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REVIEW

Risk Factors, Diagnostic Challenges, and Emerging Therapeutic Strategies for ICU-Acquired Weakness: A Brief Review

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Abstract: Intensive care unit-acquired weakness (ICU-AW) is a common complication in critically ill patients, associated with multiple risk factors and significantly impacting long-term patient outcomes. Currently, early diagnosis remains a key challenge in managing ICU-AW: clinical scales are limited by subjectivity, while muscle ultrasound and emerging biomarkers (such as the creatinine/cystatin C ratio, miR-451a, and MuRF1), though showing potential for early identification, have not yet been widely adopted in clinical practice. In terms of management, prevention is paramount. The ABCDEF bundle emphasizes early mobilization (initiated within 24–72 hours), while nutritional strategies targeting molecular pathways (such as HMB and ω-3 fatty acids) help regulate protein metabolism balance. Novel targeted therapies (eg, the myostatin inhibitor Bimagrumab) have demonstrated potential to increase muscle mass in clinical trials. Currently, early diagnosis remains the critical barrier. This review aims to synthesize the latest evidence on the risk factors, diagnostic challenges, and management strategies for ICU-AW, providing insights for clinical practice. It also underscores the need for future research to focus on developing highly sensitive diagnostic tools, optimizing preventive strategies, and promoting the clinical translation of targeted therapies. Ultimately, this will help establish a comprehensive and precise multi-level intervention framework to improve patient outcomes.

Keywords: intensive care unit-acquired weakness, neuroinflammation markers, risk factors, assessment

Introduction

Intensive care unit–acquired weakness (ICU-AW) is a common limb weakness syndrome in critically ill patients, primarily affecting the respiratory muscles and proximal limb muscles, with relatively milder involvement of facial and ocular muscles.[1] ICU-AW encompasses critical illness polyneuropathy (CIP), critical illness myopathy (CIM), or a combination of both, known as critical illness neuromyopathy (CIN).[1,2] Its pathophysiology involves complex interactions across multiple pathways, including inflammatory responses, oxidative stress, protein metabolism imbalance, microcirculatory dysfunction, impaired nerve conduction, and defective mitophagy.[1,3] The incidence of ICU-AW is as high as 40%–50% in critically ill patients,[4,5] and exceeds 79% in those with sepsis.[6] In the short term, this syndrome can prolong the duration of mechanical ventilation and ICU stay, increase medical costs, and raise the risk of hospital-acquired infections,[7–9] In the long term, it is associated with increased mortality, delayed recovery of physical function, reduced health-related quality of life, and significant consumption of societal healthcare resources.[10–12]

Current guidelines generally recommend early intervention for ICU patients, such as initiating rehabilitation activities within 24–72 hours of admission, centered around the ABCDEF bundle strategy and combined with individualized nutrition and exercise programs,[13] with the aim of improving outcomes.[14,15] However, the effective implementation of these interventions highly depends on the early identification and diagnosis of ICU-AW. At present, there is a lack of highly sensitive and specific biomarkers for the diagnosis of ICU-AW, diagnostic tools have not been standardized,[16] and

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there is a shortage of tailored intervention strategies adapted to resource settings in different regions. These issues often lead to ICU-AW being masked by the primary disease, making early identification and intervention challenging to implement.[1,17] This article aims to review the current research status of ICU-AW, focusing on risk factors, diagnostic challenges, and prevention and emerging treatment strategies, in order to provide insights for optimizing clinical practice and guiding future research directions.

Risk Factors for ICU-AW

This review adopts the pathophysiological framework of ICU-AW, focusing on five core pathways—systemic inflammation, protein metabolism imbalance, mitochondrial dysfunction, oxidative stress, and impaired nerve conduction—to categorize risk factors into "intrinsic predisposing factors" and "extrinsic precipitating factors".[18] Intrinsic predisposing factors establish the foundation for disease onset by compromising compensatory capacity, reducing protein synthesis, or increasing neuromuscular vulnerability, whereas extrinsic precipitating factors act as "accelerators" by amplifying these pathological mechanisms. Together, they collectively drive the initiation and progression of ICU-AW.[19]

Intrinsic Predisposing Factors

Patient-Related Factors

Multiple studies indicate that age and sex are closely associated with the development of ICU-AW.[17,20] The risk of ICU-AW increases with age. This may be due to the increasing average age of ICU patients, where older adults (>60 years) experience age-related muscle mass loss and factors like inflammatory responses, making them more susceptible to ICU-AW. Women appear more susceptible to ICU-AW than men, although the underlying mechanisms for this female susceptibility remain unclear.[20] Therefore, in clinical practice, we should pay greater attention to this high-risk group comprising elderly and female patients, conducting early assessment and intervention to reduce ICU-AW risk.

