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Review Article

Respiratory Dysfunction in Guillain-Barré Syndrome

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Abstract

Guillain-Barré Syndrome is the leading cause of nontraumatic acute paralysis in industrialized countries. About 30% of patients have respiratory failure requiring intensive care unit (ICU) admission and invasive mechanical ventilation. Progressive weakness of both the inspiratory and the expiratory muscles is the mechanism leading to respiratory failure. Aspiration pneumonia and atelectasis are common consequences of the bulbar muscle weakness and ineffective cough. The classical signs of respiratory distress occur too late to serve as guidelines for management, and measurements of vital capacity and static respiratory pressures are useful to determine the best times for starting and stopping mechanical ventilation. Several factors present at admission and during the ICU stay are known to predict a need for invasive mechanical ventilation. They include rapidly progressive motor weakness, involvement of both the peripheral limb and the axial muscles, ineffective cough, bulbar muscle weakness, and a rapid decrease in vital capacity. Specific treatments (plasma exchange and intravenous immunoglobulins) have decreased both the number of patients requiring ventilation and the duration of ventilation. The need for mechanical ventilation is associated with residual functional impairments, although all patients eventually recover normal respiratory muscle function.

Key Words: Guillain-Barré Syndrome (GBS); vital capacity; maximal inspiratory pressure; maximal expiratory pressure; plasma exchange; intravenous immunoglobulin.

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Introduction

Since the disappearance of poliomyelitis, Guillain-Barré Syndrome (GBS) has become the leading cause of acute nontraumatic paralysis in industrialized countries, with an incidence ranging from 0.4 to 4 per population of 100,000 *(1)* Respiratory failure is the main complication of GBS and often develops insidiously, so that waiting for signs of respiratory distress to initiate treatment may compromise the patient's chance of survival. Thus, specific monitoring measures must be taken to ensure prompt detection of criteria indicating a need for mechanical ventilation (MV) *(2,3)*, which occurs in about 30% of patients *(4)*. In the individual patient, no criteria reliably predict the durations of the progression and plateau phases of muscle weakness, the time to recovery, or whether and when MV may be required. The mortality rate has been estimated at 5% *(5)* and is higher in patients given MV *(6–8)*. Mortality and complication rates decreased when intensive care unit (ICU) management and MV were first introduced for the management of GBS, and further progress has been achieved recently with the use of specific treatments such as plasma exchange (PE) and intravenous immunoglobulins *(9,10)*. This article focuses on the characteristics, management, complications, and prognosis of respiratory failure associated with GBS.

Mechanisms Underlying Respiratory Failure in GBS

GBS causes progressive respiratory muscle weakness involving both the inspiratory and the expiratory muscles. The weakness of the diaphragm is thought to be caused by phrenic nerve demyelination. The respiratory pattern is restrictive, as expected in a neuromuscular disease: vital capacity (VC) and total lung capacity (TLC) are diminished, the residual volume (RV) usually is normal or increased, and the RV/TLC ratio is often high in the absence of airway obstruction *(11)*. Transdiaphragmatic pressure (Pdi) and static maximal inspiratory mouth pressure (PImax) are decreased; low static maximal expiratory mouth pressure (PEmax) indicates expiratory muscle failure, whereas a normal PEmax with a low PImax suggests isolated diaphragmatic weakness *(11)*. Static lung volumes and Pdi cannot be readily measured at the bedside, but paralysis of the diaphragm or other inspiratory muscles can be detected easily and noninvasively based on a decrease in VC with a decrease in PImax. The decrease in inspiratory capacity caused by paralysis of the abdominal and intercostal muscles impairs the ability to clear airway secretions by coughing, so that airway obstruction occurs, manifesting as atelectasis. Impaired swallowing caused by facial and oropharyngeal weakness leads to aspiration pneumonia *(12)*. All these pathophysiological mechanisms usually act in combination to produce respiratory failure and alveolar hypoventilation with hypercarbia, hypoxemia, and respiratory acidosis. Noninvasive mechanical ventilation (NIMV) is generally inadequate, and, therefore, MV must be used *(12–14)*.

