

Safety of Early Mobilisation and Rehabilitation in Critically Ill Patients: A Prospective Multicentre Cohort Study

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Abstract

Background

Early mobilisation and rehabilitation have become increasingly integrated into the care of critically ill patients. However, uncertainty remains regarding their safety in patients at increased haemodynamic risk, particularly those requiring vasopressor support. Evaluating safety events during these interventions and their associated factors in routine clinical practice may provide evidence to guide their implementation in this population.

Methods

This prospective multicentre cohort study was conducted in tertiary intensive care units (ICUs). Adult patients undergoing a structured early mobilisation and rehabilitation protocol were included. Patients could contribute multiple mobilisation sessions, resulting in repeated observations within individuals. Clinical characteristics, session-related variables, safety events and mobility levels, assessed using the ICU Mobility Scale (IMS), were recorded. Descriptive statistics were used to summarise the data. Exploratory analyses examined the association between vasopressor use and the occurrence of safety events using generalised estimating equation (GEE) models, with patients specified as the clustering unit to account for within-patient correlation across repeated sessions.

Results

A total of 262 patients (mean age 60 ± 19 years; 52% female) underwent 1,136 mobilisation and rehabilitation sessions. Passive and active in-bed mobilisation accounted for 32.8% and 26.4% of sessions, respectively. Overall, 26 safety events occurred (2.3% of sessions), predominantly oxygen desaturation ($n = 7$), hypotension ($n = 6$), hypertension ($n = 6$) and simple arrhythmias ($n = 5$). No safety event required session termination, and only one necessitated a transient increase in vasopressor support. Vasopressors were administered during 20.4% of sessions. In the overall GEE analysis, vasopressor use was not significantly associated with safety events (odds ratio 1.71; 95% confidence interval 0.81–3.59).

Conclusions

Safety events were infrequent during early mobilisation and rehabilitation in critically ill patients. Most events were transient, and none required session termination. No statistically significant association was observed between vasopressor use and safety events. These findings provide pragmatic data on the occurrence of safety events during mobilisation under the clinical conditions studied, while the observational design limits causal inference.

Background

In critically ill adults admitted to intensive care units (ICUs), prolonged immobilisation has been associated with several short- and long-term complications, including ICU-acquired weakness (ICUAW) (1), loss of muscle mass and strength (2, 3), reduced joint mobility and functional capacity (4, 5), pressure injuries (6), delirium (7, 8) and cognitive impairment (9). Collectively, these complications substantially reduce survivors' quality of life (10). Early mobilisation and rehabilitation have therefore become essential components of comprehensive critical care, aiming to mitigate these complications (11).

The World Health Organization (WHO) defines rehabilitation as a “set of interventions designed to optimise functioning and reduce disability in individuals with health conditions in interaction with their environment” (12). Randomised controlled trials have shown that initiating early mobilisation and rehabilitation within the first 72 hours of ICU admission may improve functional independence and cognitive function, increase ventilator-free and delirium-free days, and reduce hospital length of stay (5, 10, 13). Supporting this approach, a recent clinical practice guideline developed by an expert panel of the European Society of Intensive Care Medicine (ESICM) strongly recommends initiating mobilisation within the first 72 hours of ICU admission (14).

Despite these potential benefits, concerns remain regarding the safety of early mobilisation, particularly in patients receiving vasoactive support or experiencing haemodynamic instability. Although previous studies have suggested that these interventions are feasible and generally safe (4, 7, 15), findings from the randomised controlled *TEAM trial* (16) have renewed international debate by reporting a significantly higher incidence of adverse events in critically ill patients receiving early active mobilisation compared with those receiving usual care (9.2% vs 4.1%, respectively). These findings, together with the limited availability of pragmatic evidence on mobilisation safety at specific vasopressor doses, contribute to variability in clinical practice and may lead to the unnecessary withholding of rehabilitation because of concerns about haemodynamic complications.

In this context, evaluating the safety of early mobilisation in real-world clinical settings is essential to inform patient selection criteria and refine routine clinical protocols. This study aimed to describe the frequency of safety events during early mobilisation and rehabilitation in a cohort of critically ill patients admitted to tertiary ICUs and to explore the association between vasopressor use and the occurrence of these events.

Methods

A prospective, multicentre observational cohort study was conducted in four medical-surgical intensive care units (ICUs) at tertiary healthcare institutions in Bogotá, Colombia, between May and November 2024. The study was approved by the Research Ethics Committee of Fundación Universitaria Sanitas (CEIFUS2972-24) and registered with ClinicalTrials.gov (NCT06653998; first submitted on October 8,

2024, and first posted on October 23, 2024). Written informed consent was obtained from each patient or, when applicable, their legally authorised representative.

Study population

Adult patients (≥ 18 years) admitted to medical-surgical ICUs, with or without mechanical ventilation, were enrolled through consecutive sampling. Patients were excluded if they required extracorporeal membrane oxygenation (ECMO), were in the immediate postoperative period following transplantation, or had clinical contraindications to early mobilisation and rehabilitation. These contraindications included severe haemodynamic instability, acute brain or spinal cord injury requiring strict bed rest, haemoglobin < 8 g/dL, or a platelet count $< 50,000/\mu\text{L}$.

