubation readiness day and extubation day. Of the 37 patients with extubation delay, 21 had improved neurologic status, but 16 (43%) had no change or declining neurologic status on the day of extubation (*see* Table 6).

Complete data on all six parts of the Airway Care Score (ACS) (Table 3) for both extubation readiness day and extubation day were available for 72 of 99 nondelay patients and for 35 of 37 extubation delay patients. Analysis of the ACS is shown in Tables 5 and 6 and was limited to patients for whom there were complete data. Higher ACS, indicating worse airway function, was associated with extubation delay; however, many patients were extubated without delay despite poor

TABLE 4

ADMISSION DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

Characteristic	Total (*n = 136*)	No Delay (*n = 99*)	Delay* (*n = 37*)	p Value
Diagnosis				0.04
TBI	78 (57%)	65 (83%)	13 (17%)	0.001
SAH	26 (19%)	12 (46%)	14 (54%)	0.29
Stroke	24 (18%)	17 (71%)	7 (29%)	0.02
Other[†]	8 (6%)	5 (62%)	3 (38%)	0.50
Age, yr (range)	46 (7–89)	42 (7–89)	53 (15–81)	0.11
Male:Female	86:50 (63:37%)	69:30 (70:30%)	17:20 (46:54%)	0.01
Glasgow Coma Scale, median (range)	7 (3–11)	8 (3–11)	7 (3–11)	0.021
Coma (GCS $\leq$ 8)	86 (63%)	59 (60%)	27 (73%)	0.02
AIS-head, median (range)[‡]	4.0 (2–5)	4.0 (2–5)	4.0 (3–5)	0.3
Injury Severity Score, median (range)[‡]	20.0 (4–41)	17.0 (4–41)	22.5 (9–29)	0.4
Hunt and Hess grade, median (range)[§]	3.0 (1–5)	3.0 (1–5)	3.5 (1–5)	0.4

Definition of abbreviations: AIS = Abbreviated Injury Scale score; GCS = Glasgow Coma Scale score; SAH = aneurysmal subarachnoid hemorrhage; TBI = traumatic brain injury.

* "Delay" means extubation occurred $>$ 48 h after meeting readiness criteria.

[†] "Other diagnoses" are global ischemia, status epilepticus, and encephalitis.

[‡] AIS and ISS apply only to patients with traumatic brain injury.

[§] Hunt and Hess clinical grade applies only to patients with SAH.

TABLE 5

EXUTBATION DELAY IN THE 136 PATIENTS*

	No Delay	Delay	p Value
Factor, n (%)	99 (73%)	37 (27%)	
Days of delay	NA	3 (2–17)	NA
Intubation duration at readiness day, d	2 (1–8)	2 (1–6)	0.03
Spontaneous cough			
Readiness date	1 (0–3)	1 (0–3)	0.34
Extubation date	1 (0–3)	1 (0–3)	0.29
Gag			
Readiness date	1.0 (0–3)	1.5 (0–2)	0.04
Extubation date	1.0 (0–3)	2.0 (0–3)	0.002
Sum of airway care assessments†			
Readiness date	8.0 (1–12)	9.0 (5–11)	0.04
Extubation date	7.5 (1–12)	9.0 (2–16)	0.01
Glasgow Coma Scale (GCS)			
Readiness date	10 (4–11)	7 (3–11)	< 0.001
Extubation date	10 (4–11)	8 (3–11)	0.006
Coma (GCS ⩽ 8)			
Readiness date	31/99 (31%)	29/37 (78%)	< 0.001
Extubation date	28/99 (28%)	21/37 (57%)	0.002

Definition of abbreviations: Delay = extubation occurred < 48 h after meeting readiness criteria; NA = not applicable.

* Data are presented as medians with ranges shown in parentheses, except when specified.

