

## ***Early versus Delayed Pulmonary Rehabilitation and Short-Term ICU Outcomes in Mechanically Ventilated Patients***

Perbandingan Rehabilitasi Paru Dini dan Lambat terhadap Luaran Jangka Pendek di ICU pada Pasien dengan Ventilasi Mekanik

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### **Abstract**

*Mechanical ventilation is a life-saving intervention in the intensive care unit (ICU), yet it is commonly associated with prolonged immobilization, muscle weakness, and delayed recovery. Pulmonary rehabilitation (PR) has been applied to reduce these complications, although the optimal timing of its initiation in mechanically ventilated patients remains unclear. This study aimed to compare short-term ICU outcomes, including duration of mechanical ventilation and ICU length of stay, between patients receiving early and delayed PR. A retrospective cohort study was conducted using medical records of adult ICU patients who received pulmonary rehabilitation during mechanical ventilation from January to December 2024. Patients were grouped into early PR ( $\leq 48$  hours after ICU admission) and delayed PR ( $> 48$  hours). Baseline characteristics assessed included age, sex, primary diagnosis, and SOFA score. In total, 110 patients were included, with 27 in the early PR group and 83 in the delayed PR group. Baseline characteristics were generally comparable between groups. The early PR group experienced significantly shorter duration of mechanical ventilation ( $p < 0.001$ ) and reduced ICU length of stay ( $p < 0.001$ ) compared to the delayed PR group. These findings indicate a potential association between early pulmonary rehabilitation and short-term ICU outcomes.*

**Keywords:** *pulmonary rehabilitation; early rehabilitation; mechanical ventilation; intensive care unit; length of stay*

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**Introduction**

Mechanical ventilation is a life-saving intervention commonly used in the intensive care unit (ICU) for patients with acute respiratory failure caused by conditions such as pneumonia, acute respiratory distress syndrome (ARDS), or neurological disorders. Although mechanical ventilation is essential for survival, prolonged use is frequently associated with adverse effects, including respiratory and peripheral muscle weakness, reduced functional capacity, prolonged immobilization, delayed recovery, and psychological sequelae.<sup>1,2</sup>

Pulmonary rehabilitation (PR) has been increasingly applied as a supportive intervention to reduce the negative effects of prolonged mechanical ventilation. Pulmonary rehabilitation is a comprehensive intervention that includes respiratory muscle training, airway clearance techniques, physical mobilization, education, and psychosocial support, to improve respiratory function, muscle strength, and overall functional capacity.<sup>3</sup>

Early pulmonary rehabilitation has emerged as an important strategy to mitigate the adverse consequences of prolonged mechanical ventilation in critically ill patients. Previous studies have suggested that rehabilitation initiated during the early phase of ICU admission may improve recovery outcomes, reduce the duration of mechanical ventilation, and shorten ICU length of stay.<sup>4</sup> However, the optimal timing for initiating pulmonary rehabilitation remains controversial. Rehabilitation programs have been initiated at different time points across studies, including within 24–48 hours of admission, whereas other studies have used broader thresholds.<sup>4,5</sup> Consequently, the operational definition of early rehabilitation remains heterogeneous across the literature, limiting direct comparisons between studies and the generalizability of existing findings.

Therefore, this study aimed to evaluate the association between pulmonary rehabilitation initiated within 48 hours of ICU admission and short-term ICU outcomes, specifically the duration of mechanical ventilation and ICU length of stay, compared with rehabilitation initiated later during the ICU stay.

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## Methods

This study was a retrospective cohort study. Data was collected from the medical records of patients admitted to the Intensive Care Unit (ICU) at Saiful Anwar General Hospital in Malang between January and December 2024. Ethical approval was obtained from the Ethics Committee of Saiful Anwar General Hospital (Ethics Approval No: 400/249/K.3/102.7/2025). Inclusion criteria included adult patients ( $\geq 17$  years) who received pulmonary rehabilitation (PR) therapy during mechanical ventilation. Patients were excluded from analysis if their medical records were incomplete.

Patients were categorized into two groups based on the timing of pulmonary rehabilitation (PR) initiation: 1. early PR group: initiation of pulmonary rehabilitation within  $\leq 48$  hours of ICU admission; 2. delayed PR group: initiation of pulmonary rehabilitation more than 48 hours after ICU admission. The timing of PR initiation was determined based on documentation in the medical records. Pulmonary rehabilitation (PR) was provided as part of routine ICU care and included respiratory exercises, airway clearance techniques, positioning, range of motion exercises, and gradual mobilization according to patient tolerance. The flow diagram of patient selection, eligibility assessment, and allocation into early and delayed pulmonary rehabilitation groups is presented in Figure 1.