Neither sepsis nor vasopressor use was considered an exclusion criterion in itself. Decisions regarding whether to initiate or defer mobilisation were based on the patient's clinical stability and the recommendations of the consensus statement by Hodgson et al.(17).

Procedure

Physiotherapists from the research team screened patients and assessed their eligibility against the inclusion and exclusion criteria established in the study protocol.

Once eligibility had been confirmed, a member of the research team approached the patient or, if the patient's clinical condition prevented them from providing consent, their legally authorised representative. The study objectives, procedures, potential risks and benefits were explained, and written informed consent was obtained before enrolment.

Following enrolment, baseline demographic and clinical characteristics were recorded, including comorbidities, admission diagnosis, illness severity, and respiratory and haemodynamic support requirements. During each early mobilisation and rehabilitation session, physiotherapists systematically recorded the intervention characteristics, mobility level achieved, physiological variables before and after the intervention, vasopressor support, and occurrence of safety events. Each patient could contribute multiple mobilisation sessions during their ICU stay.

Early Mobilisation and Rehabilitation Protocol

Early mobilisation and rehabilitation were delivered by physiotherapists who had undergone prior training to standardise the use of the *Intensive Care Unit Mobility Scale* (IMS) (18), the grading of physical exertion and the recording of safety events.

Interventions were initiated within the first 72 hours of ICU admission in clinically stable patients. Activity progression was individualised and included passive mobilisation, active in-bed exercises, sitting at the

edge of the bed, standing, transfer to a chair and ambulation. Sessions were interrupted or deferred in the event of significant hypotension, refractory hypoxaemia, unstable arrhythmias, myocardial ischaemia or acute neurological deterioration.

Variables and Outcome Measures

A standardised data collection form was used to record demographic (age and sex), anthropometric (body mass index) and clinical variables (comorbidities, ICU admission diagnosis, Acute Physiology and Chronic Health Evaluation II [APACHE II] score, ICU length of stay and discharge status).

For each mobilisation session, vital signs were recorded before and after the intervention, including heart rate, respiratory rate, peripheral oxygen saturation (SpO₂) and blood pressure. Additional session-level variables included perceived exertion, assessed using the modified 10-point Borg scale; vasopressor support and noradrenaline dose; ventilatory support; intervention duration; and the highest level of mobility achieved, assessed using the ICU Mobility Scale (IMS). The time from ICU admission to the initiation of mobilisation and the total number of sessions performed per patient were also documented.

The primary outcome was the occurrence of safety events, assessed at the session level while accounting for repeated observations within patients. Safety events included cardiac arrhythmias, haemodynamic instability (mean arterial pressure > 120 mmHg or < 50 mmHg), arterial oxygen desaturation (SpO₂ <85% for more than 2 minutes), falls, syncope, cardiac arrest and accidental removal of medical devices (airway devices, chest drains, vascular catheters or tubes) regardless of whether the mobilisation session was terminated.

Secondary outcomes were the total number of mobilisation sessions per patient and the highest level of mobility achieved (IMS). In addition, the association between vasopressor use, including noradrenaline dose, and the occurrence of safety events was explored.

Safety Event Monitoring and Data Management

Data relating to each participant and their mobilisation sessions were entered into a structured Microsoft Excel® database. Each participant was assigned a unique identification code to ensure confidentiality.

Safety events occurring during mobilisation sessions were prospectively recorded by the physiotherapists delivering the interventions. In addition, an independent healthcare professional, who was not involved in the research team or study authorship, actively screened for potentially unreported events by reviewing participants' clinical records, including medical and nursing documentation. Events identified through both sources were consolidated into the study database for analysis.

As part of the quality control process, data were checked for completeness and consistency, missing values and values outside clinically plausible ranges. Any discrepancies were resolved by cross-checking the original clinical records before the database was finalised and statistical analyses were undertaken.

Sample Size

The sample size was calculated *a priori* to estimate the proportion of patients experiencing at least one safety event during early mobilisation. Using Epidat version 4.2 and the method described by Machin et al. (19), the calculation assumed an expected event proportion of 7%, a 95% confidence level, an absolute precision of 5% and a design effect of 1. Based on these assumptions, a minimum sample size of 135 patients was estimated.

Consecutive sampling was used, with all eligible patients enrolled sequentially throughout the recruitment period. Although the sample size calculation was performed at the patient level, the primary safety analysis was conducted at the session level. Multiple sessions contributed by individual patients were treated as repeated observations, and within-patient correlation was accounted for in the association analyses.

Statistical Analysis

Categorical variables were summarised as absolute and relative frequencies, while continuous variables were expressed as means (standard deviations) or medians (interquartile ranges), according to their distribution as assessed using the Shapiro–Wilk test.

