The Effects of Early Physiotherapy Intervention on Patients in Intensive Care Unit: A Systematic Review

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Abstract:

Introduction: Patients with a prolonged ICU stay may have several complications such as physical deconditioning and general body weakness which affect their overall quality of life. Physiotherapy intervention upon ICU admission may prevent such complications. Nevertheless, there is no solid conclusion on the benefits of early physiotherapy intervention on the occurrence of intensive care unit-acquired weakness (ICU-AW) syndrome and physical performance. Hence, this study is aimed to systemically synthesize the evidence of early physiotherapy intervention in decreasing the occurrence of (ICU-AW) syndrome and improving physical performance in ICU patients. **Methodology:** A systematic literature search was conducted in PubMed, Scopus, The Cochrane Library, and ScienceDirect databases. All relevant articles published in English between 2010 to 2022 were selected. The risk of bias assessment of the selected articles was performed using The McMaster Quantitative Critical Appraisal Tool (MQCAT). A narrative synthesis was employed to describe the findings. **Results:** After a thorough screening, four articles met the eligible criteria and were included in this systematic review for further analysis. The methodological quality of the selected articles was found to be satisfactory. The review revealed that positive outcomes of early physiotherapy intervention on ICU-AW were reported in three studies. Yet only one study reported positive outcome of early physiotherapy intervention on physical function outcome. **Conclusion:** This systematic review provides insight on the effects of early physiotherapy intervention on the incidence of ICU-AW as well as physical function that will inform the healthcare practitioners and future researchers.

Keywords: Early physiotherapy intervention, intensive care unit, intensive care unit-acquired weakness, physical performance

Introduction:

Intensive care unit (ICU) is a specialised comprehensive care unit for patients with any life-threatening illnesses which provide 24 hours of advance care and monitoring (Marshall et al., 2017). The length of ICU stays for each patient vary from a few days to a number of weeks and months depending on the severity of the illnesses (Toptas et al., 2018; Hunter et al., 2020; Vekaria et al., 2021; Zeleke et al., 2022). Lipshutz and Gropper (2013) stated that patients with serious medical conditions such as pulmonary edema, atelectasis, vasomotor instability, and contagious diseases require a longer period of ICU stay and bed rest.

While treatments delivered to critically ill patients in the ICU improve the survival outcomes, prolonged stay in the ICU leads to physical deconditioning and adversely affect the health status

(Hunter et al., 2020). Statistically, 40% of the ICU patients developed a neuromuscular dysfunction syndrome known as intensive care unit acquired weakness (ICU-AW) upon ICU discharge (Appleton et al., 2015). ICU-AW is a clinical diagnosis of muscle loss and weakness due to immobilization and it may exacerbate with catabolic condition associated with critical illness (Kramer, 2017). Several patients who were discharged from ICU have experienced persistent muscles weakness even after having fully recovered from the illness (Lad et al. 2020). Such complication may result in functional dependency.

Early mobilization upon ICU admission is crucial to mitigate the sequalae of bed rest (Castro-Avila, 2015; Sommers et al., 2015). According to a survey conducted by Cakmak et al. (2018), the most common treatments delivered by physiotherapists in the ICU include positioning, active range of motion (ROM) exercises, breathing exercise, passive range of motion (ROM) exercises, percussion, mobilization, vibration, and postural drainage, with the percentages of implementation were 90.8%, 90.8%, 89.2%, 87.7%, 87.7%, 86.2%, 86.2% and 86.2% respectively. Other than that, adjunct treatment such as neuromuscular electrical stimulation and cycle ergometer have been recommended for ICU patients particularly upon discharge from the critical care unit (Hashem et al., 2016).

Sommers and colleagues (2015) highlighted that early mobilization and rehabilitation for critically ill patients is essential to minimize the occurrence of ICU-AW syndrome as well as to improve patient's physical performance. Early mobilization which comprises of different types of physical exercises should be executed as early as second day of admission in the ICU (Castro-Avila, 2015). Several studies had been conducted to identify the effects of early mobilization and rehabilitation on ICU patients. However, the results are conflicting and inconsistent. Thus, this study is aimed to synthesize the published evidence on the effects of early physiotherapy intervention on patients in the ICU specifically on the occurrence of ICU-AW syndrome and also physical performance outcomes. The findings of this review may have significant impact on the clinical practice.