Baseline characteristics collected included age, sex, primary diagnosis, and severity of illness at ICU admission, assessed using the sequential organ failure assessment (SOFA) score. Primary diagnosis was categorized as respiratory-dominant or non-respiratory-dominant based on the main indication for ICU admission and mechanical ventilation. The primary outcomes were duration of mechanical ventilation and ICU length of stay (LOS).

Data was analyzed using IBM SPSS Statistics. Descriptive statistics were used to summarize demographic and clinical characteristics. Comparisons between the early and delayed PR groups for primary outcomes (duration of mechanical ventilation and ICU length of stay) were performed using the Mann–Whitney U test due to non-normal data distribution. Multivariable analysis was not performed due to the retrospective design and exploratory nature of the study. A  $p$ -value  $\leq 0.05$  was considered statistically significant.

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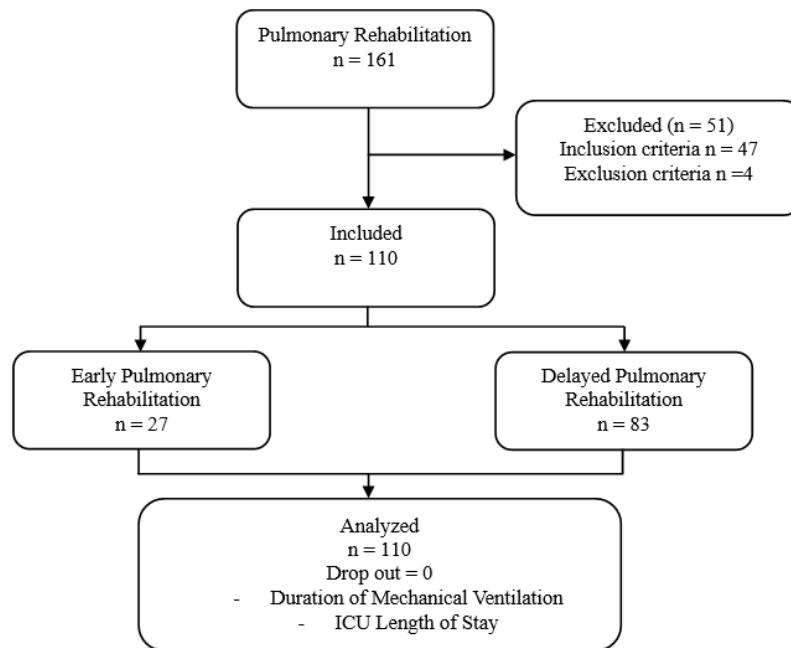


Figure 1 Patient Cohort Diagram

## Results

A total of 110 patients met the inclusion criteria and were included in the analysis. Of these, 27 patients received early pulmonary rehabilitation ( $\leq 48$  hours), while 83 patients received delayed pulmonary rehabilitation ( $> 48$  hours). Baseline demographic and clinical characteristics are shown in Table 1.

The early and delayed pulmonary rehabilitation groups showed broadly comparable baseline characteristics. Age distribution and illness severity at ICU admission were similar between groups, as reflected by comparable SOFA scores. Both groups were predominantly male. Delayed rehabilitation was more frequently administered across both respiratory and non-respiratory dominant diagnoses.

Following the analysis of baseline characteristics, the comparison of clinical outcomes among the groups was conducted. The evaluated parameters included the duration of mechanical ventilation and ICU length of stay (LOS) as summarized in Table 2.

Patients in the early pulmonary rehabilitation group demonstrated shorter duration of mechanical ventilation, with a median of 8 days (IQR 6–16). Similarly, ICU length of stay was shorter among patients receiving early rehabilitation, with a median of 11 days (IQR 7–19). Both differences were statistically significant ( $p < 0.001$ ).

To further explore whether the association between pulmonary rehabilitation timing and clinical outcomes differed according to the primary diagnosis category, subgroup analyses were

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performed for respiratory-dominant and non-respiratory-dominant patients. The results are summarized in Table 3.

Subgroup analyses according to dominant diagnosis demonstrated that early pulmonary rehabilitation was associated with significantly shorter duration of mechanical ventilation and ICU length of stay in both respiratory-dominant ( $p = 0.002$  and  $p = 0.001$ , respectively) and non-respiratory-dominant patients ( $p = 0.045$  and  $p = 0.006$ , respectively).