Clinical Aspects

GBS usually runs an uninterrupted course through four phases: a preceding phase corresponding to the delay between a preceding illness and the first signs of GBS, a phase of progressive weakness lasting less than four weeks, a plateau phase, and a recovery phase *(15)*. Rapidly progressive forms may cause quadriplegia and a need for MV within 48 hours *(6)*. An ascending pattern of weakness is the rule, with the lower limbs being affected initially, then the upper limbs, and, finally, the cranial nerves; an inability to lift the head off the bed indicates severe disease *(3)*. However, initial involvement of the cranial nerves followed by descending paralysis is also possible. Bulbar weakness is common and manifests as a nasal voice, difficulty swallowing, reduced soft palate mobility, or facial palsy on one or both sides. The severity of respiratory muscle weakness is correlated with both the severity of limb weakness *(16)*, and the pace of progression of muscle weakness *(3)*. The degree of weakness may vary across respiratory muscles, and limb weakness may not be well-correlated with diaphragm weakness *(17)*.

Pain and sensory abnormalities are common and may precede or coincide with motor loss. The sensory disturbances are usually subjective, but impairments in superficial and deep sensation may be noted *(18)*.

Dysautonomia is a dreaded manifestation of GBS. Dysautonomia is most prominent in patients with profound muscle weakness and respiratory failure and occurs during the progression phase of the disease. Hypertension, hypotension, bradycardia (most notably during tracheal aspiration), and bladder dysfunction are the most common manifestations *(19–22)*.

Early detection of respiratory failure is among the main challenges raised by the management of GBS. Careful monitoring by an experienced team of nurses and physicians is crucial. The classic signs of respiratory failure occur late, and the early manifestations consist only of tachypnea, tachycardia, air hunger, broken sentences, and a need to pause between sentences; later, use of the accessory respiratory muscles, paradoxical breathing, and orthopnea indicate severe diaphragmatic weakness *(14)*.

Rate of Occurrence of Respiratory Failure in GBS (Table 1)

Respiratory Failure Rates in Epidemiological Studies

The percentage of patients requiring MV varies across populations. In a prospective epidemiological study from Sweden, respiratory failure occurred in about 6% of patients, but the population covered the entire spectrum of GBS *(23)*, with some patients having mild patterns that usually do not require ICU admission; in addition, patients with extremely severe disease may have been excluded. In epidemiological studies from England, 25 *(24)* and 23% *(25)* of patients required MV, respectively, and the mean duration of MV was 19 days *(24)*.

Respiratory Failure Rates in Therapeutic Trials

In the large trials done to investigate PE and intravenous immunoglobulins, MV was required in 12 *(26)* to 51% of patients *(8)*. In the studies conducted by the Guillain-Barré Syndrome Study Group in North America *(27)* and the French Cooperative Group on Plasma Exchange in Guillain-Barré Syndrome in France *(28)* to compare supportive treatment with PE, MV was used in 44 *(27)* and 37% *(28)* of patients, respectively. In another study by the French Cooperative Group *(29)*, 30% of the 556 patients were receiving MV at study inclusion and the proportion of patients on MV increased with disease severity. Pooling the populations in the two French Cooperative Group studies *(28,29)* showed that among patients who were not on MV at inclusion, 43% required MV, and median time from inclusion to MV was 2 days and the median duration time of MV was 21 days *(3)*. In the study by van der Meche and Schmitz comparing PE to intravenous immunoglobulins, 19% of patients were on MV at inclusion, and among the remaining patients, 27% in the intravenous immunoglobulin group and 42% in the PE group required MV for a mean duration of 43 and 50 days, respectively *(30)*. In a trial comparing PE, intravenous immunoglobulin, and PE followed by intravenous immunoglobulin, only 12% (range: 9.9–15.6%) of patients were on MV at study inclusion, and 16.4–23.1% of the remaining patients subsequently required MV for a median of 18 to 29 days *(26)*. The relatively low MV rates in this study may be ascribable to the sizeable number of patients with milder forms of GBS as assessed by the VC values in the various treatment groups (2.3–2.4 L). In a comparison of 3 versus 6 days of intravenous immunoglobulin treatment, 51% of patients required MV, but the study included only patients with severe disease and a contraindication to PE. In a study of methylprednisolone, 34% of the patients received MV, and the median time on ventilation was 18 days in the methylprednisolone group and

Table 1
Percentage of Patients With GBS Who Required Mechanical Ventilation in Epidemiological Studies and Therapeutic Trials

