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What is new in prevention of muscle weakness in critically ill patients?

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Introduction

Muscle weakness is as common as arterial hypotension in critically ill patients, but the degree and consequences of muscle weakness vary depending on the multi-factorial pathophysiology of intensive care unit (ICU) acquired muscle weakness (ICUAW). A septic encephalopathy typically recovers with successful sepsis treatment, and difficulty in weaning from mechanical ventilation or limb muscle weakness can be the first signs noted during the early ICU stage. Multiple mechanisms of inflammation such as sepsis, trauma, injury, tumor, renal and liver failure, immobilization (due to bed rest, deep sedation, and neuromuscular blockade), and malnutrition induce persistent ICU-acquired peripheral neuromuscular diseases such as muscle wasting, critical illness myopathy, and neuropathy [1]. Critical illness myopathy and neuropathy may persist for years after discharge from the acute care hospital. Quality of life of ICU survivors is affected by impairments of functional mobility even 5 years after ICU discharge [2].

Skeletal muscle weakness involves not only the limbs, but also the respiratory muscles. Recent data suggest that ICUAW is an independent predictor of failed weaning from the ventilator and prolonged patients' dependence on the ventilator. In addition, ICUAW is associated with pharyngeal muscle dysfunction and increases the risk of symptomatic tracheal aspiration [3], which further explains the association of ICUAW with ICU length of stay, duration of hospitalization, and in-hospital mortality. Accordingly, it is important to utilize strategies that help prevent muscle weakness in the ICU.

Keep your patients moving

Rehabilitation in the ICU is rapidly gaining popularity, and a new framework of early rehabilitation is replacing the old view that rehabilitation should wait until the patient is clinically stable. Early rehabilitation can be safely implemented in the ICU, provided that patients are given little or no sedation and neuromuscular blocking agents, and the ICU staff and families are adequately prepared to face the challenge of awake intubated patients. Moderate exercise in the ICU can mitigate the adverse consequences associated with immobility by improving muscle strength and physical function, and can translate into improved patient outcomes [4]. In a well-organized setting with early rehabilitation already used in clinical practice, even the addition of 1 day of physical and occupational ICU therapy improves functional independence and quality of life at ICU discharge, and may decrease length of stay and provide benefit up to the 6-month follow-up [5].

Three prospective studies conducted in the medical ICU demonstrated improved outcomes when mobilization was made a priority: patients have less exposure to benzodiazepines, shorter durations of delirium, less time on mechanical ventilation, fewer ICU days, fewer hospital days, and better functional independence at hospital discharge. Although the impact on long-term outcome is still unclear [6, 7], early rehabilitation in the ICU can generate net financial savings in addition to improving short-term outcome [8]. Therefore, implementation of specific protocols is recommended to overcome barriers to early application of rehabilitation in the intensive care unit.

Currently, there are few data on the effects of early mobilization in the surgical ICU, with some fear that surgical patients could be harmed by premature mobilization following major surgery or trauma. Preliminary evidence from retrospective observational studies or surveys suggests that early rehabilitation can be safe in these patients [9]. The authors are currently conducting a multinational randomized controlled study to evaluate whether a validated intervention [10], the SICU optimal mobilization scale (SOMS)-guided approach to goal-directed early mobilization therapy, improves muscle strength, ICU length of stay until discharge readiness, and functional independence at ICU and hospital discharge [11].

Neuromuscular electrical stimulation added to usual care may be more effective than usual care alone for preventing skeletal-muscle weakness in critically ill patients. However, there is inconclusive evidence for its benefit in the prevention of muscle wasting [12]. Ongoing trials are expected to provide further evidence on this topic [13].

Do not immobilize the respiratory muscles unnecessarily

Postoperative pulmonary complications are responsible for significant increases in hospital cost as well as patient morbidity and mortality; respiratory muscle dysfunction represents a contributing factor. The diaphragmatic strength is very sensitive to immobilizing treatments in the ICU. In contrast to skeletal muscles that are electrically silent at rest, the respiratory muscles receive continuous phasic brainstem activations independent of volitional muscle contraction.