Methodology:

A Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) was used as a guideline in reporting the review. To preserve the methodological transparency, the protocol of this review is prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO) with the identification number of CRD42022370996. Institutional review board approval was granted prior to the initiation of the review.

Search Strategy

Searching and compiling the relevant studies were conducted through electronic databases which are PubMed, Scopus, The Cochrane Library and ScienceDirect. Boolean operators like 'AND', 'OR', or 'NOT' were employed. The searching procedure involved keywords that were related to the topic. The keywords include 'early physiotherapy mobilization', 'intensive care unit', 'intensive care unit-acquired weakness', 'physical performance', and 'ICU discharge'.

Screening and Study Selection

All retrieved articles from the databases search were collated in an electronic file. All titles of identified articles were screened preliminary by one researcher to remove any redundancies or duplicates and the remaining articles were recorded. Then, the abstracts of the articles related to the research questions and objectives of this systematic review were assessed. The remaining articles were then filtered based on the inclusion and exclusion criteria as shown in Table 1. The inclusion and exclusion criteria were defined based on PICOS framework (Table 2). The PICOS framework is convenient in addressing the criteria of the relevant study such as design of the study, population of the study, mode of treatment, outcomes of the study, and the comparison group, if any (Jain & Sharma, 2016). The excluded studies were recorded with specific reasons. The final number of studies remaining were recorded.

Methodological Quality Assessment

McMaster Quantitative Critical Appraisal Tool (MQCAT) was used to assess the methodological quality of the studies included (Law et al., 1998). This tool is relevant to all quantitative study designs. This tool examined eight main components which are study purpose, study background, study design, sample size justification, reliability and validity of outcome measures, description, contamination and co-intervention regarding intervention, statistical significance and appropriate analysis methods, dropout reporting and conclusion. The total score of the MQCAT was 14, where better methodology quality is indicated by the higher score.

Table 1: Inclusion and Exclusion Criteria

Inclusion Criteria
Studies which involve patients aged more than 18 years old
Studies include patients with any intensive care unit (ICU) admission diagnoses
Studies include patients who receive physiotherapy intervention since the first week of intensive care unit (ICU) admission
Studies include outcomes on the effects of early physiotherapy intervention on ICU-AW and physical performance
Studies published in between 2010 to 2022
Studies written in English language
Studies include any experimental study design
Exclusion Criteria
Studies include patients who receive physiotherapy intervention after intensive care unit (ICU) discharge

Table 2: PICOS Table

Population	Adult patients (>18 years old) who were admitted to the ICU more than 24 hours with any admission diagnoses
Intervention	Any early physiotherapy intervention commenced at the first week of ICU stay
Control	Receive only usual or standard care during ICU stay
Outcome	Any outcome on ICU-AW and physical performance
Study Design	Any experimental study design

Data Analysis

Information on the study design, study population, outcome measure, interventions and results were extracted by one researcher and then was crosschecked by another researcher. All extracted data were portrayed in a table. As the meta-analysis is not possible to be conducted due to heterogeneity in the intervention protocols and outcome measures used in the individuals articles, outcomes on the effects of early mobilization were synthesised narratively.

Results:

Study Selection

During the study selection, EndNote was used to collect and classify the articles. A total of 527 articles were retrieved from PubMed (n=66), ScienceDirect (n=388), The Cochrane Library (n=29) and Scopus (n=44). A total of 139 duplicate studies were identified and removed, which led to 388 articles screened by their titles and abstracts. After screening the titles and abstracts, 341 articles were excluded as they were totally not related to this study. The remaining 47 articles were then evaluated according to the pre-determined inclusion and exclusion criteria. Finally, 43 articles were excluded due to specific reasons as outlined in Figure 1. Finally, four articles were included in this systematic review.