Studies	*Percent of patients on MV*	*Duration of MV*
Cheng et al. *(23)*	6%	ND
Winer et al. *(25)*	23%	ND
Rees et al. *(24)*	25%	19 days
GBS Study Group *(27)*	44%	27 (PE) to 33 (placebo) days if ventilated before randomization 9 (PE) to 23 (placebo) days if ventilated after randomization
French Cooperative Study Group *(28)*	At randomization: 37% After randomization: 21.4%, PE group 42.6%, placebo group	ND
French Cooperative Study Group *(29)*	At randomization: 30% 2–13%, mild GBS 26–28%, moderate GBS 100%, severe GBS	 15–37 days, moderate group 34–43 days, severe group
Sharshar et al. *(3)*	43% after randomization	21 days
Dutch GBS Study Group *(30)*	At randomization: 1% After randomization: 27%, intravenous immunoglobulin group 42%, PE group	 43.3 days, intravenous immunoglobulin group 50 days, PE group
PE/Sandoglobulin GBS Trial Group *(126)*	At randomization: 12% After randomization: 22.3%, intravenous immunoglobulin group 23.1%, PE group 16.4%, intravenous immunoglobulin + PE group	 26 days, intravenous immunoglobulin group 29 days, PE group 18 days, intravenous immunoglobulin + PE group
Raphael et al. *(8)*	At randomization: 51%	33 days, intravenous immunoglobulin 3 days 28 days, intravenous immunoglobulin 6 days
GBS Steroid Trail Group *(31)*	At randomization: 18.5%, steroid group 18.6%, placebo group	 18 days, steroid group 27 days, placebo group

Abbreviations: GBS, Guillain-Barré Syndrome; MV, mechanical ventilation; ND, not documented; PE, plasma exchange.

27 days in the placebo group; however, PE was used according to each study center's usual protocol, which may have influenced the duration of MV *(31)*. The differences across study results can be ascribed to differences among study populations. For example, the French studies *(8,28,29,32)*, were done in patients admitted to ICUs for GBS, whereas the studies from the Netherlands, England, and North America *(9,10,26,27,30,31,33)* included both patients from the ICU and the neurological ward.

Respiratory Failure Rates According to the Cause of GBS

Among infectious diseases associated with GBS, *Campylobacter jejuni* infections are the most common *(34)* and are usually associated with worse outcomes *(35)*. In the epidemic that occurred in northern China, 31% of patients required respiratory support *(36)*. Cytomegalovirus (CMV) ranks second among infections associated with GBS *(34)* In a study comparing CMV-associated GBS, *Campylobacter*-associated GBS, and unexplained GBS, the patients in the CMV group were younger and more likely to have sensory symptoms and cranial nerve involvement, as compared to the other groups; they were also more likely to require MV (65%), but the difference was not quite significant in statistical tests *(37)* CMV infection also was associated with a longer time to recovery *(38)*.

Factors Predicting Respiratory Failure in GBS

Clinical Factors

Except for etiologies, clinical factors that predict respiratory failure in GBS have received little research attention (Table 2). In one study *(6)*, rapid disease progression with quadriplegia within 2 to 5 days was a risk factor for MV, with a mean duration greater than 49 days and a need for tracheostomy in 32% of patients. In a prospective study by Chevrolet and Deleamont *(13)*, VC and peak expiratory flow were monitored in 10 patients admitted to an ICU for GBS. Five patients required MV. A 50% decrease in VC was associated with a need for MV within the

Table 2
Factors Predicting a Need for Mechanical Ventilation

Predictors of MV at ICU admission	
Without VC measurement (MV >85% if four criteria are present)	*Odds ratio (95% confidence interval)*
Onset to admission less than 7 days	2.51 (1.68–3.77)
Inability to cough	9.09 (4.00–20.00)
Inability to stand	2.53 (1.40–3.30)
Inability to lift the elbow	2.99 (1.80–4.97)
Inability to lift the head	4.34 (2.70–6.66)
Liver enzyme increase	2.09 (1.38–3.17)
With VC measurement (MV >85% if all three criteria are present)	*Odds ratio (95% confidence interval)*
Onset to admission less than 7 days	5.00 (1.42–5.68)
Inability to lift the head	5.00 (1.92–12.50)
VC less than 60% of predicted	2.86 (2.43–10.00)
Predictors of MV during the ICU stay	*Odds ratio (95% confidence interval)*
Bulbar dysfunction	17.5 (5.2–59.1)
VC less than 20 mL/kg	15.0 (4.1–54.5)
Electrophysiological findings	
Low amplitude and negative peak area on phrenic nerve conduction	

