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The Current Research Status of ICU-Acquired Muscle Weakness

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Abstract: ICU-acquired weakness is the most common neuromuscular injury in critically ill patients and an important issue that affects their long-term quality of life. Although ICU-acquired weakness has received increasing attention in recent years, there is still no consensus on its pathophysiological mechanisms, and there are knowledge gaps in identifying high-risk patients and subsequent treatment. This article summarizes the research on ICU-acquired weakness in terms of pathophysiological mechanisms, diagnostic methods, and treatment through a literature review.

Keywords: ICU-acquired weakness; Pathophysiology; Diagnosis; Treatment.

1. Introduction

ICU-acquired weakness denotes a neuromuscular weakness clinical syndrome observed in the intensive care unit (ICU). The syndrome manifests as a systemic and symmetrical deterioration or loss of muscle function, primarily impacting the limbs and respiratory muscles, with minimal influence on facial and ocular muscles[1]. Patients with this ailment may experience breathing challenges, restricted mobility, and other functional limitations. Electrophysiological assessments enable the classification of ICU-acquired weakness into three distinct subtypes: critical illness polyneuropathy(CIP),critical illness myopathy (CIM) and critical illness neuromyopathy(CINM)[2].

Due to the progress in critical care medicine, the mortality rate of critically ill patients has been reduced. However, the long-term physical impairment of ICU survivors is a growing concern[3]. ICU-acquired weakness is a common complication related to muscle weakness in critically ill patients, which is associated with difficulty in weaning respiratory muscles, prolonged ICU hospital stay, increased mortality and other long-term adverse outcomes[1]. About 80% of patients admitted to ICU will have neuromuscular dysfunction in different degrees and forms[4]. Some studies have found that the incidence of ICU-acquired weakness is 26%-65% in patients who are conscious after 5-7 days of mechanical ventilation, 67% in patients who have been ventilated for more than 10 days[5], 70% in patients with sepsis and systemic inflammatory response syndrome[6], and 100% in patients with multiple organ failure. ICU-acquired weakness also increases nursing costs by 60%[7]. A multicenter prospective study conducted in Canada revealed that ICU-acquired weakness occurs in 32.8% of critically ill patients, leading to increase in-hospital mortality rates and reduced quality of life when compared to non-affected individuals[8]. A further multicenter prospective study, encompassing a cohort of relatively young patients with an average age of 58.5 years, revealed the prevalence of ICU-acquired weakness among this demographic group. These young critically ill patients exhibited elevated one-year mortality and readmission rates[9]. At present, the incidence rate of ICU-acquired weakness is relatively high, causing huge economic and medical burdens for healthcare institutions and patients' families[10]. Hence, this review consolidates the latest insights into the pathophysiology, clinical diagnostics, and management of ICU-acquired weakness to enhance comprehension among readers regarding its prevalence in critically ill patients, with the goal of advancing clinical treatment outcomes.

2. Pathophysiology

Frequent triggers of ICU-acquired weakness comprise severe systemic inflammatory states, specific medication use (such as corticosteroids, neuromuscular blocking agents, aminoglycosides[11], vasoactive drugs[12], etc.), inadequate blood glucose control, and immobility[13]. Nevertheless, the precise pathological and physiological mechanisms leading to the development of ICU-acquired weakness currently remain unclear. Animal model-based studies indicate a close connection between acquired weakness and intricate structural or functional alterations in the central nervous system, peripheral nerves, and muscle fibers[1]. This relationship often presents as muscle atrophy, impaired muscle function, and hypokalemia[14,15].

Muscle atrophy ensues from an imbalance in muscle protein synthesis and degradation, leading to notable depletion of myosin and myosin-associated proteins in individuals with ICU-acquired weakness. This phenomenon markedly contrasts with the chronic muscle wasting attributed to malnutrition[16]. At the same time, factors such as Structural muscle alterations[17], Microcirculatory disturbances[18],Mitochondrial dysfunction[1],Inadequate autophagy activation[19], ion channel dysfunction[20] can lead to muscle dysfunction in patients with ICU-acquired weakness.

In addition, during the period of critical illness, the level of glucagon will increase, which will increase the catabolism of amino acids in the liver and induce hypoaminoacidemia[21]. Moreover, experiments have proved that increasing glucagon level and amino acid infusion can increase the breakdown of amino acids in the liver, and will not prevent muscle atrophy[21].

3. Diagnosis

The diagnosis of ICU-acquired weakness primarily depends on clinical manifestations and the evaluation of peripheral and/or respiratory muscle strength.

