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Acquired Muscle Weakness in Critically ill Patients with Sepsis

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ABSTRACT

Acquired muscle weakness in ICU, also known as ICU-acquired weakness (ICUAW), encompasses critical illness polyneuropathy (CIP), critical illness myopathy (CIM), or a combination of both. It is primarily caused by systemic inflammation, immobility, metabolic and endocrine disturbances, and exposure to drugs such as corticosteroids or neuromuscular blocking agents. The incidence of ICUAW ranges from 25–50% in patients with sepsis or multi-organ failure. Diagnosis is made clinically by manual muscle testing and can be supported by electrophysiological studies. Preventive measures include early mobilization, optimal glycemic control, minimizing sedative exposure, and adequate nutrition. Rehabilitation strategies play a vital role in restoring muscle function and quality of life post-ICU discharge.

Keywords: *ICU-acquired weakness; critical illness polyneuropathy; critical illness myopathy; intensive care; muscle weakness; rehabilitation; morbidity.*

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1. INTRODUCTION

Muscle weakness is a frequent problem in the intensive care unit (ICU). The weakness can be due to primary neuromuscular disorders, such as Guillain–Barré Syndrome, myasthenia gravis, amyotrophic lateral sclerosis or multiple sclerosis, among others, but these conditions only account for < 0.5% of all ICU admissions. however, muscle weakness can develop as a secondary disorder while patients are being treated for other life-threatening conditions. The latter has been labeled “ICU-acquired weakness” with the implication that this neuromuscular dysfunction has no plausible etiology other than the critical illness and its treatments **(1)**.

ICU-acquired weakness is typically generalized, symmetrical, and affects limb (proximal more than distal) and respiratory muscles, whereas facial and ocular muscles are spared. Muscle tone is almost invariably reduced. Deep tendon reflexes can be reduced or normal. Weakness may originate from a neurogenic disturbance “critical illness polyneuropathy” (CIP), a myogenic disturbance “critical illness myopathy” (CIM), or a combination thereof labelled “critical illness neuromyopathy”. Electrophysiological examination shows typical patterns of abnormalities. Also, the pronounced loss of muscle mass, that can exceed 10% over the 1st week in ICU, has been associated with functional impairment. Severe disuse muscle atrophy has been put forward as a separate entity of ICU-acquired weakness in the absence of electrophysiological abnormalities **(2)**.

Prevalence of ICU-acquired weakness varies widely with the studied patient population and risk factors, the timing of assessment, the methods used for diagnosis, and inconsistent accounting for patients’ pre-hospital muscle function or overall functional status (often overlooking age-related frailty) **(3)**.

2. PATHOPHYSIOLOGY

The pathophysiology of ICU-acquired weakness remains incompletely understood, in part explained by practical and ethical issues complicating the study of underlying mechanisms in human patients. Indeed, mechanistic studies require harvesting of muscle or nerve biopsies, which is an invasive procedure. Also, the possibility to interfere with biological processes in human patients, e.g., by administering activators or inhibitors of assumed central players, is inherently limited in view of potential risks for the patients. However, studies in animal models have added valuable insights and, together with available patient study results, allowed to attribute ICU-acquired weakness to complex structural/functional alterations within the central nervous system, the peripheral nerves and the myofibers **(4)**.