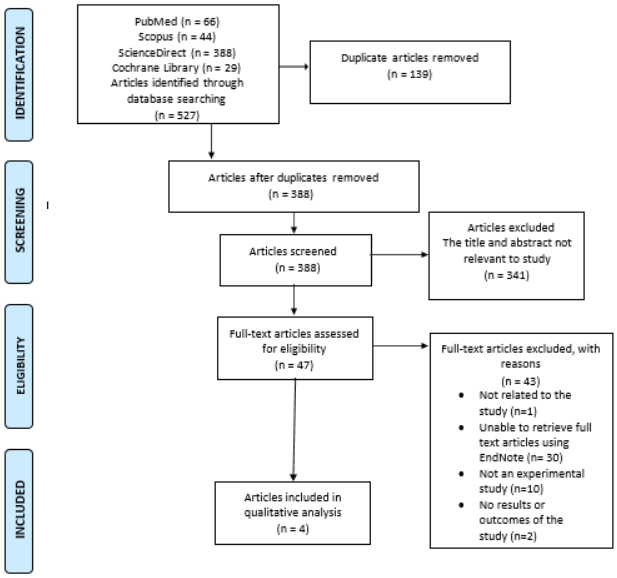

Figure 1 PRISMA flow diagram for each stage of the study (Moher et al., 2009)

Study Characteristics

There are four articles included in this study where three of them were randomised controlled trials and one article was a historical control study. The number of participants recruited in the included articles is ranged from 38 to 115 participants with various medical illness, while the mean age range is from 44 to 70 years old. All included articles mentioned that the participants began the physiotherapy rehabilitation or intervention in the early days of ICU admission. Kayambu et al. (2015) conducted the intervention within 48 hours of diagnosis in the ICU, while Machado et al. (2017) began the mobilization on the first day as patient was cooperative and responsive. Nakano et al. (2021) started the rehabilitation on the first day after ICU admission while Eggmann et al. (2018) only mention the term 'early' without mentioning the exact time. Detailed descriptions of the studies included author/year, study design, number of participants, mean age of participants, outcome measures, interventions and results of the studies are outlined in Table 3.

Table 3: Characteristics of Included Studies

Author/Year	Study design Risk of Bias	Participants Mean Age Inclusion Criteria Study Setting	Outcome measure(s) used for ICU-AW and physical performance/function	Interventions	Effects of early physiotherapy intervention on ICU-AW and physical performance/function
Kayambu et al. (2015)	Prospective double blinded RCT	n = 50 *Mean Age* • IG: 62.5 • CG: 65.5 *Inclusion Criteria* 1) ≥18-year-old 2) Remained mechanically ventilated ≥48 hours 3) Diagnosed with sepsis, severe sepsis, and septic shock *Study Setting* General ICU at the Royal Brisbane and Women's Hospital, Brisbane, Queensland, Australia	*ICU-AW*: 1) Medical Research Council Muscle Score (MRC) *Physical function*: 1) Acute Care Index of Function (ACIF) 2) Self-reported health related QoL 3) Physical functional ICU test (PFIT) *Remark*: All objective measurements for ICU-AW and physical function were taken once upon ICU discharge while subjective measurements were at 6 months of post-discharge from hospital	*IG (n = 26)* Early targeted physical rehabilitation program in the ICU (The intervention begun within 48 hours of diagnosis in the ICU) *CG (n = 24)* Standard ICU care (The first session was not determined) *Rehabilitation program (both groups)*: Ambulation, standing balance exercises, sitting balance exercises, marching on the spot, sit to stand, sitting out of bed, sitting up in bed, active resistive exercise, active ROM, passive ROM)	*ICU-AW:* MRC score for IG was high as compared to CG, indicating the occurrence of ICU-AW was low, but the difference was not significant between the IG and CG ($p>0.05$) *Physical function:* 1) Self-reported QoL: There were significant improvements in the intervention group in the domains of physical function ($p<0.05$)
Machado et al. (2017)	RCT	n = 38 *Mean Age* • IG: 45.13 ± 18.91 • CG: 44.64 ± 19.23	*ICU-AW:* 1) Medical Research Council (MRC) scale	*IG (n = 22)* Conventional physical therapy and passive exercise on leg cycle ergometer *CG (n = 16)*	*ICU-AW:* Within group analysis: Peripheral muscle strength had significantly increase at post intervention in both groups ($p<0.01$)

