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ORIGINAL ARTICLE

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Effects of mobility dose on discharge disposition in critically ill stroke patients

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Abstract

Background: Mobilization in the intensive care unit (ICU) has the potential to improve patient outcomes following acute stroke. The optimal duration and intensity of mobilization for patients with hemorrhagic or ischemic stroke in the ICU remain unclear.

Objective: To assess the effect of mobilization dose in the ICU on adverse discharge disposition in patients after stroke.

Design: This is an international, prospective, observational cohort study of critically ill stroke patients (November 2017–September 2019). Duration and intensity of mobilization was quantified daily by the mobilization quantification score (MQS).

Setting: Patients requiring ICU-level care were enrolled within 48 hours of admission at four separate academic medical centers (two in Europe, two in the United States).

Participants: Participants included individuals (>18 years old) admitted to an ICU within 48 hours of ischemic or hemorrhagic stroke onset who were functionally independent at baseline.

Interventions: Not applicable.

Nicole Mazwi and India Lissak are co-first authors with equal contribution.

Main Outcome Measure: The primary outcome was adverse discharge disposition.
Results: Of the patients screened, 163 were eligible for inclusion in the study. One patient was subsequently excluded due to insufficient data collection ($n = 162$). The dose of mobilization varied greatly between centers and patients, which could not be explained by patients' comorbidities or disease severity. High dose of mobilization (mean MQS > 7.3) was associated with a lower likelihood of adverse discharge (adjusted odds ratio, [aOR]: 0.14; 95% confidence interval [CI]: 0.06–0.31; $p < .01$).
Conclusion: The increased use of mobilization acutely in the ICU setting may improve patient outcomes.

INTRODUCTION

Stroke is a leading cause of long-term physical disability globally and creates significant challenges for patients and caregivers.[1] Survival among critically ill stroke patients has improved in recent years.[2] As a result, there is a growing patient population with long-lasting physical and neurocognitive sequelae of stroke. These sequalae significantly affect functional independence and quality of life.[3]

Traditionally, rehabilitative efforts aimed at minimizing disability have been primarily undertaken in the postacute setting. More recently, mobilization in critically ill patients has been shown to be safe,[4–8] although studies of efficacy have shown mixed results. A Very Early Rehabilitation Trial after stroke (AVERT), the largest randomized controlled trial of early mobilization after acute stroke in stroke units, found that patients who received very early mobilization (defined as mobilization initiated within 24 hours of hospital admission) had worse functional outcomes at 3 months compared with those who did not.[9] Notably, this study did not include patients in an intensive care unit (ICU) setting. However, a post hoc analysis of the same study cohort found that patients who were mobilized in shorter, more frequent sessions had improved functional outcomes.[10] In addition, a prospective single center study suggested that mobilization is feasible and safe in patients after acute aneurysmal subarachnoid hemorrhage and may improve long-term patient outcomes.[11,12] Therefore, we suspect that the varying success in neurocritical care patients may be partly due to unique medical considerations in this population as well as a lack of consensus on the definition, optimal duration and intensity of mobilization.[13,14]

In this study, we sought to determine whether mobilization dose in the ICU could predict adverse discharge disposition in patients with severe ischemic or hemorrhagic stroke. Adverse discharge is defined as discharge to a long-term care facility, skilled nursing facility, swing bed provider (eg, small hospitals that provide skilled nursing facility care), hospice at the patient's home, hospice in a health care facility, or in-hospital mortality. We used the mobilization quantification score (MQS), a mobilization assessment instrument that incorporates duration and intensity, to quantify the daily dose of mobilization.[15]

METHODS

Study design

This was an international, multicenter, observational study of patients with acute stroke in ICUs conducted at four institutions in North America and Europe. Patients were enrolled in Germany, Italy, and two centers in the United States. The research protocol was approved by the institutional review boards (IRBs) of all participating centers.

