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Perspectives in GBS

Factors Predicting Extubation Success in Patients with Guillain-Barré Syndrome

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Abstract

Introduction: Accurate prediction of successful extubation in patients with Guillain-Barré syndrome (GBS) is an important clinical problem. We hypothesized that reversal of clinical indices used to intubate a patient (i.e., declining vital capacity [VC]) predict extubation.

Methods: This was a retrospective study in neurocritical care units at two teaching hospitals identifying all mechanically-ventilated patients with GBS.

Results: A total of 44 patients with GBS were included. Of these, 14 patients were successfully extubated. There were 10 failed extubations among six patients; and 20 patients underwent tracheostomy without an extubation trial. On the day of extubation, lower negative inspiratory force (NIF) (–50.3 ± 12.7 versus –28.6 ± 16.5 cm H_2O, $p = 0.0005$) and higher VC (21.9 ± 8.4 versus 13.0 ± 5.9 mL/kg, $p = 0.003$) correlated with successful extubation. Change in VC preintubation to preextubation by greater than 4 mL/kg correlated with 82% sensitivity and 90% positive predictive value for successful extubation. Failed extubations were associated with the presence of pulmonary comorbidities (79 versus 36%, $p = 0.008$) and autonomic dysfunction (73 versus 27%, $p = 0.008$). Length of stay (LOS) in the intensive care unit (ICU) was increased in patients who failed extubation and in those patients who underwent tracheostomy (21.5 ± 11.1 versus 12.5 ± 8.7, $p = 0.005$). In multivariate analysis, higher VC at extubation was associated with successful extubation ($p = 0.05$).

Conclusions: In mechanically-ventilated patients with respiratory failure secondary to GBS, NIF less than –50 cm H_2O, and VC improvement preextubation to preintubation by 4 mL/kg were significantly associated with successful extubation. Failed extubation or need for tracheostomy correlated with autonomic dysfunction, pulmonary comorbidities, and prolonged LOS in the ICU. Such parameters may be helpful in identifying patients with GBS likely to succeed extubation versus early referral for tracheostomy.

Key Words: Extubation; Guillain-Barré syndrome; mechanical ventilation; vital capacity.

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Introduction

Approximately one-third of patients with Guillain-Barré syndrome (GBS) require mechanical ventilation *(1)*. Clinical guidelines for intubation have been studied *(2,3)*, but there is a paucity of data identifying markers that predict extubation outcome. In a study of 10 patients, serial vital capacity (VC) measurements were found helpful in determining time for weaning from mechanical ventilation and time for extubation *(4)*. Identification of specific factors that predict extubation outcome may result in aggressive extubation attempts versus early referral for tracheostomy. The goal of this study was to identify clinical markers that could predict extubation outcome in mechanically-ventilated patients with GBS. We hypothesized that reversing clinical indices indicative of respiratory failure (declining VC) are predictive of extubation success.

Methods

We retrospectively reviewed the charts of mechanically-ventilated patients with GBS admitted to the Brigham and Women's and Massachusetts General Hospitals from 1993 to 2004. Standard diagnostic criteria were used for GBS *(5,6)*. Patients were identified through an institutional patient database using International Classification of Diseases (ICD)-9 codes such as acute infective polyneuritis, paraplegia, paralysis unspecified, other specified paralytic syndrome, and polyneuropathy, and cross-searched with insertion of endotracheal tube and continuous mechanical ventilation. All patients who required mechanical ventilation for respiratory failure with GBS were included in this study. The study was reviewed and approved by an institutional review board representing both hospitals.

Data Collection

Demographic information collected included patient's age, gender, and Body Mass Index (BMI) based on the patient's actual height and weight. Neurologic variables studied included level of alertness, presence of bulbar weakness (dysarthria or dysphagia), the median-APB compound muscle action potential amplitude (CMAP) on electrodiagnostic studies, Medical Research Council (MRC) grading of weakness, the presence or absence of autonomic dysfunction, cerebrospinal fluid (CSF) protein (highest value recorded), or treatment with intravenous immunoglobulin (IVIg) or plasmapheresis. Autonomic dysfunction was considered present if there were unexplained dysrhythmias or blood pressure fluctuations, and was noted in the clinical impression of treating physicians during the patient's illness at any time during the patient's hospitalization.

