Neuromuscular Complications of Critical Illness

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Kauai
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Learning Objectives

- Become familiar with the Differential Diagnosis of weakness in the ICU
- Review some of the clinical, pathological and electrodiagnostic characteristics of neuropathy and myopathy in the ICU
- Review the electrodiagnostic approach of assessing weakness in the ICU setting
- Briefly, respectfully critique the confusing literature in CIM/CIPN
Critical Illness Neuromuscular Disorders

- Common
- Poorly understood
- Serious functional consequences

Neuromuscular Complications of Critical Illness

**History**
- Muscular wasting as a consequence of sepsis - Sir William Osler - 1892
- Unexplained neuropathic complications in critically ill patients - Olsen - 1966
- Coma-polyneuropathies - described by Mertens - 1961
- Polyneuropathy in burn patients - Henderson - 1971
- Polyneuropathy in septic patients - Bischoff - 1977
- Development of the term Critical Illness Polyneuropathy - 1984 (Belton)
- Polyneuropathy in a patient with an anoxic brain injury - Erbsloh and Abel - 1989
- Polyneuropathy associated with the use of non-depolarizing NMBA
- Myopathy in patients with asthma who were treated with NMBA and corticosteroids
- CIP is the most common acute polyneuropathy in the critically ill patient - 2003
Neuromuscular Complications of Critical Illness

Case: 51 year old male with COPD + respiratory failure
- h/o alcohol abuse and depression
- Became critically ill
- Placed on IV methylprednisolone for 27 days
- Then to prednisone
- Developed weakness that included facial muscles
- Absent tendon reflexes, CSF normal

Scully RE, et. al., Case Records of the Massachusetts General Hospital Case 11-1997

NCV Results

<table>
<thead>
<tr>
<th>Nerve and Site of Stimulation</th>
<th>Latency (msec)</th>
<th>Amplitude (μV)</th>
<th>Duration (msec)</th>
<th>Velocity (m/sec)</th>
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<tbody>
<tr>
<td>Motor nerve</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Median</td>
<td>3.5</td>
<td>1480</td>
<td>9.4</td>
<td>52</td>
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<tr>
<td>Wrist</td>
<td>2.0</td>
<td>1190</td>
<td>10.0</td>
<td></td>
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<tr>
<td>Elbow</td>
<td>5.2</td>
<td>1060</td>
<td>10.5</td>
<td>56</td>
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<tr>
<td>Ulnar</td>
<td>7.4</td>
<td>1130</td>
<td>10.6</td>
<td>68</td>
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<tr>
<td>Tibial</td>
<td>4.4</td>
<td>3120</td>
<td>6.8</td>
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<tr>
<td>Ankle</td>
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<td>2960</td>
<td>7.1</td>
<td>44</td>
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<tr>
<td>Knee</td>
<td>2.8</td>
<td>12.4</td>
<td>57</td>
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<tr>
<td>Sensory nerve</td>
<td>2.0</td>
<td>7.0</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Ulnar</td>
<td>2.8</td>
<td>7.3</td>
<td>46</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>2.3</td>
<td>12.4</td>
<td>57</td>
<td></td>
</tr>
<tr>
<td>Sural</td>
<td>2.8</td>
<td>7.3</td>
<td>46</td>
<td></td>
</tr>
</tbody>
</table>

Scully 1997

- 34th day post onset
- No conduction block
- Needle EMG
  - No fibs or PSW
  - MUPs ↑ polys
    - Nl to low amp
    - Shorter duration
    - Recruitment WNL
- F-wave lat WNL
- Low amp
- Rep stim WNL
Muscle Biopsy

- Right deltoid
- Atrophy of both Type 1&2 fibers
- No inflammation
- No fiber-type grouping

Muscle Biopsy

**Electron microscopy**

- Myofibrillar disruption
- Loss of myosin
- Normal Mitochondria
Prospective study of neuromuscular abnormalities in critical illness