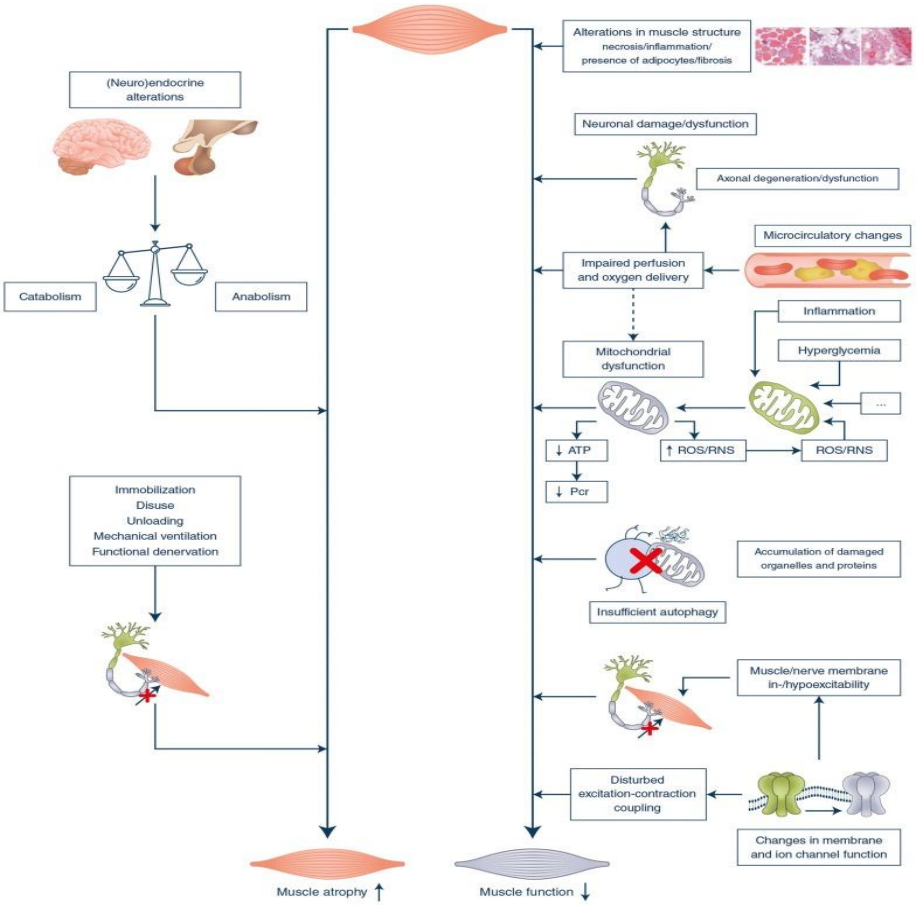

Figure 1: A concepted framework of the major pathways that contribute the development of ICU-AW

Mechanisms implicated in the development of ICU-acquired weakness. A conceptual framework of the major pathways that are assumed to be involved in the loss of muscle mass and loss of muscle function that contribute to the development of ICU-acquired weakness. ATP adenosine triphosphate, PCr phosphocreatine, ROS/RNS reactive oxygen species/reactive nitrogen species. Mitochondria, proteins, neurons and ion channels indicated in green represent healthy organelles, molecules and cells, whereas grey symbols point to damaged/dysfunctional organelles, protein aggregates, cells and ion channels **(1).**

Muscle atrophy

The catabolic state of critical illness, explain the pronounced muscle wasting that contributes to weakness of myogenic origin in ICU patients. Such loss of muscle mass is due to imbalanced protein turnover, with a reduced protein synthesis relative to accelerated breakdown by activated proteolytic systems, such as the ubiquitin–proteasome system **(5)**.

Muscle dysfunction

Several factors contribute to loss of muscle function during critical illness **(6)**.

Structural muscle alterations

Muscle biopsies show signs of inflammation or necrosis, pronounced infiltration of muscle with (or myofiber conversion to) adipose tissue and fibrosis in a remarkably high proportion of critically ill patients **(7)**.

Microcirculatory disturbances

Microcirculatory changes include vasodilation and increased permeability, which allow leukocyte extravasation and tissue infiltration, local cytokine production and edema formation with increased intercapillary distance. These changes can compromise perfusion and oxygen delivery. Involvement of edema-induced compression damage to muscles and nerves remains debated. Nevertheless, hypoperfusion may contribute to neuronal injury, axonal degeneration, and to a chronic membrane depolarization of terminal motor axons **(8)**.

Bioenergetic failure

Insufficient oxygen supply to mitochondria may compromise mitochondrial energy production. However, the mitochondrial dysfunction in critical illness appears explained by impaired oxygen utilization, due to direct mitochondrial damage further aggravated by inflammation, hyperglycemia and free radicals, rather than by impaired oxygen delivery. Dysfunctional mitochondria not only compromise energy provision but also amplify the production of free radical and reactive oxygen species, eliciting a vicious cycle of macromolecular and organelle damage **(8)**.