Disease Status

Sepsis

Sepsis is a significant risk factor for ICU-AW. Epidemiological studies indicate that its incidence among septic patients can exceed 79%, substantially higher than that in the general ICU population.[6] The systemic inflammatory response triggered by sepsis is closely associated with the development of ICU-AW.[21] Research has demonstrated that sepsis patients requiring mechanical ventilation face a significantly higher risk of muscle atrophy and weakness.[22] A study by Hadda et al revealed that septic patients experienced approximately 9–10% loss of muscle thickness during hospitalization.[23] Therefore, early control of infection and inflammation, combined with intensified rehabilitation training, can effectively reduce the incidence of ICU-AW in septic patients.

Diabetes

In a prospective study, Nanas et al found a significant association between high blood glucose levels during ICU stay and the occurrence of ICU-AW.[24] A systematic review indicated that hyperglycemia is strongly associated with the development of ICU-AW and recommended maintaining strict glycemic control within the range of 90–144 mg/dl, combined with intensive insulin therapy to reduce the risk of ICU-AW.[25] Furthermore, a study on intensive insulin therapy for neuromuscular issues in the ICU found that intensive insulin therapy reduced the incidence of CIP/CIM ($p=0.02$).[26] Therefore, real-time monitoring of patient blood glucose levels is particularly important.

Malnutrition

Malnutrition in ICU-AW patients, caused by the underlying illness, can further exacerbate muscle metabolic disorders. According to a consensus statement from the global clinical nutrition community,[27] malnutrition is typically defined as a body mass index (BMI) <18.5 kg/m^2 in individuals under 70 years of age, or a score of 5 or higher on nutritional risk screening tools such as the NRS-2002. ICU-AW is often associated with inadequate nutritional intake (especially protein) and prolonged inactivity.[28] The study by Mohamed et al[29] further confirms that a higher protein intake (averaging 0.46 g/kg/day more) can significantly improve patients' skeletal muscle strength. A randomized experiment indicated that the nutritional supplement whey protein significantly improves muscle mass and strength, while omega-3 fatty acids can improve muscle function by increasing the muscle protein synthesis rate (MPS). LI et al also showed that vitamin D significantly impacts muscle metabolism by regulating myogenesis and adipogenesis, thereby influencing muscle protein synthesis and contributing to muscle weakness.[13] Therefore, it is recommended to implement individualized nutrition plans based on the patient's condition.

Extrinsic Inducing Factors

Critically ill patients in the ICU often require prolonged bed rest, mechanical ventilation, sedative drugs, and physical restraints due to the severity of their illness, all of which are significant factors contributing to ICU-AW.

Mechanical Ventilation

Mechanical ventilation is a critical life-support measure for severely ill patients, yet it itself constitutes a significant risk factor for ICU-AW, particularly exerting direct adverse effects on the diaphragm. Studies indicate that approximately 80% of patients requiring prolonged mechanical ventilation exhibit diaphragmatic weakness.[30] Clinically, bilateral phrenic nerve magnetic stimulation is commonly employed to measure twitch transdiaphragmatic pressure (Pdi,tw) for assessing diaphragmatic function, with a Pdi,tw value below 11 cmH_2O serving as the diagnostic criterion for diaphragmatic weakness.[31] Further research demonstrates a significant negative correlation between the duration of mechanical ventilation and the decline in diaphragmatic contractility, as measured by TwPdi.[32] Longer durations of mechanical ventilation lead to longer periods of immobilization, resulting in denervation injury, muscle atrophy, and exacerbation of systemic inflammation, significantly increasing the risk of ICU-AW.[33] Therefore, we should strive to reduce mechanical ventilation time as much as the patient's condition allows and actively implement interventions to lower the risk of ICU-AW and improve patient prognosis.

