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Predictors of Extubation Success in Acute Ischemic Stroke patients

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Abstract

Background—Acute ischemic stroke (AIS) patients often undergo intubation and mechanical ventilation (MV). Prolonged intubation and MV have disadvantages and complications. Conventional extubation criteria based only on respiratory parameters are insufficient to guide extubation practices in stroke patients where capacity for airway protection is a major concern.

Objective—To identify clinical and neuroanatomical markers of successful extubation in AIS patients requiring MV.

Methods—Retrospective review of tertiary care hospital patient database from May 2009–November 2012 to identify consecutive patients with AIS intubated during hospitalization. We assessed the effect of age, sex, baseline National Institutes of Health Stroke Scale (NIHSS) score, level of consciousness, facial weakness, dysarthria, neglect, infarct location, dysphagia, respiratory parameters and history of pneumonia on successful extubation by hospital discharge using multivariate logistic regression analysis.

Results—112 subjects met study criteria and were included in the analysis. Age and NIHSS scores (mean $\pm$ standard deviation) were 74.5 ± 16.1 years and 19 ± 9.8 , respectively; 56 % were women. In multivariate analysis, NIHSS score 15 (Odds Ratio 4.6, 95% Confidence Interval 1.9–11.3, $p < 0.001$) and absence of dysarthria prior to intubation (Odds Ratio 3.0, 95% Confidence interval 1.1–8.3, $p = 0.04$) were independently associated with successful extubation. Conventional respiratory parameters had no effect on extubation success in this cohort.

Conclusions—Milder stroke and absence of dysarthria prior to intubation were independently associated with extubation success. Our findings could help inform extubation practices in patients with AIS though prospective validation is necessary.

Introduction

Acute Ischemic Stroke (AIS) stroke patients may require intubation and mechanical ventilation (MV). In the acute stroke phase, decisions regarding extubation are driven by concerns stemming from a depressed level of consciousness (LOC) and/or inability to

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handle oral secretions rather than concerns about primary respiratory failure. Patients with brain injury meet conventional extubation criteria which are classically based only on pulmonary mechanics, such as spontaneous breathing trials and rapid shallow breathing indices. Perhaps due to this fact, extubation failure rates in these patients can be as high as 40%¹. In prior studies of intubated patients with primary neurologic injury, depressed LOC and inability to follow commands, predicted extubation failure², increased mortality³ and poor long-term outcome⁴. Another small study that included only middle cerebral artery infarcts suggested that laterality might be associated with extubation success, with left hemisphere AIS having considerably better outcome⁵. However, there are no well-defined clinical tools to guide extubation practices in AIS patients⁶.

The purpose of our study was to identify early predictors of extubation success in AIS and elucidate the relative contribution of neurologic and respiratory parameters. We focused on clinical parameters that can be easily detected and recorded and are present on patient presentation, immediately preceding the initial intubation and hypothesized that there are distinct neurologic clinicoanatomical variables that are associated with successful extubation after adjusting for patient's respiratory status.

Materials and Methods

Study population

We performed a retrospective study of all patients with AIS admitted to a large academic medical center in Boston between November 2009 and May 2012. We screened consecutive patients admitted to the hospital during this period using ICD-9 codes (433.11, 433.21, 433.31, 434.01, 434.11, 459.0) and isolated those with AIS who required endotracheal intubation. Alternative neurological diagnoses, including transient ischemic attacks, seizures intracerebral hemorrhage, subarachnoid hemorrhage, subdural hemorrhage, traumatic brain injury, intracranial tumors, were excluded. Patients intubated for emergent surgery or other procedures were included in the analysis if not extubated immediately after the procedure due to concern for their ability to protect their airway. We identified 1612 patients, 1500 of which were excluded: 851 of those had AIS but did not necessitate intubation; 370 had an intracerebral hemorrhage and 279 were excluded because of alternate diagnosis. The remaining 112 patients met our inclusion criteria and were included in the final analysis. Of these 112, 7 were intubated specifically for surgical or medical procedures (6 for carotid endarterectomy, 1 for transesophageal echocardiogram). All 7 patients were extubated successfully.