Participants

We enrolled critically ill patients with ischemic or hemorrhagic stroke meeting the following inclusion criteria: (1) 18 years or older, (2) new onset anterior circulation stroke, (3) symptom onset <48 hours prior to enrollment, (4) expected ICU length of stay (LOS) ≥ 48 hours from the time of screening, and (5) functionally independent at least 2 weeks prior to symptom onset (defined by a Barthel Index score ≥ 70).[16] Patients all received guideline standard of care interventions within their local environments. Although we aimed to be broadly inclusive, we excluded patients who had been transferred from another facility with a stay exceeding 48 hours, patients for whom a goals of care discussion was ongoing and patients with lower extremity amputations. Patients with posterior circulation strokes or traumatic intracranial hemorrhage were also excluded because of the variability of these patients' presentations and courses. Written informed consent was obtained either directly from the patient or through an authorized representative in accordance with local IRB standards. Stroke severity was calculated using the clinical stroke severity score, a single scale to compare patients with both ischemic and hemorrhagic stroke.[17,18]

Power analysis

Although there has been some research conducted on early mobilization of neurocritical care patients, none of these studies provided data compatible to base power calculations for our primary aim. Therefore, for power calculations, we relied on a similar study in surgical ICU patients,[19] while acknowledging the caveat that the two groups of patients (neurocritical vs. surgical ICU) may not reflect the same cohort. We estimated a correlation of 0.25 between mobilization dose and discharge disposition. Using a two-tailed alpha error of 0.05, we calculated that a sample size of 160 patients provides a power of >0.8 for the primary outcome.

Mobility data

The health care team documented the type and duration of daily mobilization for each patient. The definitions of mobilization therapy are provided in Table 1. At all centers, mobilization was prioritized as soon as patients were deemed hemodynamically stable (no significant orthostatic blood pressure or pulse variability when mobilized). Mobility was either physical therapy (PT) or nursing led. PT-directed mobilization was documented separately by physical therapists in the medical record. Nursing-directed mobility was collected daily either from documentation in the medical record or by an interview with the nurse conducted by the research team. The data were then used to calculate the MQS, a measure adopted from the existing ICU mobility scale[20,21] to incorporate both time spent mobilized as well as mobilization level (Table 1). A description and supplemental calculations for the MQS are found in the Data S1.

Outcomes

The primary outcome was adverse discharge disposition, defined as discharge to a long-term care facility, skilled nursing facility, hospice at the patient's home, hospice in a health care facility, or in-hospital mortality. We additionally collected data on secondary outcomes including ICU and hospital LOS, transfer and ambulation subdomains of the mini-modified Functional Independence Measure at ICU and hospital discharge,[22,23] as well as the Glasgow Outcome Scale—Extended[24] and mortality assessed at 90 days following stroke onset (see Data S1).

Data indicative of harm that could possibly be linked to mobilization were also collected from nursing and physician notes. These adverse events were ascertained from the medical record and included worsened neurological deficits, falls, angina, myocardial infarction, deep vein thrombosis, dizziness, and pulmonary embolism.

Primary exposure

The primary exposure was mean daily MQS. Daily MQS from nursing and physical therapy were summed throughout the ICU stay and subsequently divided by the number of daily MQS measurements to arrive at the mean daily MQS. Nonlinearity between the mean daily dose of mobilization and log odds of adverse discharge disposition was detected; thus, the mean MQS was dichotomized to arrive at the exposure variable high versus low mean daily mobilization. The median served as a cutoff for the binary variable high versus low mobilization.

Statistical analysis

A multivariate logistic regression model was used as the primary model to assess whether mobilization dose affects discharge disposition independent of other known confounders: Barthel Index,[16] clinical stroke severity score (calculated as a percent max of the National Institutes of Health Stroke Scale/Functional Outcome in Patients With Primary Intracerebral Hemorrhage scores), Acute Physiology and Chronic Health Evaluation II (APACHE II),[25] and Charleson Comorbidity Index (CCI). The clinical stroke severity score[17,18] was used to compare stroke severity.