The frequency of safety events was calculated using the total number of mobilisation sessions as the denominator. To examine the association between vasopressor use, including dose, and the occurrence of safety events at the session level, generalised estimating equation (GEE) models were fitted using a binomial distribution, logit link function and exchangeable working correlation structure. Patients were specified as the clustering unit to account for within-patient correlation arising from repeated mobilisation sessions. Noradrenaline exposure was categorised as no noradrenaline (reference), low dose ($< 0.05 \mu\text{g/kg/min}$) and moderate-to-high dose ($\geq 0.05 \mu\text{g/kg/min}$).

A complementary patient-level analysis was conducted to examine the association between vasopressor exposure and safety events using the chi-squared test. Odds ratios (ORs) and their corresponding 95% confidence intervals (CIs) were also estimated.

All statistical analyses were performed using R version 4.4.2 (20). A two-sided p value < 0.05 was considered statistically significant.

Results

Participant Flow

Of the 272 patients initially enrolled in the study, 10 were excluded from the analysis because of incomplete clinical records. The final cohort comprised 262 patients who underwent a total of 1,136 early mobilisation and rehabilitation sessions (Fig. 1).

Demographic and Clinical Characteristics

The mean age of participants was 60 ± 19 years, and 52% were female. Overall, 80.5% ($n = 211$) had at least one comorbidity, with hypertension (44.3%, $n = 116$) and cardiovascular disease (35.5%, $n = 93$) being the most common.

The most frequent ICU admission diagnoses were sepsis of any origin (21.8%), postoperative care following abdominal surgery (18.7%) and acute hypoxaemic respiratory failure (13.4%). The mean APACHE II score at admission was 13 ± 6.6 , and the median ICU length of stay was 5 days (interquartile range [IQR] 3–8). ICU mortality was 4.6% ($n = 12$) (Table 1).

Table 1
Sociodemographic and clinical characteristics of patients at ICU admission

Variable	Overall (n = 262)
Demographic characteristics	
Age, years, mean (SD)	60 (19)
Sex, n (%)	
Male	126 (48.1)
Female	136 (51.9)
Body mass index, kg/m ² , median [IQR]	25.0 [23.0–28.0]
Comorbidities, n (%)	
At least one comorbidity	211 (80.5)
Hypertension	116 (44.3)
Cardiovascular disease	93 (35.5)
Obesity	67 (25.6)
Diabetes mellitus	58 (22.1)
Chronic pulmonary disease	36 (13.7)
Chronic kidney disease	33 (12.6)
Neurological disease	31 (11.8)
Diagnosis at ICU admission, n (%)	
Sepsis	57 (21.8)
Postoperative abdominal surgery	49 (18.7)
Type I respiratory failure	35 (13.4)
Postoperative cardiovascular surgery	26 (9.9)
Neurocritical illness	16 (6.1)
Cardiogenic shock	11 (4.2)
Postoperative neurosurgery	10 (3.8)
Coronary syndrome	10 (3.8)
Pre-eclampsia	10 (3.8)
Other diagnoses	38 (14.5)

Variable	Overall (n = 262)
Demographic characteristics	
Clinical characteristics and mobilisation	
ICU length of stay, days, median [IQR]	5 [3–8]
APACHE II score at ICU admission, mean (SD)	13 (6.6)
Number of sessions per patient, median [IQR]	2 [1–4]
Time from ICU admission to mobilisation, days, median [IQR]	2 [1–3]
ICU Mobility Scale, mean (SD)	
Initial IMS	3.0 (2.8)
Final IMS	5.0 (3.4)
ICU discharge status, n (%)	
Alive	250 (95.4)
Died	12 (4.6)

Table note: Data are presented as n (%), mean (SD), or median [IQR], as appropriate. Percentages were calculated using the total study population (n = 262). Comorbidities were not mutually exclusive.

Other diagnoses include conditions recorded in fewer than 10 patients: postoperative neck, thoracic, plastic and reconstructive, and orthopaedic surgery; type II, III, and IV respiratory failure; status epilepticus; diabetic ketoacidosis; electrolyte disturbance; anaphylaxis; polyneuropathy; hypertensive emergency; and acute kidney injury.

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit; IMS, ICU Mobility Scale; IQR, interquartile range; SD, standard deviation.

Characteristics of Mobilisation Sessions and Interventions

Early mobilisation was initiated a median of 2 days after ICU admission (interquartile range [IQR] 1–3). During the study period, 1,136 early mobilisation and rehabilitation sessions were performed, with a median of 2 sessions per patient (IQR 1–4). The most common form of respiratory support was nasal cannula oxygen therapy (44.1%; n = 501), followed by invasive mechanical ventilation (35.4%; n = 402). Overall, 11.7% (n = 133) of sessions were performed without supplemental oxygen, while 409 sessions (36.0%) were conducted during either invasive or non-invasive mechanical ventilation. Regarding airway devices, 28.2% (n = 320) of sessions involved patients with an endotracheal tube, and 15.1% (n = 172) involved patients with a tracheostomy (Table 2).

