FLEX CEUs

ICU - Early Mobilization Factors

Early mobilization of critically ill patients in the intensive care unit: A systematic review and meta-analysis

Abstract

Background

Physical therapy can prevent functional impairments and improve the quality of life of patients after hospital discharge. However, the effect of early mobilization on patients with a critical illness remains unclear. This study was performed to assess the evidence available regarding the effect of early mobilization on critically ill patients in the intensive care unit (ICU).

Methods

Electronic databases were searched from their inception to March 21, 2019. Randomized controlled trials (RCTs) comprising critically ill patients who received early mobilization were included. The methodological quality and risk of bias of each eligible trial were assessed using the Cochrane Collaboration tool. Data were extracted using a standard collection form each included study, and processed using the Mantel-Haenszel (M-H) or inverse-variance (I-V) test in the STATA v12.0 statistical software.

Results

A total of 1,898 records were screened. Twenty-three RCTs comprising 2,308 critically ill patients were ultimately included. Early mobilization decreased the incidence of ICU-acquired weakness (ICU-AW) at hospital discharge (three studies, 190 patients, relative risk (RR): 0.60, 95% confidence interval (CI) [0.40, 0.90]; $p = 0.013$, $I^2 = 0.0\%$), increased the number of patients who were able to stand (one study, 50 patients, 90% vs. 62%, $p = 0.02$), increased the number of ventilator-free days (six studies, 745 patients, standardized mean difference (SMD): 0.17, 95% CI [0.02, 0.31]; $p = 0.023$, $I^2 = 35.5\%$) during hospitalization, increased the distance the patient was able to walk unassisted (one study, 104 patients, 33.4 (0–91.4) meters vs. 0 (0–30.4) meters, $p = 0.004$) at hospital discharge, and increased the discharged-to-home rate (seven studies, 793 patients, RR: 1.16, 95% CI [1.00, 1.34]; $p = 0.046$). The mortality (28-day, ICU and hospital) and adverse event rates were moderately

increased by early mobilization, but the differences were statistically non-significant. However, due to the substantial heterogeneity among the included studies, and the low quality of the evidence, the results of this study should be interpreted with caution. Publication bias was not identified.

Conclusions

Early mobilization appears to decrease the incidence of ICU-AW, improve the functional capacity, and increase the number of ventilator-free days and the discharged-to-home rate for patients with a critical illness in the ICU setting.

Introduction

Approximately 20–50% of critically ill patients experience intensive care unit-acquired weakness (ICU-AW) [1–3]. ICU-AW includes a wide variety of disorders caused by polyneuropathy and myopathy after ICU admission, and it is associated with reductions in health-related quality of life and increased risks of death after hospital discharge [4–7]. ICU-AW is potentially aggravated by long periods of bed rest due to routinely managed sedation and immobility [8]. Currently, mobilization interventions delivered in the ICU setting are accepted as a therapeutic intervention that potentially prevents or attenuates functional impairment and ICU-AW [9–11]. However, the timing of the initiation of mobilization is still being debated.

Early mobilization has been proposed as a promising intervention to counteract ICU-AW because it attenuates critical illness-associated muscle weakness [12]. In 2013, Berry et al. reported that early exercise has the potential to decrease the length of the hospital stay and improve function in patients with acute respiratory failure [13]. In 2017, Ramos Dos et al. proposed that early mobilization appears to be important for preventing postoperative complications, improving functional capacity and reducing the length of hospital stay of patients who underwent cardiac surgery [14]. In the same year, a study by Nydahl reported that early mobilization and physical rehabilitation for critically ill patients appear to be safe and have a low risk of potential adverse events [15]. According to the 2018 study by Zhang et al., early mobilization in the ICU exerts a positive and safe effect on hospital outcomes for patients who require mechanical ventilation (MV) because it confers the significant benefit of decreasing the duration of MV and the length of stay in the ICU [16].

However, numerous opposing opinions have been reported in many published papers. In 2015, a meta-analysis conducted by Castro-Avila et al. argued that early rehabilitation during the ICU stay is not associated with improvements in the functional status, muscle strength, quality of life or health care utilization outcomes [17]. In 2016, a qualitative review suggested that early exercise in the ICU is feasible and safe, but the potential benefit of earlier program initiation has not been clearly shown [18]. In 2018, Doiron et al. reported mixed results for the effect of early movement or exercise on physical function, and described the difficulty in determining whether early movement or exercise performed by critically ill people in the ICU improves their abilities to perform daily activities, muscle strength, or quality of life [19].

In addition to the data presented above, the most recent Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption (PADIS) guideline (2018) suggests that rehabilitation or mobilization can be safely initiated in critically ill adults when the cardiovascular, respiratory, and neurological statuses are stable [20]. Moreover, many recent studies focusing on the effect of early rehabilitation within the ICU have been published. Thus, the effect of early

mobilization on critically ill patients in the ICU should be re-examined. Based on these, we conducted this study aim to comprehensively assess the evidence available regarding the effect of early mobilization on critically ill patients in the ICU.

Materials and methods

This meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (S1 Text) [21]. Ethical approval was not required for this study.

Search strategy

PubMed, EMBASE, Web of Science, and the Cochrane Library were independently searched from their inception to March 21, 2019 by two investigators using the keywords "early ambulation", "mobilization", "rehabilitation", "physical therapy", "intensive care unit", and "randomized controlled trial", as well as their respective synonyms and derivations (S2 Text). The publication language was restricted to English. Relevant articles were also identified by reviewing the reference lists of the retrieved papers and conference literature.

Study selection

Two investigators independently reviewed all the studies. Disagreements were resolved through a discussion with a third investigator.

The following inclusion criteria were used for the primary studies: (1) Population: adult patients (≥18 years old or according to local law), (2) Design: randomized controlled trial (RCT), and (3) Intervention: patients in the intervention group received early mobilization. The eligibility criteria for "early mobilization" was based on previously published meta-analyses and the new PADIS guideline [20,22,23]. Early mobilization was initiated when (1) the cardiovascular, respiratory, and neurological statuses of patients were stable and (2) patients in the intervention group began mobilization interventions earlier than the control group. Mobilization was defined as follows: (1) range of motion; (2) motion involving axial loading exercises, movements against gravity, active activities, and activities requiring energy expenditure of patients; (3) 'active' was indicated in the early mobilization definitions as patients with muscle strength and an ability to control the activities, a conscious muscle activation (except breathing) and certain types of activities, such as activities with physiological benefits, strengthening and mobility exercises and assisted exercises. Patients in the control group received the standard or usual treatment. (4) Outcomes included muscle strength (such as the Medical Research Council (MRC) sum score, ICU-AW, handgrip force, and quadriceps force), functional mobility capacity (ablity to stand, unassisted walking distance, time to walk, and so on), duration of MV, ventilator-free days, mortality rates (28-day, ICU, and hospital), discharged-to-home rate, and adverse events.

The exclusion criteria for the primary studies were (1) patients with neurological conditions (e.g., brain injury, stroke, or spinal cord injury); (2) the inclusion of ineligible interventions, such as, neuromuscular electric muscle stimulation, continuous lateral rotation of the bed, lateral positioning in bed, inspiratory muscle training/diaphragmatic electrical stimulation/ breathing exercises, chest physiotherapy/airway clearance, massage therapy, and stroke rehabilitation; (3) exercises performed after ICU discharge; (4) reviews, abstracts, and case reports; (5) pediatric, animal or cell-based studies; and (6) duplicate publications.

Quality and risk of bias assessments

The methodological quality and risk of bias of each eligible trial were independently assessed using the Cochrane Collaboration tool for assessing risk of bias in randomized trials by two investigators [24]. Any discrepancies were resolved through discussion with a third investigator.

Data extraction

A standard collection form was used to extract related data from the included trials. The extracted data comprised the first author, year of publication, sample size, demographics, and clinical outcomes. The author was contacted by email if additional information associated with a study was needed; if a response was not obtained, the study was excluded.

Data processing and statistical analyses

The STATA v12.0 statistical software was used in the meta-analysis. For dichotomous variables (e.g., mortality rate, discharged-to-home rate, and adverse events), the relative risk (RR) and 95% confidence interval (CI) were calculated using the Mantel-Haenszel (M-H) test. For continuous variables (e.g., duration of MV, ventilator-free days, unassisted walking distance, and so on), the weighted mean difference (WMD) or standardized mean difference (SMD) and 95% CI were calculated using the inverse-variance (I-V) test.

Heterogeneity was estimated using I^2 statistics [25]. If significant heterogeneity ($I^2 \geq 50\%$) was present, the random-effects model was used. Otherwise, the fixed-effects model was used. Both sensitivity and subgroup analyses were employed to investigate possible sources of high heterogeneity ($I^2 \geq 50\%$).

A funnel plot was constructed to evaluate publication bias only if a sufficient number of studies (≥ 10) was present. The significance of the pooled index was determined using the Z test. A two-sided P-value ≤ 0.05 was considered statistically significant.

Results

Search results

As shown in Fig 1, 1,898 studies were retrieved after the initial search. After duplicates were removed, 1,058 records remained. After reading the text, 23 studies (N = 2,308 patients) were eligible for inclusion and analysis in this meta-analysis [26–48].

Demographic characteristics of the population

The demographic characteristics of the patients in the included studies are summarized in Table 1. The enrolled patients consisted of 1,352 males and 956 females. The mean age of the included patients ranged from 44.9 to 65.5 years. Eighteen studies reported Acute Physiology and Chronic Health Evaluation (APACHE) II scores; the mean APACHE II scores ranged from 15.5 to 27.5 points [26,28,29,31,33–35,37–47]. One study reported a Simplified Acute Physiology Score II [30]. One study reported an APACHE III score [36]. All included studies were performed in different countries, such as Canada, France, United Kingdom, and China.

As shown in S1 Table, the causes of the ICU stay included MV [26–31,33–41,43–46], liver transplant [28], respiratory failure and/or shock [42], prolonged ICU stay [47] and chronic obstructive pulmonary disease with respiratory failure [48]. Two studies were performed in a respiratory ICU [35,48], six studies were performed in a surgical ICU [27,34,42,45–47], and the remaining studies were performed in a general ICU. Seven studies were multicenter RCTs [26,34,35,37,42,46,47].
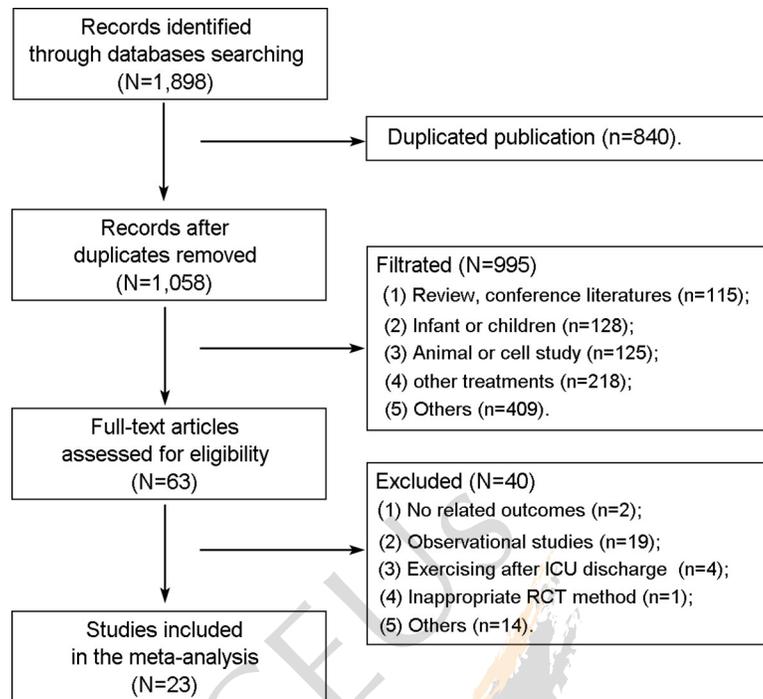
Fig 1. Flow diagram of the study selection process.

Treatment protocols

The treatment protocols used in the included studies are summarized in S2 Table. Thirteen studies reported a clear definition of 'early', such as "within five days of admission to critical care or ICU" [26,28,29,33,43,48], "within one day after trial enrollment" [34,35,37], "after coronary artery bypass grafting in the ICU" [38], "within 48 hours of the diagnosis of sepsis" [40], "during the sedated and intubated phase of their postoperative course" [32], and "at least 24 hours and not more than 48 hours of invasive MV" [39]. The remaining studies did not provide a clear definition of early mobilization but included the term "early" when describing the intervention group [27,30,31,36,41,42,44–47]. The participants in the intervention group received in-bed cycling on a cycle ergometer [26,29–31,33,39,47], mobilization or rehabilitation [27,34,36–38,40,41,43,44,46,48], enhanced or intensive rehabilitation [28,32,35], or a physiotherapy intervention [42,45]. Compared with the intervention groups, participants in the control groups received later or standardized mobilization interventions in the included studies.

Quality and risk of bias

The methodological quality and risk of bias of each eligible study were evaluated using the Cochrane Collaboration tool for assessing the risk of bias, and the results are presented in Table 2. All studies were randomized. Seventeen studies reported the method of random sequence generation, such as computer generation [26–28,30,31,33,36,38,40,42,45,46,48] internet-based access to a restricted platform [34], website randomization [39], and a random number table [43,47]. Nine studies reported allocation concealment with envelopes [27,30,31,37, 40,42,43,45,47], and three studies reported blinded allocation [28,33,46]. Two studies reported

Table 1. Demographics of patients in the included studies.

Year	Authors	Size (n)	Gender (M/F)	Age (years)	APACHE II	Region
2019	Kho et al. [26]	66	40/26	61.6±16.9	23.5±8.6	Canada
2018	Sarfati et al. [27]	145	98/47	64.0±3.5	Not reported	France
2018	McWilliams et al. [28]	102	62/40	61.5±5.6	17.5±1.8	United Kingdom
2018	Hickmann et al. [29]	19	11/8	58.5±19.5	18.5±6.6	Belgium
2018	Fossat et al. [30]	312	204/108	65.5±14.1	46.5±18.1*	France
2018	Eggmann et al. [31]	115	67/48	64.5±15.0	22.5±7.6	Switzerland
2017	Maffei et al. [32]	40	31/9	53.5±9.0	Not reported	United Kingdom
2017	Machado et al. [33]	38	23/15	44.9±19.2	17.7±6.6	Brazil
2016	Schaller et al. [34]	200	126/74	65.0±4.6	20.0±4.3	Austria, Germany, USA
2016	Moss et al. [35]	120	71/49	52.5±14.5	17.6±5.9	USA
2016	Morris et al. [36]	300	134/166	56.0±15.0	76.0±27.0 #	USA
2016	Hodgson et al. [37]	50	30/20	58.5±13.3	17.9±8.8	Australia, New Zealand
2016	Dong et al. [38]	106	42/64	61.4±14.2	16.8±4.3	China
2016	Coutinho et al. [39]	25	12/13	58.5±22.9	25.7±6.7	Brazil
2015	Kayambu et al. [40]	50	32/18	64.0±12.67	27.5±7.23	Australia
2014	Dong et al. [41]	60	41/19	55.4±16.2	15.5±4.2	China
2014	Brummel et al. [42]	87	49/38	61.0±4.7	25.1±2.8	USA
2013	Denehy et al. [43]	160	95/65	60.8±15.9	19.9±7.0	Australia
2012	Dantas et al. [44]	28	11/17	54.8±18.4	22.4±7.9	Brazil
2011	Chang et al. [45]	34	21/13	66.1±13.8	16.0±8.0	Taiwan
2009	Schweickert et al. [46]	104	52/52	56.1±6.8	19.5±2.3	USA
2009	Burtin et al. [47]	67	49/19	56.5±16.3	25.5±5.5	Belgium
1998	Nava et al. [48]	80	51/29	66.0±7.7	Not reported	Italy

* Simplified Acute Physiology Score II

\# APACHE III score

APACHE II: Acute Physiology and Chronic Health Evaluation II; USA: United States of America.

the blinding of participants and personnel [27,40], and 12 studies reported blinding of the outcome assessments [26,31,33–37,40,42,43,46].

