

Causes and Outcomes of Acute Neuromuscular Respiratory Failure

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Objective: To identify the spectrum of causes, analyze the usefulness of diagnostic tests, and recognize prognostic factors in patients with acute neuromuscular respiratory failure.

Methods: We evaluated 85 patients admitted to the intensive care unit (ICU) at Mayo Clinic, Rochester, between 2003 and 2009 with acute neuromuscular respiratory failure, defined as a need for mechanical ventilation owing to primary impairment of the peripheral nervous system. Outcome was assessed at hospital discharge and at last follow-up. Poor outcome was defined as a modified Rankin score greater than 3.

Results: The median age was 66 years; median follow-up, 5 months. The most frequent diagnoses were myasthenia gravis, Guillain-Barré syndrome, myopathies, and amyotrophic lateral sclerosis (27, 12, 12, and 12 patients, respectively). Forty-seven patients (55%) had no known neuromuscular diagnosis before admission, and 36 of them (77%) had poor short-term outcomes. In 10 patients (12%), the diagnosis remained unknown on dis-

charge; only 1 (10%) had regained independent function. Older age was associated with increased mortality during hospitalization. Longer mechanical ventilation times and ICU stays were associated with poor outcome at discharge but not at the last follow-up. Patients without a known neuromuscular diagnosis before admission had longer duration of mechanical ventilation, longer ICU stays, and worse outcomes at discharge. Electromyography was the most useful diagnostic test in patients without previously known neuromuscular diagnoses. The presence of spontaneous activity on needle insertion predicted poor short-term outcome regardless of final diagnosis. Coexistent cardiopulmonary diseases also predicted poor long-term outcome.

Conclusions: Among patients with neuromuscular respiratory failure, those without known diagnosis before admission have poorer outcomes. Patients whose diagnoses remain unclear at discharge have the highest rates of disability.

Arch Neurol. 2010;67(9):1089-1094

VARIOUS NEUROMUSCULAR diseases can produce weakness of respiratory muscles and result in ventilatory failure.^{1,2} Respiratory insufficiency occurs slowly and follows a predictable rate of worsening in patients with chronic, progressive neuromuscular diseases such as muscular dystrophies and amyotrophic lateral sclerosis (ALS). However, some neuromuscular diseases have an acute or subacute onset, and some of the chronic conditions can have sudden exacerbations, thus presenting with acute respiratory failure. These cases represent a diagnostic challenge in the intensive care unit (ICU), where clinical examination is often limited by patients' inability to communicate and cooperate with the examination owing to sedation, pharmacological paralysis, and interference from necessary medical equipment such as endotracheal tubes. In addition, the evaluation of critically ill pa-

tients with suspected acute primary neuromuscular respiratory failure may be confounded by concomitant conditions such as infections, metabolic disturbances, compressive neuropathies, muscle wasting due to immobilization, and ICU-acquired weakness from critical illness neuropathy and myopathy.³

Respiratory failure in patients with neuromuscular diseases can be initially unrecognized because, unlike in patients with respiratory diseases, they do not have frank abnormalities on auscultation or severe cyanosis. Certain signs such as paradoxical abdominal movement, use of accessory respiratory muscles, or patients becoming breathless while talking should raise a warning.^{4,5} Three groups of muscles can be implicated in neuromuscular respiratory failure. Dysfunction of inspiratory muscles can lead to failure in ventilation. Moreover, incomplete expansion of the rib cage can cause basal microatelectasis, leading to ventilation-perfusion mis-

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match. Dysfunction of expiratory muscles decreases the efficiency of cough, thus impairing clearance of secretions. Bulbar muscle weakness, when severe, can cause upper airway obstruction.⁶

Previous literature on acute neuromuscular respiratory failure has focused on specific diagnoses, most notably myasthenia gravis (MG) and Guillain-Barré syndrome (GBS).⁷⁻¹⁰ However, when patients are admitted to the ICU with acute ventilatory failure, the diagnosis is often unknown. The differential diagnosis in these cases is broad, and prognosis may vary depending on the actual cause and initial severity. Yet, the distribution of causes of acute neuromuscular respiratory failure in patients admitted to the ICU has not been formally evaluated, and little is known about the prognosis for some patients such as those who present with acute neuromuscular respiratory failure of unclear etiology.