Table 2
Clinical characteristics, activity level, and safety events across 1,136 mobilisation sessions in the ICU

Variable	Sessions (n = 1,136)
Oxygen delivery system, n (%)	
Nasal cannula	501 (44.1)
Invasive mechanical ventilation	402 (35.4)
Venturi mask	52 (4.6)
High-flow nasal cannula	28 (2.5)
Simple oxygen mask	13 (1.1)
Non-invasive ventilation	7 (0.6)
No supplemental oxygen	133 (11.7)
Airway device, n (%)	
Endotracheal tube	320 (28.2)
Tracheostomy	172 (15.1)
None	644 (56.7)
Nutritional support, n (%)	
Enteral nutrition	388 (34.2)
Oral intake	351 (30.9)
Parenteral nutrition	189 (16.6)
Mixed enteral/parenteral nutrition	27 (2.4)
No nutritional support	181 (15.9)
Maximum activity achieved, n (%)	
Passive mobilisation in bed	373 (32.8)
Active mobilisation in bed	300 (26.4)
Ambulation	139 (12.2)
Active transfer to chair	113 (9.9)
Marching on the spot	103 (9.1)
Passive transfer to chair	37 (3.3)
Sitting on the edge of the bed	35 (3.1)

Variable	Sessions (n = 1,136)
Oxygen delivery system, n (%)	
Seated leg cycle ergometry	29 (2.6)
In-bed leg cycle ergometry	7 (0.6)
Activity duration, min, mean (SD)	17.6 (4.6)
Modified Borg Rating of Perceived Exertion, mean (SD)	3.3 (1.7)
Physiological parameters, mean (SD)	
Heart rate, beats/min	
Initial	81.0 (17.8)
Final	87.0 (17.9)
Respiratory rate, breaths/min	
Initial	18.6 (3.4)
Final	20.6 (4.0)
Oxygen saturation, %	
Initial	93.5 (2.8)
Final	93.7 (2.7)
Systolic blood pressure, mmHg	
Initial	116 (18)
Final	120 (19)
Diastolic blood pressure, mmHg	
Initial	65 (6)
Final	66 (5)
Safety events, n (%)	26 (2.3)

The most frequently performed activities were passive in-bed mobilisation (32.8%; n = 373) and active in-bed mobilisation (26.4%; n = 300). A total of 726 sessions (63.9%) involved active patient participation, including more functionally demanding activities such as ambulation (12.2%; n = 139), active transfer to a chair (9.9%; n = 113) and marching on the spot (9.1%; n = 103). The mean ICU Mobility Scale (IMS) score increased from 3.0 ± 2.8 at baseline to 5.0 ± 3.4 at ICU discharge.

Safety Events

A total of 26 safety events were recorded across the 1,136 mobilisation sessions analysed (2.3%). These events occurred in 21 patients. The most frequent events were oxygen desaturation (n = 7; 26.9%), hypotension (n = 6; 23.1%) and hypertension (n = 6; 23.1%), followed by simple arrhythmias (n = 5; 19.2%) and sinus tachycardia (n = 2; 7.7%). No event required session termination, and most resolved spontaneously. One episode of hypotension in a patient with sepsis required a transient increase in vasopressor support (Table 3).

Table 3

Clinical characteristics of safety events recorded during early mobilisation and rehabilitation sessions (n = 26)

Type of safety event	n (%)	Predominant clinical context	Resolution/clinical consequence
Arterial oxygen desaturation	7 (26.9)	Sepsis, acute hypoxaemic respiratory failure, postoperative cardiovascular surgery, and pre-eclampsia	Spontaneous recovery
Arterial hypotension	6 (23.1)	Sepsis	Spontaneous resolution; one event required a transient increase in vasopressor support
Arterial hypertension	6 (23.1)	Postoperative abdominal surgery	Spontaneous resolution
Simple arrhythmia	5 (19.2)	Postoperative abdominal and orthopaedic surgery, including hip/femur fracture reduction	Transient event with spontaneous resolution
Sinus tachycardia	2 (7.7)	Acute hypoxaemic respiratory failure	Spontaneous resolution
Total	26 (100.0)	—	One event required modification of vasopressor support

Note: Percentages are based on the total number of safety events recorded (n=26). None of the safety events required interruption of the mobilisation session.

According to intervention type, 14 events occurred during 410 passive mobilisation sessions (3.4%), compared with 12 events during 726 sessions involving active patient participation (1.7%). Of all safety events, 50.0% (n = 13) occurred during passive in-bed mobilisation, followed by active in-bed mobilisation (n = 7; 26.9%), marching on the spot (n = 4; 15.4%), passive transfer to a chair (n = 1; 3.8%) and sitting at the edge of the bed (n = 1; 3.8%) (Fig. 2). Furthermore, 13 of the 26 events (50.0%) occurred during sessions performed under mechanical ventilation.

Safety events occurred across different clinical contexts. Oxygen desaturation was observed primarily in patients with sepsis, acute hypoxaemic respiratory failure, following cardiovascular surgery, and with pre-eclampsia. Haemodynamic disturbances and cardiac rhythm abnormalities were documented mainly in patients with sepsis and following abdominal or orthopaedic surgery. Sessions during which safety events occurred lasted between 10 and 20 minutes (Table 3).