† Total of six (maximum, 18).

markers of airway function and clearance. Thirty-eight of 61 patients (62%) with an ACS ⩾ the median ACS of 8 on extubation readiness day were extubated without delay; 11 of 20 patients (55%) with an ACS ⩾ 10 on extubation readiness day were extubated without delay, and 13 of 47 patients (28%) with an ACS < 8 on extubation readiness day had delayed extubation. To evaluate the possibility that physicians were using a combination of airway function and neurologic status to guide decision-making, rather than either one alone, we looked at the group of patients with poor airway function (ACS ⩾ 10) and poor neurologic status (GCS ⩽ 8). Of the 12 patients in this group on extubation readiness day, four were extubated without delay.

In a small part of this cohort, variability in extubation practice was also seen in children. There were eight patients 16 yr of age and younger, five of whom were younger than 16 and one of whom was younger than 7 yr of age. Of the eight children, four were admitted comatose (GCS ⩽ 8) and remained comatose at the time of meeting readiness criteria. Two of these patients were still comatose when extubated, and none of the eight was reintubated after extubation (all were therefore successfully extubated). The youngest patient survived and was never reintubated after being extubated without delay.

Successful Extubation;

Twenty-four patients required reintubation: seven were reintubated for unplanned surgery and four for medical complications not related to airway or pulmonary dysfunction (e.g., development of intracranial hypertension, convulsions, gastrointestinal hemorrhage). The remaining 13 patients were reintubated for acute airway or pulmonary dysfunction. Overall, reintubation occurred in 17 of 99 patients (17.2%) without extubation delay and seven of 37 (18.9%) with extubation delay (p = 0.8). Reintubation for airway or pulmonary dysfunction also was not significantly related to extubation delay (p = 0.2) or to coma at the time of extubation. Many patients were successfully extubated without requiring reintubation for airway or pulmonary reasons despite profound neurologic depression and coma on the day of extubation. Thirty-nine of 49 patients (80%) with a GCS ⩽ 8 and 10 of 11 patients (91%) with GCS scores ⩽ 4 were successfully extubated. Similarly, many patients were successfully extubated despite poor markers of airway function and clearance. The ACS was not associated with successful extubation at either extubation readiness day (p = 0.5) or extubation day (p = 0.3). Thirty-two of 36 patients (89%) with absent or weak gag were successfully extubated. Eighteen of 22 (82%) with weak or absent cough were successfully extubated. Two components of the ACS on extubation readiness day were associated with successful extubation: spontaneous cough (p = 0.01) and suctioning frequency (p = 0.02).

TABLE 6

DISTRIBUTION OF VARIATION IN PATIENTS WITH EXTUBATION DELAY FOR SELECTED PREDICTOR VARIABLES FROM THE TIME OF MEETING READINESS CRITERIA UNTIL EXTUBATION*

	Glasgow Coma Scale (*n = 136*)	Spontaneous Cough (*n = 107*)	Gag (*n = 107*)	Sum of Airway Care Parameters (*n = 107*)
Improved, n	21	6	9	14
No change or worsened, n	16	29	26	21

* *See text* for descriptions of variables. Values are numbers of patients.

Extubation Delay and Outcome

At some point during hospitalization, 35 of the 136 patients (25.7%) developed pneumonia, as shown in Table 7 and Figure 1. Extubation delay was associated with a statistically significant increase in the risk of pneumonia (relative risk [RR], 1.8; 95% confidence interval [CI], 1.0 to 3.1). This association persisted, although losing statistical significance, after controlling for coma on admission (adjusted RR, 1.72; 95% CI, 0.97 to 3.0) or coma on extubation readiness day (adjusted RR, 1.9; 95% CI, 0.9 to 3.6).

Pneumonia did not appear to be a cause for delaying extubation. Eleven of the 16 patients developing pneumonia before meeting readiness criteria (69%) were extubated without delay. There were patients who were extubated in the presence of pneumonia, including four patients who first met diagnostic criteria for pneumonia on the day of extubation.

