JOINTS (Journal Orthopaedi and Traumatology Surabaya)
October 2025; 14(2): 77-83, DOI: 10.20473/joints.v14i2.2025.77-83
Received: 27 May 2025 / Revised: 15 August 2025
Accepted: 27 August 2025 / Published: 30 October 2025

*Original Article*

# Early Application of Neuromuscular Electrical Stimulation Prevents Excessive Muscle Wasting in Critically Ill Patients in the Intensive Care Unit

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## ABSTRACT

**Background:** Intensive Care Unit-Acquired Weakness (ICU-AW) is a common neuromuscular complication in critically ill patients, leading to muscle atrophy, prolonged mechanical ventilation and impaired functional recovery. Effective rehabilitation strategies play crucial role in maintaining muscle strength. Neuromuscular electrical stimulation (NMES) had shown potential in preserving quadriceps femoris muscle thickness. This study aimed to examine the effect of NMES to quadriceps femoris muscle thickness in patient with ICU-AW.
**Methods:** Patients that stayed in ICU more than 48 hours and used mechanical ventilation for at least 24 hours enrolled in one-group pretest-posttest design. Neuromuscular electrical stimulation applied to bilateral quadriceps femoris for 30 minutes daily over five consecutive days. Bilateral quadriceps femoris muscle thickness were assessed with USG day before and after therapy.
**Results:** Twenty ICU-AW patients were enrolled from December 2023 to June 2024, and 13 of them completed the study. There were no significant changes in the thickness of the right and left quadriceps femoris muscle before and after 5-days of NMES therapy ($p = 0.910$ and $p = 0.519$, respectively). However, we preserved less than 5% decreased of muscle thickness.
**Conclusions:** Early 5-days of NMES therapy did not increase quadriceps femoris muscle thickness but effectively prevented further muscle degradation in ICU-AW patients. The potential benefits of rehabilitation therapy in ICU-AW patients should be further explored in future studies with controlled indicators and larger sample sizes.

**Keywords:** Electrical stimulation therapy; Intensive care; Muscular atrophy; Rehabilitation

## INTRODUCTION

Intensive care unit-acquired weakness (ICU-AW) is a clinical condition of severe widespread muscle weakness and atrophy that developed in critically ill patients who treated in ICU without any identifiable cause other than the critical illness itself.[1] Incidence of ICU-AW ranges from 46%-50% mostly in patient with prolonged mechanical ventilation, multi-organ failure or sepsis that can leads to a daily reduction at least 5% in muscle thickness during the first week of ICU admission and may result in persistent physical dysfunction at discharged lasting up to 5 years post-recovery.[1,2] While early rehabilitation mitigates ICU-AW and shortens hospital stays, its effectiveness is hindered in non-cooperative or sedated patients.[3] No definitive treatment exists, highlighting the urgent need for risk factor control and novel interventions.[2]

Neuromuscular electrical stimulation (NMES) combats muscle wasting by stimulating contractions that uniquely recruit large, fast-twitch fibers first (reverse of voluntary recruitment) – the fibers most prone to disuse atrophy. This allows

targeted strengthening of weakened muscles, but because these fibers fatigue rapidly, longer rest periods between contractions are essential.[4] It is applied to lower extremities serves as a viable adjunct therapy for the patient mobilization, particularly in those unable to actively participate. Evidence supports its efficacy in enhancing muscle strength among ICU patients, with study demonstrating significant improvements in Medical Research Council (MRC) scores following NMES intervention.[5,6] Neuromuscular electrical stimulation is a clinically viable method to induce muscle growth and enhance strength and endurance in patients unable to perform active exercise, making it a promising intervention for mitigating muscle mass loss.[7] Neuromuscular electrical stimulation (NMES) has shown promise in mitigating muscle loss in critically ill patients. A randomized controlled trial found that daily NMES for seven consecutive days significantly reduced quadriceps muscle thickness loss compared to controls (-6% vs -12%, $p = 0.014$).[8]

As a preliminary study, this research aims to evaluate the efficacy of a 5-day NMES protocol in prevent quadriceps femoris muscle wasting in ICU-AW patients, with particular focus on the time course of NMES effects. We hypothesized that a 5-day regimen of NMES would significantly attenuate quadriceps femoris muscle wasting in ICU-AW patients, as measured by changes in muscle thickness compared to baseline.

## MATERIAL AND METHODS

### Study Design and Setting

This is the first preliminary study with one-group pretest-posttest design using consecutive sampling technique that carried out at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from December 2023 to June 2024. Ethical clearance was granted under number 0800/KEPK/X/2023 by the Ethical Committee of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.

