CHEST Recent Advances in Chest Medicine

ICU-Acquired Weakness*

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Observational studies of patients receiving prolonged mechanical ventilation and other forms of critical care support have determined acquired neuromuscular disorders to be extremely common. Early studies used electrophysiologic investigations to diagnose critical illness polyneuropathy (CIP) and muscle biopsy to confirm critical illness myopathy (CIM). More recent approaches seek to obviate these invasive techniques and build on a standardized bedside neuromuscular examination to identify patients with acquired weakness syndromes. Serial examination in the alert patient may serve as a reasonable prognosticator for most patients.
The importance of ICU-acquired weakness syndromes is supported by the observation that muscle wasting and weakness are among the most prominent long-term complications of survivors of ARDS. In addition, a strong association appears to exist between acquired weakness and protracted ventilator dependence, an important determinant of ICU length of stay. Multivariate analysis has identified several risk factors associated with increased incidence for ICU-acquired weakness, including severe systemic inflammation, medications (specifically, corticosteroids and neuromuscular blocking agents), glycemic control, and immobility. We advocate an approach to this common syndrome that identifies risk factors early in the hope of minimizing their impact. ***(CHEST 2007; 131:1541–1549)***

Key words: critical illness; ICU-acquired weakness; myopathy; polyneuromyopathy

Abbreviations: CIM = critical illness myopathy; CIP = critical illness polyneuropathy; CMAP = compound muscle action potential; ICU-AP = ICU-associated paresis; ICU-AW = ICU-associated weakness; MRC = Medical Research Council; NMBA = neuromuscular blocking agent

Wasting syndromes associated with protracted infection have long been recognized. Osler[1] commented on the "rapid loss of flesh" observed in patients with prolonged sepsis in the preantibiotic era. With the advent of improved cardiopulmonary support for the critically ill, syndromes of pronounced neuropathy and myopathy are increasingly recognized in the survivors of acute critical illness.

Investigations of patients with prolonged sepsis and severe motor dysfunction recognized during convalescence first appeared in the 1980s.[2] Over the next 25 years, comprehensive evaluations for these disorders have supported the significance of these initial investigations. Electrophysiologic testing, histopathologic evaluation, and prospective cohort studies[3–14] have created a substantial body of literature on neuromuscular disease in critical illness that highlights common risk factors and delineates the extent of injury.

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Variation in terminology and nosology characterizes this literature. Disease states, such as critical illness polyneuropathy (CIP) and critical illness myopathy (CIM), have been defined by advanced neuromuscular testing and muscle biopsy that are not uniformly performed in routine critical care. Given the dichotomy between the commonality of weakness in the critically ill and the limited number of electrophysiology tests performed, this review embraces an overarching term for neuromuscular disease in the critically ill: *ICU-acquired weakness*

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(ICU-AW). This diagnosis, defined simply by structured examination, can be applied more generously and may permit more uniform reporting of affected patients by intensivists. Case definitions for each neuromuscular disease state will be clarified below.

Clinical Presentation

Patients with ICU-AW are usually recognized in two bedside contexts. Most commonly, the clinician struggling to liberate a patient from mechanical ventilation will entertain the diagnosis of weakness. This diagnostic evaluation focuses initially on the respiratory muscles. The patient with ICU-AW, while slowly and globally recovering, exhibits generalized weakness that impairs not only return to spontaneous breathing but mobilization in general. The second bedside context involves the patient with such profound weakness despite return of sensorium that causes of quadriplegia are entertained. In both cases, if neuromuscular function recovers, it often lags well behind other organ system repair.

Physical examination of patients for ICU-AW is dependent on the cooperation and maximal effort of the patient, an aspect of bedside assessment that can be confounded by sedation, delirium, encephalopathy, and other ICU influences on cortical brain function. When a reliable motor examination is possible, affected patients will exhibit generally symmetrical motor deficits in all limbs, ranging from paresis to true quadriplegia.[15] A standardized bedside muscle examination can be utilized to evaluate individual muscle groups. The Medical Research Council (MRC) score includes formal testing of three muscle groups in each limb on a scale from one to five (Table 1).[16] This scoring has demonstrated excellent interrater reliability, including evaluations of patients with Guillain-Barre syndrome receiving mechanical ventilation,[17] and can be utilized to document the extent of disease and track serial changes over time (assuming intact cognition).