Prolonged Immobilization

Studies indicate that in healthy individuals, complete immobilization for 1 week can reduce muscle strength by 5% to 10%, with an average daily loss of 1% to 1.3% of overall muscle strength.[19] The ICU Mobility Scale (IMS) is used to assess the mobility status of adult patients in the ICU, objectively quantifying functional mobility from bed-bound to walking into 11 hierarchical levels, thereby enabling systematic identification of their specific rehabilitation needs.[34] Patients in the ICU are typically immobilized due to critical illness requiring prolonged bed rest and mechanical ventilation. Prolonged muscle inactivity increases the production of pro-inflammatory cytokines and reactive oxygen species, further promoting muscle protein breakdown and accelerating overall muscle loss.[1] Therefore, in clinical work, we should continuously assess the patient's restraint status, remove restraints promptly based on the patient's condition, and initiate early passive and active rehabilitation training to promote muscle strength recovery.

Medications

In the ICU, the use of vasoactive drugs is closely related to the risk of ICU-AW.[1] Research indicates that the use of norepinephrine is associated with oxidative stress, microcirculatory dysfunction, and metabolic disturbances, which may collectively contribute to the development of muscle weakness.[25] A meta-analysis focusing on critically ill patients with sepsis found that corticosteroid use was linked to an increased risk of ICU-AW, potentially through mechanisms involving suppressed muscle synthesis and enhanced muscle protein breakdown.[35] Aminoglycoside antibiotics significantly increase the risk of ICU-AW by causing neuromuscular toxicity and muscle dysfunction.[10] Therefore, drug use in clinical treatment should be cautious to reduce the risk of ICU-AW.

Early Identification and Diagnostic Assessment

Clinical Scale Assessment

Clinical scales are the most commonly used bedside tools for diagnosing and monitoring ICU-AW. However, their application is heavily dependent on the patient's level of consciousness and cooperation ability, and different instruments vary in their emphasis on reliability, validity, and clinical applicability (as detailed in Table 1).

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Table 1 Comparison of Common Clinical Assessment Scales for ICU-AW

Assessment Tool	Primary Assessment Domains	Advantages	Disadvantages
Medical Research Council Sum Score (MRC-SS)[1]	Muscle strength of six muscle groups: Shoulder abduction Elbow flexion Wrist extension Hip flexion Knee extension Ankle dorsiflexion	- Simple to perform, can be completed at the bedside - Suitable for conscious and cooperative patients	**Validity/Reliability Issues**: Low sensitivity; Inter-rater reliability susceptible to subjectivity; Ceiling effect (poor discrimination between scores of 4 and 5)[1] **Clinical Applicability Issues**: Unsuitable for comatose or paralyzed patients
Physical Function in ICU Test scored (PFIT-s)[1]	Four items:[36] Shoulder flexion strength; Knee extension strength; Assisted standing duration; Number of steps in place	- Specifically designed for the ICU environment; relatively sensitive to early functional changes - Suitable for monitoring the effects of rehabilitation interventions	**Validity/Reliability Issues**: Ceiling and floor effects exist; Limited evidence for diagnostic accuracy **Clinical Applicability Issues**: Requires a certain level of patient cooperation
Chelsea Critical Care Physical Assessment Tool (CPAX)[37]	Comprehensive physical function (eg, respiratory function, mobility, balance)	- Comprehensive assessment dimensions, reflects overall functional independence level	**Validity/Reliability Issues**: Lacks sensitivity for dynamic monitoring **Clinical Applicability Issues**: Requires combination with other tools for a more comprehensive assessment
Six-Minute Walk Test (6MWT)[38]	Distance walked in six minutes	- Classic tool for assessing functional capacity in late rehabilitation phase - Effectively predicts long-term functional recovery and prognosis	**Clinical Applicability Issues**: Only applicable to stable patients; Requires specific equipment, space, and imposes high physical demands on the patient