Muscle strength

Eight studies involving 763 patients reported changes in the Medical Research Council (MRC) sum score at ICU discharge [26–28,30,31,33,40,44]. A pooled analysis of the data indicated that early mobilization did not increase the MRC sum score at ICU discharge (WMD: 0.95, 95% CI [-1.72, 3.61]; $p = 0.487$, $I^2 = 90.2\%$) (S3 Table). According to the sensitivity analyses, four studies were responsible for the high heterogeneity ($I^2 = 90.2\%$), due to the inclusion of patients who received short-term MV (≤ 4 days) [26], were treated in a surgical ICU [27], received electrical stimulation [30], and a lack of reporting of the method used for random sequence generation [44] (S1 Fig). After removing the four studies, pooled analysis of the data indicated the same result (WMD: 0.18, 95% CI [-1.13, 1.49]; $p = 0.788$, $I^2 = 0.0\%$) [28, 31,33,40] (S3 Table).

Five studies examining 414 patients reported changes in the MRC sum score at hospital discharge [26–28,37,46]. A pooled analysis of the data indicated that early mobilization did not increase the MRC sum score at hospital discharge (WMD: 0.76, 95% CI [-0.18, 1.70]; $p = 0.114$, $I^2 = 54.2\%$) (S4 Table). Based on the sensitivity analyses, one study (performed in a

Table 2. Quality and bias of the included trials.

Year	Authors	Selection bias		Performance and detection bias		Incomplete outcome data addressed	Selective reporting	Other bias
		Sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessments			
2019	Kho et al. [26]	Low risk	Unclear	High risk	Low risk	Low risk	Low risk	Low risk
2018	Sarfati et al. [27]	Low risk	Low risk	Low risk	High risk	Low risk	Low risk	Low risk
2018	McWilliams et al. [28]	Low risk	Low risk	High risk	High risk	Low risk	Low risk	Low risk
2018	Hickmann et al. [29]	Unclear	Unclear	High risk	High risk	Low risk	Low risk	Low risk
2018	Fossat et al. [30]	Low risk	Low risk	High risk	High risk	Low risk	Low risk	Low risk
2018	Eggmann et al. [31]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk
2017	Maffei et al. [32]	Unclear	Unclear	High risk	High risk	Low risk	Low risk	Low risk
2017	Machado et al. [33]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk
2016	Schaller et al. [34]	Low risk	Unclear	Low risk	Low risk	Low risk	Low risk	Low risk
2016	Moss et al. [35]	Unclear	Unclear	Low risk	Low risk	Low risk	Low risk	Low risk
2016	Morris et al. [36]	Low risk	Unclear	Low risk	Low risk	Low risk	Low risk	Low risk
2016	Hodgson et al. [37]	Unclear	Low risk	High risk	Low risk	Low risk	Low risk	Low risk
2016	Dong et al. [38]	Low risk	Unclear	High risk	Low risk	Low risk	Low risk	Low risk
2016	Coutinho et al. [39]	Low risk	Unclear	High risk	Low risk	Low risk	Low risk	Low risk
2015	Kayambu et al. [40]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
2014	Dong et al. [41]	Unclear	Unclear	High risk	Low risk	Low risk	Low risk	Low risk
2014	Brummel et al. [42]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk
2013	Denehy et al. [43]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
2012	Dantas et al. [44]	Unclear	Unclear	High risk	High risk	Low risk	Low risk	Low risk
2011	Chang et al. [45]	Low risk	Low risk	High risk	High risk	Low risk	Low risk	Low risk
2009	Schweickert et al. [46]	Low risk	Low risk	Low risk	Blinded	Low risk	Low risk	Low risk
2009	Burtin et al. [47]	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk
1998	Nava et al. [48]	Low risk	Unclear	High risk	High risk	Low risk	Low risk	Low risk

surgical ICU) performed by Sarfati et al. was responsible for the high heterogeneity (I^2 = 54.2%), and was removed [27] (S2 Fig). A pooled analysis of the data from the remaining four studies indicated that early mobilization did not increase the MRC sum score at hospital discharge (WMD: 0.20, 95% CI [-0.53, 0.92]; p = 0.594, I^2 = 45.2%) [26,28,37,46] (S4 Table).

Five studies analyzing 419 patients reported the incidence of ICU-AW (MRC sum score <48) [26,27,34,37,46]. The pooled analysis of the data indicated a decrease in the incidence of ICU-AW at hospital discharge following early mobilization (RR: 0.60, 95% CI [0.40, 0.90]; p = 0.013, I^2 = 0.0%) (Fig 2), but not at ICU discharge (RR: 0.99, 95% CI [0.80, 1.23]; p = 0.936, I^2 = 36.6%) (S3 Fig).

Four studies reported handgrip force [31,36,46,47], and three studies reported quadriceps force [31,36,47]. As shown in S5 Table, a difference was not observed between the early mobilization and control groups.
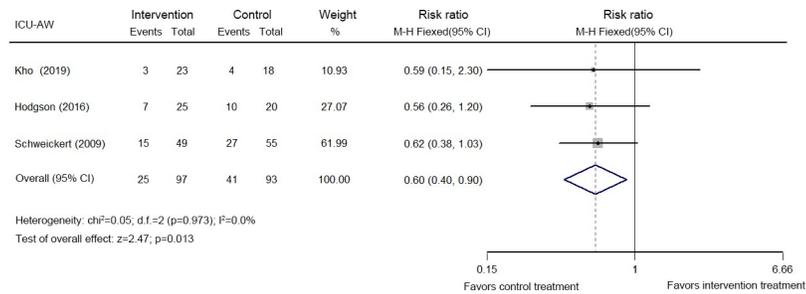
Fig 2. Forest plot of the eligible studies that reported ICU-AW at hospital discharge.

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Functional mobility capacity

Sixteen studies including 1,758 patients examined the changes in functional mobility capacity using different mobility assessments at different time points [26–28,30–32,34,35,37,40–43,46–48]. In one study, early goal-directed mobilization increased the number of patients who were able to stand during hospitalization (90% vs. 62%, p = 0.02) [37]. According to another study, patients in the early physical and occupational therapy group recorded a greater unassisted walking distance (33.4 (0–91.4) meters vs. 0 (0–30.4) meters, p = 0.004) at hospital discharge [46]. In addition to these indicators, a comprehensive analysis showed that early mobilization failed to improve functional indicators (S6 and S7 Tables). However, due to the high heterogeneity, these results should be interpreted with caution.

Mechanical ventilation and ventilator-free days

Seventeen studies including 1,501 patients reported the duration of MV [26–33,35,37–41,43, 45,46]. The pooled analysis of the data indicated that early mobilization did not decrease the duration of MV (SMD: -0.33, 95% CI [-0.66, -0.00]; p = 0.051, I^2 = 89.1%). As shown in S8 Table, analyses of different subgroups also failed to detect an effect of early mobilization on the duration of MV.

Six studies including 745 patients reported ventilator-free days [34,36,37,40,42,46]. The pooled analysis of the data indicated that early mobilization increased the number of ventilator-free days (SMD: 0.17, 95% CI [0.02, 0.31]; p = 0.023, I^2 = 35.5%) (Fig 3).

Mortality rate

Eighteen studies including 1,781 patients reported changes in the mortality rate at different time points. As shown in results of the pooled analysis of the data presented in S9 Table, early mobilization did not decrease the 28-day mortality rate (RR: 1.23, 95% CI [0.81, 1.85]; p = 0.330) [29,30,43], ICU mortality rate (RR: 1.12, 95% CI [0.82, 1.52]; p = 0.474) [26–28,30,31,35,37,40], or hospital mortality rate (RR: 1.10, 95% CI [0.89, 1.37]; p = 0.380) [34,37,38,41,42,46–48].

Discharged-to-home rate

Seven studies analyzing 793 patients reported the discharged-to-home rate [26,34,35,37,43, 46,47]. As shown in Fig 4, moderate heterogeneity existed among these studies (χ^2 = 9.76, p = 0.135, I^2 = 38.5%), and a random fixed-effects M-H model was used. Early mobilization increased the discharged-to-home rate (RR: 1.16, 95% CI [1.00, 1.34]; p = 0.046).
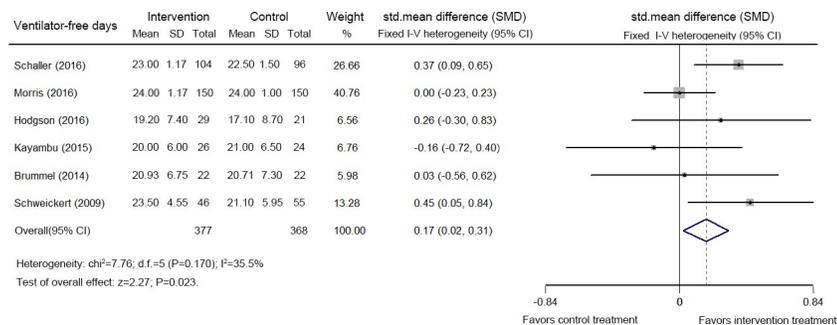
Fig 3. Forest plot of the eligible studies that reported the number of ventilator-free days.

Adverse events

Eight studies including 1,009 patients reported adverse events [26,31,34–36,41,42,46]. As shown in S4 Fig, moderate heterogeneity was observed among these studies (χ^2 = 10.04, p = 0.186, I^2 = 30.3%), and a fixed-effects M-H model was used. Early mobilization did not increase the rate of adverse events (RR: 1.35, 95% CI [0.86, 2.12]; p = 0.195).

Publication bias

The funnel plot for the duration of MV (17 studies) is shown in Fig 5, and it shows no publication bias (Z = 0.30 (continuity corrected), Pr > |z| = 0.767 >0.05).

Discussion

Twenty-three RCTs (2,308 patients) were included in this systematic review and meta-analysis. Publication bias was not identified. Based on the pooled results of this study, we concluded that regardless of the different techniques and periods of mobilization used, early mobilization of critically ill patients increased the number of people who were able to stand (90% vs. 62%, p = 0.02) and the number of ventilator-free days during hospitalization, decreased the incidence of ICU-AW, increased the walking distance at hospital discharge, and increased the discharged-to-home rate. The mortality (28-day, ICU and hospital) and adverse event rates were moderately increased by early mobilization, but the differences were not statistically significant.

Critically ill patients commonly develop severe muscle weakness due to hypercatabolism, deep sedation and immobility [49]. Muscle weakness impairs the functional capacity, leads to
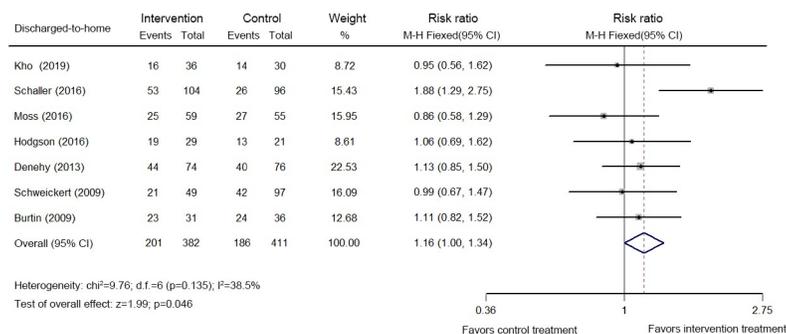

Fig 4. Forest plot of the eligible studies that reported the discharged-to-home rate.
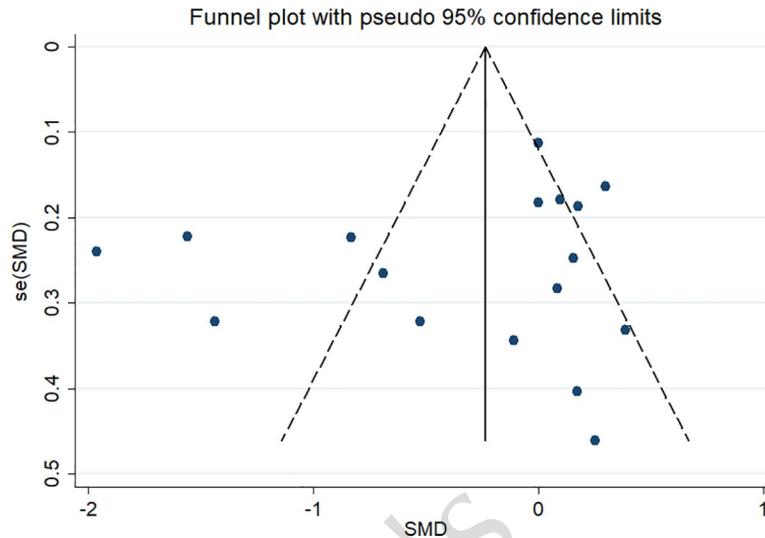
Fig 5. Funnel plot of the 17 eligible studies that reported the duration of MV.

delayed recovery, impedes weaning from MV, increases financial costs, and decreases the quality of life of survivors [50–52]. Many clinical scales and dynamometry methods have been developed by researchers to reliably measure muscle force in the ICU.

A bedside evaluation of muscle strength using the MRC sum score (<48) has been applied to diagnose ICU-AW in many current recommendations [53]. According to the present meta-analysis, early mobilization did not increase the MRC sum score at ICU and hospital discharge. However, early mobilization decreased the incidence of ICU-AW after hospital discharge. These results are consistent with two recent systematic reviews reporting that early physical therapy increases peripheral muscle strength [9, 10].

Handgrip strength, which can be measured using hand-held dynamometers, serves as an indicator of overall muscular strength [54]. Many studies have reported a lower handgrip strength in subjects with ICU-AW and an independently association with poor hospital outcomes [55–57]. Recent systematic reviews have shown that exercise training improves the skeletal muscle strength of patients with acute respiratory failure [13, 58]. However, in this systematic review, no differences in peripheral muscle strength measured using handgrip force and quadriceps force were observed between groups. A similar result was reported by Castro-Avila et al. [17].

Muscle strength maintenance is significantly correlated with an improvement in functional capacity [59–61]. Immobility is an important risk factor for functional impairment [4]. Many systematic reviews have reported that early mobilization is feasible, safe and well tolerated and promotes better functional outcomes in patients in the ICU [10,62,14,63]. Therefore, the mainstream view is that critically ill patients should receive mobilization therapy as soon as possible.

