Anticipating Mechanical Ventilation in Guillain-Barré Syndrome

Nicholas D. Lawn, FRACP; Dade D. Fletcher, MD; Robert D. Henderson, FRACP; Troy D. Wolter, MS; Eelco F. M. Wijdicks, MD

Context: The combination of multiple clinical factors culminates in neuromuscular respiratory failure in up to 30% of the patients with Guillain-Barré syndrome (GBS). Although guidelines exist as to when to proceed with intubation, early indicators of subsequent progression to respiratory failure have not been established.

Objectives: To identify clinical and respiratory features associated with progression to respiratory failure and to examine patterns of respiratory decline in patients with severe GBS.

Design: Retrospective survey.

Setting: Tertiary care hospital.

Patients: One hundred fourteen consecutive patients with severe GBS admitted to the intensive care unit between January 1, 1976, and December 31, 1996.

Main Outcome Measures: Early markers of impending respiratory failure, requirement for mechanical ventilation, and patterns of respiratory decline.

Methods: The clinical and electrophysiologic features of 60 patients receiving mechanical ventilation were compared with 54 patients with severe GBS who did not receive mechanical ventilation. Daily preventilation maximal inspiratory and maximal expiratory respiratory pressures and vital capacity were analyzed. Multivariate predictors of the necessity for mechanical ventilation were assessed using logistic regression analysis.

Results: Progression to mechanical ventilation was highly likely to occur in those patients with rapid disease progression, bulbar dysfunction, bilateral facial weakness, or dysautonomia. Factors associated with progression to respiratory failure included vital capacity of less than 20 mL/kg, maximal inspiratory pressure less than 30 cm H2O, maximal expiratory pressure less than 40 cm H2O or a reduction of more than 30% in vital capacity, maximal inspiratory pressure, or maximal expiratory pressure. No clinical features predicted the pattern of respiratory decline; however, serial measurements of pulmonary function tests allowed detection of those at risk for respiratory failure.

Conclusions: While inherently unpredictable, the course of patients with severe GBS can, to some extent, be predicted on the basis of clinical information and simple bedside tests of respiratory function. These data may be used in the decisions regarding admission to the intensive care unit and preparation for elective intubation.

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The management of patients with Guillain-Barré syndrome (GBS) can be intimidating. The unpredictable course and potential for rapidly producing life-threatening respiratory failure may prompt admission to an intensive care unit (ICU). However, it is clearly unnecessary to transfer every patient with GBS to the ICU based on the potential for deterioration alone. At present, only limited data are available to provide guidance in this situation. Although many studies have identified factors that are associated with the need for ventilation (severe generalized weakness, bulbar involvement, or rapid disease progression), these factors were variably analyzed prior to intubation. It is, therefore, difficult to know how to use this information in the assessment of a patient before the point of respiratory failure as many of the clinical findings identified may have occurred after intubation.

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In their observational series of 19 patients, Ropper and Kehne established strict criteria for intubation in GBS based on previously defined clinical and respiratory factors. Patients were intubated when clini-
PATIENTS, MATERIALS, AND METHODS

The medical records of 114 patients with GBS admitted to the ICU between January 1, 1976, and December 31, 1996, were reviewed. Standard diagnostic criteria for GBS were used. All patients were examined by a neurologist. The clinical, biochemical, and electrophysiologic features of 60 of these patients with GBS who received mechanical ventilation were compared with a group of 54 patients with GBS who were admitted to the ICU but who did not receive mechanical ventilation. These patients were admitted for many reasons including autonomic dysfunction, bulbar weakness, comorbid disease, systemic complications, and importantly, concerns regarding progression of disease and development of respiratory dysfunction.

DATA COLLECTION

All data were collected before ventilation or to peak disability in patients who had received mechanical ventilation and those who did not, respectively. Demographic features analyzed were age, sex, time to peak disability, presence of pulmonary comorbidity (chronic obstructive airways disease, asthma, or pulmonary fibrosis), and antecedent event, in particular, preceding gastrointestinal illness (diarrhea or abdominal pain). Time to peak disability was defined as time to intubation (patients who underwent ventilation), or time to worst score on the Hughes disability scale (patients who did not undergo ventilation), from onset of neuropathic symptoms. The use of specific treatment with intravenous immunoglobulin or plasma exchange was also analyzed. Clinical features analyzed were presence of bilateral facial weakness, upper limb paralysis (complete absence of movement in the upper limbs), autonomic dysfunction (unexplained blood pressure or heart rate fluctuations or significant bladder or bowel dysfunction), and bulbar weakness (dysarthria, dysphagia or impairment of the gag reflex).