Inadequate autophagy activation

Initially, increased autophagy was assigned a detrimental role as a contributor to muscle atrophy. However, it has become clear that this important cellular quality control mechanism is actually insufficiently activated during critical illness, allowing accumulation of damage to mitochondria and other cellular components. Impaired clearance of such damage results in degenerative changes which compromise muscle function, thus contributing to ICU-acquired weakness **(9)**.

Membrane and ion channel dysfunction

Sodium channel inactivation is thought to contribute to the rapid, reversible hypo-excitability or in-excitability of nerve and muscle membranes in patients with ICU-acquired weakness. Altered intracellular calcium homeostasis further contributes to impaired muscle contractility by affecting the excitation–contraction coupling **(10)**.

Central nervous system involvement

Recent evidence suggests that central nervous system involvement with failure of coordinated repetitive firing within the motor neurons can be a very early event, preceding electrical failure in axons and nerve–muscle coupling **(11)**.

Risk factors of ICU acquired weakness

Several independent risk factors for developing ICU-acquired weakness have been identified, mostly from observational studies, although often not unequivocally (Figure 2) **(12)**.

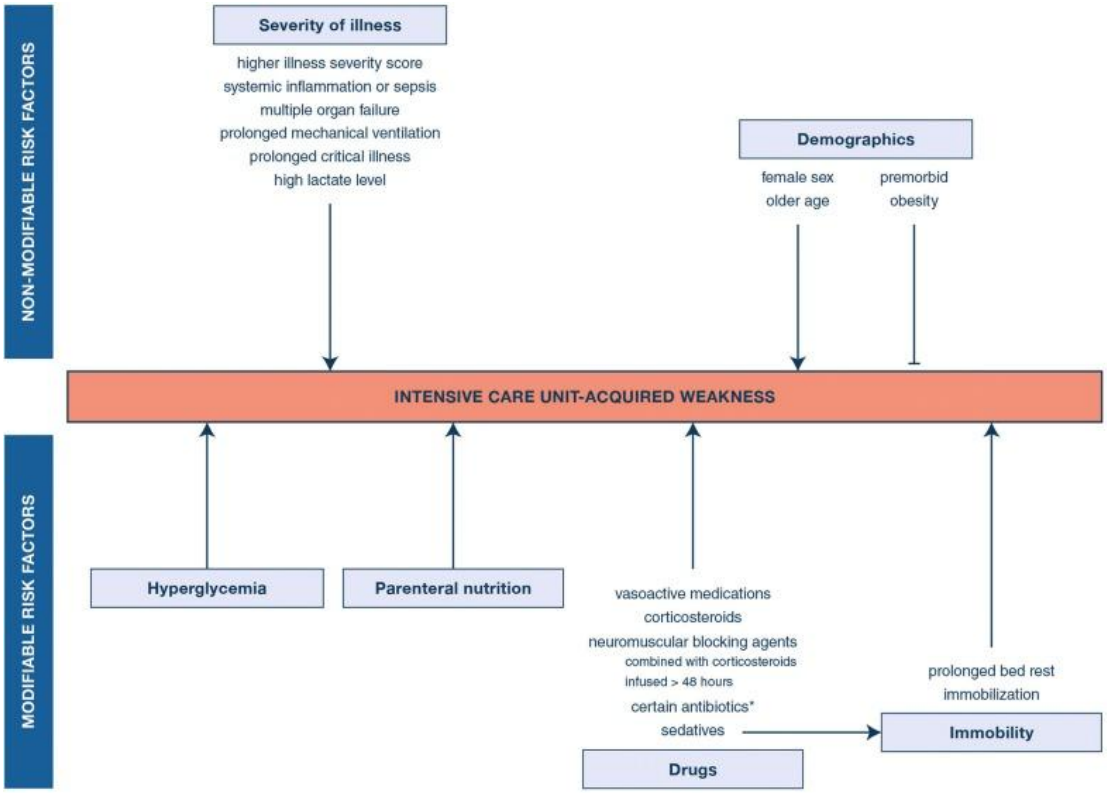

Figure 2: Overview of risk factors of ICU-acquired weakness.

Observational and randomized controlled trials have identified a wide range of non-modifiable and modifiable risk factors associated with the risk of developing weakness in the ICU. *Certain antibiotics, such as aminoglycosides and vancomycin, have been independently associated with ICU-acquired weakness, although not unequivocally. Other antibiotics, such as clindamycin, erythromycin, quinolones, polymyxin, tetracycline and vancomycin may affect the neuromuscular junction, but have so far not been independently associated with ICU-acquired weakness.