An early clue that may be noted by care providers is that painful stimulation (such as pressure on the nail bed) results in a limited to absent limb response, yet normal grimacing. This finding highlights the usual sparing of weakness in the facial muscles. Limited information is gleaned from the assessment of reflexes and the sensory examination. Reflexes are usually diminished or absent, but normal reflexes do not rule out the diagnosis. Sensory examination is often curtailed by patient sensorium, interaction with the examiner, and edema.

Once a weakness syndrome is entertained, the clinician must clearly establish the absence of a neuromuscular condition that began before admission to the ICU. Careful review of the premorbid functional status must be undertaken. Usually a determination of the performance of activities of daily living and ambulation suffices. Acute spinal cord injury, motor neuron disease, Guillain-Barre syndrome, myasthenia gravis, Lambert-Eaton syndrome, and muscular dystrophy are usually evident prior to the initiation of mechanical ventilation. However, these conditions may rarely emerge during critical illness and, in selected patients, neurologic assessment must be undertaken for these entities.[18]

Table 1—*MRC Scale for Muscle Examination

Functions assessed
Upper extremity: wrist flexion, forearm flexion, shoulder abduction
Lower extremity: ankle dorsiflexion, knee extension, hip flexion
Score for each movement
0–No visible contraction
1–Visible muscle contraction, but no limb movement
2–Active movement, but not against gravity
3–Active movement against gravity
4–Active movement against gravity and resistance
5–Active movement against full resistance
Maximum score: 60 (four limbs, maximum of 15 points per limb) [normal]
Minimum score: 0 (quadriplegia)

*Adapted with permission from Kleyweg et al.[16]

Distinction Between Polyneuropathy and Myopathy

Since delirium and sedation are frequent in ICU patients, reliable bedside examination of neuromuscular function can be difficult. Given these obstacles, (early) studies of seemingly weak patients have relied on electrophysiologic testing to provide a rigorous description of underlying neuromuscular dysfunction. Comprehensive electrophysiologic studies including motor and sensory nerve conduction studies as well as needle electromyography in the upper and lower limbs defined two broad categories of ICU-AW: CIP and CIM. Brief introductions to each entity will be described below; comprehensive reviews[7,18–20] of these entities are available.

In CIP, electrophysiologic testing usually shows sensorimotor axonopathy with decreased compound muscle action potential (CMAP) and sensory nerve action potential yet normal nerve conduction velocities (assuming the absence of persistent neuromuscular blockade).[18] Abnormalities may be detected as early as 48 h into critical illness.[21] Spontaneous muscle activity with fibrillation potentials can be detected in severe axonal disease.

An accompanying prolongation of the CMAP du-

ration suggests an associated myopathy.[7] CIM is an acute primary myopathy (not secondary to muscle denervation) and is diagnosed by abnormalities of the electromyographic tracing during a voluntary contraction (requiring patient cooperation). Affected muscle exhibits a characteristic pattern of abundant low-amplitude, short-duration polyphasic units with early recruitment.

The definitive diagnosis of muscle involvement requires examination of muscle tissue by biopsy. The reported light-microscopic findings in specimens from CIM patients include muscle fiber atrophy (preferentially type II fibers), occasional fiber necrosis, regeneration, and decreased or absent reactivity in myofibrillar adenosine triphosphatase staining, corresponding to a selective loss of myosin filaments. This selective loss of myosin is practically pathognomonic for CIM. To minimize the morbidity of an open muscle biopsy, some[22] have proposed quantification of myosin/actin ratio by gel electrophoresis in core needle specimens (conchotome muscle biopsy technique) to diagnose CIM.

To overcome the challenges of patient cooperation and completely avoid muscle biopsy, the method of direct muscle stimulation has been evaluated. First proposed by Rich et al[23,24] in 1996, direct muscle stimulation was intended to differentiate between CIM and CIP. Both conditions demonstrate reduced nerve-evoked CMAP amplitude, yet denervated muscle (as in CIP) should retain electrical excitability and the direct muscle stimulation CMAP amplitude should be normal. CIM patients should exhibit loss of electrical excitability, and both nerve- and direct muscle-stimulated CMAPs should be diminished. Several groups have since studied this modality, but analysis has been troubled by the common overlap of CIM and CIP[25] or the absence of muscle biopsy correlates.[26]

As further series of patients were described,[27] significant overlap of CIP and CIM was noted, leading to the use of a new descriptive term *critical illness polyneuromyopathy* (CIPNM, also known as *CIM and/or neuropathy*). Several investigators[14,27] have demonstrated that when sought, myopathy is often present in conjunction with the established evidence for neuropathy. For example, Latronico et al[27] demonstrated that 19 of 24 patients with CIP had evidence of myopathy when muscle biopsy was performed.

