Clinical and electrophysiological predictors of respiratory failure in Guillain-Barré syndrome: a prospective study

Marie-Christine Durand, Raphaël Porcher, David Orlikowski, Jérôme Aboab, Christian Devaux, Bernard Clair, Djillali Annane, Jean-Louis Gaillard, Frédéric Lofaso, Jean-Claude Raphael, Tarek Sharshar

Summary

Background Respiratory failure is the most serious short-term complication of Guillain-Barré syndrome and can require invasive mechanical ventilation in 20–30% of patients. We sought to identify clinical and electrophysiological predictors of respiratory failure in the disease.

Methods We prospectively assessed electrophysiological data and clinical factors, including identified predictors of delay between disease onset and admission, inability to lift head, and vital capacity, in patients admitted with Guillain-Barré syndrome. We related these factors to subsequent need for ventilatory support. Neurophysiological findings were classified as demyelinating, axonal, equivocal, unexcitable, or normal. Predictive values of clinical and electrophysiological data were tested using classification trees to build up a predictive model. This model was initially built up in a two-third (fitting set) then validated in a one-third (validation set) of the total sample. The fitting and validation sets were randomly selected. We also assessed the predictive value of this model for disability at 6 months.

Findings From 1998, to 2006, 154 patients with Guillain-Barré syndrome were included in the study and 34 (22%) were subsequently ventilated. Demyelinating Guillain-Barré syndrome was more common in patients who went on to be ventilated than in those who were not (85% *vs* 51%, p=0·0003). Vital capacity and the proximal/distal compound muscular amplitude potential (p/dCMAP) ratio of the common peroneal nerve were retained in the tree model, with a probability of needing ventilation of less than 2·5% in patients with a ratio of greater than 55·6% and a vital capacity more than 81% of predicted. A p/dCMAP ratio of the peroneal nerve less than 55·6% and age older than 40 years were retained as independent predictors of disability at 6 months.

Interpretation Neurophysiological testing is helpful for assessing risk of respiratory failure, which is highest in patients with evidence of demyelination and very low in those without both 55·6% conduction block of the common peroneal nerve and a 20% reduction in vital capacity.

Lancet Neurol 2006; 5: 1021–28

Published Online November 2, 2006 DOI:10.1016/S1474-4422(06)70603-2

See Reflection and Reaction page 991

Functional Testing Department (M-C Durand MD, F Lofaso MD), **Medical Intensive Care Unit** (D Orlikowski MD, J Aboab MD, C Devaux, B Clair MD, D Annane MD, J-C Raphael MD, T Sharshar MD), **and Microbiology Department** (J-L Gaillard MD), **Raymond Poincaré Teaching Hospital, Garches, France; and Biostatistics and Medical Informatics, Saint-Louis Teaching Hospital, Paris, France** (R Porcher PhD)

Correspondence to: Tarek Sharshar, Hôpital Raymond Poincaré, Service de Réanimation Médicale, 104 Boulevard Raymond Poincaré, 92380 Garches, France **tarek.sharshar@rpc.ap-hop-paris.fr**

Introduction

Respiratory failure is the most serious short-term complication of Guillain-Barré syndrome[1–3] and invasive mechanical ventilation is required in 20–30% of patients.[1,4–6] Moreover, 60% of those who are intubated develop major complications, including pneumonia, sepsis, gastrointestinal bleeding, and pulmonary embolism.[1,2,7] Anticipation of respiratory failure is crucial to avoid respiratory distress and aspiration,[7] but also to triage patients to the appropriate unit (ward *vs* intensive care unit). Early predictors of the need for mechanical ventilation include time between onset of the disease and hospital admission of fewer than 7 days, inability to lift the head, presence of bulbar dysfunction, and vital capacity less than 60% of that predicted.[5,6] Additionally, anti-GQ1b antibodies are identified more frequently in patients with Guillain-Barré syndrome who require mechanical ventilation than in those who do not.[8] Despite those predictors, respiratory failure can still be difficult to anticipate. Electrophysiological testing might have a role in the prediction of respiratory failure, for example by examining the phrenic nerves.[9] However, we did not find that phrenic electrophysiology was helpful in the prediction of respiratory failure.[10] Nonetheless, we reasoned that standard electrophysiological testing might have some predictive value. This hypothesis was based on a previous finding that patients with demyelinating Guillain-Barré syndrome more frequently underwent mechanical ventilation than those with axonal disease.[11] We aimed to: 1) confirm in a large cohort that demyelinating Guillain-Barré syndrome is associated with an increased rate of mechanical ventilation; 2) develop a predictive electrophysiological model; 3) compare the predictive value of this electrophysiological model with a pure clinical model including validated clinical predictors; and 4) determine whether this electrophysiological model predicts disability at 6 months.