In this meta-analysis, early mobilization increased the number of people who were able to stand during hospitalization and the walking distance at hospital discharge. These results support the previous hypothesis that early mobilization is beneficial for improving patients' functional mobility capacity.

However, early mobilization did not affect other functional scores (e.g., physical function score on the ICU test, functional status score on the ICU test, and Berg Balance Scale scores) at ICU/hospital discharge. This result differs from a previous systematic review showing that the

Functional Independence Measure (FIM) score improved in the intervention group and after rehabilitation in the post-acute setting [62]. One possible explanation for this discrepancy may be our strict definition of interventional care.

Poor peripheral muscle strength is associated with a longer duration of MV [53]. Previous studies reported positive effects of early exercise in the ICU on these measures [9,10,13]. In this meta-analysis, early mobilization increased the number of ventilator-free days during hospitalization, but not the duration of MV. A possible explanation is that many patients without MV were included [32,43,48]. Highly significant heterogeneity was observed among the 17 studies. As a result, these results should be interpreted with caution.

The mortality rate is a traditional measure of the health status of critically ill patients. Muscle weakness is associated with increased mortality [56]. Physical therapy in the ICU had no effect on mortality in many previous systematic reviews and meta-analyses [9, 10, 11]. Similar to previous studies, early mobilization did not improve ICU mortality, hospital mortality, or 28-day mortality rates in the present study. The discharged-to-home rate is an important prognostic indicator for critically ill patients. In the present study, we first showed that early mobilization increased the discharged-to-home rate compared to the control group.

According to convergent evidence-based data, physical therapy in the ICU is safe [64]. In this meta-analysis, early mobilization did not increase the rate of adverse events compared with the control group. This finding is consistent with previous studies [18,23,11,62].

Study limitations

Some important limitations of this systematic review and meta-analysis should be noted. First, the definitions, frequency, duration, intensity, volume and treatment time of early mobilization varied across the different studies. As a result, substantial variations in the results were observed. Second, most of the included studies did not adopt sufficient randomization and allocation concealment methods or appropriate blinding methods. Therefore, many sources of bias existed among the included studies. Third, some heterogeneity (e.g., type of outcomes, instruments used, and timing of assessment) existed in the included studies, which limited the possibility of performing additional meta-analyses.

Conclusions

Regardless of the different techniques and periods of mobilization applied, early mobilization may be initiated safely in the ICU setting and appears to decrease the incidence of ICU-AW, improve the functional capacity, and increase the number of patients who are able to stand, number of ventilator-free days and discharged-to-home rate without increasing the rate of adverse events. However, due to the substantial heterogeneity among the included studies, the evidence has a low quality and the results of this study should be interpreted with caution. Further large-scale and well-designed research studies are needed to provide more robust evidence to support the effectiveness and safety of the early mobilization of critically ill patients in the ICU setting.

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Early Mobilization of Patients in Intensive Care: Organization, Communication and Safety Factors that Influence Translation into Clinical Practice

Abstract

This article is one of ten reviews selected from the Annual Update in Intensive Care and Emergency Medicine 2018. Other selected articles can be found online at https://www.biomedcentral.com/collections/annualupdate2018. Further information about the Annual Update in Intensive Care and Emergency Medicine is available from http://www.springer.com/series/8901.

Background

Early mobilization in the intensive care unit (ICU) is currently a hot topic, with more than 15 randomized controlled trials (RCTs) in the past ten years including several high impact publications [1]. However, the largest studies of early mobilization have enrolled 300 patients, and the results of phase II randomized trials, pilot studies and observational studies have been used to encourage practice change [2–5]. There are currently several international practice guidelines available, and early mobilization has consistently been reported as safe and feasible in the ICU setting [6]. There is no doubt that this early intervention in ICU shows exciting potential. The reported benefits of early mobilization, include reduced ICU-acquired weakness, improved functional recovery within hospital, improved walking distance at hospital discharge and reduced hospital length of stay [1]. However, medical research has repeatedly demonstrated that the results of pilot studies and phase II studies may not result in improved patient-centered outcomes when tested in a larger trial [7, 8]. More importantly, it has been difficult to test this complex intervention, with several randomized trials delivering significantly less early mobilization than specified in the study protocol [2, 9] and observational studies reporting very low rates of early mobilization during the ICU stay [10, 11].

This chapter summarizes the considerations for patient safety during early mobilization; including the physiological assessment of the patient, the consideration of invasive lines and monitoring, the management of sedation, strategies to educate and manage the multidisciplinary team and environmental factors. Importantly, we will consider the long-term effect of early mobilization on patient outcome and the future directions for this important area of work for ICU clinicians.

Safety of Early Mobilization in the ICU: Short-Term Consequences

Early mobilization is a complex intervention that requires careful patient assessment and management, as well as interdisciplinary team cooperation and training [12]. Patient safety is one of the most commonly reported barriers to delivering early mobilization, including respiratory, cardiovascular and neurological stability and the integrity of invasive lines. In a recent systematic review and meta-analysis of patient safety during early mobilization, 48 studies were identified that reported data on safety during early mobilization, including falls, removal of endotracheal tubes (ETT), removal or dysfunction of intravascular catheters, removal of catheters or tubes, cardiac arrest, hemodynamic changes and oxygen desaturation [13]. Five studies were not included as their data were reported in other included publications. The 43 included studies had different descriptions of safety events and, in most, the criteria for ceasing early mobilization were the same

criteria used to define a safety event. The most frequently reported safety events were oxygen desaturation and hemodynamic changes, each reported in 33 (69%) of the eligible studies and removal or dysfunction of intravascu-lar catheters reported in 31 (65%) of the eligible studies. Several studies did not report on important safety events, including falls (n = 21, 43%), ETT removal (n = 17, 35%) and cardiac arrest (n = 15, 31%).

Of the 43 included studies, 23 (53%) reported conse-quences of potential safety events [13]. There were 308 potential safety events from 13,974 mobilization sessions, for an incidence of 2% potential safety events during mobilization. Of these, consequences of the safety event were reported for 78 occasions (0.6%) including 49 debridement or suturing of wounds and 11 tube re-movals with 4 of these requiring replacement. With regards to adverse events including a high heart rate, low blood pressure or oxygen desaturation, the pooled incidence for each was less than 2 per 1,000 episodes of mobilization. Safety events that resulted in additional care requirements or consequences were very rare.

There have been several publications that recommend criteria for the safe mobilization of patients receiving mechanically ventilated. The first was published approxi-mately 15 years ago, and later adopted as a recommen-dation by the European Respiratory Society and the European Society of Critical Care Medicine [12, 14]. At this time, the evidence was considered level C and D (observational studies and expert opinions). In particular, these authors recommended identification of patient characteristics that enable treatment to be prescribed and modified on an individual basis, with standardized pathways for clinical decision making. The flow diagram detailing patient assessment prior to early mobilization is a useful tool in clinical practice, and may be used to assist with staff training.

More recently, an international multidisciplinary ex-pert consensus group developed recommendations for consideration prior to mobilization of patients in the ICU during mechanical ventilation [15]. The panel consisted of 23 clinical or research experts from four countries, including 17 physiotherapists, five intensivists and one nurse. Following a modified Delphi process, the group developed a traffic light system for each of the identified safety criteria to determine the risk/benefit of performing early mobilization. Green indicated that there was a low risk of an adverse event, and the benefit outweighed the potential safety consequences of early mobilization. Yellow indicated a potential risk or conse-quence of adverse event during early mobilization, such that precautions and contraindications should be dis-cussed with the interdisciplinary team prior to mobilization. Red indicated a significant potential risk of an adverse event, where early mobilization should not occur unless it was authorized by the medical team re-sponsible for the overall patient management in ICU.

Importantly, a 'red' sign was not a contraindication to early mobilization, but rather a clear message that the risks may outweigh the benefits in this instance (Fig. 1) [15]. The safety criteria were divided into the categories of respiratory, cardiovascular, neurological and other consid-erations (e.g., securing intravascular lines). Consensus was achieved on all criteria for safe mobilization with the exception of levels of vasoactive agents, where the panel agreed that more evidence was required to guide the rec-ommendations. At an international meeting, 94 multidis-ciplinary ICU clinicians concurred with the proposed expert recommendations prior to publication.

The safety criteria developed by the group were intended to be used whenever mobilization was being considered, which might be up to several times per day for an individual patient. In considering the decision to mobilize a patient, the criteria should be assessed based on the status of the patient at the time of planned mobilization, but changes in condition, and direction of trends, in the preceding hours should also be taken into account [15]. The potential consequences of an adverse event in an individual patient should also be considered as part of the overall clinical reasoning process. This group noted that further research was required to valid-ate the traffic light system in centers of clinical expertise and in centers without clinical expertise in early mobilization. They also noted that practice may change and progress in the future, so that areas that were considered a significant potential risk (red) may change to yellow with further investigation, or *vice versa*.

Barriers and Facilitators to Mobilization Reported in Quantitative Studies

Many observational and randomized controlled trials over the past decade have demonstrated that ICU clini-cians are reluctant to mobilize mechanically ventilated patients, despite the scarcity of reported adverse events and the potential benefits [11, 16, 17]. The barriers and facilitators to early mobilization can be divided into patient factors, ICU team factors and organizational factors (Table 1). A recent systematic review identified barriers to delivering the Awakening, Breathing Coord-ination, Delirium and Early mobility/exercise (ABCDE) bundle to minimize adverse outcomes and improve pa-tient care for ICU patients [18]. This study reported 107 barriers, categorized into four classes: patient-related (patient instability); clinician-related (lack of knowledge and staff safety concerns); protocol-related (unclear protocol criteria); and ICU contextual barriers (interdis-ciplinary team coordination).

Several large, multicenter observational studies have re-ported barriers to mobilization across regions. For example,

Fig. 1 Expert consensus color coding definitions for safe early mobilization of mechanically ventilated patients [15]

a prospective, observational study of mobilization practice in mechanically ventilated patients enrolled 192 patients from 12 ICUs in Australia and New Zealand [11]. The data were collected from 1,288 physiotherapy–patient interactions and no early mobilization occurred in 1,079 (84%) of these episodes during mechanical ventilation. A total of 122 (63.5%) patients did not receive early active mobilization and the main reported barrier to mobilization was sedation, with nearly half of the cohort too sedated for active mobilization on the first two days in

Table 1 Barriers and facilitators to mobilization

Barriers	Facilitators
Patient Factors	
Physiological instability (hemodynamic, respiratory, neurological)	Manage patient physiological instability
Sedation	Management of sedation & delirium
Low Glasgow Coma Scale	Sleep
Delirium/agitation	Delirium screening/management
Psychological state	Analgesia prior to mobilization
Pain	Patient goals
Medical procedures/orders	Family engagement and education
Patient refusal/anxiety	
Intensive Care Team Factors	
Poor culture	Develop a positive team culture
Lack of communication	Ward rounds, multidisciplinary team meetings
Lack of leadership	Designated leaders
Disengaged team members	Team planning and communication
Inexperienced staff	Education and up-skilling staff
Lack of planning and coordination	Screening of appropriate patients
Unclear expectations	Flexible and cooperative team members
Risk for mobility providers	Utilization of safety criteria for mobilizing mechanically ventilated patients
Femoral lines	
Early ward transfers	
Anticipated risks	Anticipated benefits
Organizational Factors	
Lack of funding	Business case for additional staff to outline the economic benefits for the organization
Time constraints	
Lack of equipment and resources	Appropriate equipment & resources
Lack of staffing or availability	Dedicated staffing
Busy caseloads	Mobility guidelines/protocol
	Training on appropriate equipment

the ICU. The study suggests that unit culture, rather than patient-related factors, may be the main barrier to early mobilization in these ICUs. The use of vasopressors was common (n = 127, 66%), however there was no evidence to suggest the appropriate level of vasopressor support to enable safe mobilization. Similarly, a point prevalence study completed across 38 ICUs in Australia and New Zealand showed that no patients mobilized or sat out of bed during mechanical ventilation [16].

Harrold and colleagues compared early mobilization between Australian and Scottish ICUs [10]. This study found that 60.2% (209/347) patients were mobilized in the Australian cohort and 40.1% (68/167) patients were mobilized in the Scottish cohort during the ICU stay. Mobilization in the presence of an ETT was rare in both cohorts (3.4% Scotland and 2.2% in Australia). Physiological instability and the presence of an ETT were frequently reported barriers; however sedation was the most commonly reported barrier to mobilization in both the Australian and Scottish cohorts.

Randomized trials have also had difficulty delivering the planned dose of early mobilization in the intervention group. The TEAM pilot study found that early, goal-directed mobility was feasible, safe and resulted in increased duration and level of active exercise [19]. Fifty patients were randomized and the intervention group received a median duration of 20 min/day early goal-directed mobilization, despite the 30–60 min pre-specified goal of the intervention. Although the intervention group did not meet the targeted duration of early mobilization, the proportion of patients that walked in the ICU was almost doubled in the intervention group. Two of the largest randomized trials of early mobilization have also reported difficulties delivering intensive dosage of active mobilization. One study was only able to deliver the intervention on 57% of study days [9], whilst the other was able to complete physical therapy on 55% and progressive resistance exercise on 36% of study days [2]. Sedation management, in particular, limited the number of early mobilization interventions, which may have contributed to the findings that ICU-based physical rehabilitation did

not appear to improve physical outcomes at 6 months compared to standard physical rehabilitation.

To address the concern with unit culture and interdisciplinary goals and communication, a multicenter international randomized trial in five university hospitals in Austria, Germany and the USA was performed where the mobilization goal was defined during daily morning ward rounds and facilitated by interdisciplinary closed-loop communication [4]. The mobilization goal was achieved in 89% of study days in the intervention group. Early goal-directed mobilization improved patient mobilization throughout ICU admission, shortened patient length of stay in both the surgical ICU and hospital, and improved patients' functional mobility at hospital discharge (51% of patients in the intervention group vs 28% of patients in the control group). The current evidence suggests that early mobilization is safe and feasible and may improve functional recovery at hospital discharge; however ICUs are still very conservative in mobilizing mechanically ventilated patients, with some potentially avoidable barriers. Interdisciplinary communication and a clinical lead or champion may reduce barriers to early mobilization [20–22].

Themes that Identify Barriers and Facilitators to Early Mobilization

There have been several studies that have used qualitative methods to establish themes associated with barriers and facilitators to early mobilization in ICU. Barber and col-leagues used three discipline-specific focus groups to es-tablish barriers and facilitators to early mobilization amongst 25 ICU staff, including separate focus groups for doctors, nurses and physiotherapists [21]. Three key themes emerged to both barriers and facilitators across all groups. The barriers included: first, culture which included the use of sedation and the reluctance to mobilize patients with an ETT; second, communication which included contacting the appropriate physiotherapist to mobilize a patient, and doctors writing it as a care plan for the day without it being operationalized; and third, a lack of resources, which included staff, training and equipment to safely conduct mobilization in the ICU. The facilitators to early mobilization in the ICU included: organizational change, such as a dedicated mobility team; leadership including a champion who would assist with multidisciplinary team planning, team meetings and daily goal setting; and resources to provide adequate staff, training and equipment for mobilization in this complex area.