The results of cerebrospinal fluid examination (protein level and cell count) and chest radiographs performed prior to peak disability were analyzed. The compound muscle action potential (CMAP) was analyzed on the first nerve conducted study performed at the Mayo Clinic, Rochester, Minn. Low CMAP amplitude was defined as less than 20% of the lower limit of normal. Inexcitable nerves were defined as CMAP amplitude absent in all nerves tested or calculated.

10% of the lower limit of normal and absent in all other nerves tested.

Serial respiratory function tests including VC (measured in milliliters per kilograms), maximal inspiratory pressure (Pmax), maximal expiratory pressure (PEmax) (measured in centimeters of water), and arterial blood gases were analyzed daily. For Pmax, negative values are usually measured, but in this article, these values are expressed, for simplicity, as positive (eg, Pmax of 30 cm H2O is recorded as 30 cm H2O). Respiratory factors were measured by a respiratory therapist using standard techniques. For those with facial weakness, the lips would be held sealed by the respiratory technician or an anesthesia mask would be used. When multiple respiratory measurements were recorded, the best score was analyzed. We also reviewed the patterns of respiratory decline in each patient. The time of day at which intubation occurred was analyzed and, for each patient, it was determined whether this was an elective or urgent procedure.

STATISTICAL ANALYSIS

Characteristics between patients with GBS who received mechanical ventilation and those who did not were assessed for comparability using the Wilcoxon rank sum test for continuous variables and the Fisher exact test for categorical variables. Multivariate predictors of ventilation were assessed using logistic regression analysis with a backward elimination procedure of nonsignificant variables. In this model, mechanical ventilation (yes vs no) was the dependent variable and all variables with a univariate significance, as positive (eg, Pmax of –50 cm H2O is recorded as 50 cm H2O). Respiratory factors were measured by a respiratory therapist using standard techniques. For those with facial weakness, the lips would be held sealed by the respiratory technician or an anesthesia mask would be used. When multiple respiratory measurements were recorded, the best score was analyzed. We also reviewed the patterns of respiratory decline in each patient. The time of day at which intubation occurred was analyzed and, for each patient, it was determined whether this was an elective or urgent procedure.

Baseline demographic and clinical characteristics of patients with severe GBS who received mechanical ventilation and those who did not are listed in Table 1. Patients requiring mechanical ventilation tended to have more severe disease evidenced by the presence of bulbar dysfunction (P < .001), autonomic dysfunction...
Table 2: Baseline Demographics and Clinical Features of 114 Patients With Guillain-Barré Syndrome

<table>
<thead>
<tr>
<th>Variable†</th>
<th>Patients Who Received Ventilation (n = 60)</th>
<th>Patients Who Did Not Receive Ventilation (n = 54)</th>
<th>P‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median [range], y</td>
<td>59 [4-87]</td>
<td>56 [7.5-84]</td>
<td>.53</td>
</tr>
<tr>
<td>Female</td>
<td>23 (38)</td>
<td>22 (41)</td>
<td>.85</td>
</tr>
<tr>
<td>Bulbar dysfunction§</td>
<td>49 (91)</td>
<td>20 (37)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Preceding GI illness</td>
<td>8 (13)</td>
<td>7 (13)</td>
<td>.99</td>
</tr>
<tr>
<td>Upper limb paralysis</td>
<td>5 (9)</td>
<td>1 (2)</td>
<td>.21</td>
</tr>
<tr>
<td>Low CMAP amplitude¶</td>
<td>3 (17)</td>
<td>5 (19)</td>
<td>.99</td>
</tr>
<tr>
<td>Autonomic dysfunction#</td>
<td>26 (47)</td>
<td>12 (22)</td>
<td>.009</td>
</tr>
<tr>
<td>Bilateral facial palsy**</td>
<td>38 (69)</td>
<td>26 (48)</td>
<td>.03</td>
</tr>
<tr>
<td>Pulmonary disease</td>
<td>10 (17)</td>
<td>5 (9)</td>
<td>.28</td>
</tr>
<tr>
<td>Treated††</td>
<td>17 (28)</td>
<td>18 (33)</td>
<td>.68</td>
</tr>
<tr>
<td>Time to peak disability, median, d‡‡</td>
<td>7</td>
<td>10</td>
<td>.01</td>
</tr>
</tbody>
</table>