Procedures

Endotracheal intubation took place either in the Emergency Department or in the Neuro – Intensive Care Unit (ICU). All intubated patients received MV and were weaned to pressure support as tolerated if breathing spontaneously. Nursing oral and airway care was delivered according to institutional protocol. They were evaluated daily by qualified respiratory technicians and underwent daily spontaneous breathing trials to assess their readiness for extubation as indicated by institutional intensive care unit ventilator protocols. The final extubation decision was made by the treating Neuro ICU attending physician.

Data collection

Variables were determined by hospital record review: Age, sex, National Institutes of Health Stroke Scale scores (NIHSS) on presentation prior to intubation. The following parameters were recorded as binary (yes/no) smoking status, history of primary respiratory illness (Chronic obstructive respiratory disease or asthma), history of Congestive heart failure (CHF), development of ventilator-associated pneumonia (VAP), stroke location (right-, left- or bi- hemispheric, or brainstem/infratentorial), re-intubation history, terminal extubation and in-hospital mortality. When missing, NIHSS scores were estimated retrospectively using validated algorithms⁷. We also recorded the following respiratory parameters for each patient, for the duration of their intubation: Fraction of inspired oxygen (FiO₂), minute volume ventilation, total positive end expiratory pressure (PEEP) and the rapid shallow breathing index (RSBI) which is the ratio of respiratory frequency to tidal volume and used as an indicator of weaning readiness to extubation⁸. For each of the respiratory variables the average value over the length of intubation was calculated and used in the statistical analyses.

Definitions

Extubation success was defined as lack of a need for re-intubation for 48 hours after extubation. Terminal extubation, need for tracheostomy and re-intubation were classified as “extubation failures”. Terminal extubation, per our institutional nomenclature is used to imply extubation in the context of transitioning care toward comfort measures. Terminal extubation was classified as extubation failure as in the vast majority of these patients in our cohort, the decisive, explicit reason driving the decision was the necessity for tracheostomy and percutaneous gastrostomy (if care were to be continued in these group of patients, all of them would have necessitated tracheostomy). Pneumonia diagnosis was based on clinical criteria by the treating physician and confirmed by chart review. A combination of fever, leukocytosis and presence of infiltrate in chest radiograph were required to adjudicate the diagnosis. VAP was defined as pneumonia after 48 hours of ventilation with a clean chest X-ray on presentation; eventually both VAP and other cases of pneumonia were clustered together as “pneumonia”. CHF was defined as confirmed history of it or a transthoracic echocardiogram with an ejection fraction of <30%. Dysarthria and facial weakness were defined as present (score = 1 in the relevant NIHSS item) or absent (score=0). LOC was defined as awake (score=0 in item LOC1a of the NIHSS) or not awake (score = 1 in item LOC1a). Severe stroke was defined as NIHSS ≥ 15; old age as >75 years. Cutoff values were chosen based on clinical relevance and prior studies.⁹

Statistical Analysis

Patients were dichotomized in two groups based on extubation success. Descriptive statistics were obtained, using chi-squared test for categorical dichotomous variables and two-tailed Student's t-test for continuous variables. Continuous variables are expressed as means and standard deviations or median and interquartile range as specified and dichotomous variables expressed as proportions.

A multivariate logistic regression model was constructed, with extubation success as the event of interest, utilizing a priori chosen clinically relevant covariates as well as covariates

whose difference between the groups reached statistical significance, denoted as p value <0.05 (age, stroke severity, presence of pneumonia, stroke location, dysarthria, facial weakness). Data were analyzed using STATA/IC 13.1 (StataCorp, College Station, Texas, USA)

Results

Patient characteristics

Characteristics of our patient cohort are summarized in table 1. Strokes were severe as suggested by a median NIHSS severity of 19 and when dichotomized as severe vs mild, 38% were mild. 56 (50%) of the patients were extubated successfully. The median day of intubation relative to ischemic stroke was 0, range (0-8). Of the 27 infratentorial strokes, 11 were restricted to the cerebellum only, although on all occasions there was significant brain edema with compression of the brainstem.