As critical care practice has evolved to a "least sedation" model, the ability to evaluate patients with a comprehensive bedside examination has become more feasible, perhaps making extensive electrophysiologic testing less necessary. De Jonghe and colleagues[10] prospectively evaluated 95 patients who had received mechanical ventilation for > 7 days and achieved satisfactory awakenings for MRC examination. Patients with a score of < 48 were delineated to have ICU-acquired paresis (ICU-AP). All patients with ICU-AP demonstrated sensory motor axonopathy, and histologic features of primary myopathic changes were observed in all patients with paresis 1 week after the initial diagnosis. This term is essentially synonymous with the term used broadly in North America: *ICU-AW*.

These authors[10,15] have advocated using physical examination as the primary determinant of ICU-AW. Patients demonstrating the characteristic examination combined with any evidence of recovery on serial examination usually require no further investigation. Patients with a protracted altered sensorium or fixed motor deficit should undergo further testing for CNS pathology.

Controversy Regarding Neuromuscular Investigations

The decision to perform electrophysiologic testing and/or muscle biopsy in routine care, as opposed to research settings, has created an ongoing debate in the medical literature. Proponents[27] cite evidence that clinicians have predicted fatal outcomes in acutely ill, comatose patients with paralysis developing despite neurologic signs and physiologic and radiologic investigations that do not indicate irreversible brain damage. Coma, a potent predictor of mortality and morbidity in critical illness, coupled with the absence of movement, is commonly considered a "deadly sign."[19,28] However, patients with CIP and CIM, potentially reversible entities, should be carefully identified to avoid unreasonably pessimistic prognoses. Predicted outcome has been shown to alter patient treatment[29]; therefore, accurate predictions are paramount in decisions regarding goals of care in the patient with protracted critical illness.

Advocates for routine clinical examination who reserve neurophysiologic testing and biopsy for unusual or severe instances of weakness cite the limitations, costs, and risks of this testing. Edema, artifacts related to the presence of multiple electrical devices, and invasive catheters are common sources of technical difficulties with electrophysiologic testing in ICU patients.[30] In addition, neurophysiologic testing does not predict duration of mechanical ventilation nor ICU stay, and the presence of CIP and/or CIM does not ensure reversibility.[31] Importantly, there is not a specific therapy for CIP and/or CIM; therefore, establishing a highly specific or physiologically based diagnosis does not translate to a specific pharmacologic therapy. Rather, therapies currently employed to limit ICU-acquired weakness

are preemptive and should be applied to virtually all critically ill patients receiving mechanical ventilation (see discussion following).[31]

Additional practical factors may influence the decision to perform these tests. Neuromuscular specialists with expertise in electrophysiologic testing and biopsy interpretation are in limited supply, while critically ill patients undergoing mechanical ventilation are ubiquitous. In addition, the continuity of care enjoyed by intensivists is far different than the consultative role of a neuromuscular specialist. Intensivists have the opportunity to serially evaluate a patient's neuromuscular and psychological state over time, including subtle changes in performance (particularly when sedation limitations are implemented appropriately). Neuromuscular specialists are often requested for consultation during the latter stages of critical illness and asked to diagnose and prognosticate in a finite capsule of time. It is not surprising that advanced diagnostic tools would then be utilized to create a prompt and comprehensive response.

Proposed Diagnostic Algorithm

To optimize the likelihood of patient interaction for neuromuscular assessments, we advocate the implementation of sedation protocols.[32,33] Our preference, daily interruption of sedative infusions, confers the opportunity for serial neuromuscular examination and reduces the duration of mechanical ventilation.[32,34] Careful implementation of the structured MRC examination should be employed and documented serially as a matter of routine. Patients exhibiting fixed or focal motor defects or persistent altered sensorium despite adequate sedation washout should undergo more advanced diagnostics (*ie*, CNS imaging, electrophysiologic studies, and/or muscle biopsy) [Fig 1].