*Entries summarize nonmissing data and are presented as number (percentage), unless otherwise indicated.
†GI indicates gastrointestinal; CMAP, compound muscle action potential.
‡Two-tailed P value from the rank sum test or Fisher exact test comparing patients who received ventilation with patients who did not.
§Includes the presence of impaired gag reflex, dysarthria, or dysphagia. Data were missing for 6 patients who received ventilation.
¶Data were missing for 3 patients who received ventilation.
#Includes compound muscle action potential less than 20% lower limit normal in at least 2 nerves from electromyogram prior to ventilation or peak disability. Data were missing for 42 patients who received ventilation and 28 patients who did not.
†Includes unexplained dysrhythmia, blood pressure fluctuations, significant bowels or bladder involvement. Data were missing for 5 patients who received ventilation.
**Data were missing for 5 patients who received ventilation.
††Plasma exchange or intravenous immunoglobulin prior to ventilation or prior to the time of peak disability in patients who did not receive ventilation.
‡‡From the onset of neuropathic symptoms.

(P = .009), and bilateral facial palsy (P = .03). In addition, the requirement for mechanical ventilation was associated with a shorter time to peak disability following the onset of neuropathic symptoms (P = .01). No significant differences were noted between those patients who received ventilation and those who did not for age, sex, and the presence of a preceding gastrointestinal illness, upper limb paralysis, or pulmonary disease. Results of cerebrospinal fluid analysis were similar in both groups. Nerve conduction studies were comparable in both groups; however, this analysis was limited because only 18 patients who received mechanical ventilation and 26 patients who did not receive mechanical ventilation had an electromyogram prior to peak disability. No patient in either group had evidence of inexcitable nerves prior to peak disability. In this series the lack of treatment with intravenous immunoglobulin or plasma exchange was not associated with intubation and mechanical ventilation.

Baseline and subsequent respiratory measures are summarized in Table 2. Patients requiring mechanical ventilation had lower baseline VCs (P = .007) on hospital admission, lower baseline PImax (P = .01), and lower baseline PO2 (P = .01) compared with patients who did not receive mechanical ventilation. In addition, patients requiring ventilation were more likely to have a VC decrease to lower than 20 mL/kg at some stage following admission (P < .001) or a reduction in VC of at least 30% from baseline (P < .001). They were also more likely to have a reduction from baseline by 30% in PImax (P = .002) and PEmax (P = .003). Additionally, PImax less than 30 cm H2O and PEmax less than 40 cm H2O were strongly associated with eventual requirement for ventilation (P < .001 and P = .007, respectively).

We also analyzed the temporal patterns of decline in VC. Of 32 patients with severe GBS who received mechanical ventilation for whom complete data were available, 23 had a greater than 30% decline in VC. Fifteen patients experienced a rapid decompensation (over < 24 hours) whereas 8 patients were noted to have a more gradual decline (over > 24 hours) in VC. Nine patients had no appreciable decline prior to intubation. Three of these patients had an initial VC less than 20 mL/kg and were intubated soon thereafter. The other 6 patients were intubated for airway protection because of bulbar weakness or significant hypoxia related to superimposed pneumonia. Of the 42 patients with severe GBS who did not receive mechanical ventilation for whom comprehensive data were available, 36 (86%) had either no decline or an improvement in their serial VC measurements during the course of their admission. Only 6 patients had a decline in VC. All but 1 had an absolute VC greater than 20 mL/kg at their nadir. Forty-eight percent of patients were intubated between the hours of 6 PM and 8 AM, although most of these seemed to be semielective procedures. Urgent (“crash”) intubation, necessitated by respiratory or cardiac arrest or extreme respiratory distress, occurred in 16% of patients. Radiographic abnormalities on chest x-ray films were more commonly seen in patients who required ventilation (49% of the patients who received ventilation vs 29% of the patients who did not receive ventilation, P = .06). Patients usually had a combination of radiographic abnormalities including pulmonary infiltrates, atelectasis, and pleural effusion. These were often multifocal in distribution without any preponderance of right lower lobe changes despite the high frequency of significant bulbar weakness and risk for aspiration.