Between group comparisons, univariate and multivariate analyses

In the univariate analysis, stroke severity using total NIHSS scores was significantly lower in the group of successfully extubated patients and naturally the proportion of patients with “severe” stroke was significantly higher in the group that failed extubation (table 2). Presence of dysarthria and depressed LOC were also strongly associated with extubation failure. Stroke location, facial weakness, aphasia or neglect did not demonstrate a significant association with extubation success. There were no significant differences in any of the respiratory variables. (Table 2). None of the respiratory parameters were associated with extubation success

In multivariate analysis, milder stroke (OR 4.6, 95% CI 1.9-11.3) and absence of dysarthria on presentation (OR 3.0, 95% CI 1.1-8.3) were independently associated with extubation success (table 3). NIHSS score introduced as a continuous instead of dichotomous variable in the model retained a robust association with extubation success (results not shown; a dichotomized NIHSS score is presented in our analysis hereby). None of the other parameters included in our model (younger age, absence of facial weakness, left hemispheric location, absence of pneumonia) were independently associated with extubation success. The LOC term was not included in the final model due to collinearity with the total NIHSS score. The area under the ROC curve is 0.746, indicating fair model discrimination (Figure).

Discussion

In this retrospective study of intubated AIS patients, we found that milder stroke severity and absence of dysarthria prior to intubation were independently associated with extubation success, after adjusting for important respiratory parameters that usually guide extubation practices. The median day of intubation relative to the stroke symptoms onset was 0, indicating that it occurred very early and as a result of the neurologic injury.

Our findings confirm our hypothesis that accounting for standard respiratory extubation parameters, neurologic factors and especially dysarthria may be significantly contributing to

extubation success in intubated AIS patients. Intubation occurred very early on relative to the stroke, long before a respiratory complication could have occurred, with the exception, perhaps of bronchial aspiration. However, the frequency of pneumonia was not different between the two groups and it did not have an effect on final extubation success. Similarly, all direct and indirect markers of pulmonary function that are traditionally used to guide extubation readiness^{8,10} were not different in those who failed extubation compared to those who succeeded. The average RSBI of ~40 in both groups would normally favor weaning readiness across the entire cohort from a respiratory standpoint⁸ and yet half of them failed extubation. Similarly, development of pneumonia was similar between the two groups and it did not significantly affect the final extubation outcome (Table 2). Additionally, we did not identify any relationship between the anatomical location of the infarct and extubation outcome; this is in contrast to prior studies that suggested a worse prognosis for patients with infratentorial strokes¹¹, although these studies were more focused on survival and less so on extubation success.

LOC and oropharyngeal musculature compromise usually drive decisions about intubation in AIS patients. Presence of dysarthria in the relevant NIHSS item is indicative of underlying bulbar weakness or incoordination which can result in inability to handle oral secretions even with preserved LOC. Severe dysarthria can conceivably occur in otherwise mild stroke, in contrast to depressed LOC. It is, therefore an element that merits special attention and prior studies support this conclusion¹². We believe that level of arousal does affect decisions regarding extubation. However, because most strokes with impaired LOC have large deficits it is difficult to isolate the effect of impairment of consciousness on extubation success without considering the overall stroke severity. In our cohort, a strong correlation was observed between the NIHSS score and the LOC 1a item of the scale (correlation coefficient of 0.67) which did not allow us to incorporate both variables in the final multivariate model. On the contrary, other aspects of neurologic presentation often perceived in everyday practice of as negatively affecting the weaning process, such as facial weakness, aphasia and neglect were not associated with extubation success.

Early identification of candidates who can be successfully extubated has enormous clinical implications such as decreasing the time of MV and its complications, expediting tracheostomy in appropriate patients, reducing the ICU and hospital LOS and ultimately facilitating the transition to acute rehabilitation^{13,14}. A study of elective extubation in brain-injured patients meeting extubation criteria has been proven to be feasible¹⁵ but a larger, prospective randomized trial of elective extubation has not been undertaken yet. A recent pilot study evaluating the safety and feasibility of early tracheostomy in 60 patients with severe stroke showed encouraging results with decreased sedative use, ICU and 6 month mortality¹⁶ but benefits remain to be confirmed in a larger, phase 2 trial that is currently underway¹⁷.