### Participants

The inclusion criteria were: (1) age 19-60 years, (2) required mechanical ventilation >24 hours, (3) had ICU stay >48 hours, and (4) able to follow simple commands to assess muscle strength and ensure patient safety and discomfort. The exclusion criteria were: (1) pre-existing neurological condition, (2) BMI > 35 kg/m2, (3) peripheral vascular disease, (4) pre-ICU motor paralysis, (5) extremity fracture, and (6) cognitive impairment. The drop out criteria were: (1) missing ≥3 consecutive NMES session, (2) clinically significant deterioration, (3) early transfer from ICU before protocol completion, and (4) death.

### Intervention Protocol

We enrolled 20 ICU patients who underwent baseline assessments of muscle strength using Medical Research Council Sum Score (MRC-SS) and quadriceps femoris thickness prior to intervention. Participants received five consecutive days of NMES using an EMS EV-906 device delivering rectangular biphasic pulses (50Hz frequency, 300μs pulse width) with 10s on/10s off cycles (1s ramp time). Electrodes were positioned on bilateral quadriceps femoris in supine position and slight knee flexion, with intensity (0–80 mA) titrated for each patient by starting at the lowest perceivable stimulation, increasing in 2–5 mA increments until a strong, visible muscle contraction was achieved without discomfort, and adjusting at each session to the highest tolerable level that maintained contraction. Each 40-minute daily session comprised 5-minute warm-up, 30-minute stimulation, and 5-minute recovery, with continuous hemodynamic monitoring. A physiatrist and intensivist jointly recorded pre- and post-intervention outcomes using standardized forms.

### Data Collection and Analysis

All data were systematically recorded and analyzed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA). Demographic characteristics (age, sex, ICU duration) were summarized using descriptive

statistics, with continuous variables reported as mean ± standard deviation for normally distributed data or median for non-parametric distributions. We assessed data normality using the Shapiro-Wilk test. Given the non-parametric distribution of our primary outcomes, within-group comparisons of quadriceps femoris muscle thickness measurements before and after the 5-day NMES intervention were analyzed using the Wilcoxon signed-rank test. A two-tailed $p$-value < 0.05 was considered statistically significant.

## RESULTS

Twenty critically ill patients initiated the prescribed NMES protocol. Seven participants required early discontinuation following ICU discharge to general wards, while 13 completed all five NMES sessions with the baseline characteristics appear in Table 1. These dropouts may have reduced the statistical power of the study and could introduce attrition bias, particularly if the characteristics or responses of these patients differed from those who completed the intervention. Safety monitoring detected no NMES-related adverse events, including no instances of hemodynamic instability or skin injury during treatment sessions.

Quantitative ultrasound assessment, showed in Table 2, revealed no statistically significant changes in quadriceps femoris muscle thickness following the 5-day NMES intervention. Comparative analysis showed minimal alteration in the right quadriceps femoris muscle (pre-intervention: 1.43 ± 0.54 cm vs post-intervention: 1.42 ± 0.36 cm; mean difference: -0.01 ± 0.23 cm, $p$ = 0.910, Cohen's d = 0.339), representing a clinically negligible reduction of 0.7%. Similarly, the left quadriceps femoris muscle exhibited a moderate but non-significant decrease (pre-intervention: 1.47 ± 0.61 cm vs post-intervention: 1.40 ± 0.52 cm; mean difference: -0.07 ± 0.25 cm, $p$ = 0.519, Cohen's d = 0.349), corresponding to a 4.8% reduction. Although neither change reached statistical significance, the small-to-moderate effect sizes suggest potential clinical relevance that warrants further investigation in larger studies.

**Table 1.** Demographic characteristic data of ICU-AW patients

| Characteristic | $n$ = 13 | $p$ |
|---|---|---|
| Age (years) | 49 (19-60) | 0.019 |
| Body Mass Index (kg/m$^2$) | 23.41 ± 3.56 | 0.694 |
| Sedation duration (days) | 3 (2-12) | 0.001 |
| Ventilator duration (days) | 4 (2-16) | 0.003 |
| SOFA Score | 7 (4-8) | 0.076 |
| Gender | | |
| Male | 4 (30.8%) | |
| Female | 9 (69.2%) | |
| Diagnose | | |
| Renal disease | 2 (15.38%) | |
| Post elective surgery | 2 (15.38%) | |
| Post emergency surgery | 6 (46.15%) | |
| Lung disease | 3 (23.08%) | |

Shapiro-Wilk normality test. Data presented as median (min-max) or mean ± SD or n (%)