Abbreviations: MV, mechanical ventilation; ICU, intensive care unit; VC, vital capacity.

next 36 hours, and a decrease in VC to less than 1 L was associated with a need for ventilation within the next 18 hours. The five patients who required MV had a VC of 15 mL/kg body weight, whereas in the other five patients, VC remained stable and greater than 40 mL/kg *(13)*. In a retrospective study of 114 patients with GBS, a VC lower than 20 mL/kg, PImax lower than 30 cm H_2O, PEmax lower than 40 cm H_2O, or VC decrease greater than 30% was associated with progression of respiratory failure *(2)*. Bulbar dysfunction was also an independent risk factor for respiratory failure in this study *(2)*. Cranial nerve involvement was more common in children who required MV *(39)*. In a recent study pooling the patients included in two large prospective studies of PE and including 722 nonventilated patients in all, Sharshar et al. *(3)* identified six factors present at admission that were also independently predictive of MV by multivariate analysis: time from onset to admission less than seven days, inability to cough, inability to stand, inability to lift the elbows, inability to lift the head, and liver enzyme elevation.

When VC values were available, a time from onset to admission of less than seven days and an inability to left the head combined with a VC of less than 60% of the predicted value were associated with subsequent MV (Table 2). MV was required in up to 85% of the patients with four or more of the variables in the multivariate model without VC or with all three variables in the multivariate model including VC *(3)*. In this study, bulbar dysfunction at admission was not a risk factor for MV, whereas in an earlier study *(2)*, the development of bulbar dysfunction and bilateral facial weakness during the ICU stay was associated with worsening respiratory failure.

Laboratory Test Factors

Liver enzyme elevation was among the factors predicting MV in the study by Sharshar et al. *(3)*. Liver enzyme elevation is found in about 25% of patients with GBS *(40)* but is uncommon in those with *C. jejuni* infection *(41,42)*, and the role of viral agents such as CMV in the pathophysiology of acute demyelinating neuropathy needs further investigation.

Electrophysiological Factors

Prognostic information concerning patient outcome can be deduced from computation of the mean of the summed motor-evoked compound muscle action potential (CMAP) amplitudes from distal stimulation. Prior studies showed that a mean CMAP of less than 10 to 20% from all motor nerves studied correlates with a poorer prognosis overall, but their association with need for mechanical ventilation has not been assessed *(3,43,44)*.

In a recent electrophysiological study, 60 consecutive patients with GBS who were admitted to the ICU underwent standard electrophysiological testing. Patients were classified according to Hadden's criteria *(45)*, and physicians who were unaware of the electrophysiological findings determined whether MV was needed. The proportions of patients with demyelinating, equivocal, and axonal electrophysiology were comparable to previous studies *(45)*. Patients with primary demyelination had worse disability and arm grades and lower VC values. Overall, one-third (20 of 60) of patients required MV within 20 days of EMG; however, 46% of patients with primary demyelination required MV as compared to only 17% of patients in the equivocal group and no patients in the axonal group *(46)*. The importance of patients with primary demyelination, rather than equivocal or axonal, electrophysiologic features could be explained by the early testing of the electromyogram (EMG) (within 72 hours of admission) and neurophysiological features can change over the time in a given patient.

Electrophysiological studies of the phrenic nerve have shown abnormalities in latency, amplitude, duration, and area of the diaphragmatic CMAPs in patients with GBS, as compared to controls. Low median motor amplitudes and

decreased amplitude of CMAPs and negative peak area were correlated with MV. The reductions were about twofold as compared to normal subjects, but were small compared to nonventilated patients with GBS and yielded values close to the lower end of the normal range *(47)*.

Monitoring and Managing Respiratory Failure in Patients With GBS

Detecting Respiratory Failure

Delaying MV until hypercarbia occurs leads to emergent endotracheal intubation and may increase the rate of life-threatening complications such as aspiration pneumonia and respiratory arrest *(2)*. Respiratory failure in GBS results from mechanical failure, as opposed to parenchymal or airway disease. Therefore, hypoxemia and hypercarbia occur late and indicate severe respiratory muscle weakness with impending respiratory arrest. Furthermore, normal blood gas values do not exclude respiratory muscle weakness *(5,6,13)*.