Physiological and Functional Responses During Mobilisation

The mean session duration was 17.6 ± 4.6 minutes. Mean heart rate increased from 81.0 ± 17.8 to 87.0 ± 17.9 beats/min, while respiratory rate increased from 18.6 ± 3.4 to 20.6 ± 4.0 breaths/min. Mean systolic blood pressure increased from 116 ± 18 to 120 ± 19 mmHg, and diastolic blood pressure increased from 65 ± 6 to 66 ± 5 mmHg. Peripheral oxygen saturation remained similar at the beginning and end of mobilisation sessions ($93.5 \pm 2.8\%$ and $93.7 \pm 2.7\%$, respectively). The mean perceived exertion score, assessed using the modified Borg scale, was 3.3 ± 1.7 (Table 2).

Vasopressor Support and Exploratory Analysis of Associated Factors Using GEE

Of the 1,136 mobilisation sessions, 232 (20.4%) were performed during vasopressor support, predominantly with noradrenaline. The most frequently administered noradrenaline dose range was 0.05–0.2 $\mu\text{g/kg/min}$ (56.9%). Vasopressin (0.26%) and inotropic agents (1.7%), primarily milrinone, were used less frequently (Supplementary Table S1).

Among the 232 sessions involving vasopressor support, doses remained unchanged in 210 (90.5%), were reduced in 19 (8.2%), and were increased in two (0.9%). Initiation of additional vasopressor support was recorded in one session (0.4%) (Supplementary Table S1).

Safety events occurred in 3.4% of sessions performed during vasopressor support, compared with 2.0% of sessions without vasopressors. In the generalised estimating equation (GEE) analysis, which accounted for within-patient correlation across repeated mobilisation sessions, vasopressor support was not significantly associated with the occurrence of safety events (OR 1.71; 95% CI 0.81–3.59; $p = 0.156$).

In the exploratory analysis stratified by noradrenaline dose, sessions performed with doses < 0.05 $\mu\text{g/kg/min}$ were associated with higher odds of safety events than sessions without noradrenaline (OR 3.11; 95% CI 1.27–7.66; $p = 0.013$). No statistically significant association was observed for doses ≥ 0.05 $\mu\text{g/kg/min}$ (OR 0.95; 95% CI 0.29–3.06; $p = 0.930$) (Table 4).

Table 4
Association of vasopressor support with safety events at the session and patient levels

Analysis / exposure	Safety events, n/N (%)	OR (95% CI)	p-value
A. Session-level analysis¹			
No vasopressor	18/904 (2.0)	Reference	—
Any vasopressor	8/232 (3.4)	1.71 (0.81–3.59)	0.156
Norepinephrine dose²			
No norepinephrine	18/904 (2.0)	Reference	—
< 0.05 µg/kg/min	5/83 (6.0)	3.11 (1.27–7.66)	0.013
≥ 0.05 µg/kg/min	3/149 (2.0)	0.95 (0.29–3.06)	0.930
B. Patient-level analysis³			
No vasopressor exposure	18/170 (10.6)	Reference	—
Vasopressor exposure	8/92 (8.7)	0.81 (0.33–1.98)	0.625

Note: Session-level associations were estimated using generalized estimating equations (GEE) with a binomial distribution and logit link, specifying patient as the clustering unit and an exchangeable working correlation structure to account for repeated mobilisation sessions within patients. For the norepinephrine analysis, sessions without norepinephrine were used as the reference category. Patient-level vasopressor exposure was defined as at least one mobilisation session performed under vasopressor support during the ICU stay; the association with at least one safety event was assessed using a chi-square test, with ORs and 95% CIs reported. All ORs are unadjusted.

Abbreviations: CI, confidence interval; GEE, generalized estimating equations; OR, odds ratio.

Discussion

The main finding of this prospective multicentre cohort study was the low frequency of safety events during early mobilisation and rehabilitation in critically ill patients. A total of 26 events occurred across 1,136 sessions (2.3%), most of which were transient and resolved spontaneously. None required session termination, and only one episode of hypotension necessitated a transient increase in vasopressor support following mobilisation. The most frequently observed events were oxygen desaturation, hypotension, hypertension, simple arrhythmias and sinus tachycardia.

Mobilisation sessions were accompanied by minor physiological changes, characterised by modest increases in heart rate, respiratory rate and blood pressure, without clinically relevant changes in oxygen saturation. These responses, together with the limited need for therapeutic adjustments, suggest that the interventions were generally well tolerated from a cardiorespiratory perspective under the patient selection and monitoring criteria applied in this study. These findings are consistent with previous

studies which, although conducted in relatively small samples, have provided preliminary evidence supporting the safety of early mobilisation when standardised patient selection and monitoring criteria are applied (21, 22).

The low frequency of safety events observed in our cohort is consistent with previous systematic reviews reporting low rates of adverse events associated with early mobilisation in the ICU (4). However, direct comparisons should be interpreted cautiously because of heterogeneity in safety event definitions, patient characteristics, intervention intensity and progression, and the denominators used to estimate event rates. In our study, safety was assessed across 1,136 mobilisation sessions, allowing events to be characterised during repeated exposures to mobilisation.