Pulmonary data were obtained from daily nursing and respiratory therapy progress notes. Variables studied included VC, negative inspiratory force (NIF), tidal volume, respiratory rate, oxygenation, and ventilation indices (FiO_2, O_2 saturation, CO_2) prior to extubation or on the day prior to the patient's tracheostomy. Information on quantity of secretions, concomitant pulmonary processes, chest X-ray findings, history of prior intubations, days from onset of symptoms to intubation, days on the ventilator, timing of tracheostomy, and length of stay (LOS) in the intensive care unit (ICU) was collected. A pulmonary comorbidity was considered present if the patient had a history of asthma/chronic obstructive pulmonary disease, or a finding of pulmonary embolus, pneumonia, atelectasis, or pulmonary edema on imaging during hospitalization. Patients were grouped into two categories: (1) successful extubation, and (2) extubation failure or direct triage to tracheostomy. Extubation failure was defined as reintubation within 48 hours of the patient's extubation. Patients who were directly triaged to tracheostomy were classified as extubation failures.

Protocol for Mechanical Ventilation

Following intubation, mechanical ventilation was provided at the discretion of the treating clinicians. In general, patients received assist control or intermittent mandatory ventilation mode for the duration of their ventilatory support. Patients were weaned off mechanical ventilatory support as tolerated to pressure support mode at the discretion of the treating physician.

Statistical Analysis

Univariate *t*-test and Chi-square analysis were used to evaluate the effects of these variables on successful extubation, failed extubation, or direct triage to tracheostomy. Multivariate logistic regression analysis was performed using STATA v. 8.0 (Statacorp, College Station, TX).

Results

A total of 44 patients with GBS met the previously mentioned inclusion criteria. The mean age was 55 ± 22 years (range 14–89 years). There were 24 (54.5%) women and 20 (45.4%) men. Of these, 31 (70.5%) patients were intubated for decreasing VC, with mean VC of 15.2 ± 5.1 mL/kg prior to intubation. A group of four (9.0%) patients were intubated for airway protection, two (4.5%) patients were intubated for oxygenation failure, and two (4.5%) patients were intubated for combined aspiration and decreasing oxygen saturations. In addition, one patient was intubated for transfusion-associated lung injury, and another patient was intubated because of inability to speak and wheezing. The cause for intubation was unclear from the documentation in three (6.8%) patients. Following intubation, patients were initially placed on assist-control mode using volume-cycled ventilation followed by intermittent mandatory ventilation or pressure support modes. The mean number of days intubated was 11.7 ± 7.0 days.

Among the 44 patients included in this study, 14 (31.8%) were successfully extubated. In this group, one patient had GBS twice, 20 years apart, and succeeded extubation on both occasions. There were 10 failed extubations among six patients. There were no documented complications from reintubation. Reasons for reintubation were hypoxia (3/10, 30%), ventilatory failure (2/10, 20%), and aspiration or inability to tolerate secretions (4/10, 40%). In one patient, reason for reintubation was not documented. One patient failed extubation because of stridor and inability to speak, and was noted to have poor movement of the vocal cords upon reintubation. This patient succeeded extubation on a second trial. Of the six patients who failed extubation, one patient went on to successful extubation, and the other five went to tracheostomy. A total of 20 (45.5%) patients underwent tracheostomy without an extubation trial. There was a trend towards longer mean time of intubation among patients who failed extubation and required

Table 1
Multivariate Regression Analysis of Factors Associated With Extubation Success or Failure

	Coefficient	*Standard error*	*T*	*Significance (p)*	*Confidence interval*
Extubation					
VC (mL/kg)	0.034	0.015	2.26	0.05	0.0005–0.07
NIF (cm H_2O)	0.012	0.010	1.38	0.20	–0.0078–0.03
Change in VC	0.011	0.018	0.61	0.56	–0.029–0.05
Dysautonomia	17	0.24	0.69	0.51	–0.38–0.71

VC, vital capacity; NIF, negative inspiratory force.

tracheostomy, compared to patients who were directly triaged to tracheostomy (16.9 ± 6.3 versus 11.2 ± 7.4, $p = 0.07$). In this group, two patients underwent withdrawal of care because of multiple comorbidities and were considered as failures of extubation. Of these two patients, one patient underwent direct triage to tracheostomy.

Baseline demographic and clinical characteristics of patients who succeeded extubation compared to those who failed were similar. The presence of autonomic dysfunction was significantly associated with failure of extubation (73.0 versus 26.7%, $p = 0.008$). There was no significant difference in outcome of extubation by the patient's age, gender, BMI, time from onset of symptoms to intubation, presence of bulbar weakness, CSF protein, or treatment with IVIg or plasmapheresis. The median nerve CMAP amplitude was not significantly different, though quantified nerve conduction study data were missing in more than 25% of patients in each group. LOS in the ICU was increased in patients who failed extubation and in those patients who underwent tracheostomy (21.5 ± 11.1 days versus 12.5 ± 8.7 days, $p = 0.005$). There was no significant difference between patients who failed extubation compared to patients who underwent direct triage to tracheostomy by the patients' age, gender, BMI, time from onset of symptoms to intubation, presence of bulbar weakness or autonomic dysfunction, and CSF protein.

