How should we deal with muscle weakness in critically ill patients?*

Peripheral neuromuscular disorders are highly prevalent in critically ill patients. Two distinctive entities have been described: critical illness polyneuropathy and critical illness myopathy. Because of the significant overlap of these two disorders, the term "critical illness polyneuromyopathy" (CIPNM) is used by most clinicians. CIPNM is now recognized as the most common peripheral neuromuscular disorder in the intensive care unit (ICU) patients. The main symptom is symmetrical muscle weakness, which usually predominates in the proximal part of the limbs. Facial muscles are usually spared. Other clinical signs may include sensory loss, decreased deep tendon reflexes, and muscle atrophy. Involvement of the limbs carries numerous risks, such as prolonged mechanical ventilation, difficulty weaning from mechanical ventilation, prolonged ICU and hospital stay, delay in return to physical autonomy, prolonged physical dependency, and need of rehabilitation (1–5). Severity of clinical course varies from a mild temporary weakness to debilitating weakness, leading to prolonged hospital stay and even death due to secondary hospital complications. Although clinically significant muscular weakness is seen in 25% of ICU patients who remained mechanically ventilated >7 days (6), the prevalence can be as high as 70% to 100% in patients with sepsis and multiple organ failure (7). Muscular weakness may appear as early as 7 days of ICU admission and may last months after ICU discharge (8), although duration is generally unpredictable.

*See also p. 2499.

Key Words: critical illness polyneuromyopathy; muscle weakness; polyneuropathy; myopathy; exercise; mobilization

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Muscle weakness can be quantified by using the medical research council score (9), in which three muscle functions are evaluated in both upper and lower limbs, with good reproducibility, even in mechanically ventilated patients. However, a definitive diagnosis of neuromuscular disorders requires invasive measures. Electrophysiologic studies revealing sensoriomotor axonapathy with decreased muscle action potential for critical illness polyneuropathy and muscle biopsy showing loss of myosin for critical illness myopathy are needed. In clinical practice, definitive diagnostic measures are rarely utilized.

Risk factors for CIPNM include duration of ICU stay, persistent systemic inflammatory response syndrome/multiple organ failure, poor glycemic control, use of corticosteroids or neuromuscular-blocking agents, electrolyte imbalance (e.g., hyperkalemia), hypoalbuminemia, parenteral nutrition, and hyperosmolarity (10).

Although there is no specific treatment for CIPNM, several preventive measures can be considered, such as strict glucose control (11–13), avoiding unnecessary prolonged use of corticosteroids or neuromuscular-blocking agents, sedation-sparing protocols, timely electrolyte replacements, and optimal nutrition.

Early activity of immobilized ICU patients makes theoretical sense to prevent or slow down CIPNM. Earlier studies have shown the safety and feasibility of early activity (14) and decreased ICU/hospital stay (15) in critically ill patients.

In this issue of *Critical Care Medicine*, Burtin and colleagues (16) investigated the potential benefit of daily exercise by using a bedside cycle ergometer on functional exercise capacity, functional status, and quadriceps force in mechanically ventilated ICU patients. In this randomized controlled study, 90 critically ill patients were divided into two groups: 1) one group received only respiratory physiotherapy and a daily standardized passive or active motion sessions of upper and lower limbs (control, n = 32); 2) the other group received additional passive or active exercise training sessions of 20 mins every day by using a bedside ergometer (treatment group, n = 26). Both groups were well matched in terms of the proportion of patients receiving corticosteroid, neuromuscular-blocking agents, and vasopressive support, except for the treatment group that had a longer ICU stay and a longer period of intravenous sedation at the time of inclusion to the study. Six-minute walk distance, SF-36 health survey questionnaire, and quadriceps force showed significantly higher or improved results at hospital discharge in the treatment group. However, there was no difference in hand grip force and ability to stand up independently between the groups at hospital discharge. Similarly, weaning time from mechanical ventilation, length of ICU stay, hospital stay, and 1-year mortality did not differ in both groups.

Early mobilization or activity in critically ill patients as a preventive measure of CIPNM may potentially hold promise. The current study is the first randomized controlled study looking at the benefit of exercise in ICU outcome in critically ill patients with several limitations. First, it is not known whether an additional 20-min exercise session would generate the similar beneficial effects in a control group. Second, intensity of exercise treatment was not determined by objective data, such as cardiopulmonary parameters. Third, rehabilitation after ICU transfer was not standardized. Forth, there were only a limited number of patients assessed for CIPNM with electrophysiologic studies. Therefore, outcome measures could not be applied to this subgroup due to the small number of patients (four patients in each group). So, it is not known what percentage of patients really had weakness secondary to CIPNM.

Evaluation of weakness in ICU patients should probably be performed by using medical research council score be-

cause the invasive methods are not practical in our current critical care practice. Future randomized controlled studies are needed to determine whether early activity in patients with documented CIPNM would prevent or slow down the process and improve the ICU/hospital outcome. The main challenge, however, is to find an optimal exercise protocol for individual patients based on their clinical characteristics and the degree of exercise that would have positive impact on ICU outcome measures. As reported in the current article, one patient experienced Achilles' tendon rupture in the treatment group. Because there is no specific treatment for CIPNM, elimination or avoidance of risk factors should be a common practice for those who manage critically ill patients.