Using the theory of planned behavior, Holdsworth and colleagues elicited attitudinal, normative and control beliefs toward early mobilization of mechanically ventilated patients [23]. A nine-item elicitation questionnaire was administered electronically to a convenience sample of 22 staff in the ICU. Respondents wrote the most text about barriers to mobilization, including that it was time consuming, posed a safety risk to patients with line dislodgement or disconnection and unstable patient physiology and that there was a negative workplace culture.

Perhaps the most comprehensive publication in this area is a recent systematic review of quantitative and qualitative studies that identified and evaluated factors influencing physical activity in the ICU setting (and post-ICU setting) [20]. Eighty-nine papers were included with five major themes and 28 sub-themes including: first, patient physical and psychological capability to perform physical activity, including delirium, sedation, motivation, weakness and anxiety; second, safety influences, including physiological stability and invasive lines; third, culture and team influences, including leadership, communication, expertise and administrative buy-in; fourth, motivation and beliefs regarding risks versus benefits; and lastly environmental influences including funding, staffing and equipment. Many of the barriers and enablers to physical activity were consistent across both qualitative and quantitative studies and geographical regions, and they supported themes established from previous research in this area. Barriers and facilitators to physical activity were multidimensional and may be altered by raising general awareness about post-intensive care syndrome and the potential risks versus potential benefits of early mobilization in the ICU.

Drivers of Clinical Decision Making That Are Modifiable

It is possible that several of the drivers of clinical decision making with regards to early mobilization of mechanically ventilated patients are modifiable [20]. In a large prospective cohort study across 12 ICUs, the main reported barrier to early mobilization was sedation [11]. Only one of 12 ICUs in this study routinely used a sedation protocol, including sedation minimization or daily sedation interruption. Implementing a sedation protocol into routine ICU care across regions may facilitate early mobilization by allowing ICU patients to wake and participate in physical activity. These results were also identified in an international study of early mobilization practices in Australia and Scotland [10].

In another observational study, Leditschke and colleagues reported on 327 patient days audited for early mobilization or barriers to early mobilization [22]. Early mobilization did not occur on 151 (46%) of these days and the reasons for inability to deliver early mobilization was potentially avoidable in almost half of these. Potentially avoidable barriers to mobilization included femoral vascular catheters, timing of procedures, sedation management, agitation and early transfer to the hospital ward. Active identification of barriers to early mobilization and strategies to avoid these issues should be included as part of an early mobilization plan.

Early Mobilization and Long-term Consequences

The importance of completing long-term follow-up of patient outcomes after ICU has become well recognized and is now prioritized in research [24, 25]. It is recommended that studies follow up patients for a least six months after ICU admission [26]. Mortality is a commonly reported outcome in critical care research. Due to the complexities of critical care and the interventions provided to patients, it is possible that early mobilization and rehabilitation may have long-term adverse effects on our patients [1]. An updated meta-analysis of controlled and randomized trials of early mobilization and rehabilita-tion in ICU showed no significant difference in mortality at six months between the intervention and control groups (OR − 0.01, 95% CI −0.07–0.05, $p = 0.74$, seven studies, $n = 265$) (Fig. 2).

Whilst mortality is an important outcome to assess after critical illness, it is long-term physical, psychological and cognitive function that patients and their family members rate as important outcomes post-critical illness [27]. To this end, there are a large number of outcome measures available to assess the key domains after ICU discharge, including physical, cognitive and psychological function [28]. In studies of early mobilization and rehabilitation it is common that different outcome measures are used to assess the same domains across different studies [1, 20]. This makes combining the results in a meta-analysis difficult and makes it challenging to compare the results across studies.

A recent meta-analysis assessed six-month outcomes from randomized and controlled clinical trials of early mobilization and rehabilitation. It reported that there was no significant difference in timed-up-and-go test and the 36 Item Short Form Survey (SF-36) results [1]. It did, however, show significantly higher SF-36 results favoring the intervention group in the role physical and role emotional domains for high-dose rehabilitation compared to low-dose rehabilitation and significantly more days alive and out of hospital favoring the intervention group (mean difference 9.63, 95% CI 1.68–17.57, $p = 0.02$, five studies, $n = 509$). There were consistent concerns regarding the high rates of loss to follow up across the studies, making outcomes like the SF-36 and timed-up-and-go difficult to interpret as they do not
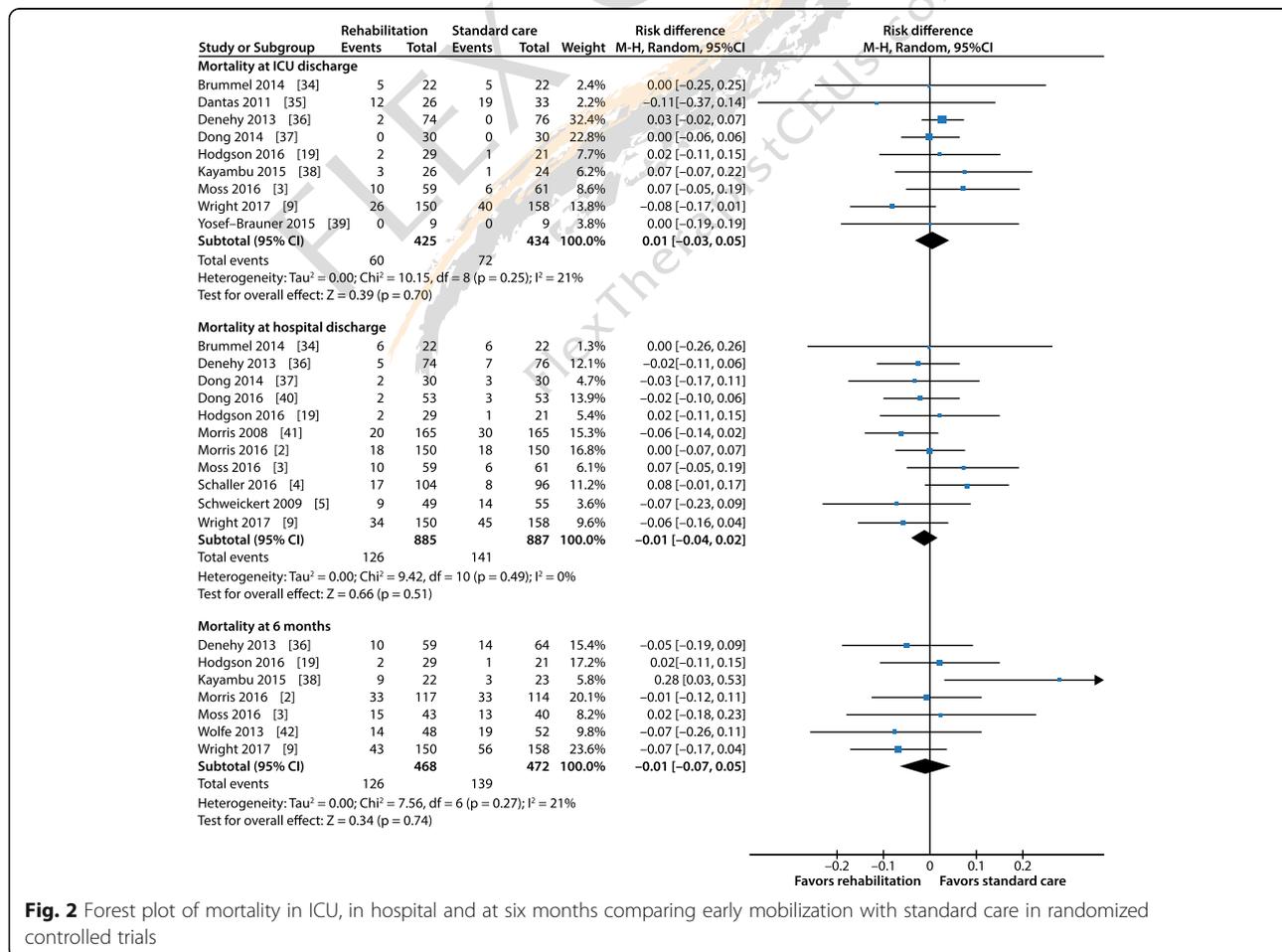

Fig. 2 Forest plot of mortality in ICU, in hospital and at six months comparing early mobilization with standard care in randomized controlled trials

account for death [1, 29]. There is currently no consistent message regarding the long-term effects of early mobilization in the ICU on physical function or quality of life [30, 31].

Do We 1Have Consensus on Long-term Outcomes for ICU Survivors?

A two-stage, international Delphi process determined that the following domains are important to assess post-ICU discharge in patients with acute respiratory failure: physical function, cognition, mental health, satisfaction with life and personal enjoyment, survival, pulmonary function, pain and muscle or nerve function [32]. The Delphi process evaluated which outcome measures should be used to assess domains identified as important. Consensus could not be reached on all domains, however the minimal acceptable outcomes to report based on this study are survival, EuroQol-5D (EQ-5D; assessing satisfaction with life and personal enjoyment), hospital anxiety and depression scale and impact of event scale revised (assessing mental health).

Perhaps we can learn some lessons from other acute areas of medicine. A dose-response analysis of early mobilization, completed on the AVERT Study stoke patient data, helps to unravel uncertainties in the dosage, timing and frequency of early mobilization interventions following stroke onset [33]. In the primary analysis, the results demonstrated that very early mobilization in stroke patients resulted in decreased odds of a favorable outcome [7]. The secondary analysis, however, showed a 13% improvement in odds of a favorable outcome with each episode of out-of-bed activity per day, keeping time to mobilization and daily amount constant. Conversely increasing the amount of time doing out-of-bed activity reduced the odds of a favorable outcome. Patients who started mobilizing earlier post-onset of stroke also had more favorable outcomes. The beneficial effect of regular short periods of out-of-bed activity was consistent across most of the analysis. These results may guide further re-search in the critical care population with regards to the prescription of early mobilization. To date, studies of early mobilization in the ICU have delivered variations in dose, timing and progression of the rehabilitation intervention [1]. This variability has made it challenging to compare the study results and to determine the most appropriate dosage and timing of early mobilization in the ICU.

Conclusion

Currently there is a divide between ICU clinicians who wish to implement early mobilization based on current evidence and clinicians who believe that early mobilization is an intervention that should be tested in a large patient-centered trial to determine long term outcomes (including functional recovery). Despite the publication of safety recommendations and clinical practice guidelines [6, 14, 15], the implementation of early mobilization remains a challenge in the ICU, with limited information on safe levels of vasoactive support, ongoing evidence of over-sedation of mechanically ventilated patients and poor staff resources limiting the ability to deliver early mobilization. Based on current evidence, early mobilization is safe during mechanical ventilation, but the conservative management of ICU patients translates into a culture of bed rest. Some of the drivers of clinical decisions may be modifiable, with better adherence to sedation and mobilization protocols, clinical leadership and increased staff resources and training. However, given our experience in other areas of medicine including stroke and traumatic brain injury, early mobilization should be tested
in a patient-centered trial with evaluation of long-term outcomes prior to implementation.

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Clinical attitudes and perceived barriers to early mobilization of critically ill patients in adult intensive care units

Atitudes clínicas e barreiras percebidas para a mobilização precoce de pacientes graves em unidades de terapia intensiva adulto

ABSTRACT

Objective: To investigate the knowledge of multi-professional staff members about the early mobilization of critically ill adult patients and identify attitudes and perceived barriers to its application.

Methods: A cross-sectional study was conducted during the second semester of 2016 with physicians, nursing professionals and physical therapists from six intensive care units at two teaching hospitals. Questions were answered on a 5-point Likert scale and analyzed as proportions of professionals who agreed or disagreed with statements. The chi-square and Fisher's exact tests were used to investigate differences in the responses according to educational/training level, previous experience with early mobilization and years of experience in intensive care units.

Results: The questionnaire was answered by 98 out of 514 professionals (response rate: 19%). The acknowledged benefits of early mobilization were maintenance of muscle strength (53%) and shortened length of mechanical ventilation (83%). Favorable attitudes toward early mobilization included recognition that its benefits for patients under mechanical ventilation exceed the risks for both patients and staff, that early mobilization should be routinely performed via nursing and physical therapy protocols, and readiness to change the parameters of mechanical ventilation and reduce sedation to facilitate the early mobilization of patients. The main barriers mentioned were the unavailability of professionals and time to mobilize patients, excessive sedation, *delirium*, risk of musculoskeletal self-injury and excessive stress at work.

Conclusion: The participants were aware of the benefits of early mobilization and manifested attitudes favorable to its application. However, the actual performance of early mobilization was perceived as a challenge, mainly due to the lack of professionals and time, excessive sedation, *delirium*, risk of musculoskeletal self-injury and excessive stress at work.

Keywords: Early ambulation; Respiration, artificial; Muscle weakness; Patient care team; Physical therapy modalities

Conflict of interest: None.

INTRODUCTION

A growing body of evidence supports the safety, feasibility and long-term functional benefits of early physical therapy, i.e., starting within the first 48 hours of mechanical ventilation (MV) and being maintained throughout the stay in the intensive care unit (ICU).[1-8] Its potential benefits notwithstanding,

effective early mobilization (EM) is not widely performed in the ICU. International multicenter studies on EM in the ICU evidence a low prevalence of out-of-bed mobilization, especially among patients under MV.[9,10] The same situation was recently described in Brazilian ICUs, where only 10% of patients under MV were mobilized out of bed.[11]

Few studies have sought to explain why EM is not effectively performed in ICU clinical practice. Some studies on improvement of the quality of care delivery investigated whether the attitudes and education of professionals relative to EM are barriers to actual performance.[12-14] These studies identified personal and patient safety and lack of clinical comprehension as potentially relevant hindrances to the performance of EM. Recent studies[15-17] found that the need of a larger number of professionals, insufficient working hours and the staff's culture regarding mobilization, including a lack of resources, prioritization and leadership, are among the main interdisciplinary barriers to the performance of EM.

A multicenter prevalence study found that the EM of patients under MV is uncommon, especially in regard to patients ventilated through endotracheal tubes, with muscle weakness, cardiovascular instability and sedation being the most commonly perceived barriers to mobilizing patients at a higher level. These difficulties might be overcome, which is relevant to increasing mobilization in Brazilian ICU.[11]

The aim of the present study was to investigate the knowledge of a multi-professional team on the EM of critically ill adult patients and identify their attitudes and perceived barriers to effective performance.

METHODS

The present cross-sectional study consisted of a survey of professionals who deliver care at six ICUs in two teaching hospitals in Brazil. The study was conducted in the second semester of 2016 and was approved by the research ethics committees of the participating hospitals, *Hospital de Clínicas de Porto Alegre* (HCPA; 1.335.156) and *Irmandade da Santa Casa de Misericórdia de Porto Alegre* (ISCMPA; 1.647.299). Informed consent was obtained through electronic means before the electronic questionnaire was answered.

All the professionals at the ICU of both hospitals were invited to participate in the study through e-mails sent by the study coordinator to service chairs, who then resent them to the professionals. Physicians, including routine and assisting physicians and medical residents, were named by the medical team chair of each ICU. Nurses, nursing technicians and physical therapists allocated to these units were named by the nursing team chair of each service and the chair of the department of physical therapy of each hospital.