		Inclusion Criteria 1) ≥18 years 2) On MV 3) Maintained at light level of sedation 4) Hemodynamically stable *Study Setting* ICU of the Santa Maria University Hospital of the Federal University of Santa Maria, Brazil		Conventional physical therapy only *Remark*: First physiotherapy session of conventional physical therapy started as early as 24-48 hours	Between group analysis: IG had significantly greater increase in the MRC scale scores than the CG ($p<0.01$)
Eggmann et al. (2018)	Single-center, parallel, two-arm, assessor-blinded RCT	n = 115 *Mean Age* • IG: 65 ± 15 • CG: 63 ± 15 *Inclusion Criteria* 1) Adult (≥18 years) 2) Expected to stay on MV for at least 72 hours 3) Independent before onset of critical illness *Study Setting* ICU of the Department of Intensive Care Medicine at the Inselspital, Bern University Hospital, Switzerland	*ICU-AW:* 1) Medical Research Council (MRC) *Physical performance:* 1) 6-Minute Walking Distance (6MWD) 2) Functional Independence Measure (FIM) 3) Timed 'Up & Go' (TUG) test 4) Short Form 36 (SF-36) *Remark*: All measurements for ICU-AW and physical performance were taken once, either at ICU discharge or hospital discharge	*IG (n = 58)* Early, progressive ERT program (motor-assisted bed-cycle, UL and LL exercises with weights or manual resistance) combined with early mobilisation. *CG (n = 57)* Early mobilisation, respiratory therapy and passive or active exercises *Early mobilisation*: On-bed exercises, progressively sitting on bedside, sitting on chair, standing and walking. *Remark*: First physiotherapy session started within 48 hours	*ICU-AW:* The incidence of ICU-AW at post intervention in IG was low 3% as compared to CG but the difference was statistically insignificant ($p>0.05$) *Physical performance:* Significant difference for physical performance parameters were not found ($p>0.05$)

Nakano et al. (2021)	Single-center, historical control study	n = 101 *Mean Age* • IG: 70.9 • CG: 70.9 *Inclusion Criteria* 1) Admitted to ICU *Study Setting* Hitachi General Hospital	*ICU-AW:* 1) Medical Research Council (MRC) *Physical performance:* 1) ICU Mobility Scale (IMS) 2) Grip strength 3) Functional status scores for ICU (FSS-ICU) 4) Barthel Index *Remark*: All measurements for ICU-AW and physical performance were taken once at ICU discharge	*IG (n = 56)* Protocol-based intervention, Intensive goal-directed rehabilitation with electrical muscle stimulation and nutrition (IGREEN) protocol. *CG (n = 45)* Standard care without NMES *Remark*: First rehabilitation session started on day 1 after entering the ICU	*ICU-AW and physical performance:* Significant difference for ICU-AW and physical performance were not found for all outcomes (p>0.05)

Note. RCT= Randomized Controlled Trial; IG= Intervention Group; CG= Control Group; MV= Mechanical Ventilation; QoL= Quality of Life; ROM= Range of Motion; ERT= Endurance and Resistance Training; UL= Upper Limb; LL= Lower Limb; NMES= Neuromuscular Electrical Stimulation; ICU= Intensive Care Unit; FMV= Femoral Muscle Volume

Methodological Quality of Included Studies

The methodological quality assessment was evaluated and the overview of the scores is displayed as in Table 4. The total score for the included studies is ranged from 10 -12 out of 14 which indicated a promising methodological quality. All of the studies did not report contamination and co-intervention regarding intervention, and almost all of the studies (n = 3) did not report the clinical importance of the results.