Epidemiology

The occurrence of ICU-acquired weakness varies substantially depending on the patient case mix, diagnostic method used, and the timing of examination. De Jonghe et al[10] found clinically significant ICU-AW in 25% of patients who received mechanical ventilation for at least 7 days. Of note, a substantial number of patients could not be evaluated by muscle strength testing, most commonly the result of death before regaining consciousness. Electrophysiologic testing to delineate CIP does not share similar limitations in the unresponsive patient, and has resulted in reports of higher incidences of acquired neuromuscular disease in similar cohorts. For exam-

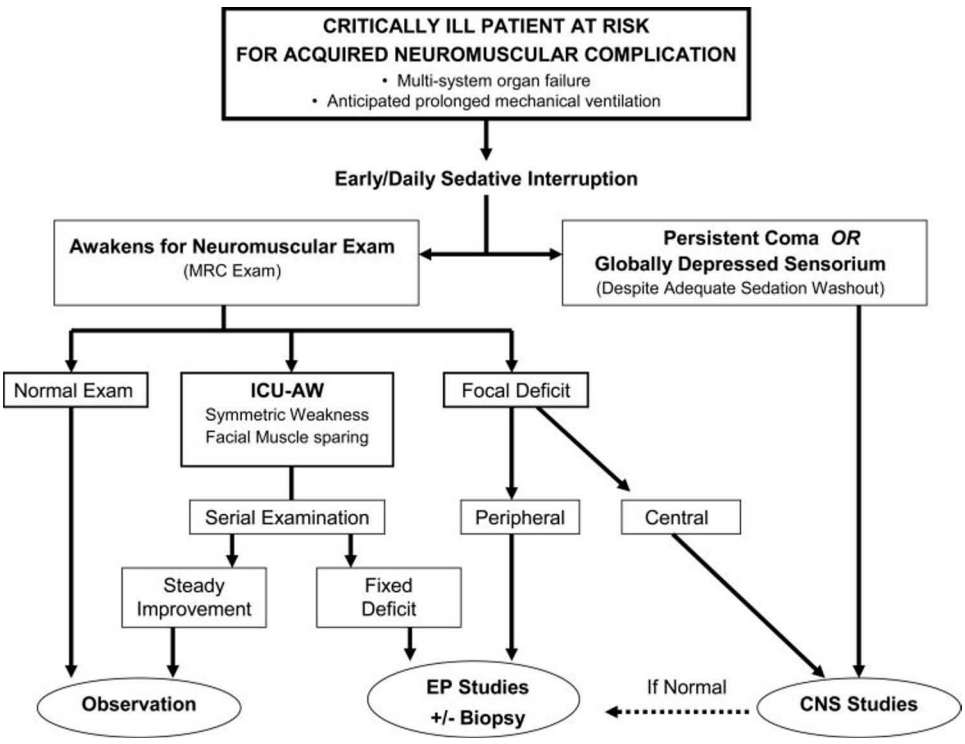

Figure 1. Proposed diagnostic algorithm for assessing neuromuscular complications in the critically ill. EP = electrophysiology; +/− = with/without.

ple, a prospective study[35] of 50 patients receiving mechanical ventilation for > 7 days documented CIP in 58%. Studies[8,36,37] using cohorts restricted to sepsis and multiorgan failure have found even higher incidences of neuromuscular disease, ranging from 50 to 100%.

Outcomes

Understanding the evolving terminology described above is important when reviewing outcome studies of these patients. The combination of varied definitions of neuromuscular impairment and selected cohort analysis creates the risk of bias and makes comparisons across studies challenging. Even with these limitations, ICU-AW appears to have a significant association with short and long-term measures of outcome.