The link to access the questionnaire was sent by e-mail to the service chairs together with the invitation to participate in the study. The service chairs resent the e-mails to the members of their teams, on which the study coordinator was copied. To make responding to the questionnaire and data collection easier, it was developed using the software SurveyMonkey®, and the results were obtained in real-time through coupling to Statistical Package for the Social Sciences (SPSS) software.

The questionnaire was adapted from the one employed in a recent study,[15] which was applied to the full intensive care team. The questionnaire included items to investigate the respondents' knowledge about the potential benefits of EM in the ICU, their attitudes regarding the application of this technique in the ICU and perceived barriers to the performance of EM. The items were answered on a 5-point Likert scale with the following options: "I fully agree", "I agree", "I neither agree nor disagree", "I disagree" and "I fully disagree".

Early mobilization was defined as any activity performed beyond the range of motion within 48 hours of the onset of MV. Experience with EM and availability of an EM protocol in the ICU were defined as present when the respective responses to the following questions were "yes": (1) "Have you had training in, have you worked at or do you work at an institution where patients under MV are actively mobilized?"; and (2) "Has an EM protocol been implemented at the ICU where you work?"

The right answers to the questions investigating knowledge about EM were defined before the onset of the survey. The answers "I disagree" and "I fully disagree" were considered the right ones for the question "Does range of motion suffice to maintain muscle strength in the ICU?" The answers "I agree" and "I fully agree" were considered the right ones for the item on whether EM is associated with a shorter duration of MV. For the remainder of the items, positive responses were "I agree" or "I fully agree" and negative answers were "I neither agree nor disagree", "I disagree" or "I fully disagree".

The questionnaire for physicians included a non-hierarchical list of potential barriers to mobilization in the ICU, including the option "other (specify)", as follows: (1) duration of nursing procedures, (2) duration of respiratory physical therapy, (3) availability of physical therapists, (4) patient undergoing procedures, (5) excessive sedation, (6) mobility is irrelevant in the ICU, (7) *delirium*, (8) access to specialized equipment, (9) personal safety, (10) patient safety, (11) cost and (12) therapy is not performed although it is recommended. The questionnaires for nurses and physical therapists also included a list, with the following items: (1) risk of musculoskeletal self-injury, (2) fatigue, (3) excessive stress at work, (4) need to work overtime, (5) other (specify). In both questionnaires, the professionals could mark any number of options they considered appropriate and add other items they held to represent potential hindrances to EM in the ICU.

The participants were given 1 month to respond to the questionnaire from the moment it was sent. An e-mail reminding the participants to respond to the questionnaire was sent one week before the deadline. To ensure that no participant would be included in the survey twice, e-mail addresses were checked against the list of participants' e-mail addresses. The questionnaires were answered anonymously and on a voluntary basis.

Descriptive statistics were performed to characterize the sample. The responses given on the Likert scale ware expressed as absolute frequencies and proportions. The chi-square test was used to investigate whether the physicians' responses differed as a function of their educational level (medical residency versus master's degree versus doctoral degree). Fisher's exact test was used to investigate significant differences in the nursing staff's responses as a function of their educational level (nursing technicians versus nurses), previous experience with EM for physicians, nursing professionals and physical therapists (yes versus no), and years of experience (< 5 years versus ≥ 5 years) for nursing professionals and physical therapists. The significance level was set at $p < 0.05$. The data were stored and analyzed using SPSS software for Windows, version 18.0.

RESULTS

Both participating institutions were university-affiliated hospitals, and the ICU types were as follows: clinical-surgical (n = 3), pneumological (n = 1), oncological (n = 1) and transplant (n = 1). A total of 514 professionals were invited to participate, including 154 physicians, 293 nursing professionals and 67 physical therapists.

Results relative to the questionnaire for physicians

Twenty-two physicians responded to the questionnaire, corresponding to a response rate of 14% (22/154). All the physicians were intensivists, and medical residency was the most prevalent educational level (Table 1). Most physicians reported having had previous experience with EM and responded that range of motion is insufficient to preserve the muscle strength of critically ill patients (n = 12; 55%) and that EM shortens the length of MV (n = 19; 86%) (Table 2), without any significant differences according to educational level or previous experience with EM.

Table 1 - Professionals' characteristics and experience with early mobilization

	n (%)
Physicians	n = 22
Medical residency	11 (50)
Master's degree	5 (23)
Doctoral degree	6 (27)
Experience with EM	19 (86)
Nursing team*	n = 61
< 5 years of experience in the ICU	8 (13)
≥ 5 years of experience in the ICU	53 (87)
Experience with EM	34 (56)
Physical therapists	n = 15
< 5 years of experience in the ICU	4 (27)
≥ 5 years of experience in the ICU	11 (73)
Experience with EM	11 (73)

EM - early mobilization; ICU - intensive care unit. * 32 (53%) nurses and 29 (47%) nursing technicians.

Twenty-one (95%) physicians agreed that the benefits of EM exceed the risks for patients under MV (Table 3). Most physicians stated they would allow EM for patients under MV (n = 20; 91%) and that they would agree to change the MV parameters (n = 19; 86%) and reduce the level of sedation to enable EM (n = 21; 95). Ten (45%) physicians did not agree with EM for patients receiving vasoactive drugs. Eighteen out of 22 physicians who responded to the questionnaire stated that EM should be routinely performed via nursing and physical therapy protocols unless explicitly contraindicated. The responses did not significantly differ in regard to educational level or previous experience with EM. The barriers to EM most frequently indicated by the physicians are described in figure 1A.

Table 2 - Knowledge about the potential benefits of early mobilization in the adult intensive care unit per professional category and educational/training level

	Disagreed n (%)
ROM suffices to preserve muscle strength in the ICU	52 (53)
Physicians	p = 0.284
Medical residency (n = 11)	6 (55)
Master's degree (n = 5)	4 (80)
Doctoral degree (n = 6)	2 (33)
Nursing team*	p = 0.255
< 5 years of experience in the ICU (n = 8)	2 (25)
≥ 5 years of experience in the ICU (n = 53)	28 (53)
Physical therapists	p = 0.560
< 5 years of experience in the ICU (n = 4)	2 (50)
≥ 5 years of experience in the ICU (n = 11)	8 (73)

	Agreed n (%)
Early mobilization shortens the length of MV	81 (83)
Physicians	p = 0.099
Medical residency (n = 11)	8 (73)
Master's degree (n = 5)	5 (100)
Doctoral degree (n = 6)	6 (100)
Nursing team*	p = 0.762
< 5 years of experience in the ICU (n = 8)	7 (88)
≥ 5 years of experience in the ICU (n = 53)	40 (75)
Physical therapists	**
< 5 years of experience in the ICU (n = 4)	4 (100)
≥ 5 years of experience in the ICU (n = 11)	11 (100)

ROM - range of motion; ICU - intensive care unit; MV - mechanical ventilation. * 32 (53%) nurses and 29 (47%) nursing technicians. p-value calculated by means of the chi-square test to compare educational level between agreement and disagreement among physicians, and by means of the Fisher's exact test to compare years of experience in the intensive care unit between agreement and disagreement among nurses and physical therapists. ** p-value was not calculated because the variable is a constant.

Results relative to the questionnaire for the nursing staff

Sixty-one members of the nursing team responded to the questionnaire, corresponding to a response rate of 21% (61/293). Of these, 29 (47%) were nursing technicians. Most nursing professionals reported having more than 5 years of experience in the ICU, and most nurses had a specialization in intensive care (n = 33; 43%). Twenty-seven (44%) respondents reported no previous experience with EM in the ICU (Table 1). Half of this group stated that range of motion is insufficient to preserve the muscle strength of critically ill patients (n = 30; 49%), and most stated that EM shortens the length of MV (n = 47;

Table 3 - Physicians' attitudes relative to the indication of early mobilization in the adult intensive care unit per educational level

Instrument item	Agreed n (%)
The benefits of EM exceed the risks for patients under MV	p = 0.488
Medical residency (n = 11)	10 (91)
Master's degree (n = 5)	5 (100)
Doctoral degree (n = 6)	6 (100)
I would agree with the EM of patients receiving vasopressors	p = 0.674
Medical residency (n = 11)	5 (45)
Master's degree (n = 5)	3 (60)
Doctoral degree (n = 6)	4 (67)
I would agree with the EM of patients under MV	p = 0.428
Medical residency (n = 11)	10 (91)
Master's degree (n = 5)	4 (80)
Doctoral degree (n = 6)	6 (100)

EM - early mobilization; MV - mechanical ventilation. p-value calculated by means of the chi-square test to compare educational level between agreement and disagreement.
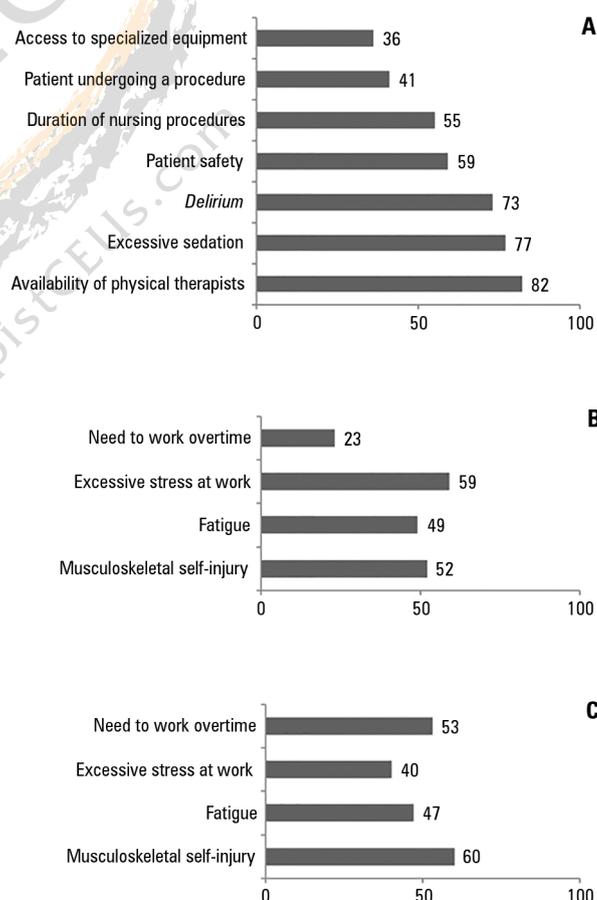

Figure 1 - Barriers reported by the professionals (A - physicians; B - nurses and nursing technicians; C - physical therapists) to early mobilization of critically ill adult patients.

Table 4 - Nursing professionals' and physical therapists' attitudes relative to the indication of early mobilization in the adult intensive care unit per educational/training level

Instrument item	Agreed n (%)
The benefits of EM exceed the risks for patients under MV	56 (74)
Nursing team*	p = 0.049
< 5 years of experience in the ICU (n = 8)	8 (100)
≥ 5 years of experience in the ICU (n = 53)	34 (64)
Physical therapists	p = 1.0
< 5 years of experience in the ICU (n = 4)	4 (100)
≥ 5 years of experience in the ICU (n = 11)	10 (91)
I agree that I have enough time to help mobilize a patient under MV once per day	48 (63)
Nursing team*	p = 0.698
< 5 years of experience in the ICU (n = 8)	6 (75)
≥ 5 years of experience in the ICU (n = 53)	32 (60)
Physical therapists	p = 0.077
< 5 years of experience in the ICU (n = 4)	1 (25)
≥ 5 years of experience in the ICU (n = 11)	9 (82)
I agree that the benefits of EM for patients under MV exceed the risks for the staff	56 (74)
Nursing team*	p = 0.091
< 5 years of experience in the ICU (n = 8)	8 (100)
≥ 5 years of experience in the ICU (n = 53)	35 (66)
Physical therapists	p = 0.476
< 5 years of experience in the ICU (n = 4)	3 (75)
≥ 5 years of experience in the ICU (n = 11)	10 (91)

EM - early mobilization; MV - mechanical ventilation; ICU - intensive care unit. * 32 (53%) nurses and 29 (47%) nursing technicians. p-value calculated by means of the Fisher's exact test to compare years of experience in the intensive care unit between agreement and disagreement among nurses and physical therapists.

77%) (Table 2). The responses did not significantly differ according to years of experience in the ICU, educational level or previous experience with EM.

Most nursing professionals agreed that the benefits of EM exceed the risks for patients under MV (n = 42; 69%). Nursing staff with more than 5 years of experience in the ICU were more likely to agree that the benefits of EM exceed the risks for patients under MV (p = 0.049) (Table 4). Most respondents stated that they had enough time to help mobilize patients under MV (n = 38; 62%) and that the benefits of EM for patients under MV exceed the risks to the team's personal and professional safety (n = 43; 70%). The nursing technicians were less likely to agree that they had enough time to help mobilize patients under MV compared with the nurses (n = 14; 48% and n = 24; 75%, respectively; p = 0.038). The responses did not differ regarding the respondents' previous experience with EM.

The barriers to EM most frequently indicated by the nursing professionals are described in figure 1B.

Results relative to the questionnaire for the physical therapists

Fifteen physical therapists responded to the questionnaire, corresponding to a response rate of 22% (15/67). Most respondents (73%) reported having more than 5 years of experience in the ICU and previous experience with EM (Table 1), being that the largest proportion had a specialization in intensive care (n = 7; 47%). Most physical therapists stated that range of motion is insufficient to preserve the muscle strength of critically ill patients in the ICU (n = 10; 67%), and all agreed that EM shortens the length of MV (Table 2), without differences according to years of experience in the ICU or previous experience with EM.

Almost all the physical therapists agreed that the benefits of EM exceed the risks for patients under MV (n = 14; 93%), and that the benefits of EM for patients under MV exceed the risks to the team's personal and

professional safety (n = 13; 87%). Most respondents (n = 10; 67%) stated that they had enough time to help mobilize patients under MV (Table 4). The responses did not differ regarding years of experience in the ICU. The physical therapists with previous experience with EM were more likely to agree that the benefits of EM for patients under MV exceed the risks to the team's personal and professional safety (p = 0.050).

The barriers to EM most frequently indicated by the physical therapists are described in figure 1C.

DISCUSSION

Among the main findings of the present study conducted in the ICU of two Brazilian teaching hospitals, we highlight that most members of the multi-professional team had knowledge about the potential benefits of EM, including the maintenance of muscle strength and a shorter duration of MV, and that most participants agreed that the benefits of EM exceed the risks to patients under MV. Similar results were reported in a previous study[15] that analyzed the knowledge and attitudes of multi-professional health team members involved in care delivery to critically ill patients.

Most physicians agreed on the EM of patients under MV; however, only half of them agreed on indicating EM for patients receiving vasoactive drugs. The physicians stated they would change the MV parameters and reduce sedation to enable the EM of patients.[15] Approximately two-thirds of the physical therapists and nursing professionals stated they had sufficient time to help mobilize patients under MV once per day. Most physical therapists and nursing professionals agreed that the benefits of EM for patients under MV exceed the risks to the team's personal and professional safety. Nursing technicians were less likely to agree that they had sufficient time to help mobilize patients under MV once per day compared to nurses. The barriers to EM most frequently cited by physicians were the unavailability of professionals on the team and of sufficient time to routinely mobilize patients, excessive sedation and *delirium*.[15,17] Risk of musculoskeletal self-injury and excessive stress at work were also mentioned by nurses and physical therapists as barriers to EM.