Previous studies have identified neuromuscular diseases as the most important cause of prolonged ventilator dependency.¹¹ The diagnostic value of electrophysiological studies in these patients has been noted.¹² Multiple other diagnostic tests can be ordered in those patients but their usefulness has not been formally assessed in a large series of cases of acute neuromuscular respiratory failure.

The purpose of our study was to identify the spectrum of causes, analyze the usefulness of diagnostic tests, and recognize prognostic factors in patients with acute neuromuscular respiratory failure, with special attention to the subgroup of patients for whom a neuromuscular diagnosis was not known before admission.

METHODS

PATIENTS

Patients admitted to an ICU at Saint Marys Hospital (Mayo Clinic, Rochester, Minnesota) with acute respiratory failure between 2003 and 2009 were identified using an electronic medical registry that includes all patients ventilated in our ICUs. Criteria for inclusion in this study were need for mechanical ventilation (invasive or noninvasive) and having an objective impairment of the peripheral nervous system—including anterior horn cell, roots, plexus, peripheral nerves, neuromuscular junction, and muscles—deemed primarily responsible for the respiratory failure. Patients with diagnosis of ICU-acquired weakness (ie, critical illness neuropathy or myopathy) or initial respiratory failure of another cause (eg, pulmonary disease, cardiac failure, sepsis) were excluded. When in question, diagnosis was reached by consensus between the investigators.

CLINICAL DATA

Information regarding age, sex, body mass index (calculated as weight in kilograms divided by height in meters squared), comorbid conditions, findings of neurological examination, time receiving mechanical ventilation (invasive or noninvasive), medical complications, and length of stay in the ICU and the hospital was gathered for each patient. Pneumonia was defined by the presence of fever or leukocytosis, appropriate semiology on physical examination, purulent respiratory secretions, and new infiltrate or consolidation on chest x-ray. Overweight was defined by a body mass index of 25 or greater and obesity by a body mass index of 30 or greater.

Patients were separated into 2 categories depending on whether they had a neuromuscular diagnosis known prior to admission that was likely responsible for the respiratory failure. Initial presumptive diagnoses on admission and final diagnoses were collected for all cases.

DIAGNOSTIC TESTS

Serum creatinine kinase (CK) levels, cerebrospinal fluid content, electromyogram (EMG) findings, and muscle and nerve biopsy results were gathered. We analyzed their diagnostic usefulness for patients without a previously known neuromuscular condition that was responsible for the respiratory failure.

OUTCOME

Outcome at discharge and at last follow-up was registered using the modified Rankin score. Poor outcome was defined as a modified Rankin score greater than 3 including death during hospitalization for outcome at discharge and death after discharge for outcome at last follow-up. We analyzed the effect of several factors on the short-term (at discharge) and longer-term (at last follow-up) outcome. Additional endpoints for the analysis included duration of mechanical ventilation and length of ICU stay.

STATISTICAL ANALYSIS

Descriptive statistics are presented as median and range. Predictors of functional outcome were analyzed using the Fisher exact and χ^2 tests for categorical variables and the Wilcoxon rank sum test for continuous variables. All tests were 2-tailed. $P < .05$ was considered statistically significant. All analyses were performed using JMP statistical software, version 8 (SAS Inc, Cary, North Carolina).

RESULTS

Eighty-five patients met the criteria to be included in the study. Ages ranged from 20 to 88 years (median, 66 years; 42 women, 43 men). The most frequent comorbid conditions were diabetes (34 patients), overweight (49 patients), obstructive respiratory disease (17 patients), and cardiac insufficiency (11 patients). Seven patients had sleep apnea, and 4 had restrictive respiratory disease. Pneumonia was the most common medical complication, occurring in 33 patients (38%). The most frequent final diagnoses were MG, GBS, ALS, and myopathies (**Table 1**). In 10 patients (12%), the diagnosis remained unknown at the last follow-up, or at discharge in those who did not have follow-up. Neurological examination showed limb weakness in 84% of patients and bulbar weakness in 74%.