- 23 patients, ICU stay > 7 days
- Neurophysiological abnormalities in all but 1 of 10 patients
  - 8 primary axonal neuropathy
  - 1 motor abnormalities only
- Abnormal muscle histology in 22 patients
  - diffuse atrophy 8 cases
  - type II fibre atrophy 2 cases
  - myopathy 8 cases (necrosis in 2)
  - neurogenic atrophy 4 cases

Coakley et al, 1993

Patterns of neurophysiological abnormality in 44 long stay critically ill patients

<table>
<thead>
<tr>
<th>Group</th>
<th>n (%)</th>
<th>CMAP</th>
<th>SAP</th>
<th>Muscle biopsy</th>
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<tbody>
<tr>
<td>I</td>
<td>7 (16)</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal (2)</td>
</tr>
<tr>
<td>II</td>
<td>4 (9)</td>
<td>Normal</td>
<td>Reduced</td>
<td>Diffuse fibre atrophy (1)</td>
</tr>
<tr>
<td>III</td>
<td>11 (25)</td>
<td>Reduced</td>
<td>Normal</td>
<td>Diffuse fibre atrophy (2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Type II fibre atrophy (1)</td>
</tr>
<tr>
<td>IV</td>
<td>19 (43)</td>
<td>Reduced</td>
<td>Reduced</td>
<td>Diffuse fibre atrophy (3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Neurogenic atrophy (3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Myopathy (9)</td>
</tr>
<tr>
<td>V</td>
<td>3 (7)</td>
<td>Not classified</td>
<td>Not classified</td>
<td>Neurogenic atrophy (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Myopathy (3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Myopathy (2)</td>
</tr>
</tbody>
</table>

Data from Coakley et al. [28*]. CMAP, compound muscle action potential; SAP, sensory action potential.

Coakley et al, 1998
Characteristics of 38 patients with and without critical illness polyneuropathy (CIP) on mechanical ventilation for more than 7 days

<table>
<thead>
<tr>
<th></th>
<th>NO CIP</th>
<th>CIP</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Number</td>
<td>20</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>54.7 ±17.3</td>
<td>58.5 ±17.0</td>
<td>0.49</td>
</tr>
<tr>
<td>Mean number of ventilation days</td>
<td>20.3 ±10.9</td>
<td>33.6 ±19.8</td>
<td>0.02</td>
</tr>
<tr>
<td>Mean APACHE II in first 24 h</td>
<td>23.1 ±6.8</td>
<td>21.9 ±9.1</td>
<td>0.66</td>
</tr>
<tr>
<td>Mean maximal Multi Organ Dysfunction Syndrome (MODS) score</td>
<td>3.6 ±1.5</td>
<td>5.3 ±1.8</td>
<td>0.003</td>
</tr>
<tr>
<td>Median number (range) of days to reach maximum MODS score</td>
<td>1 (1-2)</td>
<td>4.5 (2-9)</td>
<td>0.002</td>
</tr>
<tr>
<td>Median number (range) of different organs involved (max 6)</td>
<td>2 (1-4)</td>
<td>4 (3-5)</td>
<td>0.009</td>
</tr>
<tr>
<td>Sepsis syndrome</td>
<td>8 (40%)</td>
<td>10 (56%)</td>
<td>0.34</td>
</tr>
<tr>
<td>Number of deaths in the ICU</td>
<td>4 (20%)</td>
<td>8 (44%)</td>
<td>0.11</td>
</tr>
</tbody>
</table>


Persistent neuromuscular and neurophysiologic abnormalities in long-term survivors of prolonged critical illness

Simon N. Fletcher, FRCA; Daniel D. Kennedy, FRCA; Indrajit R. Ghosh, MRCP; Vijay P. Misra, MRCP; Kevin Kiff, FRCA; John H. Coakley, MRCP; Charles J. Hinds, FRCP, FRCA

- In 21 of 22 patients remarkably consistent neurophysiological findings indicative of denervation and subsequent reinnervation up to 5 years after discharge.
- 1 patient who had developed a necrotizing myopathy had no persisting weakness and no evidence of denervation.
Neuromuscular Complications

Diagnostic Approach

Think broadly!