Our study has limitations. The most important one is that patients were recruited retrospectively; Primary data were not recorded in a standardized manner which made the retrospective identification of certain parameters such as stridor and pneumonia difficult. We inevitably relied on clinical diagnoses as recorded in patient's charts; this may have led to some misclassification of these cases but we do not believe that this introduced any

systematic error in our analysis. We were not able to record the length of intubation. Clinical decision-making about extubation eventually depends on individual patient characteristics and care-giver preferences and practice parameters which are difficult to capture and analyze in a retrospective study of this nature. However, despite this limitation, we do not think that it introduces a systematic bias in our results as these clinical criteria would have been applied in a non-differential manner across the cohort. This limitations stress even further the necessity of prospective, randomized and protocolized trials.

Strengths of our study include use of the NIHSS to grade the clinical severity, which is a scale with significantly greater granularity compared to commonly used Glasgow Coma Scale in most prior studies; this allowed us to isolate specific aspects of the neurologic deficit in addition to the overall stroke severity. Additionally we collected detailed data on respiratory parameters throughout the duration of intubation, which allowed us to address their role in extubation success.

In conclusion, our findings suggest that milder stroke and absence of dysarthria on presentation are associated with successful extubation after accounting for conventional respiratory parameters in determining ventilator weaning readiness in this subgroup of patients. Presence or absence of these simple clinical variables can inform screening practices for extubation trials and help curtail the duration of intubation and MV in stroke patients. Our results should not be interpreted as absolute predictors of extubation success; they are intended as indicators that could be helpful in clinical decision-making. They are hypothesis-generating and highlight the need for prospective, randomized studies to further address areas of uncertainty pertaining to selection criteria of both initial intubation and subsequent extubation in patients with primary neurologic injury.

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Figure 1.
Receiver operating characteristic curve for the final multivariate model for prediction of extubation success

Table 1

Baseline characteristics of the patients in our cohort. The numbers in parentheses denote percentage of patients with the relevant characteristic.

	N=112
Age (Median,IQR)	74.5 (62-84)
NIHSS (Median $\pm$ SD)	19 (11-26)
Gender (N, % female)	63 (56)
Pneumonia (N, %)	33 (29)
Smoking (N, %)	23 (21)
Right hemisphere (N, %)	51 (46)
Left hemisphere (N, %)	69 (61)
Bihemispheric (N, %)	20 (18)
Infratentorial (N, %)	27 (24)
Mild stroke (NIHSS $\leq$ 15)	42 (38)
Absence of Dysarthria (score 0 in NIHSS)	30 (27)
Old (Age >75 years)	51 (46)

Table 2
Univariate unadjusted comparisons between the successful and failed extubation groups

	Successful (N) N _{total} = 56	Failed (N) N _{total} = 56	p value
Gender (female)	33	30	0.57
Age (continuous-mean)	68	72	0.2
Old(>75 years)	25	26	0.85
NIHSS (continuous-mean)	14	23	<0.0001 *
NIHSS<15	31	11	<0.0001 *
Dysarthria **	34	48	0.003 *
Facial Weakness **	34	32	0.7
Awake [§]	44	25	<0.0001 *
Smoking	13	10	0.5
Pneumonia	13	20	0.15
Right hemisphere	26	25	0.85
Left hemisphere	37	32	0.33
Bi-hemispheric	10	10	1
Infratentorial	11	16	0.27
FiO ₂	49.1 (±8.2)	47.7 (±7.2)	0.46
Minute ventilation	8.4 (±1.8)	9 (±1.9)	0.16
PEEP total	5.7 (±1.3)	6.5 (±2.1)	0.2
RSBI	41.1 (±13.6)	42.4 (±10.9)	0.7

* p value of <0.05 denotes statistical significance

** score 1 in the relevant NIHSS item

[§] score=0 in item LOC1a of the NIHSS

PEEP: Positive End Expiratory Pressure; FiO₂: Fraction of inspired oxygen; RSBI: Rapid shallow breathing index (defined as the ratio of respiratory frequency to the tidal volume in liters)

Table 3
Multivariate logistic regression (event of interest Successful extubation, includes only variables with independent significance)

	OR	p value	95% CI
Absence of Dysarthria	3	0.04 *	1.1-8.3
NIHSS<15	4.6	0.001 *	1.9-11.3

* p value of <0.05 denotes statistical significance