On admission, only 38 patients (45%) had previously diagnosed neuromuscular disease that was deemed responsible for the respiratory failure. Of those, the most frequent diagnoses were MG (58%), myopathies (21%), and ALS (11%). In the group without previously known neuromuscular condition responsible for the respiratory failure (n=47), the most frequent final diagnoses were GBS (26%) and ALS (17%) (**Table 2**). Ten of those patients (21%) remained without a definite diagnosis at discharge and the last follow-up. Clinical data for those patients are summarized in **Table 3**. Among patients without preexistent neurological diagnoses, the rate of agreement between the initial presumptive diagnosis made

on admission and the final diagnosis was 68%. The cases in which the presumptive initial diagnosis did not match the final diagnosis are presented on **Table 4**.

The median time of mechanical ventilation for the study population was 9 days (range, 1-109 days). Patients with GBS had the longest ventilation duration (median, 15 days; range, 2-109 days) followed by myopathies (median, 12 days; range, 1-47 days), ALS (median, 12 days; range, 1-40 days), and MG (median, 5 days; range, 1-34 days). The median length of ICU stay for the sample was 16 days (range, 1-111 days). Patients with GBS again had the longest ICU stays (median, 23 days; range, 5-111 days), followed by myopathies (median, 19 days; range, 1-51 days), ALS (median, 9 days; range, 2-40 days), and MG (median, 9 days, range, 2-41 days). Patients without known neuromuscular diagnosis on admission had a median time of mechanical ventilation of 14 days (range, 1-109 days) and median length of ICU stay of 18 days (range, 1-111 days). In the group whose diagnosis remained unknown at discharge, the median time receiving mechanical ventilation was 13 days (range, 1-39 days) and the median length of ICU stay was 17 days (range, 3-59 days).

DIAGNOSTIC TESTS

An EMG was performed in 44 patients. In 38 cases, the EMG was compatible with the final diagnosis, whether it was neuropathic, myopathic, or indicative of neuromuscular junction disorder. One patient had a neuropathic pattern on EMG but a final diagnosis of MG. Serum CK levels were measured in 37 patients and were elevated in 7 (19%). Three of the 7 and another 4 patients with CK levels in the reference range had final diagnoses of myopathy. Levels of CK were not measured in the other 5 cases of myopathy. One patient with final diagnosis of GBS, 1 with botulism, and 1 with ALS had mild CK elevations. One patient with final diagnosis of GBS had high levels of CK related to a concomitant rhabdomyolysis of unclear cause. The sensitivity of increased CK level for detecting myopathies was 0.42 and the specificity was 0.87.

Lumbar punctures were performed in 28 patients. Twelve of 14 inflammatory radiculoneuropathies showed the characteristic albumino-cytological dissociation. However, 2 patients with ALS also had this finding. The sensitivity of cerebrospinal fluid testing for the diagnosis of inflammatory radiculoneuropathies was 0.85 and the specificity was 0.80.

Muscle biopsies were performed in 11 patients; the findings of 10 were abnormal. Three of the patients were eventually diagnosed with myopathies, 4 with neuropathic disease (chronic inflammatory demyelinating polyneuropathy and ALS), and 1 with MG; 3 had unknown diagnoses. One of the myopathies was a necrotizing myopathy with anti-signal recognition particle antibody. The biopsy findings of this patient showed the characteristic changes, leading to the final diagnosis and antibody determination. Another patient had a toxic necrotizing myopathy secondary to chemotherapy with FOLFOX (5-fluorouracil, leucovorin, and oxaliplatin). His biopsy showed necrotizing changes that, together with a history of exposure to the drug, led to the final diagnosis. The third patient with myopathy had a biopsy showing a severely damaged muscle

Table 1. Final Diagnoses of Patients Admitted to the ICU With Acute Neuromuscular Respiratory Failure