The findings of the present study confirm the hypothesis that there is a gap between evidence-based knowledge and its application in clinical practice. Several authors admit that while knowledge continues to advance, practice remains one step behind.[18,19] The multi-professional participants in the present study exhibited knowledge about the potential benefits of and a favorable attitude toward EM in the ICU but identified several barriers to its actual application in clinical practice. The barriers to EM are patient-related, such as patient symptoms and conditions; structural, such as human and technical resources; related to the ICU culture, including habits and the particular attitudes at each institution; and process-related, from lack of coordination to lack of rules for the distribution of tasks and responsibilities.[20] These multiple barriers were also detected in the present study.

More than 80% of the physicians stated that EM should be routinely performed via nursing and physical therapy protocols, unless explicitly contraindicated. In addition, they stated they would agree to change MV parameters and reduce sedation to enable the EM of patients. Nurse-oriented mobility protocols point to increased mobility and functional benefits for patients.[21,22] However, the workload of the ICU nursing team is admittedly high, which might impact safety and the quality of care delivered.[23,24] These facts confirm the results of the present study, as only 62% of the nurses agreed that they had sufficient time to help mobilize patients under MV once per day.

Although most nursing professionals and physical therapists agreed that they had sufficient time to help mobilize patients under MV once per day, the need to work overtime was one of the main barriers to EM that they mentioned. The unavailability of physical therapists was the main barrier to EM mentioned by the participating physicians. These findings confirm the ICU culture- and process-related barriers already established in the literature.[20]

Several barriers were mentioned by all the groups of participants, including the unavailability of professionals and insufficient time to perform EM with critically ill patients. These barriers were also reported by members of multi-professional teams in the United States[15] and Canada.[17] Time and the professionals required to mobilize critically ill patients might be considerable hindrances to EM in the ICU. In addition, they represent a frequently reported concern in regard to the improvement of the quality of care needed to facilitate the acceptance of mobilization.[12-15] A solution developed at some centers

was to shift the perception and revise priorities in the daily care delivery routine to include mobilization.[1,25,26] Creation and implementation of a dedicated ICU mobility team might also represent an option to increase the mobility of patients and was proven safe and viable. This approach allowed the mobilized patients to get out of bed on 2.5 more days, without any adverse events, resulting in better clinical outcomes and functional independence, in addition to reducing hospital costs.[27]

Concerns about musculoskeletal self-injury, stress and overtime work were barriers mentioned by the nursing professionals and physical therapists who participated in the present study; these findings corroborate the reports in the literature.[15] Although EM was shown to be safe and feasible for patients, there is no information in regard to the staff safety, which might constitute a considerable barrier to EM in the ICU.[28]

Our study has potential limitations. First, the results are subjected to selection bias as a function of the low response rate. Second, the fact that we did not calculate the sample size needed to ensure that the number of participants was sufficient to detect significant differences might have resulted in a type II error in the data analysis. Finally, the responses to the questions investigating "knowledge" might have been influenced by the fact that the literature on EM is scarce and reduced the potential for the generalization of clinical trials on EM. As strengths, the present was the first study that investigated the full

staff that provides care to critically ill patients at academic institutions, including nursing technicians, to better understand interdisciplinary concerns about EM.

CONCLUSION

Most participants had information about the benefits and significance of early mobilization for critically ill patients and exhibited a favorable attitude toward the performance of early mobilization in the intensive care unit. However, they mentioned countless barriers related to the work routine, staff interaction, unit operation and clinical conditions of patients. Early mobilization in the intensive care unit was perceived as a challenge, mainly due to the lack of professionals, insufficient time, excessive sedation, *delirium*, risk of musculoskeletal self-injury and excessive stress at work. We detected considerable barriers to the early mobilization of critically ill adult patients admitted to the intensive care unit. This information might serve to initiate the training of professionals involved in this procedure and in the implementation of institutional protocols.

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Teamwork enables high level of early mobilization in critically ill patients

Abstract

Background: Early mobilization in critically ill patients has been shown to prevent bed-rest-associated morbidity. Reported reasons for not mobilizing patients, thereby excluding or delaying such intervention, are diverse and comprise safety considerations for high-risk critically ill patients with multiple organ support systems. This study sought to demonstrate that early mobilization performed within the first 24 h of ICU admission proves to be feasible and well tolerated in the vast majority of critically ill patients.

Results: General practice data were collected for 171 consecutive admissions to our ICU over a 2-month period according to a local, standardized, early mobilization protocol. The total period covered 731 patient-days, 22 (3 %) of which met our local exclusion criteria for mobilization. Of the remaining 709 patient-days, early mobilization was achieved on 86 % of them, bed-to-chair transfer on 74 %, and at least one physical therapy session on 59 %. Median time interval from ICU admission to the first early mobilization activity was 19 h (IQR = 15–23). In patients on mechanical ventilation (51 %), accounting for 46 % of patient-days, 35 % were administered vasopressors and 11 % continuous renal replacement therapy. Within this group, bed-to-chair transfer was achieved on 68 % of patient-days and at least one early mobilization activity on 80 %. Limiting factors to start early mobilization included restricted staffing capacities, diagnostic or surgical procedures, patients' refusal, as well as severe hemodynamic instability. Hemodynamic parameters were rarely affected during mobilization, causing interruption in only 0.8 % of all activities, primarily due to reversible hypotension or arrhythmia. In general, all activities were well tolerated, while patients were able to self-regulate their active early mobilization. Patients' subjective perception of physical therapy was reported to be enjoyable.

Conclusions: Mobilization within the first 24 h of ICU admission is achievable in the majority of critical ill patients, in spite of mechanical ventilation, vasopressor administration, or renal replacement therapy.

Keywords: Teamwork, Intensive care unit, Mechanical ventilation, Early mobilization, Physical therapy, Perception

Background

Early mobilization referring to initiating physical exercise or mobilization within the early illness phase is an increasingly common practice in intensive care units (ICU) [1]. Yet the definition of early mobilization is rather vague, as it encompasses a wide range of techniques practiced on different ICU populations [2, 3]. Nevertheless, early mobility interventions in critically ill patients prove to be feasible and safe in preventing bed-rest-associated morbidity [4–6], while improving patients' physical function [7], psychological condition [8], and quality of life [9]. Mobilizing patients at an early time point has been associated with reduced health care costs [10], as such intervention decreases invasive mechanical ventilation (MV) duration, delirium [7, 11], and hospital length of stay [12]. Recent observations suggest that providing mobility as early as possible and extending it to weekends could further improve patient outcomes [13–15].

Reported reasons for not mobilizing patients vary widely and include mechanical ventilation [16],

catecholamine infusion [17], impaired consciousness [16], poor functional status [7, 12], safety considerations [9], limited staff capacities, or lack of protocols [18–20]. Safety considerations are indeed crucial in order to prevent additional risks, yet several reported safety issues are instrumental in excluding or delaying intervention in critically ill patients on multiple support systems, whereby this group runs the greatest risk of developing neuromuscular abnormalities.

At the same time, communication [21] and muscular activity [7] remain possible by means of limiting sedation, in line with current recommendations. Nevertheless, there is a lack of data available reporting patients' perceptions in such settings.

In our experience, early mobilization is an integral part of standard care, requiring teamwork combined with either limited sedation or none at all. The primary objective of this study was to demonstrate that early mobilization is feasible in the vast majority of critically ill patients, independently of their severity assessed by the need of MV, high FiO_2, vasopressor doses, or renal replacement therapy (RRT). The secondary objectives included safety of early mobilization, early mobilization rate in MV according to hypoxemia severity and patients' perception. Preliminary data were reported in an Abstract book [22].

Methods

Setting and patients

This was an observational study performed in a tertiary, 14-bed, mixed ICU at Saint-Luc University Hospital. Data were collected from all consecutive patients either already hospitalized in or newly admitted to our ICU between December 1, 2014, and January 31, 2015. The Ethics Committee of the Cliniques universitaires Saint-Luc, Brussels, Belgium, approved the study protocol. A waiver was obtained for written informed consent, given that the described interventions were considered to be part of standard care. Early unwanted effects of mobility, in addition to monitoring data, were anonymously recorded in accordance with Belgian and European law.

Early mobilization and standard care

In accordance with the literature, we define early mobilization as a series of progressive physical activities able to induce acute physiological responses (enhancing ventilation, central and peripheral circulation, muscle metabolism, and alertness) [23] and beginning within 24 h of ICU admission. Our early mobilization protocol includes a few prior contraindications (Fig. 1) [24], such as acute myocardial infarction, active bleeding, increased intracranial pressure with major instability, unstable pelvic fractures, and therapy withdrawal. Moreover, during the morning

medical rounds, a multidisciplinary team (physicians, physical therapists, and nurses) evaluates each patient in order to identify limitations to early mobilization. These include low blood pressure despite increasing dose of vasopressors, severe hypoxemia requiring a rapid increase in FiO_2 or prone position, seizures, and patients' refusal.

According to the routine procedure for basic treatment, ICU team first transfers patients out of their beds. The ensuing physical therapy sessions are then designed as passive, active, or manual resistance exercise; cycle ergometer or leg press training; standing; verticalization by means of a tilt table; standing and assisted walking [25]. Activities are selected depending on patients' consciousness; hemodynamic/respiratory stability, as perceived by the team; as well as patients' preferences and physical capabilities. The complete therapeutic regime included getting out of bed together with physical therapy sessions twice a day. The daily mobilization program is otherwise considered to be incomplete.

Physical therapists are present at the ICU from Monday to Friday (7:30 am–5:00 pm), and the senior physical therapist-to-patient ratio is 1:14. The ratio of physical therapy students to senior physical therapists is 2:1. Furthermore, one resident physical therapist is present in the hospital at all times in case of respiratory emergencies. The nurse to patient ratio is 1:1.6 from 7:30 am to 4:00 pm.

Our standard care program consists in limited sedative administration in order to keep patients dozy and calm (RASS score between −1 and +1), combined with appropriate analgesia. Our preferred mechanical ventilation mode is pressure support, irrespective of hypoxemia severity or ARDS, provided that the protective volume and pressures guidelines were adhered to [26]. Controlled ventilation modes are mainly restricted to patients undergoing prone position or very severe hypoxemia despite PEEP adjustment.

Data collection

All medical and monitoring data were collected on a routine basis using our software of choice (*Qcare* 4.6 Build 154/2, C3 Critical Care Company NV, Sint-Martens-Latem, Belgium), with subsequent analysis performed by means of a data extraction tool. We extracted from our routine database: demographic characteristics, severity scores, monitoring data, early mobilization activities, reasons for not providing such therapy, as well as any adverse events. Predefined adverse events included death, cardiac or respiratory arrest, falls, medical device removal, and abnormal physiological responses requiring activity interruption [27].

For the first patients' transfer to chair, the nurse monitored hemodynamic and respiratory parameters at
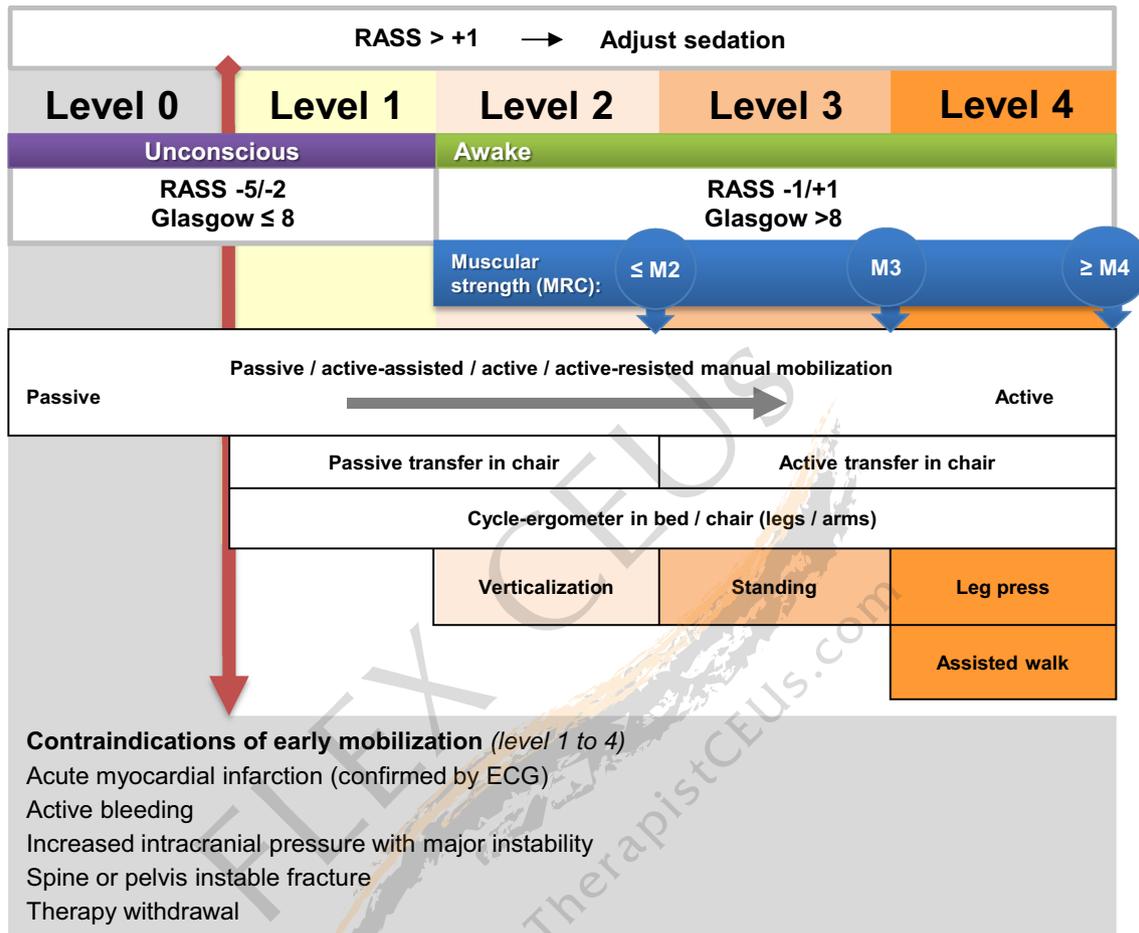
Fig. 1 Early mobilization protocol of ICU at Saint-Luc University Hospital. Modified with authorization [24]

baseline (in bed), and after 5 and 30 min, respectively. Through physical therapy sessions, hemodynamic and respiratory parameters, along with pain scores, were monitored at baseline, as well as at 0 and 15 min afterward, respectively. Pain was assessed in communicative patients on a score of 0 (no pain) to 10 (maximum pain). Patients' perceived exertion was rated from 0 to 10 immediately following physical therapy sessions based on the Borg RPE scale [28], with a similar rating employed to measure perceived enjoyment (0 = no enjoyment, 10 = maximum enjoyment) [29, 30].