Thus, other tools are needed to ensure early detection of respiratory failure in GBS. Among them, repeated VC measurements and determination of PImax and PEmax are useful for managing respiratory failure in GBS *(3,5,13,48)*. VC measurement is highly standardized and reproducible and has an additional advantage in that validated reference values are available. VC is sensitive for monitoring the course of moderate-to-severe respiratory muscle weakness. However, VC lacks specificity for the diagnosis of respiratory muscle weakness and, in patients with mild weakness, VC is less sensitive than PImax/PEmax *(11)*. All VC measurements at the bedside must be done in the same positions: the supine position and the 45° semirecumbent position. Similarly to other neuromuscular diseases, a VC drop between the supine and the semirecumbent positions indicates diaphragmatic failure, and a 30% or greater decrease generally is associated with severe diaphragmatic weakness *(49)*. PImax and PEmax measurement is a simple way to gage inspiratory and expiratory muscle strength. The results reflect the pressure generated by both the respiratory muscles and the passive elastic pressure of the chest wall and lung. PImax usually is measured at the RV and PEmax at TLC; both are measured using a flanged mouthpiece *(11)*.

Because VC and PImax/PEmax are linked by a curvilinear relationship, one of these three measures can be used to predict the other two *(11)*. A discordance between the pressure values and the VC values should suggest a technical problem or a parenchymal abnormality such as atelectasis or pneumonia.

MV is required in patients with evidence of respiratory distress (Table 3; i.e., impairment of consciousness, tachypnea >30/minute or bradypnea, use of accessory respiratory muscles and paradoxical breathing, shock, or cardiac arrhythmia). However, because these abnormalities occur late in patients with GBS at a stage when respiratory arrest is imminent *(14)*, every effort must be made to start MV before they develop. Blood gas abnormalities indicate a need for MV. It has been suggested that even in the absence of signs of respiratory distress, major criteria for MV include hypercarbia (carbon dioxide partial pressure in arterial blood [$PaCO_2$] > 6.4 kPa), hypoxemia (oxygen partial pressure in arterial blood [PaO_2] < 7.5 kPa on room air) and VC less than 15 mL/kg. Inefficient cough, impaired swallowing, and atelectasis may serve as minor criteria. MV ventilation may be required in patients with at least one major criterion or at least two minor criteria *(5,14)*. Absolute values of PImax less than 25 cm H_2O and of PEmax leass than 40 cm H_2O also have been proposed as criteria for MV *(14)*.

Table 3
Signs of Respiratory Distress

Early signs	*Late signs*
Tachypnea	Bradypnea
Tachycardia	Cardiac arrhythmias
Air hunger	Loss of consciousness
Interrupted speech	Respiratory arrest
Paradoxical breathing	
Use of accessory muscles	

Mechanical Ventilation

Although MV is the reference standard for managing patients with GBS in the ICU, the role for noninvasive mechanical ventilation (NIMV) needs to be defined. NIMV may be unsafe in patients with impaired swallowing, ineffective cough, dysautonomia, and rapidly declining values of VC or PImax/PEmax *(2,13,50)*. The total duration of ventilatory support for GBS is unpredictable in the individual patient. Total prolonged paralysis of the respiratory muscles occurs in some patients, and NIMV is difficult to handle in this situation.

Endotracheal intubation in patients with GBS and respiratory failure carries major risks. Dysautonomia can induce severe hypotension or cardiac arrhythmias associated with the use of sedatives. Depolarizing agents used for neuromuscular blockade can induce severe hyperkaliemia in patients with paralysis. On the other hand, nondepolarizing agents can increase the neuromuscular deficit and delay recovery. Blind nasal intubation has been suggested, because this method requires only topical anesthesia of the upper airways and is performed while the patient is awake and breathing spontaneously *(51)*. Although nasal intubation is more comfortable for patients who have to stay on the ventilator for a long time, it is associated with nosocomial sinusitis and pneumonia *(52)*.