Short-term Outcomes

Two studies[38,39] have demonstrated that weakness is an independent predictor of prolonged mechanical ventilation. Garnacho-Montero and colleagues[38] evaluated septic patients receiving ventilation for at least 7 days for CIP. Patients with electrophysiologic evidence of CIP had longer duration of mechanical ventilation than patients who did not (median, 34 days vs 14 days; $p < 0.001$). This finding was explained by a longer period required for weaning and was associated with an increased length of ICU and hospital stay. De Jonghe and colleagues[39] evaluated ICU patients receiving ventilation for at least 7 days who were sufficiently awake to permit evaluation for ICU-AP. Of the 95 patients enrolled, 24 patients (25%) had ICU-AP. The weak patients exhibited a similarly increased period of weaning and duration of mechanical ventilation as compared to the nonweak cohort. In the multivariate analysis incorporating severity of illness scoring, disease states, and duration of multiple organ dysfunction, the two independent predictors of prolonged weaning, were ICU-AP (hazard ratio, 2.4) and COPD (hazard ratio, 2.7). [39]

Two studies[35,40] have demonstrated increased mortality in patients with CIP. Garnacho-Montero et al[40] studied a very select population of severely ill patients: septic patients with multiple organ dysfunction syndrome requiring mechanical ventilation for > 10 days. Patients with CIP had higher in-hospital mortality rates than those without CIP (84% vs 56.5%, $p = 0.01$). Similarly, Leijten et al[35] found that in 50 patients receiving mechanical ventilation for > 7 days, ICU mortality was higher in the CIP group (48% vs 19%, $p = 0.03$).

Despite the demonstrated associations between ICU-AW and poor short-term outcomes, there is no clear cause-and-effect relationship. Attempts have been made to statistically adjust for imbalances between weak and nonweak cohorts,[39] yet no conclusive evidence exists to refute the possibility that poor outcomes and weakness may simply reflect the type and/or severity of the patient's underlying condition.

Long-term Outcomes

Muscle wasting and weakness are common and often striking in survivors of critical illness. In a comprehensive evaluation of a cohort of 100 survivors of ARDS, patients were evaluated at 3, 6, and 12 months following critical illness via physical examination, pulmonary function testing, 6-min walk testing, and quality of life evaluation.[41] Extrapulmonary conditions, specifically muscle wasting and weakness, were the most prominent complications and were responsible for much of the persistent functional disability. Retrospective data[42] suggest that in high-risk groups such as patients with ARDS, CIP and/or CIM may be present in as many as 60% of patients.

Latronico and colleagues[43] made a composite evaluation of studies reporting long-term outcomes in patients with CIP and CIM. Inclusion of 36 studies provided information on the outcomes of 263 patients. Mean duration of follow-up was 3 to 6 months (range, 2 days to 8 years). Complete functional recovery with patients regaining the ability to breathe spontaneously and to walk independently was reported in 68% (180 of 263 patients). Severe disability with quadriparesis, quadriplegia, or paraplegia was reported in 28% (74 of 263 patients). Persisting milder disabilities were common even in patients with complete functional recovery, and included reduced or absent deep tendon reflexes, stocking and glove sensory loss, muscle atrophy, painful hyperesthesia, and foot drop.[44]

Risk Factors

Factors such as systemic inflammation, medications, electrolyte disturbances, and immobility have been implicated in the pathogenesis of ICU-AW. In the absence of an experimental model to explore mechanisms of injury, current information derives largely from prospective cohort studies of patients utilizing multivariate analyses to assess independent risk factors.

Systemic Inflammation

Pioneers in the field of neuromuscular disease in the critically ill recognized the correlation of ac-

quired weakness with the systemic inflammatory response syndrome, sepsis, and multisystem organ dysfunction.[4,8,45,46] Two prospective studies[9,10] have further validated the relationship to inflammation. de Letter et al,[9] coupling clinical examination and electrophysiology, demonstrated that acute physiology and chronic health evaluation (APACHE) III scores and the presence of systemic inflammatory response syndrome were independently associated with the development of CIPNM. Based on the distribution of the predictive index of these two variables, three risk groups were determined to assist in risk stratification for the development of CIPNM. This model has yet to be tested prospectively. De Jonghe et al[10] demonstrated that prolonged multisystem organ failure is strongly associated with the development of ICU-AP. How systemic inflammation would produce nerve and muscle injury is unclear; commonly invoked pathways include ischemia or injury via mediators of inflammation. de Letter et al[47] have additionally demonstrated evidence for low-level, local immune system activation with release of both proinflammatory and antiinflammatory cytokines in the muscle of patients with critical illness polyneuromyopathy. Tissue injury may lead to the influx of inflammatory cells and the release of such cytokines. The expression of adhesion molecules on vascular endothelium suggests the possible contribution of increased vascular permeability. While these local phenomena may be important, measurement of more global markers of inflammation, such as interleukin-6 and tumor necrosis factor, has not shown them to be elevated in the serum of patients with CIP as compared to nonweak, critically ill control subjects.[48]