Notably, the TEAM trial (16) raised concerns by reporting a higher incidence of adverse events during early active mobilisation in patients receiving invasive mechanical ventilation. However, TEAM evaluated a protocolised early active mobilisation strategy in invasively ventilated patients, whereas our cohort included a broader range of patients and interventions, from passive mobilisation to ambulation, with activity progression tailored to each patient's clinical and functional status. Differences in study populations, intervention intensity, safety criteria and study design therefore limit direct comparisons between the two studies.

An important finding was the distribution of safety events according to intervention type. Fourteen events occurred during 410 passive mobilisation sessions (3.4%), compared with 12 events during 726 sessions involving active patient participation (1.7%). This descriptive difference should not be interpreted as evidence that passive mobilisation carries a higher risk, as the study was not designed to compare safety between intervention types. Confounding by indication may partly explain this observation, since patients requiring passive mobilisation may have greater illness severity, reduced ability to participate and lower physiological reserve than those able to undertake active interventions. These findings highlight the importance of interpreting safety events in the context of patients' clinical condition rather than solely according to the type of mobilisation performed.

As a secondary finding, a descriptive increase in IMS scores was observed during the ICU stay, with patients progressing to more functionally demanding activities, including active transfers to a chair and ambulation. These findings are consistent with previous studies examining functional recovery and the effects of mobilisation and rehabilitation strategies in critically ill patients (23–27). However, given the observational design and absence of a comparator group, the functional changes observed in our cohort cannot be directly attributed to the intervention and should be interpreted as a description of mobility progression during the ICU stay.

An important aspect of this study was the inclusion of patients receiving haemodynamic support, allowing us to assess the safety of early mobilisation in a clinically complex subgroup. Approximately one-fifth of mobilisation sessions were performed in patients receiving vasopressors, predominantly noradrenaline at low to moderate doses, consistent with previous studies (28, 29). After accounting for

within-patient correlation across repeated sessions using generalised estimating equation (GEE) models, vasopressor use was not significantly associated with the occurrence of safety events.

In the exploratory analysis, sessions performed with low-dose noradrenaline ($< 0.05 \mu\text{g/kg/min}$) were associated with higher odds of safety events than those performed without noradrenaline, whereas no such association was observed at doses $\geq 0.05 \mu\text{g/kg/min}$. The absence of a dose–response relationship, together with the small absolute number of events, precludes interpreting this finding as evidence of a causal relationship between noradrenaline dose and safety events. One possible explanation is that patients receiving higher doses may have been selected for less intensive interventions, potentially limiting comparability between groups. In this context, vasoactive support remained stable during most sessions, and dose adjustments following mobilisation were uncommon.

The low overall frequency of safety events observed in our cohort is consistent with the findings of Parada et al. (15), who conducted a systematic review of eight observational studies involving 13,143 patients, five of which were included in the meta-analysis. The authors reported a pooled safety event rate of 2% (95% CI 1–4%), although substantial heterogeneity was observed ($I^2 = 74.9\%$). Therefore, our findings regarding noradrenaline dose should be considered exploratory and hypothesis-generating. They do not establish a specific dose threshold for initiating or withholding mobilisation.

From a clinical perspective, these findings highlight the importance of establishing clearly defined safety criteria for mobilising patients receiving haemodynamic support. Implementing structured protocols that incorporate comprehensive safety assessments before and during mobilisation, together with appropriate monitoring and careful patient selection, may facilitate safe mobilisation in this setting (30, 31). Such assessments should consider not only cardiovascular and respiratory stability but also relevant laboratory parameters and, importantly, their trends over time.

A recent expert consensus on laboratory criteria for early mobilisation proposed incorporating variables such as haemoglobin, platelet count, lactate, blood glucose, the international normalised ratio (INR) and acid–base balance into pre-mobilisation assessments, emphasising the importance of interpreting these parameters within the patient's overall clinical context (32). Rather than considering vasopressor use alone as a contraindication, our findings support a comprehensive assessment of clinical stability, trends in haemodynamic support requirements and the patient's physiological response during mobilisation. Accordingly, our results provide additional evidence supporting the feasibility of early mobilisation in selected critically ill patients receiving vasoactive support. However, these findings should not be extrapolated to patients with haemodynamic instability who were not represented in our study.

Strengths and Limitations

The main strengths of this study include its prospective multicentre design, the large number of mobilisation sessions evaluated and the prospective recording of safety events, supplemented by an independent review of clinical records to identify potentially unreported events. Furthermore, the

inclusion of patients receiving mechanical ventilation and vasopressor support provides relevant evidence regarding the feasibility of early mobilisation in complex critical care settings.

Nevertheless, several limitations should be acknowledged. First, the observational design and absence of a control group preclude establishing causal relationships between early mobilisation and the observed outcomes. Although the study protocol included formal adjudication of the causality and preventability of safety events using predefined criteria, this procedure was not implemented during the study. Consequently, the identified events should be interpreted as safety events occurring during or temporally associated with mobilisation sessions, without formal determination of their causality or preventability.

