

# Critical Illness Myopathy: Pathophysiology and Management Strategies

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## Abstract

Critical illness myopathy is a significant neuromuscular complication in critically ill patients, characterized by early proximal muscle weakness. It has varying incidences, significantly impacting mortality and morbidity among critically ill patients. This article aims to discuss the pathophysiology and evidence-based management strategies, which may help to improve patient outcomes in critically ill individuals.

**Keywords:** Critical Illness Myopathy; Early Mobilisation; Sedation

## Abbreviations

CIM - Critical Illness Myopathy.

NMBAs - Neuro Muscular Blocking Agents.

CIPNM - Critical Illness Polyneuromyopathy.

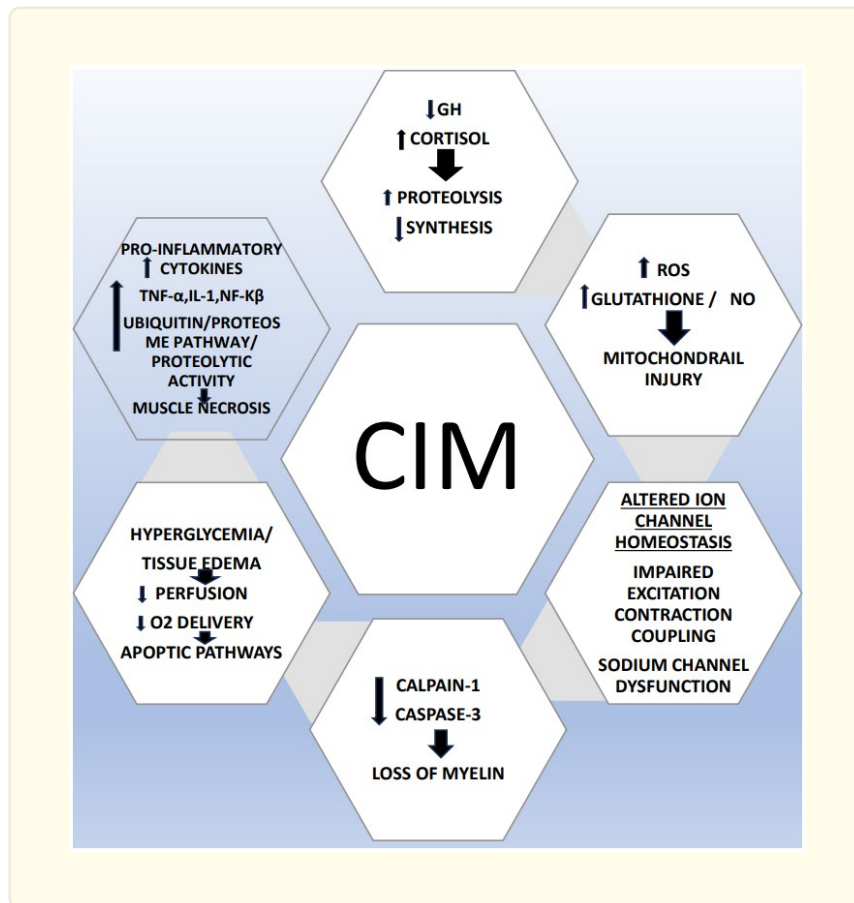
ICU - Intensive Care Unit.

## Introduction

Critical illness myopathy represents a significant neuromuscular complication observed in critically ill patients, characterized by profound muscle weakness and dysfunction. It is often diagnosed late, typically recognized during weaning failure from mechanical ventilation. The incidence of CIM varies widely ranging from 20-80 % with one meta-analysis reporting an incidence of 40 % [1]. CIM typically manifests as symmetrical muscle weakness involving respiratory muscles and skeletal muscles (both proximal and distal) with proximal muscles affected earlier. It significantly increases mortality and morbidity in intensive care unit patients.

This article aims to provide a comprehensive overview of critical illness myopathy, highlighting its pathophysiology, clinical presentation, diagnostic approach, management strategies, and long-term outcomes. Enhancing understanding of CIM and its implications in critical care can help in optimizing therapeutic interventions and improve outcomes.