- Long differential diagnosis, depending on the clinical context

- History
  - Medication (intravenous administration of corticosteroids - pancuronium, vecuronium, metronidazole, amiodarone)
  - Undiagnosed neuromuscular disorder (PM, DM, ALS, GBS, MG, LEMS, acid maltase deficiency, mitochondrial myopathy, musc. dystrophy)
  - Spinal cord damage (ischemic, compressive hematoma, trauma)
  - Critical illness neuromuscular disorder
  - Loss of muscle mass (disuse atrophy, rhabdomyolysis, catabolic state)
  - Electrolyte disorders (hypokalemia, hypermagnesemia, hypophosphatemia)
  - Systemic illness (acute prophyria, AIDS, vasculitis neuropathy, endocrine myopathies)

Diagnostic Approach

Examine the patient! Confirm weakness!

- Unexpected lack of ventilatory weaning
- Accelerated peripheral muscle atrophy
- Inability to hold head/limb off bed

Diagnostic Clues

- Mental status - not affected
- Pattern of weakness
  - symmetric, facial sparing
  - CN weakness - think GBS, MG, stroke
- MSR - usually decreased
  - if increased, suggests central lesion
THE DEVELOPMENT OF CRITICAL ILLNESS RELATED WEAKNESS INFLUENCES SHORT TERM OUTCOME

**Important to Know Because:**
- Time on ventilator
- Time in intensive care
- Time in hospital
- Mortality
- Morbidity

ICU acquired paresis is an independent predictor of prolonged weaning

- Multivariate analysis
  ICUAP independent predictors of prolonged weaning

Neuromuscular Complications of Critical Illness

**SIRS**
- *Systemic Inflammatory Response Syndrome (SIRS)* - The Society of Critical Care Medicine and The American College of Chest Physicians consensus conference 1992
- The severe systemic response that occurs in critically ill patients
- Etiology varied: infection (sepsis), trauma, burns etc.
- Septic Shock is a term reserved for individuals with organ dysfunction and hypoperfusion

Neuromuscular Complications of Critical Illness

**Physiology of SIRS**
- Activation of humoral responses primarily involving the cytokines (interleukins, tumor necrosis factor, arachidonic acid, free oxygen radicals and proteases)
- Activation of cellular responses primarily involving lymphocytes, monocytes and neutrophils
Neuromuscular Complications of Critical Illness

Physiology of SIRS

- Activation increases capillary permeability
- Inadequate nutrient delivery
- Oxygen debt within the tissue
- Vulnerable nervous system
Myopathy in Critically Ill Individuals

- Acute corticosteroid myopathy
- Acute quadriplegic myopathy (AQM)
- Acute myopathy in Status Asthmaticus
- (Acute) (necrotizing) myopathy of intensive care
- Critical care myopathy
- ICU myopathy
- Myopathy with thick filament (myosin) loss

Neuromuscular Complications of Critical Illness*

- Neuropathy
  - *Critical Illness Polyneuropathy*
  - *Acute Motor Neuropathy Associated with Non-Depolarizing Neuromuscular Blocking Agents*

- Critical Illness Myopathy
  - Thick Filament Myopathy
  - Acute Necrotizing Myopathy of Intensive Care
  - Catabolic Myopathy

- Neuromuscular Junction Abnormalities
- Neuromyopathy

*Studies in the pediatric population find a similar pattern of distribution*
Critical Illness Polyneuropathy

Neuromuscular Complications of Critical Illness
I. Neuropathy

**Critical Illness Polyneuropathy**
- Acute, diffuse, mainly motor neuropathy due to axonal dysfunction
- Patients with sepsis or multiple organ dysfunction
- Incidence in this patient population ranges from 50-75%
- Severity proportional to length of time in the ICU
Neuromuscular Complications of Critical Illness

I. Neuropathy

Critical Illness Polyneuropathy

- The earliest sign - difficulty weaning from the ventilator
- Can present with tetraplegia, absent deep tendon reflexes
- Blood CPK levels are normal

Septic Encephalopathy usually precedes the diagnosis of Critical Illness Polyneuropathy by two weeks

- Impaired attention, concentration, orientation and writing
- CSF studies are normal or show mild elevations in protein