Tracheostomy

Tracheostomy is more comfortable for patients than oro- or nasotracheal intubation, because it permits oral hygiene and speech and also facilitates weaning off the ventilator. However, tracheostomy is an invasive procedure associated with complications and a residual unbecoming scar *(51)*. The optimal time for performing tracheostomy is not known *(53)*. Early tracheostomy may be unnecessary in patients who experience a prompt improvement allowing rapid successful extubation, and late tracheostomy may increase the rate of complications associated with the tracheal tube, such as tracheal stenosis or tracheomalacia. When prolonged ventilatory support is needed, tracheostomy is often considered after three weeks *(54)*. Tracheostomy is needed in patients with factors that predict prolonged ventilatory assistance or weaning problems, namely, older age or underlying pulmonary disease *(55)*. Lawn and Wijdicks *(56)* sought to determine whether a composite lung function indicator (PF score) based on summation of the VC (mL/kg), PImax (cm H_2O), and PEmax (cm H_2O) could be used to predict a need for ventilation of more than 3 weeks and,

consequently, a need for tracheostomy. This score represented a comprehensive assessment of neuromuscular pulmonary function. In this study, if the ratio of the PF score on day 12 divided by the PF score from the day of intubation was less than one, the need for prolonged ventilation was predictable with a specificity and positive predictive value of 100% *(56)*.

Complications

The total duration of MV in patients with GBS often exceeds 3 weeks, even when specific treatments are given *(8,27–29,56)* Preventing complications and delivering careful nursing care are essential. Special attention is needed to minimize the risk of ventilator-associated pneumonia: the patient's head should be elevated at 30°, continuous enteral feeding should be started early, and the residual gastric volume should be measured every 6 hours *(51)*. Gastroprotective therapy is recommended only in patients at high risk for gastrointestinal bleeding *(57)*. Posture therapy and chest physiotherapy are highly effective in preventing atelectasis and pneumonia *(58)*.

Morbidity is linked to severity of the disease and use of treatments. Respiratory complications are the main source of morbidity in patients with GBS admitted to the ICU. In a retrospective study of 114 patients, the respiratory complication rate was 59%. Tracheobronchitis and pneumonia occurred in 45% of patients, pulmonary embolism in 3%, and pneumothorax in 4% *(59)*. In a French multicenter study comparing different numbers of PE procedures, pneumonia occurred in 22 to 28% of the patients who were unable to walk and in 60 to 74% of the patients requiring MV; pneumonia was more common among the patients with the highest number of PE procedures *(29)*. In the same study, intubation-related complications occurred in 3 to 7% of patients and pulmonary embolism occurred in 1 to 3%, with no differences among groups. Ventilator-associated pneumonia is the leading primary event responsible for death in patients with GBS managed in the ICU, with underlying pulmonary disease being an additional risk factor *(60)*. The risk of ventilator-associated pneumonia should be carefully evaluated before choosing a treatment by PE, because a fatal case of pneumonia after PE treatment has been reported in a patient with GBS *(28)*. Other complications associated with PE include systolic blood pressure instability (which increases with the number of PE procedures), bradycardia, and infectious complications. The main indirect complications related to PE are events related to vascular access, such as hematomas, venous thrombosis, and pneumothorax after subclavian venous catheterization *(27–29,61)*. The main reported side effects of intravenous immunoglobulin are dyspnea, fever, flu-like symptoms, hypotension, nausea, and possible myocardial infarction *(8,26,30)*. Acute renal failure has not been reported, even with high doses of intravenous immunoglobulin *(62)*, but exacerbation of chronic renal failure has occurred *(10)*. Liver enzyme elevation has been reported after infusion of intravenous immunoglobulin *(30,40)*.

Weaning

The optimal time for starting to wean the patient off the ventilator is not easily determined. In contrast with other ICU patients, patients with GBS require gradual weaning, and extubation must be put off until respiratory muscle strength is sufficiently recovered. Bulbar dysfunction may require a return to MV even after successful weaning and extubation. Chevrolet and Deléamont *(13)* started the weaning process when VC rose above 7 mL/kg, using a T-piece to alternate between periods on the machine and increasingly long periods of spontaneous breathing. The total time on spontaneous breathing increased in parallel with the increase in VC. An algorithm for predicting the maximal time on spontaneous breathing was developed. In this study, the patients were extubated when their VC exceeded 15 mL/kg of their body weight and they were able to breathe on their own for 24 hours *(13)*.