Clinical and respiratory features found to be predictive on univariate analysis were included in the model for multivariate analysis. Owing to missing more than 25% of the data, PO2 and the percentage of reduction variables for VC, PImax, and PEmax were excluded from the
The presence of bulbar dysfunction ($P < .001$) and having a VC less than 20 mL/kg at some time during hospitalization ($P < .001$) were found to be independently predictive of the requirement for mechanical ventilation. Odds ratios and 95% confidence intervals for these predictors are given in Table 3.

Results from the analysis on the data that included only the patients with complete data (ie, patients with missing data were omitted, missing data were not imputed) were comparable (bulbar dysfunction, $P < .001$; VC $< 20$ mL/kg, $P < .001$). Owing to missing data, the effective total sample size for this analysis was reduced to only 68 patients. The proportion of patients omitted from this analysis in the group who received mechanical ventilation was significantly higher compared with the group who did not receive mechanical ventilation (33 patients who received ventilation and 13 patients who did not receive ventilation, $P = .001$).

The results of our study suggest that a decline in neuromuscular respiratory function and progression to mechanical ventilation should be anticipated in patients with severe GBS who have bulbar dysfunction or a VC of less than 20 mL/kg. The presence of bilateral facial palsy, autonomic dysfunction, and rapid disease progression were also associated with an increased likelihood of mechanical ventilation. Upper limb paralysis was identified in a higher proportion of patients who subsequently received mechanical ventilation, but this did not reach statistical significance. Patient-dependent factors such as age and the presence of preexisting chronic pulmonary disease did not predict the progression to mechanical ventilation.

Our study confirms that serial measurements of respiratory factors are an important component of the assessment of patients with severe GBS and clearly contribute to respiratory management.7,11,15 Chevrolet and Deleamont11 studied serial VC in 10 patients, 5 of whom received mechanical ventilation. They identified that a decline in VC of 50% from baseline was associated with subsequent ventilation within 36 hours and a drop in VC to an absolute value less than 1 L was associated with ventilation within 18 hours. Conversely, the serial VC measurements were stable and greater than 40 mL/kg in all patients who did not receive mechanical ventilation.11 Our findings are comparable, but on detailed analysis of day-to-day changes we found that a 30% reduction in VC, Pmax, or PEmax was highly correlated with
a subsequent progression to respiratory failure and intubation. In addition, certain “threshold” respiratory values were identified that indicate that progression to respiratory failure was highly likely to occur. These were as follows: VC less than 20 mL/kg, Pmax less than 30 cm H2O, and PEmax of less than 40 cm H2O. The use of these data (“20/30/40 rule”) may allow identification of patients at risk of respiratory failure early and the institution of preemptive measures such as admission to the ICU. This may avoid waiting until critical values are reached where respiratory failure is established and urgent intubation under suboptimal circumstances is necessary. A proposed guideline for the use of clinical data and respiratory function tests in the management of GBS is shown in the Figure.

Serial measurement of respiratory factors revealed the following 3 patterns: gradual decline (>30% reduction in VC over >24 hours), rapid decline (>30% reduction in VC in <24 hours), and no decline. The vast majority of patients (86%) without a decline in VC did not require ventilation. The patients who received mechanical ventilation but who did not have a decline in VC were primarily intubated for bulbar weakness and airway protection or because of low baseline respiratory function test results. No clinical features predicted those at risk of a decline in VC. However, gradual decline should allow elective intubation. Rapid decompensation, which occurred in a significant number of patients, was only detected by serial measurements combined with clinical examination. Because rapid decompensation can occur, even in those with a seemingly predictable course, ICU admission should be considered when the above threshold respiratory values are reached, or if there is significant bulbar weakness. The optimal frequency of VC measurement was not specifically addressed by this study. However, we believe it is reasonable to recommend that respiratory function tests be performed at least 3 times daily during the period of disease progression to enable detection of significant decline. If values are low, the tests should be repeated, ensuring full patient cooperation, prior to any major change in management. The frequency of monitoring is in accord with that used by Chevrolet and Deleamont. More frequent measurements may result in unnecessary fatigue.