Methods

Patients

We gathered data prospectively for all adult patients referred to the intensive care unit of the Raymond Poincaré Teaching Hospital (Garches, France) if they fulfilled standard diagnostic criteria for Guillain-Barré syndrome,[12] had undergone complete electrophysiological testing, and were not mechanically ventilated before or within 24 h of electrophysiological testing. Patients were excluded if they had non-idiopathic Guillain-Barré

syndrome, Miller-Fisher syndrome, or if electrophysiological testing was done by a neurophysiologist other than the study neurophysiologist (MCD). Our ethics committee waived informed consent because electrophysical testing is routinely done and not taken into account in the decision for mechanical ventilation. Data management was performed in accordance with the French law *Loi informatique et liberté* (Loi 78–17). Part of this cohort was previously published in two studies.[10,11] 60 patients were enrolled in the first study,[10] which described neurophysiological differences between ventilated and non-ventilated patients. Ten additional patients were included in the second study,[11] which determined neurophysiological abnormalities of the phrenic nerves in patients with Guillain-Barré syndrome. Therefore, 84 new patients took part in our study.

	All groups (n=154)	Fitting group (n=103)	Validation group (n=51)
Age (years)	52 (19)	51 (17)	52 (21)
Women	78 (51%)	50 (49%)	28 (55%)
Diarrhoea	40 (26%)	25 (24%)	15 (29%)
GBS onset to admission (days)	5 (3–8)	5 (3–8)	5 (3–8)
Admission to inclusion* (days)	2 (1–3)	2 (1–3)	2 (1–3)
Disability grade >3†	83 (54%)	55 (53%)	28 (56%)
Arm grade >2‡	24 (16%)	14 (14%)	10 (20%)
Bulbar dysfunction	25 (16%)	15 (15%)	10 (20%)
Inability to lift head	43 (28%)	30 (29%)	13 (25%)
Pure motor	14 (9%)	6 (6%)	8 (16%)
CSF protein (g/L)	0·8 (0·5–1·3)	0·8 (0·5–1·3)	0·8 (0·5–1·3)
Liver dysfunction	32 (21%)	26 (25%)	6 (12%)
Positive serology for CJ§	26 (21%)	15 (19%)	11 (24%)
Positive serology for CMV§	20 (16%)	13 (16%)	7 (15%)
Negative serological test§	75 (59%)	48 (59%)	27 (59%)
No anti-ganglioside Ab¶	46 (55%)	29 (56%)	17 (53%)
VC (% of predicted value)	77 (21)	78 (20)	75 (23)
Subsequent MV	34 (22%)	23 (22%)	11 (22%)
Time from inclusion to MV (days)‖	2 (1–3)	2 (1–4)	1 (1–2)
Demyelinating electrophysiology	90 (58%)	63 (61%)	27 (53%)
Equivocal electrophysiology	37 (24%)	22 (21%)	15 (29%)
Axonal electrophysiology	10 (6%)	7 (7%)	3 (6%)
Plasma exchange	65 (42%)	48 (47%)	17 (33%)
IvIg	72 (47%)	46 (45%)	26 (51%)