One reason physicians may keep patients intubated despite meeting extubation readiness criteria is to maintain an artificial airway to prevent aspiration and pneumonia. To evaluate

TABLE 7

EXBUTATION DELAY AND OUTCOME

	No Delay	Extubation Delay	p Value
Factor, n (%)	99 (73%)	37 (27%)	
Pneumonia, n (%)	21 (21.2%)	14 (37.8%)	0.048
Intensive care unit length of stay, d	3 (1–15)	8 (3–22)	< 0.001
Hospital length of stay, d	11 (1–39)	17 (3–61)	0.009
Cost, $ (range)	41,824 (6,576–165,994)	70,881 (27,051–193,109)	< 0.001
Mortality, n (%)	12 (12.1%)	10 (27.0%)	0.04
Tracheotomy, n (%)	4 (4.0%)	0 (0.0%)	0.6

* Data are presented as medians with ranges shown in parentheses, except when specified.

whether extubation delay prevented subsequent pneumonia, we separated pneumonias into three groups: those that occurred prior to extubation readiness day (which presumably would be "unpreventable" even with timely extubation), those that occurred after extubation readiness date but prior to extubation (and therefore theoretically could be prevented by a change in airway management), and those that occurred after extubation. Thirty-five patients developed pneumonia in the cohort: 16 before extubation readiness day and 19 after extubation readiness day. Of the 19 patients who developed pneumonia after meeting the extubation readiness criteria, nine cases occurred during extubation delay and 10 cases after extubation (Figure 1). Extubation delay was associated with an increase in the risk of developing pneumonia after the extubation readiness date (RR, 2.4; 95% CI, 1.1 to 5.5); however, patients comatose at the time of meeting readiness criteria who also had delayed extubation had a 3.7-fold increased incidence of pneumonia as compared with comatose patients extubated within 48 h.

Patients with extubation delay had statistically significantly longer ICU and hospital lengths of stay (LOS) than did those without extubation delay, as shown in Table 7. Mean ICU LOS was 4.8 d longer and mean hospital LOS was 6.7 d longer in the extubation delay group. Patients with extubation delay had statistically significantly higher hospital charges than did those without extubation delay, as shown in Table 7. Mean hospital charges were $34,859.00 more in patients with extubation delay. Even after controlling for coma on admission, diagnosis, pneumonia, and age using a regression analysis of log-transformed cost, extubation delay was statistically significantly associated with higher charges ($p < 0.001$).

There were 22 in-hospital deaths among the 136 study patients (16.2%). Extubation delay was statistically significantly associated with mortality (RR for death, 2.2; 95% CI, 1.0 to 4.7). Patients who died in the hospital were more likely to have had extubation delay ($p = 0.04$) and lower admission GCS scores ($p = 0.002$). In a logistic regression model, controlling for coma on admission, diagnosis, pneumonia, and age, the association between death and extubation delay remained but was no longer statistically significant (multivariate odds ratio, 2.6; 95% CI, 0.76 to 8.9).

Six of the 146 patients who met extubation readiness criteria received a tracheotomy as their study end point. Two of these were among the 10 patients excluded from the final study cohort because they received tracheotomy or died before a trial of extubation. The other four (3% of the study cohort) received a tracheotomy, all after successful extubation. Patients who received tracheotomy after reintubation were not captured in our study since reintubation was a study end point.

DISCUSSION

This prospective observation of current extubation practices documented variation in extubation timing and its associated morbidity and mortality for acutely brain-injured patients who met standard weaning criteria. Our results show that timely extubation (within 48 h of meeting standard weaning criteria) in selected patients is safe. Patients who met criteria for cardiovascular stability, lack of neurologic deterioration, no planned interventions requiring mechanical ventilation, adequate gas exchange, and acceptable spontaneous ventilatory parameters, were extubated without a significantly increased risk of reintubation, pneumonia, or death. Even after stratifying patients for differences in illness severity (GCS, ACS, a combination of ACS and GCS, changes in ACS or GCS, and duration of prior intubation), we observed clinically significant variability in the timing of extubation within a single institution and relatively homogeneous patient population.