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Among specific assessment tools, the Medical Research Council Sum Score (MRC-SS) quantifies muscle strength by evaluating six specific muscle groups and remains one of the most widely utilized instruments in clinical research. The MRC score has a maximum of 60 points; significant weakness is defined as a score <48, and severe weakness as <36. The original Physical Function ICU Test (PFIT) was developed in 2007. Skinner et al[39] reported in 2009, in a small sample of post-tracheostomy patients, that PFIT demonstrated excellent reliability (ICC range: 0.996–1.00) in assessing changes in cadence, knee extension strength, and shoulder flexion strength. To facilitate subsequent statistical analysis and clinical application, Denehy et al optimized the scoring system and streamlined the content, developing the Physical Function ICU Test Score (PFIT-s).[36] It is used to assess muscle strength, endurance, and mobility, comprising four items: shoulder flexion strength, knee extension strength, assisted standing time, and step cadence (stepping in place). It assesses muscle strength, endurance, and functional mobility, comprising four items scored on a 0–3 scale. The Chelsea Critical Care Physical Assessment tool (CPAx) is a simple scale developed by Corner et al to assess the recovery of physical function in ICU patients.[37] The scale includes 10 assessment items: respiratory function, cough effectiveness, bed mobility, rolling from supine to sitting edge of bed, sitting or standing balance, sit-to-stand transfer, transferring from bed to chair, walking ability, and grip strength. Each dimension is scored from 0 to 5, with a total score of 50; 0 indicates complete dependence, and 50 indicates complete independence.[37] The Six-Minute Walk Test (6MWT) is a classic tool for assessing overall function, suitable for ICU patients in the late rehabilitation phase. By measuring the maximum distance a patient can walk in six minutes, the 6MWT reflects cardiopulmonary function and muscle endurance, predicting long-term functional recovery after discharge.[38]

In summary, although the aforementioned clinical scales provide a structured approach for assessing ICU-AW, they share a core limitation: reliance on clinical judgment. Their results are susceptible to influences such as the patient's level of consciousness, cooperation, and the operator's experience. Therefore, future research must focus on developing instrument-based quantitative tools to enable more accurate and reproducible assessments.

Imaging Examination

Skeletal Muscle Ultrasound (SMUS) and Neuromuscular Ultrasound (NMUS) have seen increasing application in ICUs in recent years. A recent systematic review suggests that muscle ultrasound may be a reliable tool for ICU-AW detection, with high sensitivity (0.76) and specificity (0.80).[40] The vastus intermedius muscle is considered a key site for monitoring, as it exhibits the greatest changes in muscle mass and has the strongest relationship with functional measures.[41] However, ultrasound still faces methodological challenges in muscle quantification, requiring further standardization of techniques, particularly in nutritionally vulnerable patients, to better predict muscle function, nutritional status, and survival. Combining ultrasound with metabolic and functional markers is considered optimal for assessment and prognosis.[42,43] One study indicated that NMUS cannot reliably diagnose ICU-AW in ICU patients relatively early in the disease course, possibly because changes in muscle thickness and echo intensity are not significantly different in the early stages, and these indicators may be confounded by factors like fluid overload.[44] In 2023, Klawitter et al demonstrated that NMUS can detect and monitor changes in muscle and nerve and may help predict patient outcomes.[45] Therefore, neuromuscular ultrasound warrants further research and exploration of its applications.

Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) provide precise measurements of muscle cross-sectional area and mass, suitable for patients with severe fluid overload.[46] However, due to various limitations, they are not typically used as routine bedside tools. Bioelectrical Impedance Analysis (BIA) and Dual-Energy X-ray Absorptiometry (DXA) are also used for muscle assessment in ICU patients.[47] BIA estimates muscle and fat proportions by measuring electrical impedance, offering advantages of non-invasiveness, convenience, and repeatable monitoring, but its accuracy is affected by body water content and positional changes. DXA accurately measures lean body tissue; although limited by equipment availability in ICUs, it remains a useful tool under specific conditions.[1]

Muscle Biopsy

Muscle biopsy allows analysis of microscopic structure and pathological changes in muscle tissue, such as nerve fiber degeneration, myelin status, muscle fiber atrophy, necrosis, inflammation, fatty infiltration, fibrosis, and vacuolation.

However, muscle biopsy only reflects the state of a localized muscle area, which may not represent the overall situation. It is an invasive procedure carrying risks of infection and bleeding for the patient and is rarely used clinically.[1]

Biomarkers

Biomarkers represent a new direction for breaking through the bottleneck of early diagnosis. Recent literature reviews indicate that various biomarkers, such as the creatinine to cystatin C ratio (Cr/CysC), inflammatory markers (IL-6, TNF-α), metabolic markers (eg, albumin, amino acid levels), and miRNAs, show potential value in the diagnosis and monitoring of ICU-AW. For example, the Cr/CysC ratio has moderate diagnostic accuracy and has been widely studied for muscle mass assessment. However, the diagnostic performance of these markers varies across studies, possibly due to differences in diagnostic criteria and population characteristics. Furthermore, dynamic changes in miRNAs (eg, miR-451a) during muscle injury and repair provide new insights for the early diagnosis of ICU-AW.[48,49] Research in sarcopenia and neurodegenerative diseases has found associations between biomarkers like neurofilament light chain (NfL) and phosphorylated tau protein (p-tau181) and declines in muscle mass and function, offering new directions for biomarker research in ICU-AW.[50,51] Simultaneously, the critical role of the muscle atrophy-related E3 ubiquitin ligase MuRF1/TRIM63 in the muscle atrophy process has been revealed, providing potential targets for the diagnosis and treatment of ICU-AW.[52] Nevertheless, the diagnostic accuracy of current biomarkers is still insufficient for clinical application and usually requires combination with other detection methods (like muscle ultrasound) for comprehensive assessment. Future research should focus on developing multi-biomarker models and validating their efficacy and specificity in diagnosing ICU-AW through clinical trials.