![Graph](image.png)

Fig. 1. The typical series of neurological complications after the onset of the septic syndrome. The time course may vary from weeks to months.
Neuromuscular Complications of Critical Illness

I. Neuropathy

Critical Illness Polyneuropathy
- Development associated with hyperglycemia
- Development associated with hypoalbuminemia
- Neuropathy occurs more often in patients getting parenteral nutrition

Mechanisms proposed for nutritional axonal injury are:
- Glucose-induced depletion of intracellular phosphate stores with subsequent depletion of high-energy phosphate compounds
- Oxidative modification of dietary lipid
Neuromuscular Complications of Critical Illness

I. Neuropathy

Critical Illness Polyneuropathy

- Prognosis depends on the underlying disease process
- Recovery usually occurs over weeks to months depending on neuropathy severity

Electrodiagnostic Findings in Critical Illness Polyneuropathy

- Nerve conduction velocities and distal latencies are normal
- Reduction in the CMAP and SNAP amplitude
- No evidence of conduction block
- Repetitive nerve stimulation does not show a defect
Neuromuscular Complications of Critical Illness

I. Neuropathy

Critical Illness Polyneuropathy

- **Severe**: absent SNAP, fibrillation potentials in all muscle groups, and multiple CMAP amplitudes less than 1mv amplitude
- **Moderate**: SNAP amplitudes <5uv, multiple CMAP amplitudes between 1 and 3 mV, fibrillation potentials and positive sharp waves in distal muscles and occasionally present in more proximal muscles
- **Mild**: SNAP amplitudes >5uv, CMAP amplitudes >3mv, occasional positive sharp waves in distal muscles

Spitzer AR, Giancarlo T, Maher L, et al. 1992

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Nerve Biopsy

- Severe primary axonal degeneration of motor and sensory fibers
- Affects distal segments primarily
- No evidence of inflammation
Neuromuscular Complications of Critical Illness

I. Neuropathy

Muscle Biopsy

- Scattered atrophic fibers in the acute phase

BIOPSY

- Grouped fiber atrophy in the chronic phase
- Autopsy studies also may reveal central chromatolysis of anterior horn cells

Spinal Cord
Muscle
Acute Motor Neuropathy Associated with Non-Depolarizing Neuromuscular Blocking Agents

Neuromuscular Complications of Critical Illness
1. Neuropathy

Acute Motor Neuropathy Associated with Non-Depolarizing Neuromuscular Blocking Agents
- Associated with the administration of pancuronium or vecuronium
- 3-hydroxy metabolites of pancuronium (3-desacetylpancuronium) and vecuronium (3-desacetylvecuronium) retain neuromuscular blocking activity and accumulate in the body with prolonged use
Neuromuscular Complications of Critical Illness
I. Neuropathy

Acute Motor Neuropathy Associated with Non-Depolarizing Neuromuscular Blocking Agents
- Occurs more readily in patients with renal or hepatobiliary disease
- Neuropathy occurs as a result of a toxic effect of the non-depolarizing agent in a patient with SIRS
- Neuropathy is more likely the longer these agents are used

Significant increase in the incidence when these agents are used for >48 hours
- Presents as difficulty weaning from the ventilator and limb weakness
Neuromuscular Complications of Critical Illness

I. Neuropathy

Electrodiagnostic Findings in Acute Motor Neuropathy Associated with Non-Depolarizing Neuromuscular Blocking Agents

- Primary axonal degeneration of mostly motor fibers

Neuromuscular Complications of Critical Illness

I. Neuropathy

Muscle Biopsy Finding in Acute Motor Neuropathy Associated with Non-Depolarizing Neuromuscular Blocking Agents

- Varying degrees of denervation, atrophy, and muscle necrosis
Thick Filament Myopathy

Neuromuscular Complications of Critical Illness
II. Myopathy

Thick Filament Myopathy
- Occurs in patients with a sudden severe asthma exacerbation
- Patients who receive NMBA and high dose corticosteroids
- Incidence associated with the length of chemical paralysis
Neuromuscular Complications of Critical Illness
II. Myopathy

