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## Review

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# Recent Advances in Pulmonary Rehabilitation for Patients in the Intensive Care Unit (ICU)

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## ABSTRACT

Pulmonary rehabilitation is important to prevent complications in critically ill patients in the intensive care unit (ICU) who are on mechanical ventilation. However, the effectiveness and adverse events related to pulmonary rehabilitation for patients in the ICU are largely unclear because of the diversity of diseases and various levels of severity in this situation. This review aims to clarify the evidence currently available for pulmonary rehabilitation in critically ill adult patients requiring mechanical ventilation, with a focus on positioning and early mobilization. Prone positioning (PP) does not seem to benefit adults with hypoxemia mechanically ventilated in the ICU. However, it improved survival among patient subgroups like those enrolled within 48 h of meeting the trial entry criteria, those treated with PP for  $\geq 16$  h per day, and those with severe hypoxemia at trial entry. PP using the protective lung ventilation strategy for patients with acute respiratory distress syndrome was associated with reduced mortality. On the other hand, PP may cause pressure sores and tracheal tube obstruction. The semi-recumbent position may prevent ventilator-associated pneumonia with no adverse events. Early mobilization (EM) enhances mobility status and muscle strength and increases days of life and out of the hospital for up to 6 months; it also shortens the duration of delirium. The main adverse events with EM are hemodynamic changes and desaturation. Therefore, medical staff should carry out pulmonary rehabilitation for patients in the ICU, given the effectiveness and adverse events. Future studies should identify diseases that would benefit from pulmonary rehabilitation and optimize the method.

**KEY WORDS:** Pulmonary rehabilitation; Intensive care unit (ICU); Positioning; Early mobilization

**ABBREVIATIONS:** ICU: Intensive Care Unit; PP: Prone Positioning; EM: Early Mobilization; RR: Risk Ratio; CI: Confidence Interval; ARDS: Acute Respiratory Distress Syndrome; VAP: Ventilator-associated pneumonia; OR: Odds Ratio; MRC: Medical Research Council; IL: Interleukin; COPD: Chronic Obstructive Pulmonary Disease.

## INTRODUCTION

All mechanically-ventilated critically ill patients in the intensive care unit (ICU) may experience difficulty coughing and excreting secretions. This in turn predisposes them to severe lung complications, decreases ventilator-free days, increases the length of ICU and hospital stay, and may consequently increase in mortality rates.<sup>1,2</sup> Pulmonary rehabilitation is a major step in the management of patients in the ICU, in order to prevent complications.<sup>3</sup> Physical therapy including pulmonary rehabilitation in the ICU has been shown to improve quality of

life (QoL), physical function, and respiratory muscle strength; increase ventilator-free days; and decrease the length of hospital and ICU stay.<sup>4</sup> However, limited information is available on the effectiveness of pulmonary rehabilitation and associated adverse events in patients who are in the ICU for different diseases or conditions of varying severity.<sup>5</sup> The objective of this review is to confirm the evidence currently available for pulmonary rehabilitation of critically ill adult patients on mechanical ventilation, with a focus on positioning and early mobilization (EM).

## POSITIONING

Positioning refers to the use of body position as a specific treatment technique. Positioning strategies used in the ICU include prone positioning (PP), semi-recumbent positioning, upright positioning, and lateral positioning.<sup>3</sup> This review describes PP and semi-recumbent positioning.

A recent systematic review of clinical trials showed that PP did not appear to be beneficial for adults with hypoxemia mechanically ventilated in the ICU, but certain subgroups may show improved survival with the use of this position: those enrolled within 48 h of meeting the entry criteria (risk ratio [RR], 0.75; 95% confidence interval [CI], 0.59-0.94), those placed in PP for  $\geq 16$  h per day (RR, 0.77; 95% CI, 0.61-0.99), and those with severe hypoxemia at trial entry (RR, 0.77; 95% CI, 0.65-0.92).<sup>6</sup> Additionally, subgroup analyses of short- and long-term mortality showed an RR of 0.79-0.85 for PP among patients with acute respiratory distress syndrome (ARDS), although the findings were not statistically significant. It has also been reported that compared with supine positioning, PP along with a protective lung ventilation strategy (tidal volume  $< 8$  mL/kg) significantly reduced mortality among patients with ARDS (RR, 0.74; 95% CI, 0.59-0.95).<sup>7</sup> PP is considered to improve survival rate by reducing the extent and duration of severe hypoxemia, propensity to ventilator-induced lung injury, or occurrence of nosocomial or ventilator-associated pneumonia (VAP).<sup>6</sup> Because recent studies showed that the incidence rate of pneumonia in patients with acute respiratory failure was not significantly different between the prone and supine position groups,<sup>2,6</sup> the main mechanism of improvement in mortality rates might not be prevention of pneumonia. However, PP may have some adverse effects, namely, pressure sores (RR, 1.37; 95% CI, 1.05-1.79) and tracheal tube obstruction (RR, 1.78; 95% CI, 1.22-2.60).<sup>6</sup>