A first group of risk factors are not modifiable the severity of critical illness is an important determinant. Thus, a higher severity of illness score, sepsis and inflammation, multiple organ failure, as well as a longer duration of mechanical ventilation and ICU stay, were found to be predictive. In fact, ICU-acquired weakness is most frequent in patients with persistent critical illness. The relationship with mechanical ventilation could be reciprocal given that prolonged ventilation increases the risk of ICU-acquired weakness and diaphragmatic dysfunction which, vice versa, increase the risk of prolonged ventilation and failed weaning **(13)**.

Another illness-related risk factor is a high lactate level. Further, a higher risk of weakness may apply to women than to men, and to older as compared with younger patients. Also, premorbid disability and frailty may predispose to the severity of weakness. premorbid obesity was found to be an independent protective factor against development of ICU-acquired weakness and against muscle atrophy **(14)**.

Some risk factors are modifiable These include the degree of hyperglycemia that develops in response to the severe stress of critical illness and the administration of parenteral nutrition, but also several drugs that are used to treat critically ill patients. For example, dose and duration of vasoactive medications, mostly β-agonists, are associated with a higher risk of ICU-acquired weakness. The reported adverse relationship between the use of neuromuscular blocking agents and muscle weakness remains uncertain. An RCT comparing 48-h infusion of cisatracurium with placebo, both under deep sedation, in ARDS patients did not observe a significant impact **(15)**.

However, a 48-h infusion of cisatracurium with concomitant deep sedation tended to increase the risk of ICU-acquired weakness as compared with absence of routine neuromuscular blockade and lighter sedation targets, with significance reached for weakness present on day 28, but not for weakness present on day 7 or at any time through day 28. Also, when co-administered with corticosteroids or infused for > 48 h, NMBAs may promote weakness. Certain antibiotics, including aminoglycosides and vancomycin, have also been independently associated with ICU-acquired weakness. The association between sedatives and weakness may be indirect, as separating effects of sedatives from those of sedation-induced immobility and bed rest is difficult. Continued sedation is thought to have a more pronounced effect on muscle atrophy and weakness than when a patient is conscious but immobile in the absence of sedation **(16)**.

Sepsis-induced muscle wasting and ICUAW

A considerable amount of patients with sepsis were observed with signs of severe muscle wasting and/or ICU-acquired weakness (ICUAW), which described a frequently observed complication in critically ill patients and refers to clinically weak ICU patients in whom there is no plausible aetiology other than critical illness **(17)**.

William Osler first commented on the “rapid loss of flesh” that occurs with severe sepsis in 1892. Today, this phenomenon remains a frequent complication of critical illness—particularly sepsis—and is often referred to as muscle wasting. However, because sepsis led to a fairly rapid death in Osler’s days, the primary focus was rather survival than sepsis-associated long-term complications. Yet, once ICU and artificial organ support therapies are available, more patients survive the initial stages of systemic inflammation/sepsis and critical care specialists are increasingly confronted with profound muscle weakness, which is often accompanied by difficulties in weaning from respiratory support. Sepsis-induced multiple organ failure has been identified as one of the primary risk factors for this major and frequent complication of critical illness **(18)**.

As a confusing number of various terminologies referred to similar or identical clinical presentations of this neuromuscular disorder, a recent round table conference held in 2009 proposed the mutual term “ICUAW”.Whereas ICUAW is usually accompanied by muscle wasting, muscle wasting does not necessarily lead to neuromuscular dysfunction, since overall muscle strength depends both on total muscle mass and force generating capacity (force per cross-sectional area), which is affected in ICUAW but not necessarily in muscle wasting syndromes (Figure 3) **(19)**.