**Table 2.** Inter group changes difference of quadriceps femoris muscle thickness

| Measurement | Mean ± SD (cm) | Mean Change ± SD (%) | $p^a$ | Effect size[b] |
|---|---|---|---|---|
| Right quadriceps femoris thickness pre | 1.43 ± 0.54 | -0.01 ± 0.23 cm (-0.7%) | 0.910 | 0.339 |
| Right quadriceps femoris thickness post | 1.42 ± 0.36 | | | |
| Left quadriceps femoris thickness pre | 1.47 ± 0.61 | -0.07 ± 0.25 cm (-4.8%) | 0.519 | 0.349 |
| Left quadriceps femoris thickness post | 1.40 ± 0.52 | | | |

a) Paired Sample t Test. b) Cohen's d

## DISCUSSION

To our knowledge, this represents the first investigation of neuromuscular electrical stimulation effects on quadriceps femoris muscle thickness in intensive care unit-acquired weakness patients at Dr. Soetomo General Academic Hospital's intensive care unit, Surabaya from December 2023 to June 2024. From an initial cohort of 20 enrolled participants, seven were dropped out due to early ward transfer before completed NMES therapy. Thirteen patients successfully completed the 5-day NMES protocol without adverse events, demonstrating the feasibility of this intervention in our ICU setting.

Critical illness triggers sexually dimorphic pathophysiological responses, with females exhibiting greater metabolic dysregulation, including impaired insulin sensitivity and reduced type IIA muscle fiber cross-sectional area, which accelerates muscle catabolism.[9,10] Critically ill males exhibit a distinct endocrine vulnerability characterized by suppressed testosterone activity, where low plasma testosterone and elevated estradiol-to-testosterone ratios correlate strongly with muscle weakness and worse clinical outcomes, including higher mortality risk.[11] These sex-specific differences—metabolic dysfunction in females and hormonal imbalance in males—highlight the need for tailored therapeutic strategies to address distinct pathways, such as targeting insulin resistance and muscle preservation in females or modulating androgen-estrogen ratios in males to optimize recovery outcomes.

Recent evidence suggests that obesity may not protect against ICUAW, but instead may increase the risk of early severe muscle wasting, particularly in patients with high subcutaneous fat accumulation. This paradox may be linked to suppressed ketogenesis in obese patients during critical illness, alongside stronger acute inflammatory responses, both of which can exacerbate skeletal muscle loss.[12] These findings highlight the complex interplay between fat accumulation, metabolic responses, and muscle preservation in the ICU, underscoring the need for targeted strategies to prevent ICUAW in obese patients.

Sedation is essential for patient comfort but prolongs mechanical ventilation and ICU stays when overused. Prolonged sedation reduces mobility, increases agitation, and elevates risks of post-ICU depression and PTSD. Neuromuscular blockers, though rarely used, worsen complications in patients with renal or hepatic impairment. Current guidelines therefore recommend protocolized light sedation with daily interruptions to balance comfort and recovery.[13] Our study found median durations of 3 days for sedation and 5 days for mechanical ventilation. Prolonged sedation and mechanical ventilation increase risks of intensive care unit -acquired weakness and ventilator-associated complications, though their direct mortality impact remains debated.

The sequential organ failure assessment (SOFA) score serves as an important clinical tool for assessing organ dysfunction severity in ICU patients, with higher scores indicating greater disease severity and increased risk of intensive care unit-acquired weakness.[14] Our study found a median SOFA score of 7, with elevated scores correlating with greater infection susceptibility in immunocompromised patients and subsequent systemic inflammatory responses that may contribute to ICU-AW development. Research indicates that tracking SOFA score trends during the initial ICU week can help predict patient outcomes, including neuromuscular complications.[15]

Critically ill ICU patients experience rapid quadriceps femoris muscle loss (15-30% thickness reduction) within 5-10 days of admission, as demonstrated by ultrasound measurements of the rectus femoris and vastus intermedius. This early muscle wasting strongly predicts poor discharge outcomes and long-term functional impairments.[16] A longitudinal study of 37 ICU patients revealed significantly greater muscle wasting (rectus femoris, vastus intermedius, and biceps brachii) in those with ICU-AW compared to non-ICU-AW counterparts, with progressive declines observed at days 4, 7, and 10 of ICU stay.[17]

As a foundational component of early

mobilization, NMES effectively prevents muscle atrophy in sedated ICU patients by inducing non-volitional contractions. Clinical evidence demonstrates its benefits in preserving muscle mass, reducing ICU-acquired weakness, and potentially decreasing ventilation duration.[18] A recent study by Yustiawan et al. further established that 5-day NMES protocols significantly enhance quadriceps femoris muscle strength, global muscle function, and reduce serum CK levels in mechanically ventilated patients, highlighting its therapeutic potential even before active participation becomes feasible.[19]

Quantitative ultrasound assessment revealed no statistically significant alterations in quadriceps femoris muscle thickness following the 5-day NMES intervention. The right quadriceps femoris muscle demonstrated minimal changes (mean difference: −0.01 ± 0.23 cm, $p = 0.910$), reflecting a clinically insignificant reduction of 0.7%. Similarly, the left quadriceps femoris exhibited a moderate but non-significant decrease (mean difference: −0.07 ± 0.25 cm, $p = 0.519$), corresponding to a 4.8% decline. Several factors may have contributed to the lack of significant results. Critically ill patients with established or evolving ICUAW exhibit rapid catabolic muscle loss that often overwhelms short-term NMES anabolic stimulation. The 5-day intervention duration was likely insufficient, as positive structural adaptations typically require longer protocols. Inter-individual variability in clinical factors (disease severity, sedation, mobility) and comorbidities (malnutrition, corticosteroids) further limited NMES efficacy.

