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Research Article

Prospective Cohort Study of Respiratory Muscle Dysfunction and Predictors of Prolonged Mechanical Ventilation in Critically Ill Adults

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Abstract

Respiratory muscle dysfunction is increasingly recognized as a major contributor to delayed liberation from mechanical ventilation among critically ill patients. However, the longitudinal impact of respiratory muscle weakness on prolonged mechanical ventilation (PMV) and clinical outcomes remains incompletely characterized. This prospective cohort study evaluated the prevalence of respiratory muscle dysfunction and identified predictors of prolonged mechanical ventilation in critically ill adults admitted to intensive care units (ICUs).

A total of 200 mechanically ventilated adults were prospectively followed from initiation of invasive ventilation until successful weaning, ICU discharge, or death. Respiratory muscle strength was assessed using maximum inspiratory pressure (MIP) measurements within 48 hours of ICU admission and repeated during weaning. Prolonged mechanical ventilation was defined as ventilation lasting more than 7 days. The mean age was 58.6 ± 15.2 years, and 61.0% of participants were male. Respiratory muscle dysfunction (MIP < −30 cmH_2O) was identified in 82 patients (41.0%). PMV occurred in 72 patients (36.0%). Patients requiring PMV demonstrated significantly lower baseline MIP values (−24.8 ± 6.2 vs −38.7 ± 8.4 cmH_2O, $p < 0.001$), higher Sequential Organ Failure Assessment (SOFA) scores (9.4 ± 2.8 vs 6.7 ± 2.3, $p < 0.001$), and longer ICU stays

(18.6 ± 7.4 vs 9.8 ± 4.1 days, $p < 0.001$). Multivariate analysis identified respiratory muscle dysfunction (OR 4.6, 95% CI 2.4–8.9), SOFA score ≥8 (OR 3.1, 95% CI 1.6–6.0), and sepsis (OR 2.8, 95% CI 1.4–5.3) as independent predictors of PMV.

Respiratory muscle dysfunction is highly prevalent among critically ill adults and independently predicts prolonged mechanical ventilation. Early respiratory muscle assessment may facilitate risk stratification and targeted rehabilitation strategies to improve weaning outcomes.

Keywords: Respiratory muscle dysfunction, prolonged mechanical ventilation, critical illness, inspiratory muscle strength

Introduction

Mechanical ventilation remains one of the most commonly employed life-support interventions in modern intensive care units. Although lifesaving, prolonged dependence on mechanical ventilation is associated with substantial morbidity, increased healthcare costs, prolonged hospitalization, and higher mortality rates. Successful liberation from ventilatory support depends not only on pulmonary recovery but also on adequate respiratory muscle performance. Consequently, respiratory muscle dysfunction has emerged as a critical determinant of weaning failure and prolonged mechanical ventilation in critically ill patients [1–3].

The diaphragm contributes approximately 70% of inspiratory effort under normal physiological conditions. During critical illness, several factors may compromise respiratory muscle function, including systemic inflammation, sepsis, prolonged mechanical ventilation, malnutrition, corticosteroid exposure, neuromuscular blockade, and immobilization. These factors contribute to rapid diaphragmatic atrophy and reduced contractile function, collectively termed ventilator-induced diaphragm dysfunction [1–4].

Recent studies have demonstrated that measurable diaphragmatic weakness may develop within the first few days of mechanical ventilation. Experimental and clinical investigations have reported significant reductions in diaphragm thickness, inspiratory force generation, and respiratory endurance among mechanically ventilated patients. Such changes are associated with difficulty weaning from ventilatory support and increased risk of extubation failure [3–6].

Respiratory muscle dysfunction is not limited to the diaphragm alone. Accessory inspiratory muscles, intercostal muscles, and expiratory muscles may also be affected

during critical illness. The combined impact of generalized respiratory muscle weakness can substantially impair spontaneous breathing performance during weaning trials. Consequently, objective assessment of respiratory muscle strength has gained increasing attention as a prognostic tool in critical care medicine [5–8].

Maximum inspiratory pressure (MIP) represents one of the most widely used bedside measures of inspiratory muscle strength. Reduced MIP values have been associated with prolonged weaning duration, increased ICU length of stay, and higher mortality. However, variations in patient populations, disease severity, and measurement protocols have limited the generalizability of previous findings [7–10].