Statistical analysis

Analyses were conducted using the software program SPSS software (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, version 20.0. Armonk, NY, USA:

IBM Corp). Study periods were expressed in patient-days in terms of performing early mobilization therapy or lack thereof. Descriptive statistics were conducted for demographic, clinical, and activity data and expressed as mean and standard deviation or confidence interval at 95 % (95 % CI) for normally distributed continuous variables, or as median and interquartile range (IQR) for non-normally distributed continuous variables. Categorical data were summarized using numbers or percentages. Characteristics between mobilized and non-mobilized patients were compared using unpaired Student's t test or Mann–Whitney U test when appropriate. Categorical data were compared with Chi-squared test between groups. One-way repeated measures ANOVA was employed with time as a random factor in order to compare the effect of each activity on hemodynamic and respiratory parameters.

To clearly demonstrate the safety of early mobilization, a multivariate analysis was performed by logistic regression. Adjusted odds ratio (AOR) for 28-day, ICU, and hospital mortality was calculated as follows: Univariate logistic regression analysis was previously performed to identify every numerical instability or collinearity of different factors associated with mortalities. Validated covariates were selected to be entered into a complete multivariate logistic regression model. Variable selection was performed with a method of backward elimination, using a criterion of p value less than 0.20 for retention in the model. Final analysis was performed between covariates reaching a significant p value. Statistical tests were two-sided, and significance was set at the 0.05 probability level.

Results

Population description

In total, 160 consecutive patients were admitted to the ICU over a 2-month period, and 11 others were already being hospitalized at the start of the study period. The overall characteristics of the 171 included patients are presented in Table 1. The mean APACHE II score was 18 ± 7 for the entire ICU population, 20 ± 8 for mechanically ventilated patients, and 22 ± 7 for those affected by severe sepsis or septic shock. Comorbidities were present in 60 % of patients including; active cancer (32 %), end stage cirrhosis (14 %), neurologic disorders (9 %), chronic obstructive pulmonary disease (8 %), and pancreatitis (4 %). MV was provided to 51 % of patients, including 14 % with tracheostomy. Spontaneous modes, principally pressure support, were provided in 96 % of days and controlled modes in only 4 % of the mechanical ventilated population. Remaining patients had oxygenation by mask (13 %), high-flow oxygen therapy (6 %), noninvasive mechanical ventilation (1 %), or nasal cannula (21 %). The mean inspired oxygen fraction (FiO_2) in mechanically ventilated patients was 0.46 ± 0.17. Noradrenaline was the only vasopressor administered, with a mean dose of 0.16 ± 0.23 $\mu g \, kg^{-1} \, min^{-1}$. The primary sedatives employed were propofol (93 %) and clonidine (23 %). Neuromuscular blocking agents were only administered during tracheal intubation maneuvers, as necessary. Sedatives were administered to 84 % of mechanically ventilated patients. The main analgesic medications, namely opioids and paracetamol, were administrated by means of intravenous bolus, patient-controlled analgesia systems, epidural, or oral route.

Early mobilization therapy

Overall, 139 (81 %) patients underwent early mobilization therapy. The median (IQR) delay from ICU admission to patients' first activity was 19 h [15–23]. Seating in a chair was the first activity for 79 % of patients. In these patients, proportion of hypoxemia according to Berlin classification [31] was as follows: without ($n = 33$), mild ($n = 19$), moderate ($n = 40$), and severe ($n = 19$). The 171 ICU admissions translated to 731 patient-days. Subjects displayed protocol exclusion criteria on 3 % of patient-days. Reasons for this included active bleeding ($n = 7$), increased intracranial pressure with major instability ($n = 3$), unstable pelvic fractures ($n = 2$), and therapy withdrawal ($n = 10$). The remaining 709 were considered to be patient-days on which early mobilization was possible, thus accounting for 709 potential bed-to-chair transfers and 1418 potential physical therapy sessions (Fig. 2), according to our protocol. Based on these totals, complete and partial mobility regimes were carried out on 48 and 86 % of patient-days, respectively, and therefore incorporated into the treatment plan of 81 % of admitted patients. Subjects were transferred from their beds to chairs on 74 % of patient-days, with at least one physical therapy session provided on 59 % of patient-days.

Mobilized and non-mobilized patients' characteristics are described in Table 2. MV, vasopressors, and RRT were provided on 46, 30, and 16 % of patient-days, respectively. Patients treated using all the aforementioned support systems were transferred out of their beds on 60 % of patient-days.

Description of early mobilization

Patients were transferred from bed to chair with assistance in standing upright in 60 % of cases. They were manually lifted up by an ICU team in 36 % of cases, with a motorized lift employed in the remaining 4 %. Patients remained in their chairs for a median (IQR) duration of 300 (152–300) min. Hemodynamic variations during the first sitting session did not differ between patients on mechanical ventilation and those without it (Additional file 1).

Active physical therapy sessions were provided to 61 % of cases. Median (IQR) potency during active leg cycle ergometer sessions in seated and lying positions was recorded at 4 [3–5] watts and 3 [3–5] watts, respectively. Median (IQR) durations and RASS scores recorded during each activity are documented in Table 3.

The subjective perceptions of communicative patients were recorded on each physical therapy session (Table 3). Overall exertion ratings were moderate (5 ± 3); however, patients' enjoyment scores following physical therapy sessions were higher, indicating pleasant perceptions of their activity (8 ± 3), with even better values observed after more demanding activities, such as walking or active cycling. It is worth noting that pain was not significantly affected by physical activity.

Table 1 Descriptive patient characteristics

All admissions (n = 171)	Mobilized n = 139	Never mobilized n = 32	p value
Age[a]	59 ± 17	62 ± 17	0.36
Male[b]	80 (58 %)	18 (56 %)	0.99
SOFA score[a]	5 ± 3	8 ± 5	0.01
APACHE II score[a]	17 ± 7	22 ± 9	<0.001
Predicted mortality (APACHE II)	29 %	44 %	0.017
In-hospital mortality[b]	26 (19 %)	16 (50 %)	<0.001
In ICU mortality[b]	11 (8 %)	13 (41 %)	<0.001
28-day mortality[b]	15 (11 %)	15 (47 %)	<0.001
ICU length of stay[a]	6.4 ± 11.7	1.4 ± 2.1	0.017
Vasoactive drug use[b]	47 (34 %)	11 (34 %)	0.99
Sedative drug use[b]	68 (49 %)	13 (41 %)	0.43
Opioids use[b]	86 (62 %)	15 (47 %)	0.16
Renal replacement therapy[b]	12 (9 %)	5 (16 %)	0.32
Admission cause			
Medical[b]	74 (53 %)	15 (47 %)	0.56
Elective surgery[b]	49 (35 %)	9 (28 %)	0.54
Urgent surgery[b]	16 (12 %)	8 (25 %)	0.08

Mechanically ventilated patients (n = 88)	Mobilized n = 69	Never mobilized n = 19	p value
Age[a]	61 ± 16	66 ± 14	0.24
Male[b]	40 (58 %)	12 (63 %)	0.79
SOFA score[a]	7 ± 4	10 ± 5	0.01
APACHE II score[a]	19 ± 7	25 ± 9	0.005
Predicted mortality (APACHE II)	36 %	60 %	0.003
In-hospital mortality[b]	20 (29 %)	13 (68 %)	0.002
In ICU mortality[b]	11 (16 %)	12 (63 %)	<0.001
28-day mortality[b]	10 (14 %)	13 (68 %)	<0.001
ICU length of stay (days)[a]	10.7 ± 15.5	1.7 ± 2.6	<0.001
MV duration (days)[a]	4.9 ± 7.7	1.3 ± 1.1	0.04
Vasoactive drug use[b]	39 (57 %)	10 (53 %)	0.79
Sedative drug use[b]	58 (84 %)	13 (68 %)	0.18
Opioids use[b]	47 (68 %)	9 (47 %)	0.18
Renal replacement therapy[b]	10 (14 %)	5 (26 %)	0.30
PaO$_2$/FiO$_2$ ratio[b]			
>300 (n = 11)	10 (91 %)	1 (9 %)	0.44
201–300 (mild) (n = 13)	9 (69 %)	4 (31 %)	0.46
101–200 (moderate) (n = 42)	34 (81 %)	8 (19 %)	0.61
≤100 (severe) (n = 22)	16 (73 %)	6 (27 %)	0.55

Non-mechanically ventilated (n = 83)	Mobilized n = 70	Never mobilized n = 13	p value
Age[a]	56 ± 17	56 ± 20	0.96
Male[b]	40 (57 %)	6 (46 %)	0.54
SOFA score[a]	4 ± 3	5 ± 5	0.56
APACHE II score[a]	15 ± 6	16 ± 8	0.67
Predicted mortality (APACHE II)	22 %	19 %	0.69

Table 1 continued

Non-mechanically ventilated (n = 83)	Mobilized n = 70	Never mobilized n = 13	p value
In-hospital mortality[b]	6 (8 %)	3 (23 %)	0.14
In ICU mortality[b]	0 (0 %)	1 (8 %)	0.15
28-day mortality[b]	5 (7 %)	2 (15 %)	0.30
ICU length of stay[a]	2.2 ± 1.6	0.8 ± 0.5	<0.001
Vasoactive drug use[b]	8 (11 %)	1 (8 %)	0.99
Sedative drug use[b]	10 (14 %)	0 (0 %)	0.34
Opioids use[b]	39 (56 %)	6 (46 %)	0.55
Renal replacement therapy[b]	2 (3 %)	0 (0 %)	0.99
PaO$_2$/FiO$_2$ ratio[b]			
> 300 (n = 37)	29 (78 %)	8 (22 %)	0.22
201–300 (mild) (n = 22)	19 (86 %)	3 (14 %)	0.99
101–200 (moderate) (n = 16)	15 (94 %)	1 (6 %)	0.44
≤100 (severe) (n = 8)	7 (88 %)	1 (13 %)	0.99

APACHE II acute physiology and chronic health evaluation II score, *SOFA* sequential organ failure assessment score

[a] Values expressed as mean ± SD

[b] Values expressed as number (percentage)

Hemodynamic parameters were recorded for 242 activities, 95 of which carried out by patients on MV while 147 involved no MV (Additional file 2). Heart rate, respiratory rate, or arterial pressure variations observed immediately after active exercises like walking, cycling, or manual mobilization were not clinically significant, returning to baseline values after 15 min. Hemodynamic variations on active mobilization were similar for MV and non-MV patients.

Limiting factors for mobilization activities

Table 4 summarizes the limiting factors for early mobilization. ICU procedures (surgery, medical/nursing intervention, and imaging) were the most common reasons for patients not to perform mobilization activities, followed by physiological instability as perceived by the team, and then patients' refusal. The failure to provide any given physical therapy session was primarily accounted for by staff limitations on weekends, and the same applies to several physical therapist consultations during the week. To a lesser extent, mobilization activities were limited due to patients' refusal, ICU procedures, or physiological instability.

Hemodynamic instability was the most commonly reported physiological limitation to mobility, in patients receiving a mean dose of noradrenaline at 0.31 (95 % CI 0.15–0.47) µg kg^{-1} min^{-1}. Noradrenaline was administered during 361 mobilization activities at a mean dose of 0.10 (95 % CI 0.09–0.11) µg kg^{-1} min^{-1}. Active physical therapy was successfully performed for eight sessions, while the patients were on noradrenaline >0.2 µg kg^{-1} min^{-1} [mean
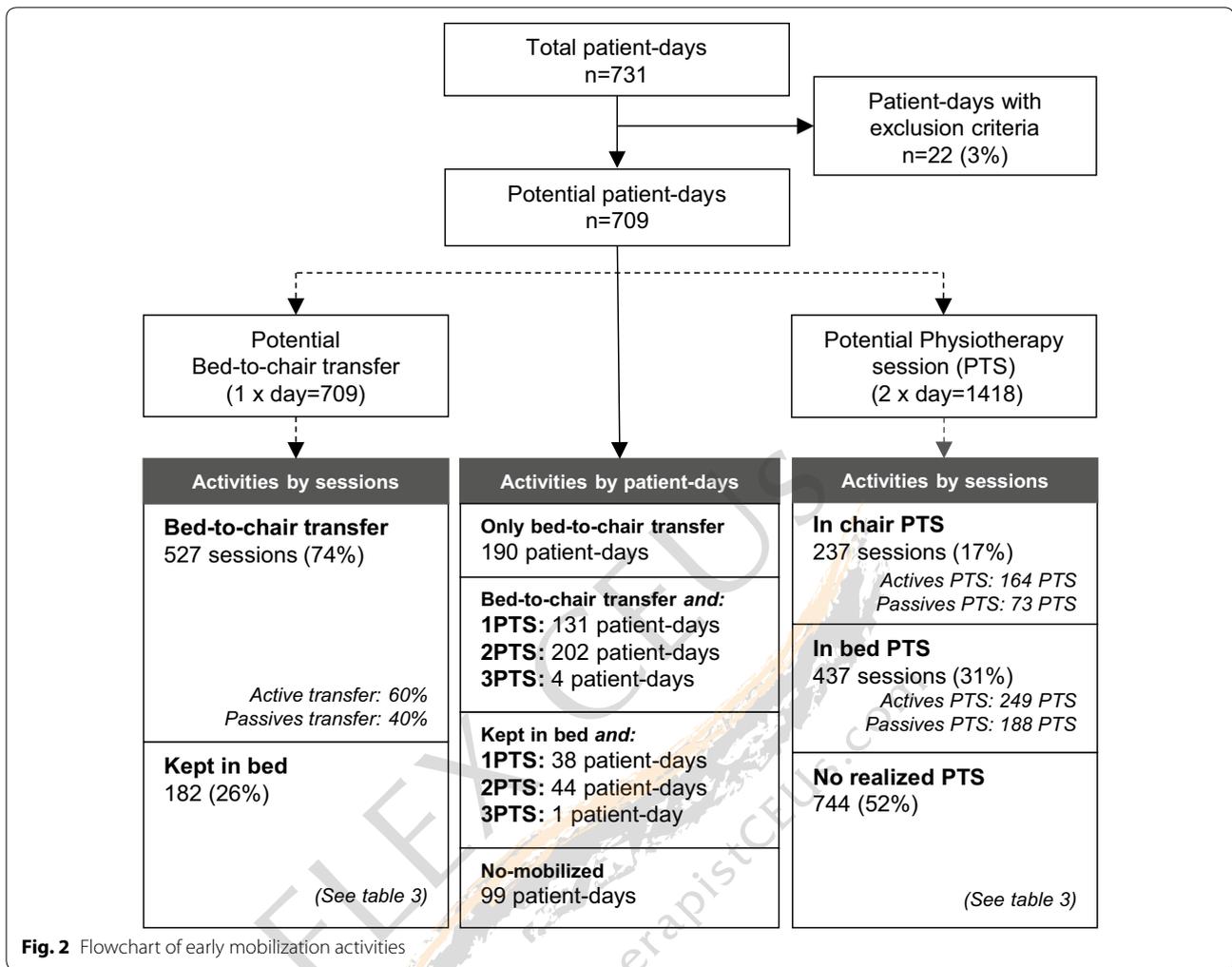
Fig. 2 Flowchart of early mobilization activities

dose: 0.34 (95 % CI 0.11–0.44)] and transfer from bed to chair was performed for 11 sessions in the same condition [mean dose: 0.30 (95 % CI 0.22–0.37)].