Medications

Many medications have been implicated as causes of weakness. Corticosteroids, the most widely studied,[10,41,49] have a significant association with the development of ICU-AW. In animal models, administration of corticosteroids can produce selective muscle atrophy, particularly of fast-twitch fibers.[50] However, a thick filament myopathy identical to CIM can be best produced by combining denervation injury and corticosteroids.[51] In such an animal model, complete loss of muscle excitability was found, now ascribed to the inactivation of fast sodium channels.[52] This "two-hit" hypothesis has been invoked to explain the profound forms of CIM described in patients with status asthmaticus.

A recent prospective, randomized trial[53] of methylprednisolone for persistent ARDS demonstrated no improvement in 60-day mortality despite evidence for early physiologic improvement of gas exchange and lung mechanics. The small number of patients with significant complications attributed to neuromyopathy were all in the methylprednisolone-treated arm. It is plausible that some benefits of corticosteroid treatment on lung function were offset by the adverse effects on strength.

The association of neuromuscular weakness with prolonged use of neuromuscular blocking agents (NMBAs) has long been recognized and is the most prominent reason for a shift away from NMBA use in the critically ill. An association of NMBA use with CIP has been noted in one study[40] but was absent in others. While the association of NMBAs with CIP remains unclear, there are well described scenarios of ICU-AW with these agents. One scenario is that of prolonged neuromuscular blockade arising from persistent drug effect, such as that occurring with agents (or their metabolites) that accumulate in the setting of renal and liver failure. The second scenario involves patients with severe acute asthma and ventilatory failure who undergo treatment with high-dose corticosteroids in combination with NMBAs. These patients may exhibit severe and protracted myopathy.[54–56]

Glycemic Control

The link between elevated blood glucose levels and ICU-AW was established in an early study[8] of critically ill patients with multisystem organ failure. More recently, a large randomized trial[57] of surgical patients undergoing tight glycemic control with insulin infusions vs conventional insulin therapy demonstrated a 50% reduction in the evolution of CIP. Secondary evaluations of this data set link the protective effect to strict glycemic control as opposed to the insulin effect.[58] The impact of tight glycemic control on preservation of neuromuscular function in medical ICU patients has yet to be described.[59] However, given other proven salutary effects of such management (including reductions in days to weaning of mechanical ventilation, ICU and hospital length of stay, and development of renal injury), we do advocate the application of tight glycemic control in patients receiving mechanical ventilation.

Immobility

Bed rest and deep sedation have been suggested to potentiate ICU-AW. Three pieces of indirect evidence support such speculation. De Jonghe et al[10] found that duration of mechanical ventilation prior to "awakening" to establish the diagnosis of ICU-AP was a significant risk factor, independent of the duration of multiple organ failure. Contributors to alterations in patient sensorium delaying the diagnosis might be causal (*ie*, sedatives). Second, a rabbit

model utilizing controlled mechanical ventilation demonstrated atrophy of the diaphragm within a few days of respiratory-muscle inactivity.[60] Finally, repeated daily passive mobilization has prevented muscle atrophy on serial muscle biopsies in patients receiving mechanical ventilation and NMBAs.[61]

In contrast, Eikermann et al,[62] utilizing electrophysiologic studies and direct muscle stimulation, demonstrated that septic patients with multiple organ failure have reduced muscle force without evidence for increased fatigability. Healthy patients undergoing limb immobilization did not exhibit reductions in force or fatigability. Seemingly, immobilization alone cannot create CIM.

