Intensive Care Unit–acquired Muscle Weakness

An Ounce of Prevention Is Worth a Pound of Cure

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INTENSIVE care unit–acquired weakness (ICUAW) is defined as bilateral symmetrical limb weakness in critically ill patients. ICUAW is the clinical manifestation of critical illness neuromyopathy and is unrelated to any other etiology. It typically presents as flaccid quadiparesis with hyporeflexia or areflexia; the cranial nerves are usually spared. ICUAW presents a grave public health problem: it is a common complication of critical illness and has a profound impact on outcomes, increasing the duration of mechanical ventilation, prolonging intensive care unit (ICU) and hospital length of stay, worsening long-term functional status, and increasing mortality.[1–5] The majority of literature on ICUAW focuses on the medical ICU population. However, patients in the surgical ICU differ from those in the medical ICU—they experience surgical trauma, pain, inflammation, and lingering effects of anesthetic medications—making ICUAW more common in the surgical population. In this issue of Anesthesiology, Farhan *et al.*[6] provide the most thorough discussion of muscle weakness in the surgical ICU to date. They review the etiology and consequences of ICUAW in the surgical ICU, and, most importantly, they provide a lengthy discussion of preventative measures to assist the practicing clinician in averting muscle weakness in critical illness. The goal of this editorial is to highlight the key messages from their review, focusing on the impact of ICUAW in terms of incidence and long-term implications, as well as methods that can be used to prevent weakness in critical illness.

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ICUAW occurs because of the physiologic and immunologic effects of critical illness, immobilization and mechanical unloading of muscles, prolonged mechanical ventilation, medications, and inadequate nutrition. This weakness affects half to three quarters of patients admitted to the surgical ICU.[7,8] ICUAW impairs the long-term functional status of ICU survivors.[9] A study of survivors of acute respiratory distress syndrome found that, despite improvement in lung function, all patients complained of decreased physical function 1 yr after ICU discharge.[3] Patients blamed this decrease on fatigue, weakness, and diminished muscle mass. Less than half of survivors had returned to work in this time period. And, these complaints persisted over time—at 5 yr after ICU discharge, all patients complained of weakness and decreased ability to exercise compared with before their ICU stay, and only 77% had returned to work.[4] Those who had returned to work often required a modified work schedule or other accommodation. Patients' mental health was also affected by their illness, with more than 50% of survivors suffering from depression or anxiety. And, survivors incurred healthcare costs that were higher than those incurred by their healthy peers. Similarly, a study of long-term outcomes in survivors of severe sepsis showed that severe sepsis was associated with functional disability and cognitive impairment that persisted for at least 8 yr.[5]

Fortunately, there are steps the practicing clinician can take to help prevent ICUAW, which Farhan *et al.* describe in detail. In our opinion, the most important of these preventative measures is early mobilization. Early mobilization of critically ill patients is feasible, safe, and effective, and results in improvements in functional and neuropsychiatric outcomes.[9] Early literature on mobilization focused on the medical ICU population,[10–14] perhaps because of fewer perceived barriers to exercise in medical patients. However, recent studies have shown its safety and effectiveness in surgical,[15] trauma,[16] and neurosurgical ICU patients.[17] At our institution, we routinely mobilize our surgical patients, including those requiring mechanical ventilation, vasopressor therapy, renal replacement therapy, and extracorporeal

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life support. We believe that early mobilization should be considered the standard of care, and all critically ill patients should be evaluated for participation.

Judicious use of medications is also of utmost importance. Farhan *et al.* specifically address the use of opioids and neuromuscular-blocking agents in the surgical ICU. Opioids are recommended for the treatment of pain. Pain management is especially important in the surgical ICU, where patients suffer from the pain and muscle trauma associated with surgery. The goal is to provide adequate pain control without oversedation, because both untreated pain and excessive use of opioids can contribute to delirium and poor outcomes. Neuromuscular-blocking agents can be used safely for a short period. Their use in the operating room results in transient weakness but has not been shown to contribute to the development of ICUAW. The short-term use of cisatracurium, when used early in the course of severe acute respiratory distress syndrome, may even improve outcomes.[18] But, the long-term use of neuromuscular-blocking agents may lead to prolonged weakness and thus should be avoided. Farhan *et al.* fail to discuss the choice of sedative medications and to reference the Clinical Practice Guidelines for the Management of Pain, Agitation, and Delirium in Adult Patients in the Intensive Care Unit put forth by the Society of Critical Care Medicine in 2013.[19] These guidelines recommend the use of nonbenzodiazapine sedatives (such as propofol or dexmedetomidine) because benzodiazepines are associated with increased incidence of delirium and prolonged duration of mechanical ventilation and may indirectly increase the incidence of ICUAW.

Whatever drug choices are ultimately made, Farhan *et al.* appropriately recommend regular drug review and drug holidays. At our institution, we include ICU pharmacists in daily rounds to facilitate regular medication review. And, daily drug holidays or sedation wake-ups have been shown to decrease the duration of mechanical ventilation and length of stay in the ICU.[20] When paired with spontaneous breathing trials, these drug holidays are associated with decreased mortality.[21]

Early recognition of sepsis is another important preventive measure. Providers must keep in mind that the potential sources of sepsis in surgical patients include not only those commonly considered in medical ICU patients (such as urinary tract infections, central line–associated blood stream infections, and ventilator-associated pneumonia) but also those associated with recent surgery such as wound infections and abscesses. Regardless of the source, sepsis must be treated aggressively, with particular emphasis on prompt administration of appropriate antibiotics.[22]

And, nutrition should be optimized to avoid underfeeding or overfeeding, and electrolytes should be monitored and repleted as needed. Unfortunately, there is conflicting evidence on the optimal time to initiate nutrition, the most accurate way to calculate energy needs, and the best mix of nutrients.[23,24] In general, enteral nutrition is preferred, but for patients in whom the enteral route is not an option because of the severity of their critical illness or the type/location of their surgery, parenteral nutrition may be considered.

Many of the aforementioned interventions can be instituted as a part of the "ABCDE" bundle, which aims to *a*ssess, prevent, and manage pain; perform *b*oth spontaneous awakening trials and spontaneous breathing trials; *c*hoose analgesia and sedation appropriately; assess, prevent, and manage *d*elirium; and promote *e*arly mobility and exercise.[25] Recently, the "ABCDE" bundle became the "ABCDEF" bundle, to recognize and promote *f*amily engagement in critical care. Patients and families should be empowered to participate in care to decrease complications, including ICUAW.

Overall, Farhan *et al.* should be congratulated for their outstanding contribution to the literature on ICUAW. It is now up to the frontline clinician to work arduously to avert ICUAW by understanding its presentation, consequences, and methods of prevention.

Competing Interests

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