Second, the small absolute number of safety events limited the statistical power of inferential analyses and precluded robust multivariable adjustment. Furthermore, decisions regarding mobilisation in patients receiving vasopressor support were based on clinical judgement and institutional protocols, introducing potential selection bias. This, together with the absence of adjustment for illness severity and mobilisation intensity, particularly limits the interpretation of the exploratory associations observed across noradrenaline dose categories.

Outcomes were assessed only during the index hospitalisation and up to discharge. Operational differences between participating centres cannot be excluded. In addition, mobilisation interventions encompassed activities with varying levels of functional complexity and physiological intensity, ranging from passive mobilisation to ambulation. This heterogeneity may have influenced the occurrence of safety events and was not specifically accounted for in the GEE models, potentially introducing residual confounding into the exploratory analyses. Finally, definitions of early mobilisation remain heterogeneous across the literature, which may limit comparisons between studies.

These limitations highlight several priorities for future research. Further studies should adopt standardised definitions of safety events, incorporate formal procedures for adjudicating event causality and severity, and include sufficient events to support adjusted models that simultaneously account for patient characteristics and session-specific factors. Future research should also investigate the relationships between vasopressor dose and its temporal trajectory, mobilisation intensity and the occurrence of safety events. Such studies may help refine patient selection criteria and intervention progression protocols while avoiding the establishment of universal vasopressor dose thresholds based solely on exploratory associations.

Conclusions

In this prospective multicentre cohort study, safety events were infrequent during early mobilisation and rehabilitation in selected critically ill patients, occurring in 2.3% of mobilisation sessions, and none required session termination. Overall vasopressor support was not significantly associated with safety events after accounting for repeated sessions within patients. The exploratory findings according to noradrenaline dose do not support the use of a specific dose threshold for initiating or withholding

mobilisation. These findings suggest that early mobilisation can be performed in selected critically ill patients receiving haemodynamic support when clinical stability is assessed and appropriate monitoring and safety criteria are applied. Further studies are needed to determine how vasopressor exposure, mobilisation intensity and patient-level factors jointly influence the risk of safety events.

Declarations

Ethics approval and consent to participate

This study was approved by the Research Ethics Committee of Fundación Universitaria Sanitas (CEIFUS2972-24) and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from each participant or, where applicable, their legally authorised representative before enrolment.

Consent for publication

Not applicable.

Availability of Data and Materials

The datasets generated and analysed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' Contributions

HMPG: Conceptualisation, methodology, writing – review and editing, and visualisation.

JB, MPD, NR, DSV, JEM, FAA, AA, MC, CR and MO: Delivery of interventions and data collection.

JMA: Delivery of interventions, data collection, writing – review and editing.

PMM.: Delivery of interventions, data collection, writing – review and editing.

RM: Methodology, supervision, project administration, and writing – review and editing.

JM-P: Methodology, data curation, formal analysis and validation.

JB-: Methodology, formal analysis and validation.

HG-D: Methodology, validation, and writing – review and editing.

All authors have read and approved the final version of the manuscript and agreed to its submission for publication.