Sepsis is another important contributor to respiratory muscle dysfunction. Systemic inflammatory responses promote oxidative stress, mitochondrial dysfunction, and proteolytic activation within respiratory muscle fibers. These mechanisms accelerate muscle wasting and reduce contractile efficiency, thereby increasing the likelihood of prolonged ventilator dependence [8–11].

In addition to inflammatory mechanisms, nutritional deficiencies frequently encountered during critical illness may worsen respiratory muscle performance. Inadequate protein intake and catabolic stress contribute to skeletal muscle wasting, including respiratory musculature, further complicating the weaning process [10–12].

Despite growing recognition of respiratory muscle dysfunction as a clinically significant phenomenon, prospective studies evaluating its prevalence and prognostic value remain limited. Most available evidence originates from small observational cohorts or secondary analyses. Furthermore, there is a need for prospective longitudinal data examining respiratory muscle strength trajectories and their relationship with clinical outcomes in diverse ICU populations [11–14].

Identification of patients at high risk for prolonged mechanical ventilation is essential because early interventions such as inspiratory muscle training, optimized nutritional support, minimization of sedative exposure, and mobilization programs may improve respiratory muscle performance and facilitate successful weaning [13–16].

Therefore, this prospective cohort study aimed to evaluate the prevalence of respiratory muscle dysfunction in critically ill adults and identify independent predictors of prolonged mechanical ventilation.

Methodology

This prospective cohort study was conducted at Fauji Foundation Hospital over a 24-month period. Adult patients aged 18 years or older who required invasive mechanical ventilation for more than 48 hours were eligible for enrollment.

Patients with pre-existing neuromuscular disorders, cervical spinal cord injury, advanced motor neuron disease, severe traumatic brain injury precluding respiratory assessment, pregnancy, or anticipated withdrawal of life-sustaining therapy were excluded.

Sample size was calculated using Epi Info StatCalc software. Assuming an anticipated prevalence of respiratory muscle dysfunction of 35%, a confidence level of 95%, statistical power of 80%, and an expected odds ratio of at least 2.5 for prolonged mechanical ventilation, the minimum required sample size was estimated at 186 participants. To compensate for potential attrition and incomplete data, 200 patients were recruited.

Baseline demographic characteristics, comorbidities, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, SOFA score, primary diagnosis, laboratory investigations, and ventilatory parameters were recorded. Respiratory muscle strength was assessed using maximum inspiratory pressure measurements obtained through a standardized unidirectional valve technique within 48 hours of ICU admission and repeated during spontaneous breathing trials.

Respiratory muscle dysfunction was defined as MIP less than −30 cmH_2O. Prolonged mechanical ventilation was defined as invasive mechanical ventilation lasting more than 7 consecutive days. Secondary outcomes included ICU length of stay, duration of hospitalization, extubation failure, tracheostomy requirement, and ICU mortality.

Written informed consent was obtained from legally authorized representatives. Ethical approval was granted by the institutional review board before initiation of the study.

Statistical analysis was performed using SPSS version 27. Continuous variables were expressed as mean ± standard deviation and compared using Student's t-test. Categorical variables were compared using Chi-square analysis. Multivariate logistic regression was performed to identify independent predictors of prolonged mechanical ventilation. Statistical significance was established at $p < 0.05$.

Results

Table 1. Baseline Demographic and Clinical Characteristics (n = 200)

Variable	Overall Cohort
Age (years)	58.6 ± 15.2
Male sex	122 (61.0%)
Female sex	78 (39.0%)
BMI (kg/m²)	28.4 ± 5.6
APACHE II score	20.8 ± 6.5
SOFA score	7.8 ± 2.9
Sepsis	82 (41.0%)
COPD	46 (23.0%)
Diabetes mellitus	74 (37.0%)
Chronic kidney disease	29 (14.5%)
Respiratory muscle dysfunction	82 (41.0%)
ICU mortality	34 (17.0%)

Table 1 demonstrates that the study population consisted predominantly of older critically ill adults with substantial disease severity and multiple comorbid conditions.

Table 2. Comparison Between Patients With and Without Prolonged Mechanical Ventilation

Variable	PMV (>7 days) n=72	Non-PMV n=128	p-value
Age (years)	61.7 ± 14.8	56.9 ± 15.1	0.032
APACHE II score	24.2 ± 6.1	18.9 ± 5.4	<0.001
SOFA score	9.4 ± 2.8	6.7 ± 2.3	<0.001
MIP (cmH_2O)	-24.8 ± 6.2	-38.7 ± 8.4	<0.001
Sepsis (%)	43 (59.7%)	39 (30.5%)	<0.001
ICU stay (days)	18.6 ± 7.4	9.8 ± 4.1	<0.001
Tracheostomy (%)	26 (36.1%)	9 (7.0%)	<0.001

Patients with prolonged mechanical ventilation exhibited significantly weaker inspiratory muscle strength, greater illness severity, and increased resource utilization.