On average, patients with worse neurologic condition had more delay; however, patients in good neurologic condition were kept intubated after extubation readiness day, whereas some patients in coma were successfully extubated. Patients with extubation delay were not necessarily improving neurologically in the time between meeting weaning readiness and extubation. Differences in airway care did not fully explain the reasons for extubation delay. Patients whose extubation was delayed did have worse ACS; however, more than one third of patients were successfully extubated with ACS below the median. Patients were successfully extubated despite absent cough, gag, or increased suctioning needs. These data confirm our hypothesis that the uncertainty in extubating brain-injured patients meeting standard weaning criteria lies with patients who are not awake at the time of meeting those criteria. Nearly half of the patients who were comatose on extubation readiness day had extubation delay, and 84% of the patients with extubation delay were comatose on either extubation readiness day or extubation day.

Delayed extubation was associated with increased costs. The 37 patients whose extubation was delayed experienced 165 extra days of mechanical ventilation during the 7-mo study period. This is important in a hospital where all acutely ill, mechanically ventilated patients remain in the ICU, and where they might be able to go to a step-down unit were it not for the

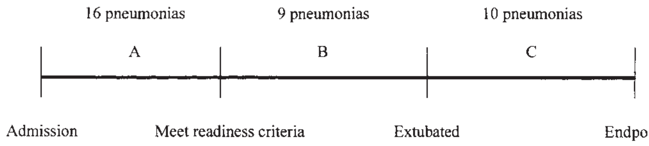

Figure 1. Study timeline and the relation of developing pneumonia. Extubation delay indicates B > 48 h. "Unpreventable," pneumonias occurred before meeting readiness criteria (A). All pneumonias during time B occurred in extubation delay patients. There was borderline association between extubation delay and developing pneumonia after meeting readiness criteria ($p = 0.05$).

ventilator. Extubation delay was associated with increased ICU and hospital LOS and hospital charges.

Extubation delay was associated with morbidity and mortality. The endotracheal tube is a known conduit for lower airway contamination, and pneumonia develops frequently and early in patients intubated after brain injury (11). Intubation duration and extubation delay appear to be risks for developing pneumonia. Patients with lower GCS scores were more likely to have delayed extubation and also to develop pneumonia. All extubation delay patients who developed pneumonia did so while awaiting extubation after meeting readiness criteria (Figure 1). The pneumonia rate was more than doubled (24 versus 10%) in patients whose extubation was delayed; conversely, those extubated within 48 h of meeting readiness criteria had less than half the pneumonia rate. Although our data are consistent with the conclusion that extubation delay led to the development of pneumonia in these patients, this observational study cannot establish the validity of such a hypothesis. We can only state that extubation delay was associated with an increased incidence of pneumonia and that patients did not appear to have pneumonia as a cause for their extubation delay.

Traditional predictors of successful weaning from mechanical ventilation and subsequent extubation may not apply to the neurologically injured patient as the ability to protect the airway and to clear secretions may be impaired independently of the ability to ventilate (15). Reintubation rates in various studies have ranged from 6 to 25% (9, 15–17). Practically all prior studies have looked at patients with normal or only mildly depressed levels of consciousness and have not included children younger than 7 yr of age (of which there was one in the present cohort.) This difference in cohort age is unlikely to explain the 18% reintubation rate in our study versus slightly higher rates in studies not including children (15).

Several studies have shown benefit from early extubation, particularly in the immediate postoperative period. Extubation upon meeting standard gas exchange and spontaneous ventilatory criteria, versus “prophylactic” overnight mechanical ventilation, can reduce sedative use and perhaps postoperative morbidity (18, 19). In a prospective study of 142 patients after cardiac surgery, 87% met standard spontaneous ventilatory and gas exchange criteria and were safely extubated within 3 h of surgery (20). In another study, 90 of 100 patients were safely extubated quickly after cardiac valve replacement, without reintubation (21). In both of these studies, cardiovascular rather than respiratory parameters better predicted the need for continued ventilatory support.