Prevention/Treatment

Data supporting specific approaches to prevent or treat ICU-AW are limited. For the practicing clinician, it is reasonable for ICU-AW to be approached as a syndrome with a large number of potential associations. Akin to the approach to delirium, the causes are multiple and overlapping.[63,64] We advocate that the clinician seek potentially reversible risk factors and adjust care accordingly (Fig 2).[65]

The best evidence for prevention comes from a secondary end point of a trial of strict glycemic control via insulin infusion in critically ill surgical patients. Intensive insulin therapy (maintenance of a blood glucose level from 80 to 110 mg/dL) demonstrated a mortality benefit and fewer cases of CIP detected by routine electrophysiologic testing after day 7 (28.7% vs 51.9%, $p < 0.001$).[57] This management seems appropriate assuming a careful implementation with safeguards against potentially injurious hypoglycemia.[59]

Given the evidence for reduced muscle atrophy with passive limb muscle stretching,[61] strategies to mobilize patients, either with passive stretching or active exercises with physical and occupational therapy, seem reasonable when approached in a safe, systematic manner. At the least, sedation protocols designed to minimize the use of sedatives and analgesics have been shown to decrease duration of mechanical ventilation.[32,66] This strategy may help to promote earlier patient wakefulness, minimize sedative-induced immobility, and permit earlier recognition of weakness with earlier mobilization as tolerated.

Medications that may increase the risk of weakness should undergo careful review. Corticosteroids should be used with caution, if at all, in circumstances in which benefit is obscure, such as late-phase ARDS.[53] Ideally, further investigations will help guide use of corticosteroids in the critically ill, extending the observations already made in patients with severe community-acquired pneumonia[67] and septic shock.[68]

It also seems prudent to maintain the internal milieu of the patient, with attention to electrolyte disorders, including phosphate and magnesium depletion. Although not proven, adequate nutrition supplementation seems a necessity, as the body will otherwise cannibalize muscle for sources of energy.

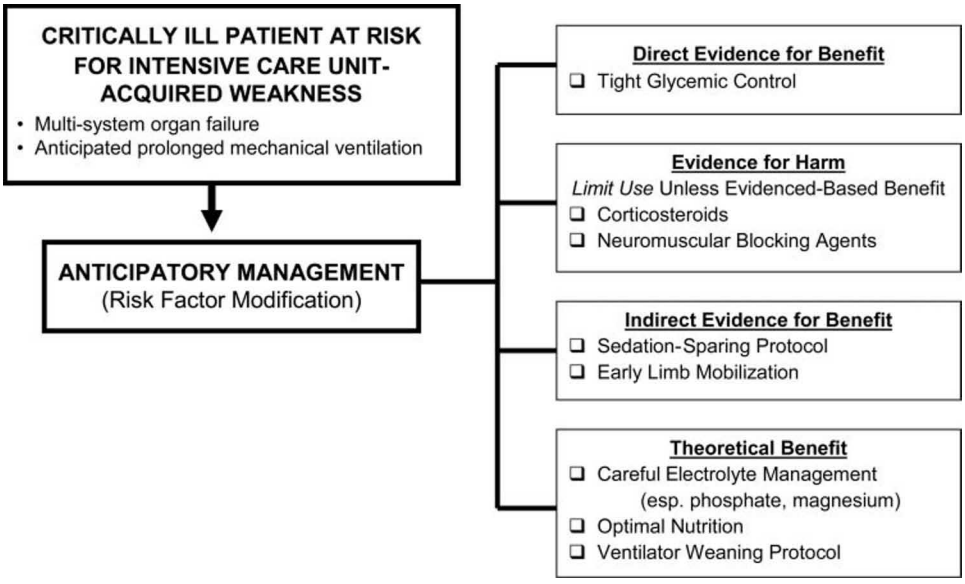

Figure 2. Risk factor modification schema for patients at risk for ICU-acquired weakness. esp = especially.

Finally, standardized approaches to ventilator weaning, such as a respiratory therapist-driven protocol, must be employed to minimize the duration of ventilator dependence.[69]

In contrast to the study-limited approach for clinical care, research mandates a more comprehensive evaluation. Study patients may require the coupling of physical examination with comprehensive electrophysiologic testing and biopsy results. Furthermore, the contribution of the diaphragm must be better understood.

Conclusions

An aging baby boomer population combined with increasing numbers of patients needing and seeking ICU services creates an environment in which critical care delivery must be optimal. Longer-term outcomes focusing on neuromuscular strength and patient functional autonomy need to be considered when evaluating the quality of interventions. Although it seems doubtful that a single therapy might prevent weakness in such varied populations, the meticulous application of a multipronged therapeutic approach including tight glycemic control, optimal nutrition, early limb mobilization, and avoidance of risk factors such as excessive sedation, high-dose steroids, and paralytics may help to ensure maximal functional status for survivors of critical illness.

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