Final Diagnosis	Patients, No. (%)
Myasthenia	27 (32)
GBS	12 (14)
Myopathies	12 (14)
Dermatomyositis	2
α -sarcoglycanopathy	1
Toxic necrotizing myopathy	1
Hypernatremic myopathy	1
Myotonic dystrophy	1
Myopathy with anti-SRP antibodies	1
Undetermined	5
ALS	12 (14)
Postpolio syndrome	3 (4)
CIDP	2 (2)
West Nile infection polyradiculoneuropathy	2 (2)
Amyloid polyradiculoneuropathy	1 (1)
Kennedy syndrome	1 (1)
Congenital myasthenic syndrome	1 (1)
Pseudocholinesterase deficiency	1 (1)
Myelopathy	1 (1)
Unknown	10 (12)

Abbreviations: ALS, amyotrophic lateral sclerosis; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; GBS, Guillain-Barré syndrome; ICU, intensive care unit; SRP, signal recognition particle.

Table 2. Final Diagnoses in Patients Without Known Neuromuscular Disease at Admission

Final Diagnosis	Patients, No.
GBS	12
ALS	8
Myasthenia	4
Myopathies	4
Hypernatremic myopathy	1
Toxic necrotizing myopathy	1
Myopathy with anti-SRP antibodies	1
Undetermined	1
CIDP	2
West Nile polyradiculoneuropathy	2
Postpolio syndrome	1
Kennedy disease	1
Pseudocholinesterase deficiency	1
Probable botulism	1
Amyloidosis	1
Unknown	10

Abbreviations: ALS, amyotrophic lateral sclerosis; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; GBS, Guillain-Barré syndrome; SRP, signal recognition particle.

with chronic changes such as fibrosis; these findings were helpful to establish the diagnosis of myopathy but could not determine the specific type of muscle disease, which remained unknown. All neuropathic cases showed denervation atrophy in the muscles biopsied, which did not define a final specific diagnosis but helped focus the problem at the nerve level. One patient with ALS also showed type 2 fiber atrophy of unclear significance. The biopsy of the patient with final diagnosis of MG showed severe type 2 fiber atrophy, which is known to occur in diseases with altered neuromuscular transmission.¹³ The only patient

Table 3. Summary of Findings in Patients Who Remained Without a Confirmed Diagnosis at Discharge

Sex/Age, y	Clinical Presentation at Time of Admission	Diagnostic Tests	Response to Treatment
M/70	Limb and bulbar weakness progressive over years, acute respiratory failure, fasciculations in 1 hand intrinsic muscles, hyporeflexia	CPK: normal. EMG: diffuse fibrillations at first examination, sparse in a second. Reduced CMAP and SNAP amplitudes and prolonged latency of F waves.	Steroids: no response
F/41	Proximal limb weakness progressive for 1 year, hyporeflexia	CPK: normal. EMG: fibrillations, enlarged motor unit potentials, diffusely. Muscle biopsy: denervation atrophy.	Steroids: no response; IVIG: no response
F/30	Lower limbs and bulbar progressive weakness for 2 y	CPK: normal. CSF: acellular with mild protein elevation. EMG: reduced CMAP, spread fibrillations. No demyelinating signs. Nerve biopsy: perivascular epineural inflammation.	Steroids: No response; IVIG: no response
F/74	Progressive dyspnea	CPK: normal. EMG: bilateral phrenic neuropathy (absence of CMAP in diaphragm). Sparse fasciculations in left first dorsal interossei and diaphragm.	Steroids: no response; IVIG: no response
M/69	Subacute left arm weakness, dysphagia, dyspnea, hyporeflexia, facial diplegia, fever	CSF: 8 white blood cells; protein, 87 mg/dL. Microbiological studies: negative. EMG: reduced CMAP and SNAP, with normal conduction velocities, prolonged latencies of F waves, and blink reflex.	Steroids: no response; IVIG: no response
F/71	Proximal limb weakness and dysphagia progressive for 2 mo	CPK: normal. CSF: unrevealing. EMG: reduced SNAP and CMAPs. Myopathic pattern in proximal muscles.	Steroids: no response; plasma exchange: no response
F/22	Proximal and distal weakness in lower limbs, fatigue	CPK: normal. CSF: unrevealing. AChR Ab and MuSK Ab: negative. EMG: reduced CMAP.	Pyridostigmine: no response; steroids: partial response; IVIG: no response
F/64	Dyspnea and bulbar weakness progressive for 2 mo	CPK: normal. AChR AB, MuSK AB: negative. EMG: myopathic pattern involving bulbar and respiratory muscles. No neuromuscular transmission dysfunction. Muscle biopsy: type 2 atrophy.	
F/20	Fatigue and weakness in limbs and bulbar muscles for 3 mo	CPK: normal. CSF: 5/86. Microbiological studies: negative. EMG: reduced CMAP amplitudes. No demyelinating signs. No neuromuscular transmission dysfunction. Muscle biopsy: normal.	Steroids: no response; IVIG: no response
M/73	Subacute limb proximal weakness and dysphagia	CPK: normal. CSF: acellular with mild protein elevation. EMG: diffuse fibrillations. Reduced CMAPs. Prolonged F wave latency. Myopathic pattern in proximal muscles.	IVIG: no response