Nocturnal decompensation was frequently seen and resulted in semielective intubation either late at night or in the early morning hours in a significant proportion of these patients. This most likely was due to a combination of poor pulmonary mechanics while the patient was in the supine position, which can result in up to 50% reduction in VC, and impairment of central respiratory drive. There was no correlation between long-term outcome and urgency of intubation but whether any short-term morbidity occurs remains to be determined.

Noninvasive methods of respiratory support such as continuous or bilevel positive airway pressure have a limited role in patients with severe GBS with borderline pulmonary mechanics. In patients with bulbar weakness, the use these modalities is particularly limited as upper airway collapse may significantly increase airway resistance. Additionally, continuous positive airway pressure does not provide any airway protection from secretions that are often difficult for these patients to control. The use of these measures to prevent nocturnal decompensation in patients without bulbar dysfunction and relatively preserved VC may warrant further study.

We acknowledge that the amount of missing respiratory data is potentially a limitation of this study. However, the subgroup of patients with comprehensive data available were representative of the group as a whole as suggested by the comparability with the imputed data. Analysis of the contribution of electrophysiologic variables in predicting progression to respiratory failure was also limited by the amount of missing data. Low CMAP and more recently inexcitable nerves have been associated with an ad-

Table 3. Multivariate Predictors of Mechanical Ventilation

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds Ratio*</th>
<th>Estimate</th>
<th>95% Confidence Interval</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bulbar dysfunction†</td>
<td></td>
<td>1.0</td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>No</td>
<td></td>
<td>17.5</td>
<td>5.2-59.1</td>
<td></td>
</tr>
<tr>
<td>Vital capacity, mL/kg</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>≥20</td>
<td></td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td></td>
<td>15.0</td>
<td>4.1-54.5</td>
<td></td>
</tr>
</tbody>
</table>

*From a multivariate logistic regression analysis with mechanical ventilation (yes vs no) as the dependent variable and factors in Tables 1 and 2 with univariate P values less than .10 included as independent variables. Odds ratio refers to the odds of requiring mechanical ventilation. For each predictor, an odds ratio of 1.0 is used to indicate the reference group. Results are based on the imputed data analysis for missing data values. Ellipsis indicates not applicable.

†Includes the presence of impaired gag reflex, dysphagia, or clinical history of dysphagia.
verse outcome, but these have not been evaluated specifically in regard to predicting ventilation. Inexcitable nerves were eventually detected on subsequent electromyograms, after intubation, in 7 patients who received mechanical ventilation. None of the patients who did not receive mechanical ventilation developed inexcitable nerves at any stage. Evaluation of phrenic nerve conduction and diaphragmatic electromyograms have been shown to predict the need for ventilation, but this technique is not universally available and was performed prior to ventilation in very few of our patients. Bifacial palsy occurred in more than 50% of our patients and could have confounded measurement of pulmonary function tests. However, because the decisions for intubation were based largely on the interpretation of serial measurements in the same patient, a poor seal, if any, should not be a major factor. Intubation remains an arbitrary decision, based on multiple factors and important clinical considerations including physician experience and comfort level, which would not have been recorded in the medical records, and cannot be assessed by this study. The finding that a low VC or bulbar dysfunction was associated with a high likelihood of progression to respiratory failure should be analyzed in the context of the study design. Both of these are reasons to intubate and are, therefore, inextricably linked to the institution of mechanical ventilation. Nevertheless, the findings identified in our study can be used in early management decisions in patients with GBS. Moreover, this study has also demonstrated that a 30% reduction in respiratory factors and certain threshold values were associated with subsequent intubation. These values may provide early warning signs of significant respiratory decline, which are independent of values that necessitate intubation, allowing opportunity for intervention or closer observation.

While no single factor can be established that encompasses all patients, our data can be synthesized as follows: an admission VC or fall in VC to less than 20 mL/kg, a decrease of VC, Pimax, and/or Pemax more than 30% from baseline and evidence of bulbar dysfunction should alert the physician that progression to respiratory failure is highly likely to occur. The presence of these factors alone or in combination may not necessitate immediate support with mechanical ventilation but may be used in the decision to admit the patient to the ICU and prepare for elective intubation. Regular assessment of the patient with these simple bedside measurements should continue until a clear and sustained improvement is observed.

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Corresponding author: Eelco F. M. Wijdicks, MD, Department of Neurology, Mayo Clinic–WBA, 200 First St SW, Rochester, MN 55905 (e-mail: wijde@mayo.edu).

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