Intervention Strategies for ICU-Acquired Weakness

Early Mobilization and Rehabilitation

The 2018 clinical practice guidelines recommend early physical rehabilitation interventions to reduce the negative impacts during critical illness and improve patients' long-term outcomes.[53] Initiating early mobilization within 24–72 hours of ICU admission[54] may be a core strategy for reducing ICU-AW risk. A randomized controlled trial demonstrated that a comprehensive rehabilitation strategy improved short-term functional outcomes, such as reducing delirium duration, enhancing muscle strength, and improving quality of life.[55] Another systematic review found that initiating early rehabilitation therapy within 72 hours of ICU admission improved physical and cognitive function and prevented Post-Intensive Care Syndrome (PICS), although it did not reveal any improvement in psychological health.[56] However, individualized interventions face challenges related to technical heterogeneity. Wright et al argued that intensive rehabilitation did not show significant superiority over standard rehabilitation in terms of long-term functional outcomes and survival rates.[57] This may be because the average treatment effect in randomized trials masks individual differences, necessitating more nuanced analysis and reporting methods to accurately reflect these variations.[58] The upgraded application of the "ABCDEF bundle strategy", adding "F (Family Engagement)", introduces a new dimension of social support by involving family members in supervising early mobilization.

Nutritional Intervention

Nutritional intervention is evolving from a traditional supportive strategy into a molecular mechanism-guided precision therapeutic approach targeting the modulation of muscle protein synthesis-breakdown balance. Emerging evidence demonstrates that enteral administration of specific amino acids and their metabolites significantly impacts muscle protein turnover: branched-chain amino acids (BCAAs) combined with dialanine (Di-Ala) prevent myofiber loss in cancer cachexia mice by suppressing the ubiquitin-proteasome pathway,[59] while a meta-analysis of adult data indicates β-hydroxy-β-methylbutyrate (HMB) yields muscle mass and strength effect sizes of 0.21 and 0.27, respectively, offering quantifiable benefits for metabolically stressed ICU patients.[60] Antioxidants, as an important component of nutritional supplements, have a positive effect on improving muscle condition in older adults, and their combination with exercise demonstrates a more pronounced effect.[61] Although significant heterogeneity exists across 30 randomized controlled trials examining HMB or composite amino acids in critically ill populations,[62] the established nutritional paradigm for geriatric sarcopenia—featuring a comprehensive regimen of leucine-rich whey protein, vitamin D, omega-3, and probiotics—demonstrates synergistic potential in preserving muscle strength and function during hospitalization.[63] Furthermore, omega-3 fatty acids (EPA/DHA) exert dual anti-inflammatory and antioxidant effects, enhancing aged rat stride length by 14.82% when combined with exercise,[64] suggesting therapeutic relevance for the oxidative stress-inflammation axis in ICU-acquired weakness (ICU-AW). Optimal timing, dosing, and drug-nutrient interactions nevertheless require validation through larger prospective ICU studies.

Combined nutrition and exercise interventions hold potential advantages for improving muscle health, but their effects may vary depending on study design and intervention methods. Kim et al's study showed that after 3 months of combined nutrition and exercise intervention, there was no significant change in appendicular skeletal muscle mass (ASM) between groups ($P = 0.26$).[65] However, a randomized controlled trial indicated that combining nutritional supplementation with exercise training yielded better results than either intervention alone, significantly improving muscle mass and strength.[13] A recent meta-analysis focusing on older adults with osteosarcopenia further confirms that strength training can effectively improve their skeletal muscle mass, grip strength, and protein intake.[66] This conclusion echoes the findings of Kim et al regarding the combined intervention of nutritional supplementation and exercise training, collectively underscoring the superiority of integrated interventional strategies.