Abbreviations: AChR Ab, acetylcholine receptor antibody; CMAP, compound muscle action potential; CPK, creatine phosphokinase; CSF, cerebrospinal fluid (cells/protein content in milligrams per deciliter); EMG, electromyograph; IVIG, intravenous immunoglobulins; SNAP, sensory nerve action potential; MuSK Ab, muscle-specific tyrosine kinase antibody.

whose muscle biopsy findings were normal was discharged with unknown diagnosis.

Sural nerve biopsies were performed in 7 patients. One was eventually diagnosed with GBS; 1, chronic inflammatory demyelinating polyneuropathy; 3, ALS; and 1, amyloid neuropathy; in 1 case, the diagnosis remained unknown. In all cases of ALS, the nerve biopsy showed axonal degeneration. In both demyelinating inflammatory neuropathies, the biopsy showed definite signs of demyelination. One biopsy had congophilic deposits considered diagnostic of amyloid neuropathy. The biopsy of the patient whose diagnosis remained unknown showed normal density of myelinated fibers, decrease in large fibers, borderline increased rate of axonal degeneration, and increased rate of segmental demyelination with few epineurial mononuclear inflammatory infiltrates, thus indicating a neurogenic process but not finding enough evidence to establish a specific diagnosis. One area of inflammation involved a vessel wall, raising the possibility of vasculitis. However, this patient was treated with immunosuppressants without improvement.

OUTCOME

Twelve patients (14%) died during hospitalization. Seven had final diagnoses of ALS; 3, myopathies; 1, amyloid neu-

ropathy; and 1, MG. On discharge, 43 patients (51%) were severely disabled (modified Rankin score >3). Eighteen patients (21%) remained ventilator dependent at discharge, and 8 required nocturnal ventilatory assistance. Forty-eight had follow-up after discharge (median follow-up, 5 months; range, 1-48 months). In this group, 25 (52%) were discharged with severe disability. Eight (17%) were dead, and 12 (25%) were severely disabled at last follow-up. Fourteen of the patients who had follow-up (30%) were ventilator dependent at discharge; 7 (15%) were still receiving mechanical ventilation at the last follow-up.

Of the 47 patients without known neuromuscular disease before hospitalization, 7 (15%) died in the hospital. At discharge, 29 (62%) were severely disabled (including 13 [28%] who were ventilator-dependent), and 11 (23%) were independent at discharge. Twenty-five patients in this group had follow-up including 17 (68%) who were discharged with severe disability. By last follow-up, 6 patients in this group were dead (24%), 7 (28%) were severely disabled, and 6 (24%) remained ventilator-dependent.

Of the 10 patients whose diagnoses remained unknown on discharge, 9 (90%) were dead (n=2) or severely disabled at discharge. Two others died during follow-up (at 3 and 12 months) without having recovered independent respiratory function. Two patients remained

severely disabled at the 4-month follow-up; 2 experienced some degree of slow improvement over time but remained disabled at 27 and 33 months, respectively; and 1 patient was discharged to a nursing home facility in another state and was subsequently lost to follow-up. Only 1 patient was independent at discharge and last follow-up.