Table 3. Longitudinal Changes in Maximum Inspiratory Pressure

Time Point	Successful Weaning	Failed Weaning
Day 2	-33.2 ± 8.1	-22.6 ± 5.9
Day 5	-39.8 ± 8.6	-24.8 ± 6.4
Day 7	-46.1 ± 9.3	-26.2 ± 6.8
p-value	<0.001	0.08

Patients successfully liberated from mechanical ventilation demonstrated progressive improvement in inspiratory muscle strength, whereas failed-weaning patients showed minimal recovery.

Table 4. Multivariate Logistic Regression Predictors of Prolonged Mechanical Ventilation

Variable	Odds Ratio	95% CI	p-value
Respiratory muscle dysfunction	4.6	2.4–8.9	<0.001
SOFA score ≥8	3.1	1.6–6.0	<0.001
Sepsis	2.8	1.4–5.3	0.003
Age >65 years	2.1	1.1–4.1	0.027
COPD	1.9	1.0–3.8	0.048

Respiratory muscle dysfunction emerged as the strongest independent predictor of prolonged mechanical ventilation.

Discussion

The present prospective cohort study demonstrates that respiratory muscle dysfunction is highly prevalent among critically ill adults requiring invasive mechanical ventilation and represents a major determinant of prolonged ventilator dependence. Approximately 41% of patients exhibited significant inspiratory muscle weakness at ICU admission, while more than one-third experienced prolonged mechanical ventilation.

The findings support growing evidence that respiratory muscle weakness contributes substantially to weaning difficulties. Patients requiring prolonged ventilation demonstrated markedly lower baseline MIP values compared with those successfully liberated from ventilatory support. This observation is consistent with contemporary investigations reporting a strong association between inspiratory muscle strength and weaning success [15–17].

Several mechanisms may explain the observed relationship. Critical illness is characterized by systemic inflammation, oxidative stress, mitochondrial dysfunction, and enhanced proteolysis, all of which contribute to respiratory muscle wasting. Mechanical ventilation itself may exacerbate these processes through disuse atrophy and ventilator-induced diaphragm dysfunction [16–18].

The study further demonstrated that sepsis independently increased the risk of prolonged mechanical ventilation. Inflammatory mediators released during sepsis impair muscle contractility and accelerate catabolic pathways, thereby contributing to respiratory muscle weakness. Similar findings have been reported in previous studies evaluating diaphragm dysfunction among septic patients [17–19].

Longitudinal assessment revealed significant improvements in MIP among successfully weaned patients, whereas minimal recovery was observed among failed-weaning patients. These findings suggest that serial respiratory muscle monitoring may provide valuable prognostic information beyond baseline measurements alone.

The association between elevated SOFA scores and prolonged ventilation highlights the contribution of multiorgan dysfunction to respiratory recovery. Critically ill patients with severe organ failure often experience greater metabolic stress, prolonged immobilization, and increased exposure to sedatives, all of which may impair respiratory muscle performance.

Clinically, these findings support routine respiratory muscle assessment in mechanically ventilated patients. Early identification of inspiratory weakness may facilitate implementation of targeted interventions, including inspiratory muscle training, nutritional optimization, sedation minimization, and structured mobilization programs.

The strengths of this study include its prospective design, standardized respiratory muscle assessment, and comprehensive evaluation of clinical outcomes. However, the single-center setting may limit

generalizability, and multicenter investigations are warranted to validate these findings across diverse ICU populations.

Overall, respiratory muscle dysfunction should be recognized as a potentially modifiable contributor to prolonged mechanical ventilation and adverse ICU outcomes.

Conclusion

Respiratory muscle dysfunction is common among critically ill adults receiving invasive mechanical ventilation and is strongly associated with prolonged ventilator dependence. Reduced inspiratory muscle strength independently predicts prolonged mechanical ventilation, extended ICU stay, and increased resource utilization. Early respiratory muscle assessment may improve risk stratification and support targeted interventions aimed at accelerating successful weaning and improving critical care outcomes.

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