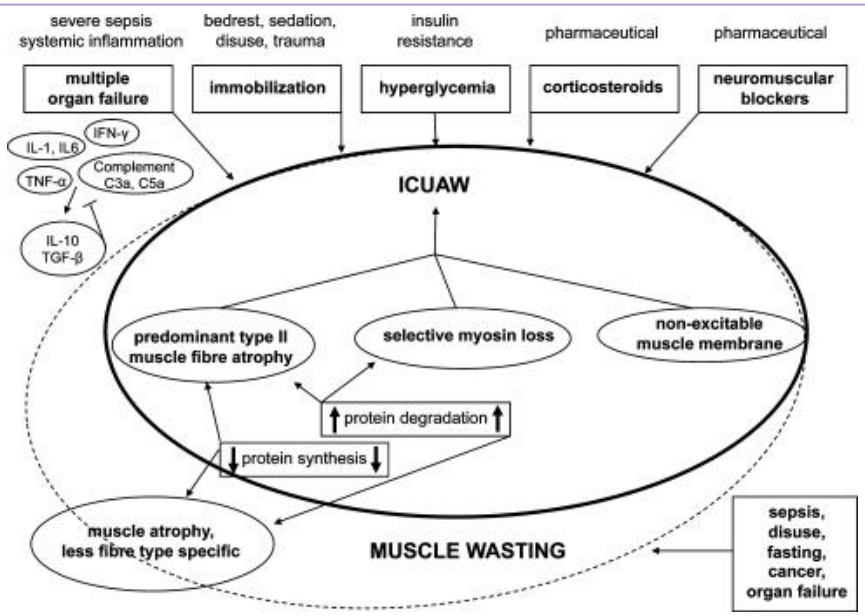

Figure 3: Risk factors involved in muscle wasting and ICUAW.

Both complications may overlap in septic patients, yet they present two distinct entities that should not be used synonymously. Whereas ICUAW is most likely accompanied by muscle wasting, muscle wasting is not necessarily associated with ICUAW **(20).**

As mentioned above, muscle force capacity may remain stable in muscle wasting syndromes. Muscle wasting can be triggered by other conditions than sepsis, including disuse, denervation, fasting, cancer, cardiac failure and renal dysfunction. As these conditions frequently coincide with sepsis, systematic research of sepsis-specific muscle wasting and ICUAW may be challenging in humans. This seems especially the case as sepsis is often accompanied by prolonged bedrest/immobilisation, application of sedatives, acute or chronic organ dysfunction, malignancy as an underlying disease, medication using glucocorticoids and others **(21)**.

An imbalance between muscle protein synthesis and muscle protein degradation causing net loss of muscle mass is considered to present the main mechanism of muscle atrophy in muscle wasting and may result from decreased protein synthesis and/or increased protein degradation (Figure 3) **(22)**.

Decreased muscle protein synthesis during sepsis

Even though studies on sepsis-induced muscle protein degradation received more attention, animal models of sepsis clearly indicate that sepsis also decreases protein synthesis in skeletal muscles and inhibits protein synthesis within fast twitch muscles **(23)**.

Further indirect evidence for contribution of impaired insulin signalling to decreased protein synthesis comes from the observation that the proinflammatory cytokines IL-6 and TNF-α have been linked to both insulin resistance and muscle atrophy and that local IGF-1 application prevents sepsis-induced muscle atrophy, possibly by inhibition of sepsis-induced increases of muscle atrogin-1 and the proinflammatory cytokine IL-6. IL-1 may lead to decreased protein synthesis. There is evidence that systemic cytokine response in sepsis results in local amplification of proinflammatory cytokines within muscle, possibly aggravating decreased protein synthesis in skeletal muscle during sepsis **(24)**.

Nutritional aspects may contribute to decreased muscle protein synthesis as well. Administration of the essential branched chain amino acid leucine has been shown to increase protein synthesis in rat skeletal muscles during ageing, exercise or food-deprivation. However, under certain conditions including sepsis, the muscle may be resistant to leucine-stimulated protein synthesis. Although the exact mechanisms of sepsis-induced leucine resistance remain to be elucidated. **(25)**.

3. DIAGNOSIS OF ICU-ACQUIRED WEAKNESS

Several techniques are used to diagnose ICU-acquired weakness. These methods assess peripheral and/or respiratory muscles **(26)**.