Thick Filament Myopathy
- Douglass found an elevated CPK in 76% of patients ventilated with severe asthma
- 36% of these developed a symptomatic myopathy
- Dubois and Almon found the number of glucocorticoid receptors increase to three times normal after surgical interruption of nerve supply
- Suggests that a denervated muscle may be hypersensitive to treatment with corticosteroids
Neuromuscular Complications of Critical Illness

II. Myopathy

Thick Filament Myopathy
- Patients present with failure to wean and flaccid limb weakness of distal and proximal muscles
- Facial muscles are often affected
- Peripheral sensation is normal
- CPK levels are significantly increased
- Recovery is usually rapid

Electrodiagnostic Findings in Thick Filament Myopathy
- Motor nerve conduction velocities are usually normal
- Low amplitude CMAP
- Sensory studies are normal
- Repetitive nerve stimulation is normal
- Needle EMG reveals motor unit action potentials that are of short duration, low amplitude and polyphasic
Neuromuscular Complications of Critical Illness
II. Myopathy

Muscle Biopsy Finding in Thick Filament Myopathy
- Loss of structure centrally that is a result of destruction of the thick myosin filaments
- Pattern of atrophy, necrosis, and regeneration of type I and II muscle fibers
- Little or no associated inflammation

Normal

Central necrosis and atrophy

Enhanced calcium-induced proteolysis

Loss of A Bands (EM)
Acute Necrotizing Myopathy of Intensive Care

Occurs in the presence of overwhelming infections, with viruses, Escherichia coli, Leptospirosis, Legionnaires disease, and organisms that cause toxic shock syndrome.

Presents with severe weakness and myalgias, high concentrations of CPK and myoglobinuria.
Neuromuscular Complications of Critical Illness

II. Myopathy

Acute Necrotizing Myopathy of Intensive Care

- Electrodiagnosis is consistent with a severe myopathy
- Muscle biopsy shows severe widespread muscle fiber necrosis
- Prognosis correlates with the severity of the myopathy

Catabolic Myopathy
Neuromuscular Complications of Critical Illness

II. Myopathy

Catabolic Myopathy

- Ill-defined
- Believed to result from the action of Interleukin-1 and tumor necrosis factor
- Defects in high-energy metabolites in patients with respiratory failure, cardiogenic shock, severe congestive heart failure, and sepsis

Direct Muscle Stimulation

- Direct Muscle Stimulation can help in distinguishing myopathy from peripheral neuropathy in the critically ill.
- In CIP the denervated muscles should retain electrical excitability and direct muscle stimulated CMAP should be normal. In Critical Illness Myopathy the muscle fibers lose excitability and thus the direct muscle and nerve stimulated CMAP are reduced.
Neuromuscular Complications of Critical Illness

Direct Muscle Stimulation

Neuromuscular Junction Abnormalities
Neuromuscular Complications of Critical Illness

III. Neuromuscular Junction Abnormalities

- Transient persistent neuromuscular blockade occurs with the use of non-depolarizing NMBA long after the medications are discontinued
- More likely to occur in patients with renal or liver disease
- Repetitive Nerve Stimulation reveals a neuromuscular transmission defect (decremental response)

Patients present with failure to wean from the ventilator and flaccid limbs

Recovery over the course of several weeks or months

Segredo et al. associated metabolic acidosis, elevated plasma concentrations of magnesium and female gender as variables with the presence of prolonged neuromuscular blockade

Vecuronium total dose, rate of administration and duration of treatment did not correlate with the presence of prolonged neuromuscular blockade
Neuromyopathy

Neuromuscular Complications of Critical Illness

III. Neuromyopathy

- Refers to the coexistence of neuropathy and myopathy in patients with critical illness
- Critical Illness Polyneuropathy and Acute Necrotizing Myopathy of Intensive Care
- Incidence = 6% of patients with neurologic illness secondary to critical illness
- Nates felt that the presence of one neuromuscular complication of critical illness may provide an environment in which the second process is encouraged
Neuromuscular Complications of Critical Illness Management