PREDICTORS OF OUTCOME

Older age was the only variable associated with increased mortality during hospitalization ($P = .04$). Longer mechanical ventilation duration and length of ICU stay were associated with poor outcome at discharge ($P = .004$ and $.001$, respectively) but not at last follow-up among survivors. Patients treated only with noninvasive ventilation ($n = 12$) had shorter ICU stays ($P = .002$) but no difference in functional outcome when compared with those treated with invasive ventilation.

Overweight and obesity were not found to have a significant effect on short- or longer-term outcome, duration of mechanical ventilation, or length of ICU stay. Patients with diabetes and those who developed pneumonia as a medical complication during hospitalization had longer times of mechanical ventilation ($P = .008$ and $.02$, respectively) and ICU stay ($P = .003$ and $.01$, respectively) but not a significantly different functional outcome. Patients with cardiopulmonary diseases such as ischemic cardiopathy, cardiac failure, obstructive chronic pulmonary disease, and restrictive lung diseases had worse outcomes at the last follow-up ($P = .01$).

We then analyzed differences in outcome between patients with or without a known neuromuscular diagnoses prior to admission. Patients without previous neuromuscular diagnoses had longer duration of mechanical ventilation ($P = .009$), longer ICU stays ($P < .001$), and worse outcomes at discharge ($P = .01$) despite having similar ages as the rest of the population. Among this group of patients, those who had spontaneous activity on EMG had worse short-term outcomes ($P < .001$) independently of the underlying disease.

COMMENT

This study is the first, to our knowledge, to analyze a series of patients with acute neuromuscular respiratory failure of all causes. The main interest of our study design is that it incorporates patients without recognized neuromuscular diagnosis, as these patients had not been the subjects of formal analysis before. Surprisingly, the proportion of patients without known neuromuscular diagnosis on admission was high (55%) in our sample despite most of the final diagnoses eventually corresponding to chronic and slowly progressive diseases. The absence of a known neuromuscular diagnosis prior to admission was a predictor of poor outcome. Furthermore, our most novel and clinically relevant finding was that patients whose diagnosis remained unknown on discharge had particularly high rates of severe disability.

The poorer initial outcomes of patients without a known neuromuscular diagnosis on admission may be explained by the predominance of GBS in this group and of MG among

Table 4. Patients Presenting With Acute Neuromuscular Respiratory Failure Whose Initial Presumptive Diagnosis Was Different From the Final Diagnosis

Initial Presumptive Diagnosis	Final Diagnosis
Unknown: presentation as an isolated respiratory insufficiency	MG
Myopathy: very high CK	GBS
Meningitis: presentation with headache, profuse nausea and vomiting; pleocytosis in CSF; later diagnosed with Behçet disease	GBS
Vasculitic neuropathy: stepwise onset and secondary progressive weakness studied initially as an outpatient with a nerve biopsy that showed a nerve fascicle infarct pointing to a small vessel vasculitis; a new nerve biopsy during hospitalization revealed inflammatory demyelinating neuropathy	CIDP
GBS	CIDP
Unknown: presentation as isolated shortness of breath initially attributed to cardiac disease	ALS
Unknown	ALS
Unknown: patient taking lithium for bipolar disorder developed diabetes insipidus and secondary severe hyponatremia and myonecrosis	Hypernatremic myopathy
Myasthenia: patient with important background of autoimmune disease presenting with weakness and positive anti-AChR antibodies.	Myopathy with anti-SRP antibodies
Myasthenia	Botulism
Histoplasmosis: immunocompromised patient who presented with fever, diaphoresis, and shortness of breath; systemic histoplasmosis was diagnosed through a lung biopsy and serologic tests; with infection under control and improvement in mental status, quadriplegia and respiratory insufficiency became evident; myelitis and radiculoneuritis secondary to West Nile infection were found to be the underlying causes	West Nile infection
POEMS: polyneuropathy associated to monoclonal IgA paraprotein; bone marrow biopsy showed 10% of plasma cells; osteolytic lesions and hepatomegaly were present; nerve biopsy revealed amyloid neuropathy; the latter autopsy revealed systemic amyloidosis	Amyloidosis