### Pathophysiology [2-7]



### Clinical Features

Many risk factors have been identified as contributing to CIM and the common factors are premorbid health status, duration of critical illness, duration of mechanical ventilation and presence of multi organ dysfunction [8].

Diagnosis of CIM is often delayed as symptoms may become apparent when sedation is discontinued and weaning from mechanical ventilation begins. CIM typically manifests as symmetrical muscle weakness involving skeletal muscles and even respiratory muscles both proximal and distal and early involvement of proximal muscle weakness should raise suspicion of CIM.

A diagnostic framework proposed by Lacomis D. et al. [9] and Stevens et al. [10] includes the following clinical and EMG criteria for diagnosing Critical Illness Myopathy (CIM):

The patient meets the criteria for intensive care unit-acquired weakness.

Sensory nerve action potential amplitudes are >80% of the lower limit of normal in at least two nerves.

Needle electromyography (EMG) in at least two muscle groups reveals short duration, low-amplitude motor unit potentials with early or normal full recruitment, with or without fibrillation potentials.

Direct muscle stimulation demonstrates reduced excitability (muscle/nerve ratio >0.5) in at least two muscle groups.

Muscle histology consistent with myopathy, characterized by myosin loss, muscle atrophy, and necrosis.

### ***Myths/Controversies***

Recent evidence regarding the impact of steroid usage and neuromuscular blocking agents (NMBAs) is conflicting. Studies have not consistently identified them as risk factors for Critical Illness Polyneuromyopathy (CIPNM). Bednarik et al [11], did not find them to be significant risk factors, while Hermans et al [12], reported that the presence and duration of systemic inflammatory response syndrome (SIRS) and the severity of multi-organ involvement increase the risk of CIPNM, rather than steroids. Additionally, some studies suggest that steroids may even be protective against Critical Illness Myopathy (CIM) [13].

It is evident that the NF- $\kappa$ B (nuclear factor kappa-light-chain-enhancer of activated B cells) pathway and the ubiquitin-proteasome pathway play roles in the development of CIM. Recent evidence suggests that steroids interact with NF- $\kappa$ B and the ubiquitin-proteasome pathway, exhibiting anti-inflammatory properties.

### ***Prevention/Treatment***

Treatment is usually supportive and early rehabilitation.

### ***Sedation and Mobilization***

The use of a sedation protocol reduces the duration of mechanical ventilation and contributes to respiratory training, which may not directly treat the condition but influences patient mobilization and early mobilization helps prevent the loss of muscle bulk [14]. The infusion of dexmedetomidine in the ICU not only helps prevent delirium but also contributes to facilitating early mobilization with active training [15]. Animal studies suggest that early initiation of spontaneous breathing and early mobilization can prevent the activation of calpain and ubiquitin-proteasome activity [16, 17].

Recent randomized controlled trials (RCTs) suggest that electromechanical stimulation can prevent the development of Critical Illness Myopathy (CIM) in critically ill patients [18].

### ***Insulin Therapy***

Avoiding hyperglycemia and implementing insulin therapy protocols may play a role in preventing Critical Illness Myopathy (CIM) [19].

### ***Pharmacological Management***

Recent evidence suggests that BGP-15 (an insulin sensitizer) [20], Vamorolone (a partial agonist of the glucocorticoid receptor) [21], and Ruxolitinib (a JAK inhibitor) [22] have demonstrated survival benefits in experimental models.

### **Conclusion**

Critical Illness Myopathy (CIM) represents a significant neuromuscular complication observed in critically ill patients, characterized by profound muscle weakness and dysfunction. Despite its multifactorial etiology and delayed diagnosis, early recognition and proactive management strategies are essential for better patient outcomes. Supportive care, including early mobilization and pharmacological interventions targeting inflammatory pathways, shows promise in preventing and managing CIM. Ongoing research into novel therapies, such as insulin sensitizers and glucocorticoid receptor agonists, as new strategies in the management of CIM. A multidisciplinary approach and understanding of the context-sensitive half-life of drugs are crucial for optimizing drug therapy in

critically ill patients.

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