A randomized trial demonstrated that early NMES significantly attenuated quadriceps muscle mass loss in critically ill patients compared to the non-stimulated control leg (−6% vs. −12%, $p = 0.014$), coinciding with a shift toward larger myofiber size and higher MyHC-I gene expression in stimulated muscles.[8] Another study found no significant difference in quadriceps muscle mass preservation between medium-frequency (45 Hz) and high-frequency (75 Hz) NMES protocols in critically ill ICU patients, with both groups showing similar reductions in muscle layer thickness after 10 days. This suggests that the specific NMES frequency used (within the tested range) may not be a critical factor for mitigating muscle wasting in this population.[7] Notably, a recent trial implementing a comparable 5-day NMES protocol combined with early mobilization in ICU patients demonstrated superior preservation of muscle cross-sectional area in the biceps brachii (−2.7%) and rectus femoris (−1.7%) compared to early mobilization alone, which resulted in greater atrophy (−10% and −10.4%, respectively).[20] This contrast highlights the potential synergistic benefits of NMES with mobilization, though the mechanisms underlying differential effects across muscle groups warrant further investigation.

Observational evidence underscores the clinical ramifications of ICU-acquired muscle loss, which correlates strongly with prolonged mechanical ventilation, mortality risk, and long-term functional impairment. Muscle wasting occurs rapidly during critical illness, with reported rates of 1.75–2.10% per day during the first week of ICU admission, escalating to 2–3% daily in some cohorts.[21,22] Such accelerated atrophy may precipitate physical disability and increase susceptibility to adverse outcomes, emphasizing the need for timely, multimodal interventions to mitigate muscle degradation. While NMES shows promise in attenuating atrophy, its role as a standalone therapy remains equivocal, particularly in hypercatabolic states.

NMES is generally safe and feasible in critically ill patients, with a randomized trial reporting no skin injuries or hemodynamic instability during its use for pressure injury prevention in the ICU.[23] A randomized trial found that medium-frequency NMES combined with conventional therapy improved functional outcomes, muscle strength, and reduced hospital stay compared with low-frequency stimulation.[24] Additionally, a meta-analysis demonstrated that NMES integrated with physical therapy significantly increased extubation success in mechanically ventilated patients, supporting its role as part of a multimodal rehabilitation approach.[25]

This study did not account for potentially confounding variables such as baseline nutritional status and corticosteroid use, both of which may influence muscle mass preservation in critically ill patients. Including these parameters in future research could provide deeper insights into the interaction between NMES and patient-specific factors. Additionally, no post-intervention follow-up was conducted to evaluate sustained effects on muscle mass and functional recovery. Incorporating follow-up assessments at 1 week, 1 month, or longer would help clarify the durability of NMES benefits.

## CONCLUSION

This investigation provides novel evidence that a short-term, 5-day NMES protocol is safe, feasible, and capable of mitigating progressive quadriceps femoris muscle atrophy in patients with ICU-acquired weakness, even in those unable to actively participate in rehabilitation. While the intervention did not produce significant hypertrophy, the absence of any NMES-related adverse events underscores its suitability for critically ill populations. Compared with prior studies, our findings extend existing evidence by demonstrating the practicality and tolerability of NMES in a highly acute, short-term ICU setting, supporting its potential as an early preventive strategy against muscle wasting.

To strengthen these preliminary findings, future studies should recruit a larger, adequately powered cohort with parallel control groups and incorporate extended follow-up periods to evaluate the durability of NMES effects on muscle morphology and function. Research should also address potentially influential factors, such as nutritional status and corticosteroid use, to better interpret outcomes. Longer NMES intervention durations, integration with complementary rehabilitation modalities, and the use of standardized, clinically meaningful outcome measures are recommended to fully elucidate its therapeutic potential in preventing ICU-acquired weakness and muscle wasting.

## ACKNOWLEDGMENTS

The authors would like to thank the manager of Dr. Soetomo General Academic Hospital, Surabaya and the head of the Intensive Care Unit for their valuable contribution to data recording.

## FUNDING

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## CONFLICT OF INTEREST

The authors declare no conflicts of interest.

## ETHICAL APPROVAL

Ethical clearance was granted under number 0800/KEPK/X/2023 by the Ethical Committee of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.

## DATA AVAILABILITY STATMENT

The data that support the findings of this study are not publicly available due to patient confidentiality. However, data may be made available upon reasonable request directed to J.H.

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