From a pulmonary perspective, a higher VC (1.5 ± 0.5 L versus 1.0 ± 0.5 L, $p = 0.004$, or 21.9 ± 8.4 mL/kg versus 13.0 ± 5.9 mL/kg, $p = 0.003$), or lower NIF on the day of extubation (–50.3 ± 12.7 cm H_2O versus –28.6 ± 16.5 cm H_2O, $p = 0.0005$) correlated with successful extubation. A VC greater than 20 mL/kg had a positive predictive value of 70% (7/10 patients). At a higher threshold, VC greater than 25 mL/kg had a positive predictive value of 100% for extubation success, but there were only four patients with a VC this high.

Improvement in VC from day of extubation compared to day of intubation was also predictive of successful extubation outcome (5.45 mL/kg versus –3.53 mL/kg, $p = 0.003$). An improved VC greater than 4 mL/kg carried an 82% sensitivity (9/11 patients) and 90% positive predictive value of successful extubation. A change in VC less than 4 mL/kg correlated with 95% specificity (19/20 patients) and 90% positive predictive value of extubation failure. Therefore, this cutoff value correlated with a high positive predictive value for extubation success.

Multivariate regression analysis was performed, adjusting for VC at extubation (mL/kg), improvement in VC, NIF at extubation, and dysautonomia (Table 1). In this analysis, higher VC at extubation was significantly associated with extubation success ($p = 0.05$).

There were more pulmonary comorbidities in patients who failed extubation or triaged to tracheostomy compared to patients who succeeded extubation (79 versus 36%, $p = 0.008$). In most patients, arterial blood gas samples were obtained post-intubation, and therefore mean $PaCO_2$ and PaO_2 reflected initial mechanical ventilator settings rather than preintubation gas exchange. The NIF was not protocoled as part of respiratory mechanics to measure for preintubation of patients with GBS, and therefore change in NIF preintubation to postintubation could not be assessed. There was no significant difference in extubation outcome based on the patient's admission chest X-ray, preintubation VC, and preextubation tidal volumes.

Discussion

In mechanically-ventilated patients admitted to a medical ICU, the rapid shallow breathing index (respiratory frequency/tidal volume, f/Vt) has been identified as a useful marker in predicting successful weaning from mechanical ventilation *(7)*. Presence of a good cough and low level of secretions predicted extubation success in a series of postoperative neurosurgical patients *(8)*. However, such parameters may not apply to patients with GBS, as the mechanism leading to their respiratory compromise is different from that of patients with cardiopulmonary disease or those who are postsurgical. In GBS, acute demyelination or axonal injury to nerves innervating the diaphragm and intercostal muscles leads to neuromuscular weakness and respiratory failure *(3)*.

In one series of intubated patients with GBS, extubation was attempted when continuous positive airway pressure could be tolerated at 5 to 7 cm H_2O without fatigue for 12 to 24 hours, arterial PO_2 was greater than 80 mmHg on room air, and bulbar paresis improved *(3)*. All patients who met these criteria succeeded extubation, but the mean number of days intubated was long (51 ± 53 days). A delay in extubation can increase the risk of ventilator-related complications such as pneumonia, tracheobronchitis, barotrauma, or laryngotracheal stenosis *(2,10)*. On the other hand, premature extubation may lead to the necessity of reestablishing an airway by reintubation, with an associated increase in the risk of ventilator-associated pneumonia and airway trauma. Therefore, identification of parameters that predict successful extubation is important to triage patients with GBS to carefully timed extubation versus early referral for tracheostomy.

Previous reports have demonstrated that trends in VC and NIF, which are dependent on volitional effort, can predict

Table 2
Features of Mechanical Respiratory Failure in Present and Past Series

	Mayo Clinic Gracey et al.	*MGH Ropper and Kehne*	*Mayo Clinic Lawn et al.*	*MGH/BWH Nguyen et al.*
Years of study	1974–1979	1981–1984	1976–1996	1993–2004
Number of patients	13	18	60	44
Age	55 ± 22	53 ± 14	59	55 ± 22
Days to intubation	–	9 ± 8	7	11 ± 8.6
VC preintubation	–	14 mL/kg	25 mL/kg[a]	17 ± 8 mL/kg
	1.6 + 0.46 L	1.8 + 0.7 L	–	1.5 ± 0.5 L
VC "at weaning"	–	28 mL/kg	–	22 ± 8 mL/kg
NIF "at weaning"	48 ± 21cm H_2O	43 ± 15 cm H_2O	–	50 ± 13cm H_2O
Days intubated	54 (10–104)	51 ± 53 (8–220)	–	12 ± 7 (4–42)
Tracheostomy	100%	63%	–	50%
Hospital ICU days	82 ± 30	105 ± 83	–	18 ± 11