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Figures

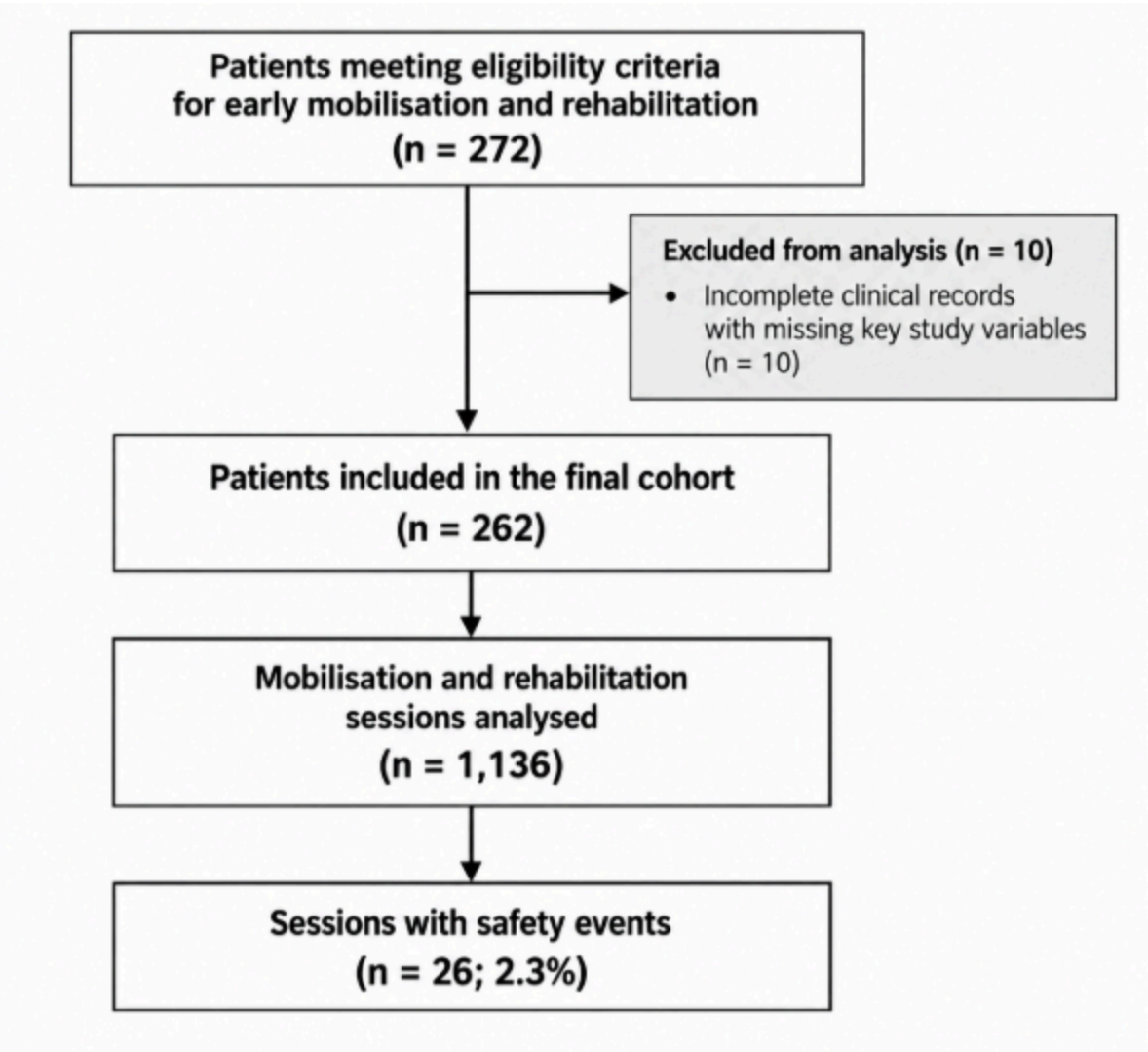


Figure 1

Study flow diagram.

Flow of patients from eligibility assessment to inclusion in the final cohort and analysis of mobilisation and rehabilitation sessions and safety events. Ten patients were excluded from the final analysis because of incomplete clinical records with missing key study variables.

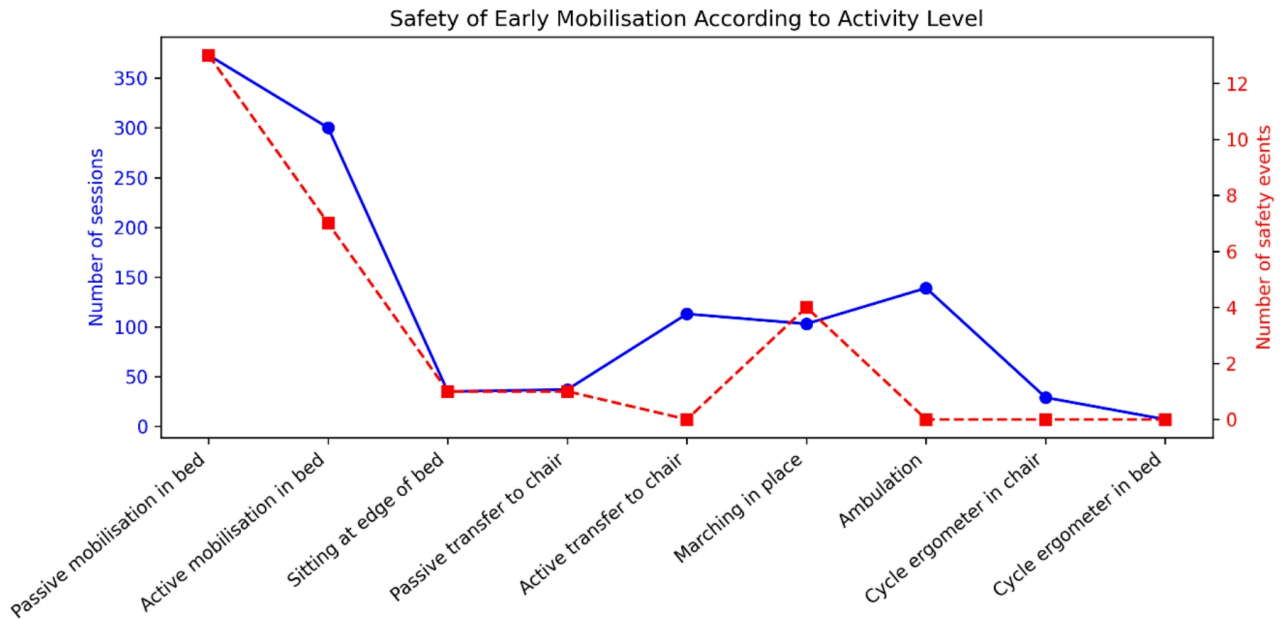


Figure 2

Distribution of mobilisation sessions and reported safety events according to the level of activity achieved.

Note: The solid blue line represents the number of mobilisation sessions (left y-axis), while the dashed red line represents the number of safety events (right y-axis). Data are presented as absolute frequencies.

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