1. Assessment of peripheral muscle strength

To diagnose ICU-acquired weakness, ideally, a clinical quantification of muscle strength should be performed. This inherently implies a volitional technique, which has the drawback that the patients must be awake and cooperative and

must comprehend the assessor's instructions. As patients are often unconscious or uncooperative, due to sedation or delirium, such clinical diagnosis is often not possible or is delayed. The most widely used volitional technique is the 6-grade Medical Research Council (MRC) sum score. This score yields a global estimation of motor function, pointing to clinically relevant muscle weakness when below 48 and severe muscle weakness when below 36 **(27)**.

However, differentiation in the higher range is difficult. The ordinal scale of the MRC sum score limits the sensitivity to detect more subtle changes in muscle function. In contrast, hand-held dynamometry for measuring handgrip and quadriceps strength provides a continuous quantitative measure, but representativeness for global muscle strength has been questioned.

Electrophysiological assessments are also used to diagnose ICU-acquired weakness and can be applied to unconscious/uncooperative patients. Although CIP and CIM share many features on nerve conduction studies and electromyography, differentiation is possible in ideal circumstances, particularly when the patient is cooperative and voluntary muscle activation is possible. Single nerve conduction studies have shown promise as alternative for time-consuming full electrophysiological studies. For differential diagnosis of CIP and CIM in uncooperative patients, direct muscle stimulation shows normal muscle excitability in CIP and reduced muscle excitability in CIM. However, expertise is not widely available and differential diagnosis is further complicated by the high co-occurrence of CIP and CIM **(28)**.

A variety of imaging techniques have been evaluated to assess muscle mass, as a surrogate of muscle strength, some of which also can visualize muscle quality. Of these, ultrasonography is considered most promising. Although ultrasonography allows quick and repeated bedside evaluation of measures of muscle quantity and quality, it may underestimate muscle and protein loss. Furthermore, interpretation of the available studies is complicated by significant methodological defects, small sample sizes, and lack of standardization to control for operator dependency **(29)**.

Finally, nerve and muscle biopsies can provide important information and have increased mechanistic understanding but are invasive with potential for complications and require specialized expertise for obtaining the samples and interpreting findings. Biopsy analyses may allow differential diagnosis of CIP and CIM, but nerve biopsy is too invasive for routine clinical use and hence is no longer advised except in the context of scientific research **(30)**.

Assessment of respiratory muscle strength

Volitional testing of global respiratory muscle strength via maximal inspiratory and expiratory pressure or of diaphragm strength via transdiaphragmatic pressure is again limited by the requirement of an awake and cooperative patient. Measurement of transdiaphragmatic or endotracheal tube pressure in response to phrenic nerve stimulation can circumvent this problem, but it is invasive, requires magnetic stimulation and is technically difficult. Also imaging techniques are being used. However, chest X-rays have low sensitivity and specificity and ultrasonography has limited value during assisted breathing **(31)**.

4. MANAGEMENT OF ICU ACQUIRED WEAKNESS

The management of ICU-acquired weakness (ICU-AW) necessitates a comprehensive and multidisciplinary strategy encompassing prevention, early recognition, and effective treatment. These three phases often occur concurrently, reflecting the complexity and dynamic nature of critical care settings **(1)**.

1. Prevention

Preventive strategies focus primarily on mitigating known risk factors for ICU-AW. Early and aggressive treatment of sepsis is pivotal, as sepsis-induced cytokine release contributes significantly to neuromuscular dysfunction and multi-organ impairment. Reducing ICU length of stay and minimizing mechanical ventilation duration are also critical, given the strong association between prolonged immobility and the development of neuromyopathy. Early mobilization protocols not only help preserve muscle strength but also improve ventilator weaning outcomes and metabolic control **(1)**.

Hyperglycemia has been recognized as a modifiable risk factor for ICU-AW. Tight glycemic control through insulin therapy has demonstrated beneficial effects on neuromuscular function; however, early mobilization itself may promote euglycemia and mitigate insulin resistance. Moreover, careful selection and prudent use of pharmacologic agents, particularly corticosteroids and neuromuscular blocking agents, remain fundamental to minimizing iatrogenic contributors to ICU-AW. While recent evidence has questioned the direct causative role of these drugs, cautious administration, dose adjustment, and minimizing treatment duration are generally advocated **(1)**.