Data are number (%), mean (SD), or median (IQR). GBS=Guillain-Barré syndrome. MV=mechanical ventilation. CSF=cerebrospinal fluid. CJ=*Campylobacter jejuni*. CMV=cytomegalovirus. Ab=antibodies. VC=vital capacity. IvIg=intravenous immunoglobulin. *Inclusion is time of electrophysiological testing; in all patients who required mechanical ventilation, the time from inclusion to MV was longer than 12 h. †Disability grade: 0=healthy, no signs or symptoms; 1=minor symptoms or signs and able to run; 2=able to walk 5 m across an open space without assistance; 3=able to walk 5 m across an open space with the help of one person and a waist-level walking-frame; 4=chairbound/bedbound, unable to walk as in 3; 5=requires assisted ventilation; 6=dead.[11] ‡Arm grade: 0=normal; 1=minor symptoms or signs but able to put hand on top of head when sitting with head upright and able to oppose the thumb to each fingertip; 2=able to do either of the tasks in 1 but not both; 3=some movements but unable to perform either of the tasks in 2; 4=no movement; 5=dead.[11] §Available in 84 (55%) patients, including 52 and 32 in fitting and validation set, respectively. ¶Decision for MV was based on presence of one major criterion or two minor criteria. Major criteria: 1) intolerable respiratory distress; 2) $PaCO_2$ >6·4 kPa; 3) PaO_2 <7·5 kPa breathing room air; and 4) VC of 15 mL/kg or less. Minor criteria: 1) inefficient cough reflex; 2) inability to clear bronchial secretions despite vigorous chest physiotherapy; 3) severe bulbar dysfunction defined as repeated coughing and aspiration after swallowing; and 4) atelectasis on a chest radiograph.[18] ‖Not available in 120 (78%) patients, including 80 and 40 in fitting and validation set, respectively.

Table 1: **Clinical and laboratory characteristics at inclusion**

Procedures

Inclusion was defined as the date of electrophysiological testing. The following data were recorded: 1) pre-Guillain-Barré syndrome events such as diarrhoea; 2) time from motor symptom onset to admission; 3) severity of muscle weakness assessed according to disability grade and arm grade[13] (table 1); 4) presence of sensory loss; 5) inability to lift the head, bulbar dysfunction, and facial palsy; 6) cerebrospinal fluid parameters; and 7) liver function tests. Slow inspiratory vital capacity was measured in triplicate with a spirometer (Morgan, UK), with the patient seated with the back reclined at 30° to 60°, wearing a noseclip, and breathing through a flange-type mouthpiece. Serum obtained at admission was studied for the presence of antibodies to *Campylobacter jejuni*, *Mycoplasma pneumoniae*, cytomegalovirus, and Epstein-Barr virus as well as for antibodies to the gangliosides GM1, GM2, GD1a, GD1b, and GQ1b.

Electrophysiological testing was done at inclusion by use of a NEUROPACK SIGMA electromyographic device (MESA Nihon Kohden). All electrophysiological tests were undertaken by the same experienced neurophysiologist (MCD) who was asked to communicate only whether the electrophysiological data lent supported to the diagnosis of Guillain-Barré syndrome. Compound muscle action potential (CMAP) after distal (d) and proximal (p) stimulation, conduction velocity (m/s), distal latency (ms), and F-wave latency (ms) were recorded in four motor nerves (median, ulnar, and right and left common peroneal nerves), as described elsewhere.[11] Electrophysiological data were classified according to Hadden and colleagues' definition[14] as primary demyelinating, primary axonal, unexcitable, equivocal, or normal. To allow identification of conduction block, dCMAP amplitude had to be at least 20% of the lower limit of normal.[14]

The decision to use mechanical ventilation was left at the discretion of the physician in charge of the patient. However, mechanical ventilation was used routinely in patients who met at least one major criterion or two minor criteria, as follows: major criteria, 1) intolerable respiratory distress, 2) $PaCO_2$ >6·4 kPa, 3) PaO_2 <7·5 kPa breathing room air, and 4) vital capacity of 15 mL/kg or less;[15–18] minor criteria, 1) inefficient cough, 2) inability to clear bronchial secretions despite vigorous chest physiotherapy, 3) severe bulbar dysfunction defined as repeated coughing and aspiration after swallowing, and 4) atelectasis on a chest radiograph.[15–18] Mechanical ventilation was always invasive.

The physicians who decided to start mechanical ventilation were unaware of the details of electrophysiological testing. In all patients who required the procedure, the time from inclusion to mechanical