The figure illustrates the clinically important interplay between conditions that activate and immobilize respiratory muscles in critically ill patients. Excessive contractions of the respiratory pump muscles due to impaired gas exchange and air hunger may increase the risk of traumatic lung injury as a consequence of high transpulmonary pressure [14]. Opioids and sedatives may be used to counterbalance excessive contractions of the respiratory pump muscles in patients on mechanical ventilation; however, these respiratory depressants decrease the drive to the phrenic nerve and may lead to diaphragm atrophy. Recent data suggest that the time course as well as the mechanisms of immobilization-induced diaphragmatic weakness observed in preclinical models including early disruption of the myofilament protein structure translates to ICU patients [15, 16]. In a clinical scenario, high-dose opioids and propofol infusions to enable volume control ventilation result in ventilator-induced diaphragmatic weakness that delays weaning from the ventilator. Spontaneous breathing on the ventilator appears to protect the diaphragm, unless high doses of anesthetic agents such as propofol are being given. Neuromuscular blocking agents exert a dose-dependent decrease in diaphragmatic contractility inducing atrophy, while the motor neuron drive remains high. This clinical scenario increases vulnerability to posttraumatic stress disorder [17].

Management strategies that help decrease the incidence of respiratory muscle dysfunction in the ICU include early and optimal mobilization of respiratory muscles while on mechanical ventilation, judicious use of respiratory depressant anesthetics and neuromuscular blocking agents, and ventilation modes that allow for spontaneous breathing or noninvasive ventilation whenever possible (Fig. 1).

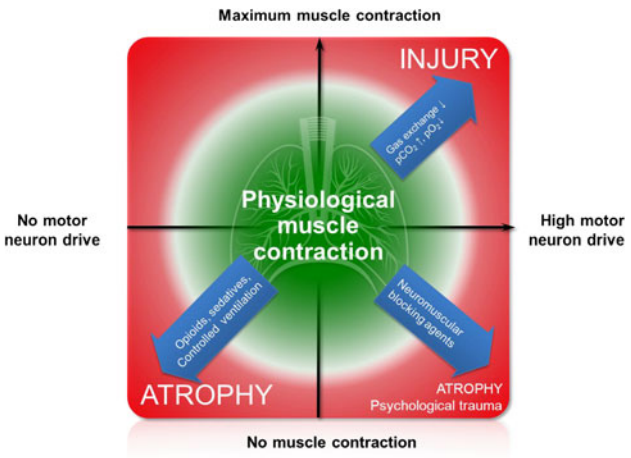

Fig. 1 Optimal activation of respiratory muscles in critically ill patients. The center of the figure (in *green*) illustrates ideal physiological muscle contractions of the respiratory pump muscles. The edges of the figure (in *red*) illustrate harmful states of forced output that occur when the drive to motor neuron and/or evoked muscle strength are either markedly depressed or excessive. The three *blue arrows* describe clinical scenarios that may change the balance between harmful and beneficial muscle contractions. The *left* lower quadrant illustrates a clinical scenario where opioids and sedatives are given to accomplish volume control ventilation leading to ventilator-induced diaphragmatic weakness. The *upper right* quadrant illustrates a clinical scenario where ARDS or sepsis leading to hypercarbia and hypoxia may induce a pathological increase in transpulmonary pressure leading to barotrauma

Aggressive and early treatment of sepsis

The degree of muscle wasting as well as the incidence and severity of critical illness polyneuropathy and myopathy increases with the duration of sepsis, and early and aggressive sepsis treatment helps prevent ICUAW. Several studies show that outcomes of patients with sepsis are improved with early, goal-directed therapy in septic shock and protocolized care driven by the Surviving Sepsis Campaign recommendations.

Nutrition

Immobilization, inflammation, and reduced nutrient intake or use may all contribute to muscle hypercatabolism and wasting during critical illness. Early enteral feeding improves the mortality and morbidity of ICU patients. Autophagy, a survival mechanism that provides cells with alternative sources of substrates in case of starvation, also contributes to increased muscle protein catabolism. Recent evidence suggests, however, that tolerating a substantial macronutrient deficit early during critical illness by delaying supplemental parenteral nutrition can be associated with increased activation of muscle autophagy and reduced incidence of ICUAW [18]. Postulated mechanisms include a more efficient removal of damaged intracellular organelles with improved cellular conditions for effective muscle contraction and strength generation [19]. Though fascinating, this hypothesis needs to be evaluated in future efficacy trials. Early enteral nutrition is beneficial and should not be restricted [20].

In summary, the important strategies to prevent ICU-acquired muscle weakness include early and aggressive treatment of the underlying condition, a cultural change toward early rehabilitation in the ICU where patients are given little or no sedation and neuromuscular blocking agents, limb mobilization, optimal activation of the respiratory pump muscles, and early enteral feeding.

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