Abbreviations: AChR, acetylcholine receptor; ALS, amyotrophic lateral sclerosis; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; CK, creatinine kinase; CSF, cerebrospinal fluid; GBS, Guillain-Barré syndrome; MG, myasthenia gravis; POEMS, plasma cell dyscrasia with polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, and skin changes; SRP, signal recognition particle.

patients with previously known diagnoses. With appropriate treatment, myasthenic crises can resolve after a couple of weeks,^{7,8,14-16} while recovery usually takes much longer after severe GBS.¹⁷⁻¹⁹ However, it is also possible that earlier correct management that avoids unnecessary treatment and diagnostic tests is most likely to be responsible for the better short-term outcomes in patients with known diagnoses before admission. This notion is also supported by the very poor outcomes of patients whose diagnoses remained unknown on discharge. The presence of coexistent cardiopulmonary diseases had a strong negative effect on long-term outcome. These results suggest that early treatment of patients with acute neuromuscular respiratory failure influence the short-term outcome, and the underlying

specific neuromuscular disease and comorbid conditions such as cardiopulmonary diseases are major determinants of long-term outcome.

The finding that 17% of patients without a known diagnosis prior to admission were diagnosed with ALS is particularly interesting. Furthermore, 8 of 12 patients with ALS in this study were newly diagnosed at the time of presentation with acute respiratory failure. Although ALS is a chronic neurodegenerative disease that typically presents insidiously, acute presentations of ALS have been previously reported.²⁰ It is therefore important that physicians consider ALS when investigating patients with unexplained acute respiratory failure of presumed neuromuscular cause. Careful monitoring of patients with documented ALS may explain the infrequent occurrence of respiratory failure in patients with previously recognized ALS in our series.

Use of EMG had the greatest diagnostic yield of all tests analyzed in this study. Its usefulness varied depending on the specific diagnostic category but it often provided evidence to establish the diagnosis or, alternatively, offered clues guiding further appropriate evaluations that proved confirmatory. Furthermore, phrenic nerve EMG may predict prognosis in conditions such as GBS.²¹ Cerebrospinal fluid analysis was only performed in 60% of patients with unclear diagnoses and was helpful in nearly 40% of cases. It was most valuable in patients with inflammatory polyradiculoneuropathies. Serum CK measurement and muscle and nerve biopsies were only useful in specific cases, suggesting that patient selection is essential before ordering those tests to optimize their yield. Nerve biopsy provided the diagnosis in 3 cases: in 1, amyloid neuropathy, and in 2, inflammatory radiculoneuropathies. However, both inflammatory polyradiculoneuropathies had also proven albuminocytological dissociation and fairly characteristic electrophysiological findings (prolonged F-wave latencies in one case and slow conduction velocities, prolonged distal latencies, and absent F waves in the other), which provided enough evidence, along with the clinical findings, to confirm the diagnosis.

Our study has limitations including those inherent in a retrospective study design. It represents the distribution and prognosis of patients with neuromuscular respiratory failure treated at a tertiary referral center. The length of follow-up among patients without specific neuromuscular diagnosis was variable and, overall, relatively short; thus, more delayed recovery in survivors cannot be excluded.

In conclusion, patients admitted to the ICU with acute neuromuscular respiratory failure have high rates of death and short- and long-term disability. In this series, absence of a previously known neuromuscular disease was common and those patients had significantly worse short-term prognoses. Chances of recovery were particularly poor among patients without specific neuromuscular diagnoses despite extensive investigations.

Accepted for Publication: April 9, 2010.

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Author Contributions: Study concept and design: Rabinstein. Acquisition of data: Cabrera Serrano and Rabinstein. Analysis and interpretation of data: Cabrera Serrano and Rabinstein. Drafting of the manuscript: Cabrera Serrano. Critical revision of the manuscript for important intellectual content: Rabinstein. Study supervision: Rabinstein.

Financial Disclosure: None reported.

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