**Table 1 Baseline Demographic and Clinical Characteristics of Patients**

| Variable                 | Early PR   | Delayed PR | <i>p</i>           |
|--------------------------|------------|------------|--------------------|
| Sample size (n)          | 27         | 83         |                    |
| Age, median (IQR)        | 55 (48-65) | 59 (41-67) | 0.994 <sup>1</sup> |
| Gender, n (%)            |            |            | 0.421 <sup>2</sup> |
| Male                     | 18 (66.7)  | 46 (55.4)  |                    |
| Female                   | 9 (33.3)   | 37 (44.6)  |                    |
| Primary Diagnosis, n (%) |            |            | 0.118 <sup>3</sup> |
| Respiratory dominant     | 24 (88.9)  | 61 (73.5)  |                    |
| Non-respiratory dominant | 3 (11.1)   | 22 (26.5)  |                    |
| SOFA Score, median (IQR) | 7 (6-9)    | 7 (6-9)    | 0.992 <sup>1</sup> |
| Discharge Status, n (%)  |            |            | 0.006 <sup>3</sup> |
| Alive                    | 5 (18.5)   | 40 (48.2)  |                    |
| Deceased                 | 22 (81.5)  | 43 (51.8)  |                    |

For continuous variables, the median (interquartile range) is given. For binary ones absolute and relative frequencies are shown. IQR - Interquartile Range; PR - Pulmonary Rehabilitation; SOFA - Sequential Organ Failure Assessment. Statistical tests: <sup>1</sup>Mann-Whitney U test <sup>2</sup>Pearson Chi-square test <sup>3</sup>Fisher's Exact test

**Table 2 Comparison of Clinical Outcomes**

|                                     | Early PR  | Delayed PR | <i>p</i> |
|-------------------------------------|-----------|------------|----------|
| Duration of MV (days), median (IQR) | 8 (6-16)  | 22 (13-32) | < 0.001  |
| ICU LOS (days), median (IQR)        | 11 (7-19) | 25 (16-34) | < 0.001  |

ICU LOS - Intensive Care Unit Length of Stay; IQR - Interquartile Range; MV - Mechanical Ventilation; PR - Pulmonary Rehabilitation.

**Table 3 Subgroup Analysis According to Diagnosis**

| Outcome                             | Early PR        | Delayed PR       | <i>p</i> |
|-------------------------------------|-----------------|------------------|----------|
| Respiratory Dominant                |                 |                  |          |
| Duration of MV (days), median (IQR) | 10.0 (6.5-17.5) | 22.0 (13.0-32.0) | 0.002    |
| ICU LOS (days), median (IQR)        | 11.5 (7.0-23.0) | 25.0 (18.0-33.0) | 0.001    |
| Non-Respiratory Dominant            |                 |                  |          |
| Duration of MV (days), median (IQR) | 6.0 (5.0-10.0)  | 24.5 (15.0-32.0) | 0.045    |
| ICU LOS (days), median (IQR)        | 6.0 (5.0-10.0)  | 27.5 (15.0-35.0) | 0.006    |

ICU LOS - Intensive Care Unit Length of Stay; IQR - Interquartile Range; MV - Mechanical Ventilation; PR - Pulmonary Rehabilitation.

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## Discussion

In this study, earlier initiation of pulmonary rehabilitation (PR) within 48 hours of ICU admission was associated with shorter duration of mechanical ventilation and ICU length of stay compared with delayed initiation. Similar associations were observed across respiratory-dominant and non-respiratory-dominant diagnostic subgroups. Baseline demographic characteristics and illness severity at ICU admission were largely comparable between groups, as reflected by similar age distribution, sex distribution, primary diagnosis category, and SOFA scores.

These findings are consistent with previous studies demonstrating that rehabilitation initiated during the very early phase of ICU care is associated with clinically meaningful benefits. Although the optimal timing for initiating pulmonary rehabilitation remains controversial, increasing evidence suggests that rehabilitation commenced within the first 48 hours of ICU admission is safe, feasible, and associated with improved clinical outcomes.<sup>6,7</sup> A nationwide cohort study reported that rehabilitation initiated within the first 48 hours was associated with a significantly shorter hospital length of stay (−9.8 days;  $p < 0.001$ ).<sup>8</sup> Our results are also consistent with earlier studies and systematic reviews demonstrating that rehabilitation initiated during the early phase of critical illness may reduce the duration of mechanical ventilation and ICU length of stay. While some previous investigations have used broader definitions of early rehabilitation, the overall direction of evidence suggests that earlier initiation of rehabilitation is associated with more favorable recovery outcomes.<sup>9,10</sup> The shorter duration of mechanical ventilation and ICU stay observed in our study further supports the potential benefits of implementing pulmonary rehabilitation at the earliest feasible stage of critical illness. Given the ongoing uncertainty regarding the optimal timing of pulmonary rehabilitation, the 48-hour threshold was selected to represent early rehabilitation.

Overall, recent evidence indicates that early PR in mechanically ventilated ICU patients is associated with shorter duration of mechanical ventilation, reduced ICU-acquired weakness, and shorter ICU and hospital length of stay, while effects on mortality remain uncertain.<sup>11</sup> Early PR, including respiratory-targeted interventions such as inspiratory muscle training, may be particularly beneficial in patients with severe respiratory disease, although practical barriers to consistent delivery in routine ICU practice persist.<sup>12,13</sup>

In the present study, similar associations were observed across both respiratory-dominant and non-respiratory-dominant diagnostic subgroups. The consistency of findings across diagnostic subgroups supports the robustness of the observed association between earlier initiation of pulmonary rehabilitation and improved short-term ICU outcomes. This suggests that

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the potential benefits of early pulmonary rehabilitation may extend beyond specific diagnostic categories among mechanically ventilated ICU patients.