The evaluation of peripheral muscle strength can be conducted through various methods:1) the clinical quantification of muscle strength involves the Medical Research Council sum score (MRC-SS) and handgrip dynamometry[22]. This assessment necessitates patient alertness and cooperation for executing actions as directed by the evaluator. Nevertheless, critically ill patients commonly face challenges in cooperation due to sedation, delirium, and other factors [22]. As a result, this approach is mainly employed for muscle strength assessment in patients at discharge or during follow-up[23]. 2) Nerve conduction studies(NCS): This method can be used for unconscious and uncooperative patients, and the test is fast, safe, and easy to administer. It is a common neuroelectrophysiological examination method that evaluates the normalcy of nerve conduction function by measuring the conduction velocity and response time of nerve fibers, thereby assisting in the diagnosis and treatment of neurological diseases.[24]. Relevant studies have shown that the sensitivity of single peroneal NCS for neuromuscular diseases is 100%, with a specificity of 81%[25]. Additionally, the specificity of this test in patients with ICU-acquired weakness is 75%, while it is 36% in healthy controls[26]. 3) Ultrasonic examination: ultrasound examination enables rapid and repetitive assessment of changes in the quantity, quality, and structure of patient muscles at the bedside[27]. A study involving 63 critically ill patients suggested that the predictive sensitivity of lateral femoral ultrasonography for fiber necrosis in muscle biopsy specimens was 74%, and the sensitivity was 85% in patients without potential iatrogenic causes of muscle necrosis[14]. Although muscle ultrasonography is a potential marker for the diagnosis of ICU-acquired weakness[28], it relies on the operator's skill and experience and may underestimate muscle and protein loss[29]. 4) nerve and muscle biopsies are characterized by their high invasiveness and the numerous complications they entail, which has hindered their widespread adoption in routine clinical practice [27].

Assessment of respiratory muscles can be performed by: 1) measuring maximal inspiratory pressure and expiratory pressure to evaluate the overall strength of respiratory muscles, where high values can indicate the absence of respiratory muscle weakness[30]; 2) assessing diaphragmatic muscle pressure, where elevated values can suggest the absence of respiratory muscle weakness. However, this technique is invasive and challenging to perform, thereby restricting its clinical utility[31]; 3) conducting chest X-ray and lung ultrasound examinations. Both methods are straightforward, convenient, and reproducible tests with relatively good diagnostic accuracy, albeit with lower sensitivity and specificity[32].

4. Preventive and Therapeutic Measures

Various approaches are employed in clinical settings to prevent and manage ICU-acquired weakness; however, the outcomes remain unsatisfactory[19]. Established treatments currently include: 1) Glycemic control: Although an optimal blood glucose target is not yet defined, maintaining fasting blood sugar levels within the normal range in ICU patients exerts a protective effect on both the central and peripheral nervous systems[33], leading to a significant decrease in the occurrence of ICU-acquired weakness[34]. 2) Minimization of unnecessary sedation and early mobilization: Early mobilization is effective in mitigating muscle atrophy, reducing hospital stays, and preventing respiratory muscle-related pneumonia, thereby playing a crucial role in the prevention of ICU-acquired weakness[35]. 3) Rehabilitation training: Studies have demonstrated that ICU patients undergoing rehabilitation training exhibit substantial improvement in activity levels and muscle strength upon ICU discharge compared to those without such intervention, and also experience a higher 6-month survival rate[36]. 4) Neuromuscular electrical stimulation (NMES) is a technique that uses low-frequency electrical current to stimulate specific muscle groups through electrodes[37], and it has been proven to be effective in treating damaged muscles[38]. Studies have shown that NMES can effectively improve muscle strength, shorten the duration of mechanical ventilation, ICU stay, and total hospital stay for ICU patients, while also enhancing patients' autonomy in daily life and improving their activity status at discharge. However, the impact of NMES on the functional status, level of consciousness, and mortality rate of ICU patients during hospitalization is still unclear. Furthermore, there is no evidence that NMES treatment can reduce the mortality rate of ICU patients[39].

5. Conclusion

ICU-acquired weakness is a prevalent complication in ICU patients, deeply affecting short-term and long-term clinical outcomes. Given the absence of specific treatment protocols for this condition, early mobilization has proven to be crucial in preventing ICU-acquired weakness. Consequently, it is imperative to advance comprehension of ICU-acquired weakness and enforce early prevention strategies to enhance the long-term prognosis of patients.

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