Extubation, when unlikely to be successful, may increase morbidity (9, 11, 22, 23), although several studies have found that premature extubation, after which urgent reintubation is required, may not necessarily increase mortality. A previous retrospective study from our institution found no increase in pneumonia after earlier extubation in patients with TBI (11). In that study, Hsieh and colleagues reviewed 174 patients with isolated TBI during a 2-yr period. They found that extubation of patients with TBI did not tend to increase pneumonia incidence, but that pneumonia prolonged ICU and hospital stay in patients with TBI. Additionally, the GCS was not predictive of pneumonia, and extubation of comatose patients did not appear to increase the risk of developing this complication. That retrospective study also did not support leaving patients with TBI intubated to reduce the incidence of pneumonia. The present study confirms the assertions of others that, within 3 to 4 d, intubation is associated with a higher risk of pneumonia (11, 14).

Extubation failure (e.g., reintubation or tracheotomy after a trial of extubation) may reflect inability to control the underlying disease process that prompted intubation initially. In one study, postsurgical patients had a reintubation rate of 4 to 5.5% within 7 d (23). Morbidity (pneumonia or pulmonary edema) was 36% for reintubated patients who had a hospital mortality of 40%. In that study’s awake patients with TBI, the major reason for reintubation was airway protection. Their average intubation time was 6 d, with a mean time to reintubation of 2 d. This group had a 60% incidence of new pulmonary infiltrates and a 10% mortality. Others have found reintubation rates of 4 to 19% (9, 22). As in the present study, standard criteria for the adequacy of spontaneous ventilation and gas exchange have been poor predictors of the need for reintubation (16).

Our study have has important economic implications. There are approximately 500,000 new cases of TBI requiring hospitalization each year in the United States (24). The present study found a savings of 165 patient-days of mechanical ventilation for a population of 136 brain-injured patients, albeit a population of TBI plus other acute neurologic conditions, when these patients were extubated within 48 h of meeting standard accepted SVPs. The group extubated in a timely fashion also experienced shorter ICU and hospital LOS. Timely extubation was not associated with increased morbidity or mortality and, in fact, may have been associated with less pneumonia and shorter hospital stays. Delaying extubation, when the only indication for prolonged intubation is neurologic status, may not improve patient outcome and may serve only to increase cost.

There were several limitations of our study. It is possible that clinicians used some factor other than those we measured or some unexplored combination of measured factors to decide on extubation. If this were the case, then the apparent variation in practice would be explained by these factors. However, we recorded every variable that both the literature and our experience at our institution led us to believe important. Some may question the criteria we used to establish extubation readiness date. If these were too strict, then patients may appear to have delayed extubation because of extrapulmonary factors, when, in fact, the delay was due to our definition of readiness. This is unlikely because no patients were extubated prior to meeting our readiness criteria and we used published and well established criteria for extubation readiness. In fact, throughout our study we made decisions to bias our analysis to the conservative side. Where several options existed for a parameter, we chose the extreme that would tend to identify extubation readiness later in the course of the patient’s illness rather than earlier. This is also why we chose to use a 48-h grace period in identifying patients with delay. If every patient who was kept intubated beyond the 24 h of the extubation readiness day had been included as extubation delay patients, we would have concluded that 58 instead of 37 patients had extubation delay. By excluding patients with non-neurologic diseases and those who developed non-neurologic complications, we studied a group of patients whose only reason for continued intubation and mechanical ventilation related to airway management. Finally, it would have been interesting to compare extubation delay in these patients with a group of mechanically ventilated patients without neurologic injury to further evaluate our hypothesis that extubation delay was associated with uncertainty surrounding airway management in unconscious patients. However, the fact that nearly all patients with extubation delay were comatose supports this conclusion.

Timely extubation of brain-injured patients who meet standard weaning criteria appears to be safe (no increased risk of reintubation or subsequent tracheotomy), potentially beneficial (associated with a lower incidence of pneumonia), and less expensive (shorter ICU and hospital costs and LOS). Our data provide no justification for delaying extubation in patients whose only indication for prolonged intubation is a depressed level of consciousness. Extubation of patients with acute brain injury, directed by existing readiness criteria for weaning from mechanical ventilation, may decrease the incidence of pneumonia and reduce ICU and hospital stays and charges. Timely extubation cannot prevent all pneumonias as some are likely related to aspiration at the time of the initial neurologic event. These data justify a randomized controlled trial of early extubation for brain-injured patients based on the extubation readiness criteria used in this study.

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