2. Early Recognition

Prompt identification of ICU-AW facilitates early intervention and may limit progression. Despite the absence of a definitive gold standard for diagnosis, clinical tools such as the Medical Research Council (MRC) muscle strength grading scale are commonly employed in cooperative patients. In non-cooperative or sedated patients, electrophysiological techniques such as nerve conduction studies (NCS) and electromyography (EMG) provide valuable diagnostic information, although they are technically demanding **(4)**.

3. Effective Treatment

Effective management of ICU-AW is rooted in two main therapeutic pillars: early mobilization and nutritional optimization. Early physical rehabilitation has consistently been shown to maintain muscle mass, preserve respiratory muscle function, and improve glycemic control. Advanced modalities, such as functional electrical stimulation (FES)-cycling, have demonstrated additional benefits in enhancing muscle strength and reducing delirium incidence among critically ill patients **(32)**.

Nutritional support is equally critical, with emphasis on early initiation of enteral nutrition (EN) within 24–48 hours of ICU admission. Current guidelines recommend moderate protein targets of 1.2–1.5 g/kg/day to support muscle anabolism without overwhelming the metabolic capacity, especially in septic patients where excessive protein intake might impair autophagic processes essential for cellular homeostasis. Experimental therapies, such as beta-hydroxybutyrate supplementation and modulation of the ubiquitin-proteasome system, show promise but remain investigational **(32)**.

Ultimately, the successful management of ICU-AW requires coordinated care involving intensivists, physiotherapists, nutritionists, and nursing staff, aiming for individualized, dynamic patient-centered care plans **(32)**.

REFERENCES

[1] Vanhorebeek, I., Latronico, N. & Van den Berghe, G. 2020. ICU-acquired weakness. Intensive Care Med, 46, 637-653.

[2] Chen, J. & Huang, M. 2024. Intensive care unit-acquired weakness: Recent insights. J Intensive Med, 4, 73-80.

[3] Egger, M., Finsterhölzl, M., Farabegoli, D., et al. 2024. Comprehensive assessment and progression of health status during neurorehabilitation in survivors of critical illness: a prospective cohort study. Annals of Intensive Care, 14, 175.

[4] Petrucci, M., Gemma, S., Carbone, L., et al. 2025. ICU-Acquired Weakness: From Pathophysiology to Management in Critical Care. Emergency Care and Medicine, 2, 4.

[5] Lad, H., Saumur, T. M., Herridge, M. S., et al. 2020. Intensive Care Unit-Acquired Weakness: Not just Another Muscle Atrophying Condition. Int J Mol Sci, 21.

[6] Fazzini, B., Märkl, T., Costas, C., et al. 2023. The rate and assessment of muscle wasting during critical illness: a systematic review and meta-analysis. Crit Care, 27, 2.

[7] Tedesco, F. S., Moyle, L. A. & Perdiguero, E. 2017. Muscle Interstitial Cells: A Brief Field Guide to Non-satellite Cell Populations in Skeletal Muscle. Methods Mol Biol, 1556, 129-147.

[8] Zedde, M. & Pascarella, R. 2024. The Cerebrovascular Side of Plasticity: Microvascular Architecture across Health and Neurodegenerative and Vascular Diseases. Brain Sci, 14.

[9] Gómez-Virgilio, L., Silva-Lucero, M.-d.-C., Flores-Morelos, D.-S., et al. 2022. Autophagy: a key regulator of homeostasis and disease: an overview of molecular mechanisms and modulators. Cells, 11, 2262.

[10] Kovalchuk, M. O., Franssen, H., van den Berg, H., et al., 2020. Excitability of motor and sensory axons in multifocal motor neuropathy. Clin Neurophysiol, 131, 2641-2650.

[11] Tortuyaux, R., Davion, J. B. & Jourdain, M. 2022. Intensive care unit-acquired weakness: Questions the clinician should ask. Rev Neurol (Paris), 178, 84-92.

[12] Meyer-Frießem, C. H., Malewicz, N. M., Rath, S., et al. 2021. Incidence, Time Course and Influence on Quality of Life of Intensive Care Unit-Acquired Weakness Symptoms in Long-Term Intensive Care Survivors. J Intensive Care Med, 36, 1313-1322.

[13] Sinha, R. K., Sinha, S., Nishant, P. et al., 2024. Intensive care unit-acquired weakness and mechanical ventilation: A reciprocal relationship. World J Clin Cases, 12, 3644-3647.