Pharmacological Interventions

Simultaneously, significant progress has been made in pharmacological research targeting ICU-AW, offering new possibilities for future treatment. Bimagrumab, by inhibiting myostatin activity, demonstrated good safety and tolerability in healthy older adults and obese adults, increasing lean body mass and muscle strength, thus providing a potential solution for ICU-AW treatment.[67,68] Elamipretide (ELAM), as a mitochondria-targeted peptide, improves cardiac and skeletal muscle function during aging, mitigating signs of sarcopenia and cardiac dysfunction.[69] Furthermore, novel compounds like GDF-15 monoclonal antibodies have shown potential for improving muscle mass and function in clinical trials.[70] However, the application of these drugs in ICU-AW is still exploratory, requiring more clinical research to validate their efficacy and safety. Concurrently, biomarkers are gaining attention in ICU-AW diagnosis; for instance, detecting GDF-15 levels might aid in early identification and monitoring of muscle wasting,[70] although current diagnostic tools still have limitations and require further optimization and standardization. Based on the advances in non-pharmacological and pharmacological interventions mentioned above, future directions should integrate multimodal strategies, incorporating bundled prevention, precision rehabilitation techniques, and targeted drugs into a stratified intervention framework.

Summary

ICU-AW is a common complication in critically ill patients resulting from multiple risk factors, which significantly impairs functional recovery and quality of life. This study integrates the latest research advances in the field of ICU-AW to develop a comprehensive framework that connects pathological mechanisms to clinical management. At the pathophysiological level, this review revolves around core mechanisms including systemic inflammation, oxidative stress, mitochondrial dysfunction, and protein metabolism imbalance, elucidating the multi-pathway interactions underlying ICU-AW. Taking sepsis as an example, it serves as a key extrinsic precipitating factor that initiates a systemic inflammatory response, exacerbates oxidative stress, and induces mitochondrial dysfunction, collectively forming a vicious pathway leading to muscle structural damage. This process is simultaneously accompanied by suppressed protein synthesis and diminished muscle regeneration capacity. The in-depth understanding of these mechanisms establishes a molecular theoretical foundation for early identification of high-risk populations and the development of targeted intervention strategies. In terms of diagnosis, while existing clinical scales are convenient for bedside use, they are limited by subjectivity and insufficient sensitivity. Imaging techniques such as muscle ultrasound, along with emerging biomarkers like the creatinine/cystatin C ratio, offer promising directions for early and objective diagnosis. However, the lack of standardized protocols currently hinders their widespread adoption. Regarding treatment strategies, early mobilization based on the "ABCDEF bundle" has been proven to significantly reduce the incidence of ICU-AW. Nutritional support interventions, such as β-hydroxy-β-methylbutyrate (HMB) supplementation, have demonstrated effect sizes of 0.21 for muscle mass and 0.27 for muscle strength. Particularly, emerging pharmacological strategies—including targeted therapies like the myostatin inhibitor Bimagrumab and the mitochondrial-targeted peptide Elamipretide—have shown potential in preclinical and early clinical trials to improve muscle structure and function, opening new avenues for ICU-AW treatment.

The implementation of these integrated interventions not only enhances muscle strength and physical function but also plays a critical role in the overall clinical pathway: early mobilization combined with structured rehabilitation shortens the duration of mechanical ventilation and ICU stay, thereby reducing the risk of complications such as ventilator-associated pneumonia and alleviating healthcare costs. Meanwhile, precision nutrition and pharmacological interventions mitigate muscle loss and accelerate functional recovery, improving long-term independent living ability and reducing post-discharge reliance on rehabilitation and nursing care, thereby indirectly saving long-term medical and social resources.

Although current evidence provides multiple strategies for the prevention and management of ICU-AW, early identification and personalized adaptation of interventions remain core challenges. Future research should focus on the following directions: developing multimodal early diagnostic tools that integrate biomarkers (eg, Cr/CysC, miR-451a, MuRF1) and muscle ultrasound to overcome existing diagnostic bottlenecks; validating the effectiveness of bundled prevention strategies in different high-risk populations (eg, the elderly, septic patients) through randomized controlled trials, and determine the optimal intervention timing and dosage; and prioritizing clinical translation research on emerging targeted therapies to establish individualized intervention frameworks based on risk stratification and molecular phenotypes. By systematically advancing these strategies, we can not only improve functional outcomes for patients but also optimize the allocation of healthcare resources, achieving a comprehensive transition from short-term disease management to long-term health outcomes.

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