The semi-recumbent position, in which the head of the bed is elevated by tilting, might prevent VAP. The results of a recent meta-analysis showed that the semi-recumbent position (30° to 60°) significantly reduced the risk of clinically suspected VAP compared to the 0° to 10° supine position (RR, 0.36; 95% CI, 0.25-0.50), although the number of studies with this finding and quality of evidence were low.<sup>8</sup> A randomized crossover study using radiolabeled gastric contents showed that reflux of contaminated gastric contents and aspiration were reduced in patients on mechanical ventilation placed in the semi-recumbent

position.<sup>9</sup> The results of this crossover study prove that to prevent clinically suspected VAP, patients should be placed in the semi-recumbent position. This position might not have adverse effects, although some effects such as pressure ulcers, thromboembolism, and heart rate or blood pressure effects have been noted.<sup>8</sup>

## EARLY MOBILIZATION

Mobilization strategies include passive and active turning and moving in bed, active-assisted and active training, cycling pedals in bed, sitting on the edge of the bed, standing, stamping, transferring from the bed, chair exercises, and walking.<sup>10</sup> EM is the application of physical therapy within the first 2-5 days of critical illness.<sup>11</sup> EM has received substantial attention because of the increasingly recognized sequelae of polyneuropathy and myopathy in critically ill patients.

A meta-analysis conducted in 2017 found that active mobilization in the ICU increased the probability of walking without assistance at hospital discharge (odds ratio [OR], 2.13; 95% CI, 1.19-3.83), greater muscle strength at ICU discharge as measured using the Medical Research Council (MRC) Sum Score (mean difference, 8.62 points; 95% CI, 1.39-15.86), and more days of life and out of hospital for 6 months (mean difference, 9.69; 95% CI, 1.7-17.66), although no impact on short- or long-term mortality was evident.<sup>12</sup> This meta-analysis also showed that early low-dose rehabilitation defined as commencing within 3 days of admission for less than 30 min per day favored days alive and out of the hospital for 6 months. Further, the results of randomized controlled trials showed that EM led to a shortened duration of delirium.<sup>13,14</sup> The mechanisms underlying the effects of EM have been examined in a few studies.<sup>15,16</sup> For example, it has been reported that the average ratio of interleukin-6 (IL-6) to IL-10 improves after low levels of passive physical activity in patients with prolonged critical illness.<sup>15</sup> However, we must take into account the peculiarities of the patient population and the time to the first mobilization. In patients with stroke (infarct or intracerebral hemorrhage), very early mobilization intervention started at a median of 18.5 h after onset and was associated with a reduction in favorable outcomes 3 months after stroke.<sup>17</sup> Similarly, in patients with acute exacerbation of chronic obstructive pulmonary disease (COPD), EM started within 48 h of hospital admission was associated with an increase in mortality at 1 year (OR, 1.74; 95% CI, 1.05-2.88).<sup>18</sup> The main adverse events during active mobilization include hemodynamic changes (pooled incidences per 1,000 mobilization/rehabilitation sessions, 3.8; 95% CI, 1.3-11.4) and desaturation defined as oxygen saturation of 80-90% (pooled incidences per 1,000 mobilization/rehabilitation sessions, 1.9; 95% CI, 0.9-4.3).<sup>19</sup>

## CONCLUSION

Our review presents an overview of positioning and EM examined in high-evidence studies. Positioning and EM in critically ill

Table 1: Effectiveness of and Adverse Events Related to Pulmonary Rehabilitation for Patients in the ICU.		
Pulmonary rehabilitation	Effectiveness	Adverse events
Prone positioning	Reduced mortality  Patients with acute hypoxemia: those enrolled within 48 h of meeting entry criteria; those treated with PP for $\geq 16$ h per day; and participants with more severe hypoxemia at trial entry.  Patients with ARDS: using protective lung ventilation strategy (tidal volume $< 8$ mL/kg)	Pressure sores  Tracheal tube obstruction
Semi-recumbent position	Prevented VAP	No adverse events
Early mobilization	Improved mobility status and muscle strength and increased days alive and out of the hospital for up to 6 months  Shortened the duration of delirium	Hemodynamic changes  Desaturation

ICU: Intensive care unit; PP: Prone positioning; ARDS: Acute respiratory distress syndrome; VAP: Ventilator-associated pneumonia.

adult patients have both positive and negative effects. Similarly, certain patient populations may or may not benefit from pulmonary rehabilitation in the ICU, although research on this topic is not extensive. Thus, medical staff should carry out pulmonary rehabilitation for patients in the ICU, given the effectiveness and adverse events. Studies should be conducted to identify the conditions that benefit from these treatment strategies and the optimal parameters of the method (e.g., time of initiation, intensity, frequency, and duration) (Table 1).

#### CONFLICTS OF INTEREST

All authors declare that they have no competing interests.

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