[14] Shawky, H. N., Kamel, H. M., Sayed, Z. E. A. et al., 2024. Role of lactate level in predicting admission need to intensive care unit and short term outcomes in patients with acute gastrointestinal bleeding. The Egyptian Journal of Internal Medicine, 36, 10.

[15] Rahimpour, F., Nejati, M., Farsaei, S., et al., 2024. Nutritional modifications to ameliorate stress hyperglycemia in critically ill patients: a systematic review. The Egyptian Journal of Internal Medicine, 36, 95.

[16] Hraiech, S., Yoshida, T., Annane, D., et al. 2020. Myorelaxants in ARDS patients. Intensive Care Med, 46, 2357-2372.

[17] Yang, T., Li, Z., Jiang, L. et al., 2021. Hyperlactacidemia as a risk factor for intensive care unit-acquired weakness in critically ill adult patients. Muscle Nerve, 64, 77-82.

[18] Plaut, T. & Weiss, L. 2025. Electrodiagnostic Evaluation of Critical Illness Neuropathy. StatPearls. Treasure Island (FL) ineligible companies. Disclosure: Lyn Weiss declares no relevant financial relationships with ineligible companies.: StatPearls Publishing Copyright © 2025, StatPearls Publishing LLC.

[19] Tashjian, H. 2024. downloaded from the King's Research Portal at https://kclpure. kcl. ac. uk/portal.

[20] Schefold, J. C., Bierbrauer, J. & Weber-Carstens, S. 2010. Intensive care unit-acquired weakness (ICUAW) and muscle wasting in critically ill patients with severe sepsis and septic shock. J Cachexia Sarcopenia Muscle, 1, 147-157.

[21] Rodgers, B. D. & Ward, C. W. 2022. Myostatin/Activin Receptor Ligands in Muscle and the Development Status of Attenuating Drugs. Endocr Rev, 43, 329-365.

[22] Martín, A. I., Priego, T. & López-Calderón, A. 2018. Hormones and Muscle Atrophy. Adv Exp Med Biol, 1088, 207-233.

[23] Haberecht-Müller, S., Krüger, E. & Fielitz, J. 2021. Out of control: the role of the ubiquitin proteasome system in skeletal muscle during inflammation. Biomolecules, 11, 1327.

[24] Zatterale, F., Longo, M., Naderi, J., et al. 2019. Chronic Adipose Tissue Inflammation Linking Obesity to Insulin Resistance and Type 2 Diabetes. Front Physiol, 10, 1607.

[25] Rehman, S. U., Ali, R., Zhang, H., Zafar, M. H. et al., 2023. Research progress in the role and mechanism of Leucine in regulating animal growth and development. Front Physiol, 14, 1252089.

[26] Eggmann, S., Luder, G., Verra, M. L., et al., 2020. Functional ability and quality of life in critical illness survivors with intensive care unit acquired weakness: A secondary analysis of a randomised controlled trial. PLoS One, 15, e0229725.

[27] Kennouche, D., Luneau, E., Lapole, T., et al., 2021. Bedside voluntary and evoked forces evaluation in intensive care unit patients: a narrative review. Crit Care, 25, 157.

[28] Piva, S., Fagoni, N. & Latronico, N. 2019. Intensive care unit-acquired weakness: unanswered questions and targets for future research. F1000Res, 8.

[29] Sabatino, A., Sola, K. H., Brismar, T. B., Lindholm, B., et al., 2024. Making the invisible visible: imaging techniques for assessing muscle mass and muscle quality in chronic kidney disease. Clin Kidney J, 17, sfae028.

[30] Mohamed, A. A., Caussat, T., Mouhawasse, E., et al., 2024. Neurosurgical Intervention for Nerve and Muscle Biopsies. Diagnostics, 14, 1169.

[31] Santos, D. B., Desmarais, G., Falaize, L., et al. 2017. Twitch mouth pressure for detecting respiratory muscle weakness in suspicion of neuromuscular disorder. Neuromuscul Disord, 27, 518-525.

[32] Ji, H. M. & Won, Y. H. 2024. Early Mobilization and Rehabilitation of Critically-Ill Patients. Tuberc Respir Dis (Seoul), 87, 115-122.