Table 4: Quality Assessment for Included Studies

Authors	Criteria																
	1	2	3	4a	4b	4c	5a	5b	6a	6b	6c	7a	7b	7c	7d	8	TS
Kayambu et al. (2015)	Y	Y	RCT	50	Y	Y	Y	Y	Y	N	N	Y	Y	N	Y	Y	11
Machado et al. (2017)	Y	Y	RCT	38	Y	N	Y	Y	Y	N	N	Y	Y	N	Y	Y	10
Eggmann et al. (2018)	Y	Y	RCT	115	Y	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	12
Nakano et al. (2021)	Y	Y	HCS	101	Y	Y	Y	Y	Y	N	N	Y	Y	N	Y	Y	11

Abbreviations: N, no/not addressed/not applicable (0 point); Y, yes (1 point); RCT, randomized control trial; HCS, historical control study; TS, total score

1, study purpose stated clearly; 2, relevant background literature reviewed; 3, research design appropriate; 4a, sample size; 4b, sample described in detail; 4c, sample size justified; 5a, outcome measures reliable; 5b, outcome measures valid; 6a, intervention/exposure described in detail; 6b, contamination avoided; 6c, co-intervention avoided; 7a, results were reported in terms of statistical significance; 7b, appropriate analysis methods; 7c, clinical importance; 7d, dropouts avoided; 8, appropriate conclusions

Table 5: Effects of Early Physiotherapy Intervention

Articles	Effects of early physiotherapy intervention on	
	ICU-AW	Physical performance/function
Kayambu et al. (2015)	Muscles strength score increase in the IG but there is no significant difference between the IG and CG ($p>0.05$)	Significant improvement in physical function domain ($p<0.05$)
Machado et al. (2017)	Significant improvement of muscles strength at post intervention ($p<0.01$).	Not reported
Eggmann et al. (2018)	Number of ICU-AW in IG was low as compared to CG but insignificant ($p>0.05$)	No significant improvement ($p>0.05$)
Nakano et al. (2021)	% of muscle loss is low in both groups ($p<0.05$). MRC score did not differ between IG and CG ($p>0.05$)	No significant improvement ($p>0.05$)

The Effects of Early Physiotherapy Intervention on ICU-AW and Physical Performance

All the included articles in this systematic review examined the effects of early physiotherapy intervention in ICU patients by comparing the early physiotherapy mobilization in combination with adjunct exercises with the standard early physiotherapy mobilization alone. To measure the outcomes, all the four included articles used MRC grading scale to indicate the incidence of ICU-AW. For physical function or physical performance, there are various outcome measures used by the studies such as Acute Care Index of Function (ACIF), Physical Functional ICU test (PFIT), 6-Minute Walking Distance (6MWD), and Functional Independence Measure (FIM). Eggmann et al. (2018) and Nakano et al. (2021) reported that ICU-AW and physical performance outcomes are only measured at post-intervention. The possible explanation was that the researchers only measured when the patients are physically stable as the assessments requires patients who are responsive and cooperative.

As shown in Table 5, three studies found that participants who received early physiotherapy had improved MRC scores and reduced occurrence of ICU-AW syndrome, however, the score was higher in those who received adjunct treatments as compared to the early mobilization alone (Kayambu et al., 2015, Eggmann et al., 2018). Furthermore, according to between group analysis, there was no significant difference between the two groups ($p > 0.05$). In contrast, Machado et al. (2017) found significant difference between the groups with and without adjunct interventions in which the improvement is evident in the group that received combination treatments as compared to group with early mobilization alone (Machado et al., 2017).

In this review, Nakano et al (2021) revealed that the percentage of muscle loss is significantly lower among those who received early mobilisation and adjunct intervention ($p < 0.05$). Nevertheless, the MRC scores did not differ between the two groups. As for physical performance, Kayambu et al. (2015) reported that early mobilization with adjunct intervention significantly improved functional performance ($p < 0.05$). While Eggmann et al. (2018) and Nakano et al. (2021) found the results to be different from those of Kayambu et. al. (2015). Machado et al. (2015), in this review, did not measure the effects of early mobilization on physical function.