The second limiting factor was related to respiratory dysfunction on account of recent intubation/extubation ($n = 12$), prone position ($n = 2$), or occurrence of severe hypoxemia ($n = 19$). In these patients, mean FiO_2 was 0.62 (95 % CI 0.51–0.73). Nevertheless, 78 % of MV patients were successfully mobilized with a mean FiO_2 at 0.47 (95 %CI 0.46–0.49). We carried out 23 active and 49 passive physical therapy sessions with $FiO_2 \geq 0.60$ (mean FiO_2 at 0.83 (95 %CI 0.77–0.88) and 0.71 (95 %CI 0.67–0.76), respectively), as well as 50 bed-to-chair transfers with mean FiO_2 of 0.78 (95 %CI 0.74–0.82). Maximum FiO_2 at 1.0 was observed during 18 mobility activities: nine chair sittings and nine physiotherapy activities.

Adverse events

Activities were discontinued due to medical/nursing procedures in 11 cases and at patient request (pain, high perceived exertion, or digestive transit acceleration) in eight cases. Adverse events occurred in 10 interventions, representing 0.8 % of total mobilizations; hypotension occurred in two patients receiving low-dose vasopressors, hypertension in two, and tachycardia in three. In the sitting position, one patient experienced faintness and was subsequently diagnosed with pulmonary embolism, while another epileptic patient experienced seizures. Moreover, one patient's operative wound exhibited slight oozing after a walking session. All events were reversible following activity interruption, displaying no impact on clinical outcome. There was no evidence of induced tissue hypoxia, as confirmed by means of steady lactate levels after mobilization available for 370 patients-days.

Table 2 Characteristics of mobilized and non-mobilized patients

| | ICU patient-days | EM performed | | | In bed PTS+ | No EM performed |
| | | Sitting in chair | | | | |
		All sitting in chair	PTS+	PTS-		
Total	709	527	337	190	83	99
Invasive mechanical ventilation (MV)	327	223 (68 %)	142 (43 %)	81 (25 %)	40 (12 %)	64 (20 %)
Severe sepsis/sepsis shock	241	166 (69 %)	102 (42 %)	64 (27 %)	28 (12 %)	47 (20 %)
Vasoactive drugs (VAD)	211	149 (71 %)	99 (47 %)	50 (24 %)	25 (12 %)	37 (18 %)
Renal replacement therapy (RRT)	115	76 (66 %)	59 (51 %)	17 (15 %)	11 (10 %)	28 (24 %)
Sedatives (SD)	260	193 (74 %)	122 (47 %)	71 (27 %)	22 (8 %)	45 (17 %)
MV + VAD	158	104 (66 %)	72 (46 %)	32 (20 %)	21 (13 %)	33 (21 %)
MV + VAD + RRT	77	46 (60 %)	38 (49 %)	8 (10 %)	8 (10 %)	23 (30 %)
MV + without SD	122	77 (63 %)	49 (40 %)	28 (23 %)	22 (18 %)	23 (19 %)
RASS −1 to +1	576	454 (79 %)	284 (49 %)	170 (30 %)	58 (10 %)	64 (11 %)
RASS >+1	25	21 (84 %)	18 (72 %)	3 (12 %)	1 (0.4 %)	3 (12 %)
RASS <−1	108	50 (46 %)	33 (31 %)	17 (16 %)	22 (20 %)	36 (33 %)

Values expressed as number (percentage)

MV mechanical ventilation, *VAD* vasoactive drugs, *RRT* renal replacement therapy, *SD* sedatives drug, *RASS* Richmond agitation-sedation scale, *PTS+* physical therapy session carried out, *PTS−* no physical therapy session carried out, *EM* early mobilization

Table 3 Early mobilization activities and patients' perception

| | Total | Duration[a] | RASS[a] | Patient perception (0–10)[b] | | | | n | Fatigue | Enjoyment |
| | | | | Pain | | | | | | |
	n	min	(−5 to +4)	n	Before	0 min	15 min		0 min	0 min
In-bed passive mobilization	151	17 [15–20]	−2 [−4 to 0]	11	4 ± 3	3 ± 3	3 ± 3	11	6 ± 3	8 ± 1
In-bed active mobilization	177	18 [15–22]	0 [0 to 0]	121	4 ± 3	4 ± 3	4 ± 3	108	6 ± 3	7 ± 3
In-bed passive cycling (legs/arms)	37	20 [15–21]	−1 [−4 to 0]	7	2 ± 3	2 ± 3	2 ± 3	7	5 ± 3	8 ± 2
In-bed active cycling (legs/arms)	69	20 [15–22]	0 [0 to 0]	64	2 ± 2	2 ± 2	3 ± 2	65	5 ± 3	9 ± 2
In-bed leg press	3	16 [10–20]	0 [0 to 0]	3	3 ± 1	3 ± 1	3 ± 1	3	5 ± 1	9 ± 1
In-chair sitting	526	300 [152–300]	0 [0 to 0]	–	–	–	–	–	–	–
In-chair passive mobilization	14	15 [12–18]	−2 [−5 to 0]	3	4 ± 4	4 ± 4	5 ± 5	1	3	5
In-chair active mobilization	41	15 [13–20]	0 [0 to 0]	22	4 ± 3	4 ± 3	4 ± 3	16	6 ± 2	6 ± 3
In-chair passive cycling (legs/arms)	59	20 [15–20]	0 [−1 to 0]	9	3 ± 3	4 ± 3	3 ± 3	4	4 ± 1	5 ± 1
In-chair active cycling (legs/arms)	93	20 [15–20]	0 [0 to 0]	74	4 ± 3	4 ± 3	3 ± 3	65	5 ± 3	7 ± 3
In-chair leg press	1	20	0	1	2	2	2	–	–	–
Standing/walking	29	28 [20–40]	0 [0 to 0]	24	2 ± 2	3 ± 3	3 ± 2	23	3 ± 2	9 ± 2

n Patient-days

[a] Values expressed as median [IQR]

[b] Values expressed as mean ± SD

Safety of early mobilization

By multivariate analyses, we were able to assess several risk factors associated with in ICU, 28-day, and in-hospital mortality (Additional file 3). Interestingly, after adjustment for severity covariates, early mobilization was not associated with increased mortality and was identified as a significant protective factor in all multivariate models (AOR (95 % CI): 0.06 (0.01–0.29), $p = 0.001$; 0.13 (0.04–0.47), $p = 0.002$ and 0.31 (0.11–0.91), $p = 0.03$ for ICU, 28-day, and in-hospital mortalities, respectively). Longer ICU length of stay, advanced age, severity of hypoxemia according to Berlin classification, and higher SOFA score were risk factors for ICU mortality. Vasoactive drug use and higher APACHE II score were risk factors for 28-day

Table 4 Limiting factors to early mobilization

	Limiting factors to	
	Bed-to-chair transfer	**Physical therapy sessions**
	182 out of 709 (26 %)	**744 out of 1418 (52 %)**
Patient-dependent limiting factors		
Severe physiological instability	42 (23 %)	42 (6 %)
Hemodynamic instability	21	9
Respiratory instability	5	27
Neurological instability	16	6
Patient refusal	26 (14 %)	62 (8 %)
Patient-independent limiting factor		
ICU interventions	45 (25 %)	49 (7 %)
Surgery (transferred to OR)	16	16
Medical/imaging procedures	17	22
Nurse procedures	12	13
Insufficient staff (weekend)	11 (6 %)	396 (53 %)
Insufficient staff (weekdays)	0 (0 %)	16 (2 %)
No reported physical therapist consultation during week	–	177 (24 %)
Unspecified	58 (32 %)	2 (0 %)

Values expressed as number (%)

OR operative room

mortality. Finally, tracheostomy and higher APACHE II score were identified as risk factors for hospital mortality.

Discussion

This observational study demonstrates the utility of teamwork in successfully carrying out early mobilization, as assessed on 171 consecutive critically ill patients. The study's main observation is that mobility was provided at least once in 81 % of all patients within 24 h of ICU admission. Bed-to-chair transfer was achievable in the vast majority of ICU patient-days. As shown by our study data, a teamwork approach exhibited an excellent safety profile when initiated very early after ICU admission, even in patients on support by vasoactive agents, MV, or RRT. Safety of our early mobilization approach was confirmed through a multivariate analysis taking into account patients' severity. After adjustment, early mobilization was identified not only as safe, but as a significant protective factor.

Despite the growing body of evidence confirming the feasibility, safety, and improved outcome displayed by early mobilization, it still remains a nonstandard and uncommon practice in ICUs. Moreover, initiation times vary significantly in the literature, ranging from 1.5 to 2 days [7, 32] to several days after intubation [9], or even weeks after ICU admission [33, 34]. Furthermore, several reports describe rehabilitation initiation occurring only after ICU discharge due to a lack of physical

therapists or mobility teams within the ICU in question [35, 36]. In a large-scale multicenter cohort study on MV patients, mobility was achieved in only 16 % of overall sessions, reporting intubation and sedation as the primary limiting factors. In this report, authors founded a high incidence of muscular weakness and associated with higher mortality [16]. Furthermore, no clear improvement in outcome has been reported when reinforcement of physical activity was provided only after patients' awakening [37].

Recent expert recommendations on safety criteria for early mobilization mentioned that vasopressor use [38, 39], endotracheal intubation, RRT [38], or even life support devices like ECMO [40] should not be considered as contraindications for active mobilization. Despite that, besides the study of Pohlman et al. [32] performing in-bed mobilization with maximal FiO_2 at 1.0 and vasoactive drug, no study has explored the safety of very early mobilization in critically ill patients on multiple support systems. To date, there is no consensus regarding vasoactive doses or maximum FiO_2, but <0.60 was considered safe for initiating active mobilization [38]. Some authors consider a maximum noradrenaline dose of 0.2 μg kg^{-1} min^{-1} and FiO_2 < 0.55 or 0.60 to be safe [9, 38]. In the protocol at hand, we made a conscious effort to predefine a few contraindications, in order to assess each patient's potential to undergo early activity. Our results demonstrate that mobilizing patients with

higher vasopressor doses and FiO_2 is achievable without increased risks. However, based on our data we are unable to propose theoretical limits to mobilization. Indeed, there is to our view no limiting FiO_2 or vasopressor dose, but rather a stabilized patient's condition with all supports.

Adverse event rates were shown to vary across studies. Pohlman et al. [32] reported the feasibility of early physical therapy and occupational therapy in 90 % of MV patients on life support devices combined with daily sedation interruption. In their study, the mean Apache II score was 20, and mobility was initiated within 1.5 days following intubation, with adverse events occurring in 16 % of overall sessions. In line with other studies, we clearly showed that most patients receiving MV and supportive therapy can be mobi-lized very early, within the first day of ICU admission. Furthermore, such activities were rarely interrupted due to adverse events like hypotension or arrhythmia, while requiring no additional intervention nor causing adverse outcome. We also demonstrated that mobility activities can be performed by patients following major abdominal surgery, patient that are often excluded of clinical trials.

As previously described, providing early mobilization with a high degree of supportive care requires experienced and coordinated multidisciplinary teams [41]. This is a mandatory aspect to ensure patients' security during early mobilization implementation.

Our principal limiting factor for specific physical therapy activities stemmed from staffing capacities, resulting in 28 % of overall weekend and 12 % of weekday physical therapy activities not being performed. This likewise accounted for the low rate of walks, since emphasis was placed on less time-consuming therapies, such as ergometer cycling, in an attempt to mobilize every patient. Based on our data, we estimated the ideal ratio of senior physiotherapists to patients to be 1:7 (including on weekends) in order to achieve the optimal number of daily physical therapy activities. Furthermore, the vast majority of patients were able to be moved out of bed by the nursing team on weekends. This observation confirms that a teamwork- and protocol-driven approach is recommended in order to ensure maximum mobilization, even in the presence of a limited number of physical therapists [19]. Moreover, even if more staff is required to mobilize patients out of bed, seating patients in a chair seems to be more advantageous in the ability to achieve a greater angle of inclination and to remain in a more stable position, compared with semi-recumbent position on bed, with non-additional risks [42].

Deep sedation is usually associated with limited mobility [43]. In our study, it was therefore unsurprising to observe a lower rate of bed-to-chair transfers for patients with a RASS score <-1. Current guidelines on sedation recommend maintaining consciousness with adequate analgesia, which results in a reduction in MV duration [44], vasopressor dosage, and in-hospital mortality [45]. In line with this recommendation, RASS scores in our study primarily ranged between -1 and $+1$, allowing patients to communicate and self-regulate both exercise intensity and duration. In addition, patients were also allowed to refuse mobilization initiation, when expressing their inability to leave their beds or perform any physical activity. This overall approach therefore represents our optimal strategy to individually dose activity intensity and duration, coupled with vital parameter monitoring. In terms of severely ill unconscious patients, passive mobility has previously been reported to be associated with negligible variation in oxygen consumption and hemodynamic parameters [46–48].

Emerging clinical research now takes into consideration the subjective feelings of critically ill patients undergoing physical therapy in order to better dose their activities' intensity [49]. In accordance with such methods, overall exertion values in our population were moderate, coupled with higher perceptions of enjoyment post-exercise. These observations are highly relevant for this new approach of patient-centered outcomes in critical care. Surprisingly, even during the more demanding physical activities, patients reported high enjoyment ratings.

Our study has some limitations. Firstly, this was a single-center study conducted in an ICU with a strong culture of both mobilization and minimal sedation. It may thus prove difficult to extrapolate our results to other centers. Secondly, in line with our observational study design, muscle strength or other functional outcomes were not assessed. Moreover, the protective effect of early mobilization has to be considered as an observation in our study cohort and must be confirmed by a randomized controlled trial. At last, due to the layout of the critical care units in our hospital, we did not include ischemic or heart failure patients in our study.

In conclusion, we observed that early mobilization is achievable and well tolerated in the vast majority of critically ill patients, despite commonly described contraindications such as MV, vasopressor administration, and RRT. It is of great interest to note that patients reported very positive experiences and feelings of well-being following various modalities of physical therapy sessions.
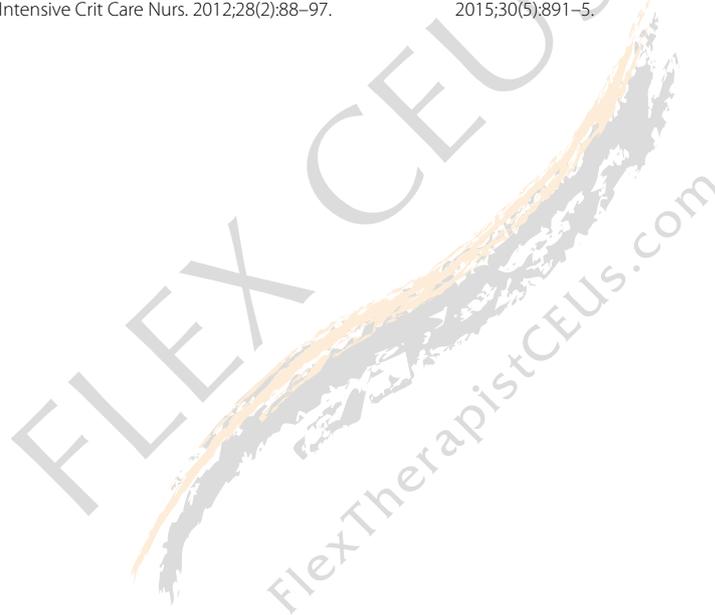
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