The association between earlier PR and reduced ventilator dependence and ICU stay is biologically plausible and aligns with established pathophysiological mechanisms of critical illness. Mechanical ventilation and immobilization induce rapid deterioration of respiratory and peripheral muscles early during ICU admission, contributing to diaphragmatic atrophy, ICU-acquired weakness, and delayed weaning. Longitudinal ultrasonographic studies have demonstrated that diaphragmatic thickness decreases within the first 48 hours after the initiation of mechanical ventilation and continues to decline over subsequent days, and early diaphragmatic thinning has been associated with prolonged ventilation and adverse ICU outcomes.<sup>14,15</sup> These early structural changes provide a mechanistic framework through which timely PR may plausibly contribute to preserved respiratory muscle function and earlier readiness for liberation from mechanical ventilation.<sup>16</sup>

In this context, early PR and mobilization target these mechanisms by preserving respiratory and limb muscle function, enhancing secretion clearance, and improving regional ventilation and ventilation–perfusion matching.<sup>17</sup> Components such as breathing exercises, inspiratory muscle training, airway clearance, positioning, and graded mobilization act synergistically: inspiratory muscle training limits diaphragmatic disuse, while mobilization attenuates systemic neuromuscular deterioration related to bed rest. Collectively, these effects may support earlier weaning, reduce ventilator duration, and shorten ICU length of stay.<sup>18,19,20</sup>

Several considerations warrant attention. Definitions of “early” rehabilitation vary across studies, commonly ranging from within 48 to 72 hours, and substantial heterogeneity exists in intervention components, frequency, and intensity, which may influence observed outcomes. Recent meta-analytic evidence suggests that early mobilization may reduce ICU length of stay and ventilator duration, although heterogeneity in protocols and safety reporting highlights the need for careful implementation. Moreover, effective early rehabilitation requires clear hemodynamic stability criteria, appropriate sedation management, and trained multidisciplinary teams, as structured evaluation and collaborative teamwork improve safety and consistency in protocolized ICU rehabilitation programs.<sup>21,22</sup> Accordingly, standardized protocols incorporating explicit safety thresholds and defined team roles are essential to optimize early PR implementation.

The clinical implications of these findings are practice oriented. Early implementation of a structured pulmonary rehabilitation (PR) protocol may reduce ventilator dependence and ICU length of stay, particularly in units with adequate resources and multidisciplinary expertise.

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Implementation should consider hemodynamic stability, sedation status, and mobilization safety criteria, supported by clear protocols and team training.<sup>23</sup> Pulmonary rehabilitation may therefore be integrated into routine ICU care for mechanically ventilated patients. However, as current evidence is largely observational, prospective studies with standardized protocols are needed to confirm effectiveness, identify key intervention components, determine optimal timing, and evaluate long-term functional and quality-of-life outcomes.<sup>24,25</sup>

The present findings were derived from routinely collected ICU medical records, with objectively measured clinical outcomes and broadly comparable baseline illness severity between groups, supporting the clinical interpretability of the observed associations. The use of a predefined operational threshold for early pulmonary rehabilitation ( $\leq 48$  hours) also enabled consistent group classification within routine clinical practice.

However, this study has several limitations. First, the retrospective design precludes causal inference. Second, analyses were based on unadjusted comparisons, and residual confounding from unmeasured variables cannot be entirely excluded despite broadly comparable baseline characteristics. In addition, pulmonary rehabilitation was delivered as part of routine care without a fully standardized protocol, which may have introduced variability in intervention delivery and exposure. The single-center setting may limit generalizability, and outcomes were restricted to short-term ICU measures, as long-term functional and post-discharge outcomes were not assessed. Furthermore, subgroup analyses were exploratory and included relatively small numbers of patients in some categories, particularly within the non-respiratory early rehabilitation subgroup. Future prospective and multicenter studies with standardized pulmonary rehabilitation protocols are needed to confirm causality and to evaluate long-term functional outcomes, generalizability, and cost-effectiveness in mechanically ventilated ICU patients.

## Conclusion

Early initiation of pulmonary rehabilitation within 48 hours of ICU admission was associated with shorter duration of mechanical ventilation and ICU length of stay in mechanically ventilated patients. Similar associations were observed across respiratory-dominant and non-respiratory-dominant diagnostic subgroups. These findings indicate that early pulmonary rehabilitation may be a beneficial component of ICU care when clinically feasible.

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