- Prompt and effective treatment of underlying disease, in particular sepsis, and prevention of MODS
- “Tight glycemic control” (reduced incidence CIP from 52% to 29% !)
- Avoid contributory factors
  - steroids
  - NMBAs
  - Hypoalbuminaemia
- Involve Rehabilitation Team

Critical Illness Polyneuropathy: A 2-Year Follow-Up Study in 19 Severe Cases

<table>
<thead>
<tr>
<th>Case</th>
<th>Day</th>
<th>Sensory findings</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12</td>
<td>Distal sensory loss</td>
<td>2 years:paraparesis</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>n.a.</td>
<td>Complete recovery within 3 m</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>Distal sensory loss</td>
<td>2 years:quadriplegia</td>
</tr>
<tr>
<td>4</td>
<td>20</td>
<td>Distal sensory loss</td>
<td>Death at day 65 without recovery</td>
</tr>
<tr>
<td>5</td>
<td>20</td>
<td>Normal</td>
<td>Complete recovery within 3 m</td>
</tr>
<tr>
<td>6</td>
<td>13</td>
<td>Distal sensory loss</td>
<td>Complete recovery within 1y</td>
</tr>
<tr>
<td>7</td>
<td>7</td>
<td>n.a.</td>
<td>Complete recovery within 3m</td>
</tr>
<tr>
<td>8</td>
<td>30</td>
<td>Distal sensory loss</td>
<td>2 years after: quadriplegia</td>
</tr>
<tr>
<td>9</td>
<td>15</td>
<td>Distal sensory loss</td>
<td>Complete recovery within 6 months</td>
</tr>
<tr>
<td>10</td>
<td>29</td>
<td>Distal sensory loss</td>
<td>Death at day 168</td>
</tr>
</tbody>
</table>

Seze et al, Eur Neurol 2000;43:61-69
Critical Illness Polyneuropathy: A 2-Year Follow-Up Study in 19 Severe Cases

<table>
<thead>
<tr>
<th>Case</th>
<th>Day</th>
<th>Sensory findings</th>
<th>Follow up</th>
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</thead>
<tbody>
<tr>
<td>11</td>
<td>33</td>
<td>Normal</td>
<td>Complete recovery within 3 m</td>
</tr>
<tr>
<td>12</td>
<td>19</td>
<td>Normal</td>
<td>Complete recovery within 6 m</td>
</tr>
<tr>
<td>13</td>
<td>23</td>
<td>Distal loss</td>
<td>Complete recovery within 1 y</td>
</tr>
<tr>
<td>14</td>
<td>30</td>
<td>Distal sensory loss</td>
<td>Complete recovery within 6 m</td>
</tr>
<tr>
<td>15</td>
<td>31</td>
<td>n.a.</td>
<td>Complete recovery within 6 m</td>
</tr>
<tr>
<td>16</td>
<td>120</td>
<td>Normal</td>
<td>Complete recovery within 1 y</td>
</tr>
<tr>
<td>17</td>
<td>10</td>
<td>Distal sensory loss</td>
<td>2 years: quadriplegia</td>
</tr>
<tr>
<td>18</td>
<td>29</td>
<td>n.a.</td>
<td>Death at day 72 without recovery</td>
</tr>
<tr>
<td>19</td>
<td>25</td>
<td>Distal sensory loss</td>
<td>Death at day 348</td>
</tr>
</tbody>
</table>

Seze et al, Eur Neurol 2000;43:61-69

Persistent neuromuscular and neurophysiologic abnormalities in long-term survivors of prolonged critical illness*

Simon N. Fletcher, FRCA; Daniel D. Kennedy, FRCA; Indrajit R. Ghosh, MRCP; Vijay P. Misra, MRCP; Kevin Kiff, FRCA; John H. Coakley, MRCP; Charles J. Hinds, FRCP, FRCA

- All 22 patients gave a clear history of prolonged weakness, fatigue and difficulty with mobility
- In some patients weakness was still clinically evident up to 4 yrs after discharge and in 1 was severe
Persistent neuromuscular and neurophysiologic abnormalities in long-term survivors of prolonged critical illness

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- Neurological examination
  - sensory deficits in 27%
  - motor weakness in 18%
  - sensory and motor deficits in 14%
  - bilateral peroneal nerve palsies in 2 patients
  - bilateral upper limb weakness in 3 patients

Outcomes
General Outcome Concepts

- Severe weakness, prolonged recovery and residual clinical motor and sensory neurological deficits are extremely common in survivors of protracted critical illness.