Discussion:

The objective of this systematic review is to determine the effects of early physiotherapy intervention on ICU-AW and physical performance among patients in the ICU. Studies included have described the time point for 'early mobilization' ICU patients, except for Eggmann et al. (2018) which did not mention the exact time for their early mobilization approaches. All studies which included leg cycle ergometer, resistive exercises, rehabilitation with NMES, and usual intervention such as positioning, sitting out of bed, active and passive ROM exercises and respiratory rehabilitation.

ICU-AW commonly occurs among critically ill patients in the ICU who are immobilized for a long period and who suffer with sepsis, multiple organ failure, persistent systemic inflammation and other critical diagnosis (Zorowitz, 2016). Several studies have found that commencing physiotherapy intervention and rehabilitation on ICU patients at the early phase of ICU stay is beneficial and has positive effects. Zang et al. (2019) stated that early mobilization could reduce the incidence of ICU-AW, improve in MRC score, and improve functional mobility at hospital discharge. This review found that early mobilization could prevent muscles loss (Nakano et al., 2021) which result in the low percentage of ICU-AW syndrome among ICU patients as reported by Eggmann et al. (2018). In addition, the MRC scores upon ICU discharge were improved with early mobilization alone or with the combination of other treatments. In this review, the researchers are aware that early mobilization alone has potential to alleviate the occurrence of ICU-AW. But at the same time, the combination with other treatments may have a more remarkable impact.

In this systematic review, significance difference in physical function between those who received early mobilization or with other treatments was not found in studies by Eggmann et al., 2018 and Nakano et al., 2021. Only Kayambu et. al., (2015) reported positive effects of early physiotherapy intervention on peripheral muscle strength. In this study, the patients received conventional physical therapy and passive leg cycle ergometer exercise. The exercise was performed for 20 minutes at a fixed rate of 20 cycles/minutes and conducted for 5 days per week until the patients discharged from the ICU. The patients are hemodynamically stable and maintained at light level of sedation. The condition of the patients might influence the effectiveness of the exercise to improve muscle strength. In addition, according to Camargo Pires-Neto et al. (2013), early passive cycling exercise conducted on sedated, critically ill and less than 72 hours mechanically ventilated patients was found to be safe and feasible as it was not associated with hemodynamic and metabolic changes.

In the ICU, patients received a range of intensive care and management from the multidisciplinary healthcare team such as from the physicians, nurses, and physiotherapists as according to their specific needs and severity of the condition (Marshall et al., 2017). The management includes mechanical ventilation (MV), medications, nutritional support, physical therapy and close monitoring equipment such as monitors to track heart rate and blood pressure, and oxygen saturation monitors (Hashem et al., 2016; Cakmak et al., 2018). These treatments might influence patients' outcome either at ICU discharge, hospital discharge or months after the discharge.

It is worth noting that there are significant findings in the improvement of quality of life in the domains of physical role in the study done by

Kayambu et al. (2015). Therefore, ICU physiotherapists are recommended to commence early physiotherapy intervention on ICU patients as it promotes positive impacts to the health domains.

Limitation of the Study

There are some limitations of this review: Firstly, it is limited to only experimental studies, although there are many observational studies related to this topic in the literature, the later was excluded in alignment with the inclusion criteria of this review. Secondly, there were limited articles available which compared the effects between early and no mobilisation in the ICU. Thirdly, the selected articles did not perform baseline measurements for ICU-AW and physical performance. This is somewhat a drawback as the researchers were unable to explore the differences between these studies in-depth.

Recommendation for Future Studies

Larger study is needed to determine the long-term effects of early mobilization in the ICU patients. Moreover, it is equally important for future research to establish a standard guideline and protocol for early mobilization approaches in order to enhance the quality of care and also upholding the best standard of practice in the critical care units.

Conclusion:

In conclusion, early physiotherapy intervention was found to be beneficial and can be considered as crucial in the prevention of ICU-AW syndrome as well as functional dependency. It is suggested that early mobilization should be conveyed to ICU patients immediately upon admission as it is safe, feasible and beneficial. Early mobilization alone or with adjunct treatments offer positive outcomes on ICU-AW and physical performance. These findings may help the clinicians to strategise the best approaches in improving the clinical outcomes for ICU survivors.

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