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REFERENCES

1. Leijten FS, Harick-de Weerd JE, Poortvliet DC, et al: The role of polyneuropathy in motor convalescence after prolonged mechanical ventilation. *JAMA* 1995; 274: 1221–1225
2. Garnacho-Montero J, Amaya-Villar R, Garcia-Garmandia JL, et al: Effect of critical illness polyneuropathy on the withdrawal from mechanical ventilation and the length of stay in septic patients. *Crit Care Med* 2005; 33: 349–354
3. De Jonghe B, Bastuji-Garin S, Sharshar T, et al: Does ICU-acquired paresis lengthen weaning from mechanical ventilation? *Intensive Care Med* 2004; 30:1117–1121
4. Latronico N, Peli E, Botteri M: Critical illness myopathy and neuropathy. *Curr Opin Crit Care* 2005; 11:126–132
5. Latronico N: Neuromuscular alterations in the critically ill patient: Critical illness myopathy, critical illness polyneuropathy or both? *Intensive Care Med* 2003; 29:1411–1413
6. De Jonghe B, Sharshar T, Lefaucheur JP, et al: Paresis acquired in the intensive care unit: A prospective multicenter study. *JAMA* 2002; 288:2859–2867
7. De Jonghe B, Cook D, Sharshar T, et al: Acquired neuromuscular disorders in critically ill patients: A systematic review. *Intensive Care Med* 1998; 24:1242–1250
8. van der Schaaf M, Beelen A, de Groot IJ, et al: Critical illness polyneuropathy: A summary of the literature on rehabilitation outcome. *Disabil Rehab* 2000; 22:808–810
9. Kleyweg RP, van der Meché FG, Meulstee J: Treatment of Guillain-Barré syndrome with high-dose gammaglobulin. *Neurology* 1988; 38:1639–1641
10. de Letter MA, Schmitz PI, Visser LH, et al: Risk factors for the development of polyneuropathy and myopathy in critically ill patients. *Crit Care Med* 2001; 29:2281–2286
11. Van den Berghe G, Wouters P, Weekers F, et al: Intensive insulin therapy in the critically ill patients. *N Engl J Med* 2001; 345: 1359–1367
12. Van der Berghe G, Wouters PJ, Bouillon R, et al: Outcome benefit of intensive insulin therapy in the critically ill: Insulin dose versus glycemic control. *Crit Care Med* 2003; 31: 359–366
13. Van den Berghe G, Wilmer A, Hermans G, et al: Intensive insulin therapy in the medical ICU. *N Engl J Med* 2006; 354:449–461
14. Bailey P, Thonsen GE, Spuhler VJ, et al: Early activity is feasible and safe in respiratory failure patients. *Crit Care Med* 2007; 35:139–145
15. Morris PE, Goad A, Thompson C, et al: Early intensive care unit mobility therapy in the treatment of acute respiratory failure. *Crit Care Med* 2008; 36:2238–2243
16. Burtin C, Clerckx B, Robbeets C, et al: Early exercise in critically ill patients enhances short-term functional recovery. *Crit Care Med* 2009; 37:2499–2505

Bending gender rules for septic patients: Are host responses positioned equally for all critically ill patients?*

The relative influences on outcomes in critically ill patients have been studied for decades. Investigators have long established that illness severity impacts intensive care unit (ICU) mortality but believe less strongly about the myriad of other factors that have been studied. Perhaps the most controversial factor that has been studied is the gender of the individual in question. Different results concerning the role of gender in predicting outcomes have arisen in different populations of human beings and laboratory animals, despite being well-analyzed studies by seemingly well-meaning, unbiased investigators.

Interestingly, in laboratory animals, depending on the species and investigational model, the results have suggested that females seem to have an immunologic advantage in septic challenges after trauma or hemorrhage (1). Androgens may have immunosuppressive effects; its administration hindered the development of fatal autoimmune disease in NZB/NZW F1 hybrid mice (2). In other murine models, Zellweger et al found that female mice sustained a significantly higher survival rate after similar infectious challenges than corresponding male mice (3).

In human beings, the data are difficult to interpret due to heterogeneous populations and varied end points. In a prospective human study, Schröder et al studied gender-related differences in outcomes of patients with surgical sepsis and observed that women fared better (4). Conversely, our group found that, in a study of 443 septic surgical ICU patients, the female gender predicted mortality (5). Croce et al studied 17,000 trauma patients and noted that, although women may have had a survival advantage and men may have had more infectious complications, no overall difference in mortality was noted (6). Other investigators found that, in the younger trauma patients, male patients had a significantly higher incidence of multiple organ failure and mortality, and longer ICU and hospital length of stay than their female counterparts (7).

In this issue of *Critical Care Medicine*, Dr. Combes and colleagues (8) recount their experience with ICU patients who develop nosocomial infections in their article titled "Gender impact on the outcomes of critically ill patients with noso-

*See also p. 2506.

Key Words: sepsis; gender; critical; illness; nosocomial

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