- In those with mild or moderate CIP recovery is often relatively rapid and complete (weeks or months).

- In some with more severe ICUAP recovery is delayed for years.

- Quality of life is often impaired.

- In a few persistent, severe neuromuscular weakness may contribute to late deaths.
ETIOLOGY & PATHOGENESIS

SIRS/SEPSIS/MODS

STEROIDS NMBAs

Hyperglycaemia
Hypoalbuminaemia
Hyperosmolality
Hyperalimentation
Hyperpyrexia

MYOPATHIES

MOTOR AXON
NEUROMUSCULAR JUNCTION
MOTOR END PLATE

Much of Newer Literature Suggests Myopathy More Common

- Acute myopathy 3x as common as polyneuropathy --Lacomis M&N May 1998.
Summary of Literature Review and Clinical Experience

- There is vast disparity in the medical literature.
- Much of the early literature appears unsatisfactory in adequately describing the conditions.
- The vast majority, at our institution, have a primarily myopathic influence.

Deficiencies in the Early Literature Include:

- Initially studied primarily severely tetraparetic patients, resulting in little motor unit evaluation
- Only sporadic use of nerve and muscle biopsies
- No use of direct muscle stimulation
- Over-interpreted absent F-waves
Complicating Factors in ICU Assessment

- Poor mobility
- Frequent cognitive impairments and sedation
- Frequent limb edema
- Often co-morbid factors (e.g., diabetes mellitus, CRF)

Myopathy not axonopathy

- Described as a “motor predominant” axonopathy because it’s a myopathy!
- Rarely sensory symptoms or signs in communicative patients
- Virtually never neuropathic pain
- Little to no membrane instability
Myopathy not Axonopathy

- Many short duration, small amplitude polyphasic MUAPs
- "Early" Recruitment!
- Little to no improvement with direct muscle stimulation
- Involves proximal and distal muscles equally

Myopathy not Axonopathy

- Recovery is generally too rapid to be attributed to re-innervation of catastrophic axonal loss.
Many Cases Appear to be “Membranopathies”

- Normal histology and rapid recovery

- Presumption: The muscle membrane becomes dysfunctional, inexcitable and leaky

- Resultant loss of myoglobin

CIM

- Others cases similar to disuse atrophy with loss of type II fibers

- Loss of thick myosin filaments more frequent seen in patients treated with corticosteroids and NMJ blocking agents

- Necrotic/muscle necrosis less common
Combination of Neuropathy and Myopathy is not Uncommon

My Opinion

- Electrodiagnosis remains the most practical and comprehensive testing for ICU weakness
Electrodiagnostic Approach

Need to assess for neuropathy, myopathy, primary NMJ disorder, motor neuron disease, central weakness

Electrodiagnostic Approach

- Neuropathy: CIP, DM, Other pre-morbid, AIDP, CIDP, MMN
- Myopathy: CIM, PM, other inflammatory, congenital
- NMJ: MG, MS, Botulinum
- MND
- Central: CVA, Cervical myelopathy
- Co-morbid conditions
**Electrodiagnostic Approach**

- Motor NCS with F-waves
- Include phrenic studies if indicated
- Sensory studies
- Repetitive Stimulation including fast stimulation or (preferably) post-exercise
- Needle EMG
- If needed, direct muscle stimulation

Note: Will generally sample at least three limbs of the above

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**Summary**

- The constellation of neuromuscular abnormalities in ICU weakness can be complex
- Caution should be used with earlier literature (ie before 1997) or more recent reviews that rely on earlier literature
- Additional studies are needed to further qualify and understand these conditions
Summary

- Comprehensive clinical and electrodiagnostic evaluation can provide an effective evaluation of generalized weakness in the ICU.