In a study on diaphragmatic performance in GBS and myasthenia gravis, diaphragmatic strength increased during the weaning period, and Pdi_{max} was a good predictor of respiratory recovery. Pdi and Pdi_{max} remained low even after weaning. Pdi_{max}, but not forced VC, was correlated with Pdi *(63)*. Pdi is a specific indicator of diaphragm contraction and is calculated as the difference between esophageal pressure (Pes) and gastric pressure (Pgas). Pdi_{max} is the maximal strength generated by the diaphragm *(11)*. Pes and Pgas are measured by inserting a double-balloon catheter through the nose and pharynx into the esophagus and stomach. The proximal balloon is in the esophagus and serves to measure Pes, whereas the distal balloon is used to measure Pgas. This method requires full and active participation of the patient, in particular for proper balloon placement and, consequently, is difficult to use in ICU patients. PImax has been suggested for weaning management in GBS *(19)* but is usually a poor predictor of successful weaning *(64)*.

Effect of Treatments in the ICU

PE and intravenous immunoglobulin modify the course of GBS and improve short-term and 1-year outcomes *(9,10)*. PE decreased the mean MV time by 24 days in the Guillain-Barré Syndrome Study Group trial *(27)* and also decreased the median MV time in those patients started on MV after study inclusion. In the French Cooperative Group Study *(28)*, PE was associated with a decreased risk of MV after study inclusion (42.6 versus 21.4%), with a faster recovery and a shorter time to weaning as compared to the controls (18 versus 31 days). In the study by the same group comparing different numbers of PEs in patients with mild, moderate, or severe GBS *(29)*, MV durations were similar in the patients with severe disease who had four and six PE procedures, whereas MV duration was significantly longer with two than with four PEs (37 versus 15 days) in the patients with moderate disease at inclusion but who experienced respiratory failure later on. In the trial by van der Meche and Schmitz *(30)* comparing PE and intravenous immunoglobulin, a difference was noted in the second week when 27% of patients given intravenous immunoglobulin and 42% of those given PE were on MV. In the Plasma Exchange/Sandoglobulin Guillain-Barré Syndrome Trial Group Study *(26)* comparing PE, intravenous immunoglobulin, and PE plus intravenous immunoglobulin, no differences were found across the groups regarding the proportions of patients requiring MV or the duration of MV, even when only those patients started on MV after randomization were considered. In the study comparing two durations of intravenous immunoglobulin therapy (3 versus 6 days) *(31)*, the proportions of patients started on MV after randomization and the

median time on MV were similar in the two treatment arms *(8)*. High-dose methylprednisolone had no effect on MV rates, MV durations, or VC values.

Long-Term Outcomes

Factors associated with poor functional outcomes of GBS are older age, a course shorter than 7 days, gastrointestinal illness, *C. jejuni* infection, evidence of axonal degeneration with diminished CMAPs, and a need for MV *(6,24,25,30,42,43,65)*. The median time to recovery of walking with assistance was 50 days in the first study regarding PE by the French Cooperative Group *(28)* and 56 to 60 days in the patients who received MV in the second study *(29)*. No patients were still on MV after 1 year. However, in a study of 1-year outcomes after ICU management *(7)*, mortality was 20% in the group that required MV and recovery was delayed in a sizeable proportion of the survivors; in addition, 7% of these patients were still on MV after 1 year. Univariate predictors of a poor 1-year outcome were older age, upper limb paralysis, longer MV duration, inexcitable nerves, transfer to a tertiary center more than two days after the primary admission, and a longer median time to peak disability. However, in the multivariate analysis, only age and delayed transfer were independently associated with poor 1-year outcomes *(7)*.

Conclusion

Respiratory failure occurs in about one-third of patients with GBS and is correlated with severe and rapidly progressive disease. The unpredictable course and potential for life-threatening complications require ICU admission. Postponing MV until the usual signs of respiratory distress develop may increase both morbidity and mortality. Early predictors of a need for MV have been identified; among them, six do and three do not require VC measurement. Patients suffering from GBS with any of these factors should be admitted to the ICU. The development of bulbar dysfunction, decreasing PImax or PEmax values, or a rapid decline in VC indicates a need for MV. Other criteria for MV should be sought. Studies are needed to investigate the influence of etiology on respiratory outcomes. Finally, whether electrophysiological testing can help to predict respiratory failure should be evaluated.

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