MGH, Massachusetts General Hospital; BWH, Brigham and Women's Hospital; VC, vital capacity; NIF, negative inspiratory force; ICU, intensive care unit.
[a] baseline vital capacity

respiratory failure, intubation requirements, timing for ventilation weaning, and extubation in patients with GBS *(3,4)*. We propose that VC, its improvement from preextubation to preintubation, can be used in identifying patients who can be successfully extubated. In our cohort of mechanically-ventilated patients with GBS, VC greater than 20 mL/kg (on average) and NIF less than –50 cm H_2O were associated with successful extubation. In multivariate analysis, higher VC at extubation was associated with extubation success. These values for respiratory mechanics are similar to previously studied parameters for ventilator weaning in intubated patients with GBS, all of whom successfully extubated. Mean VC was 1.8 L (28 mL/kg) in the Ropper et al. series, 1.6 L in the Gracey et al. series at the time of extubation, and 15 mL/kg in the Chevrolet series (Table 2). The NIFs were below –40 cm H_2O in both the Ropper and Gracey series at the time of extubation *(3,9)*. In addition, we found that an improvement in VC from day of extubation compared to day of intubation was predictive of successful extubation outcome (5.5 mL/kg versus –3.5 mL/kg, $p = 0.003$). A change in VC by 4 mL/kg was associated with an 82% sensitivity and 90% positive predictive value for successful extubation. Change in NIF could not be measured because testing of NIF in patients with GBS preintubation was not routinely measured at our institutions.

Patients who failed extubation or were directly treated with tracheostomy were analyzed together because no major clinical differences were found between the two groups. Grouping tracheostomy patients without attempted extubation as failure overestimates extubation failure.

In univariate analysis, patients who failed extubation or were directed to tracheostomy had significantly increased pulmonary comorbidities and autonomic dysfunction compared to patients who were successfully extubated. Bulbar dysfunction did not predict patients who failed extubation or who were directly triaged to tracheostomy, although a retrospective analysis may miss this entity because of lack of standardized documentation. The presence of dysarthria or dysphagia has been associated with increased likelihood of mechanical ventilation in patients with GBS *(2)*. LOS in the ICU was significantly increased in patients who failed extubation or were directed to tracheostomy versus patients who successfully extubated. Compared to previous series, LOS for mechanically-ventilated patients in the ICU was shorter in our series (LOS 18 ± 11 days) versus Ropper's series (LOS 105 ± 83 days) and Gracey's series (LOS 82 ± 30 days). This is presumably secondary to advances in ICU care over the last two decades and more aggressive efforts to extubate or direct patients to tracheostomy.

Because of the retrospective method of this study, there were limitations in the analysis of NIF preintubation, arterial blood gases, respiratory secretions, and MRC grading of strength. Most patients had arterial blood gases performed after intubation, at which point patients were placed on assist-control ventilation. In our analysis, data on ventilator weaning method, peak expiratory pressure, and ability to clear secretions could not be used because of lack of standardization in the reporting of quality and quantity of secretions. MRC grading of muscular strength was too variable in documentation to be meaningfully assessed. The lack of a standardized weaning protocol makes it difficult to determine how active respiratory weaning was in each patient. It is possible that more patients with marginal VC and NIF could have been extubated. In addition, findings are often descriptive in retrospective studies, and a clinician's criteria to extubate or directly triage a patient to tracheostomy is often unknown. It is likely that VC and NIF data were used to affect clinical decision making, which could explain our results. Future prospective studies examining the contribution of each of these variables on predicting extubation outcome in patients with GBS would be helpful.

Conclusion

In mechanically-ventilated patients with respiratory failure secondary to GBS, traditional measure of VC was found to be predictive of extubation success. In particular, with VC greater than 20 mL/kg, NIF of –50 cm H_2O at extubation, VC improvement preextubation to preintubation by 4 mL/kg, or amelioration of VC close to the point where the patient was intubated, lack of pulmonary comorbidities were all significantly associated with successful extubation. Other previously unreported factors such as autonomic dysfunction may be important.

Future prospective, multicenter studies reevaluating the contribution of change in VC, NIF, peak expiratory pressure, ventilator weaning modality, and secretions on predicting extubation outcome are needed.

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