To evaluate the performance of the primary model analyzing the effect of high versus low mean mobilization on adverse discharge disposition, we conducted a Hosmer–Lemeshow test as well as calculated the sensitivity, specificity, positive predictive value, and negative predictive value of the model. To further explore the relationship between mobilization dose (as a continuous variable) and outcomes, we used the Youden Index to investigate the optimal mean mobilization dose. We also examined the dose–response relationship between mean MQS and adverse discharge disposition using a generalized linear model. Mean MQS was assessed over the duration of hospitalization to account for LOS.

RESULTS

Patients admitted to an ICU across four institutions were screened from November 2017 to September 2019. Of these, 273 patients were eligible for inclusion, and 163 consented to participate (Figure 1). One patient was excluded from the analysis due to insufficient data collection. The median value of the composite mean daily MQS across the study cohort was 7.3. Patients with a mean MQS < 7.3 were characterized as having a low MQS ($n = 81$), and patients with mean MQS ≥ 7.3 were considered to have a high MQS ($n = 81$). A greater percentage of patients with ischemic stroke (69%) had

TABLE 1 Calculating the mobilization quantification scale (MQS).

SOMS	Modified ICU mobility scale	Mobilization level	Mobilization description	Unit definition	Calculation (level of activity x units)
0	1	Passive range of motion	Passively rolled or passively exercised by health care providers (eg, passive cycling), but not actively moving.	60 min = 1 unit	1 x units
1	1	Active sit/exercise in bed or exercise in chair	Any activity in bed, including rolling, bridging, active exercises, cycle ergometry and active assisted exercises; not moving out of bed or over the edge of the bed.	15 min = 1 unit	1 x units
2	2	Passively to/in chair	Hoist, passive lift, or slide transfer to the chair.	30 min = 1 unit	2 x units
2	3	Sitting on edge of bed	May be assisted by staff, but involves actively sitting over the side of the bed with some trunk control.	5 min = 1 unit	3 x units
3	4	Standing of any kind	Weight bearing through the feet in the standing position, with or without assistance. This may include use of a standing lifter device, tilt table or body-weight supported gait training.	5 min = 1 unit	4 x units
3	5	Active stand-step/ shuffle transfer to chair	Able to step or shuffle through standing to the chair. This involves actively transferring weight from one leg to another to move to the chair. If the patient has been stood with the assistance of a medical device, they must step to the chair (not included if the patient is wheeled in a standing lifter device).	5 min = 1 unit	5 x units
3	6	Step in place >/=4 x or walk <15 ft (5 m)	Able to walk on the spot or less than 15 ft (5 m) by lifting alternate feed (must be able to step at least 4 times, twice on each foot), with or without assistance.	5 min = 1 unit	6 x units
4	7	Walk w/2+ assist >/= 15 ft (5 m)	Walking away from the bed/chair by at least 15 ft (5 m) assisted by two or more people.	5 min = 1 unit	7 x units
4	8	Walk w/1 assist >/= 15 ft (5 m)	Walking away from the bed/chair by at least 15 ft (5 m) assisted by one person.	5 min = 1 unit	8 x units
4	9	Walk independently w/ device >/= 15 ft (5 m)	Walking away from the bed/chair by at least 15 ft (5 m) with a gait aid, but no assistance from another person. In a wheelchair-bound person, this activity level including wheeling the chair independently 15 ft (5 m) away from the bed/chair.	5 min = 1 unit	9 x units
4	10	Walk independently w/o device >/= 15 ft (5 m)	Walking away from the bed/chair by at least 15 ft (5 m) without a gait aid or assistance from another person.	5 min = 1 unit	10 x units

Abbreviation: ICU, intensive care unit; SOMS, surgical intensive care unit optimal mobilisation score.

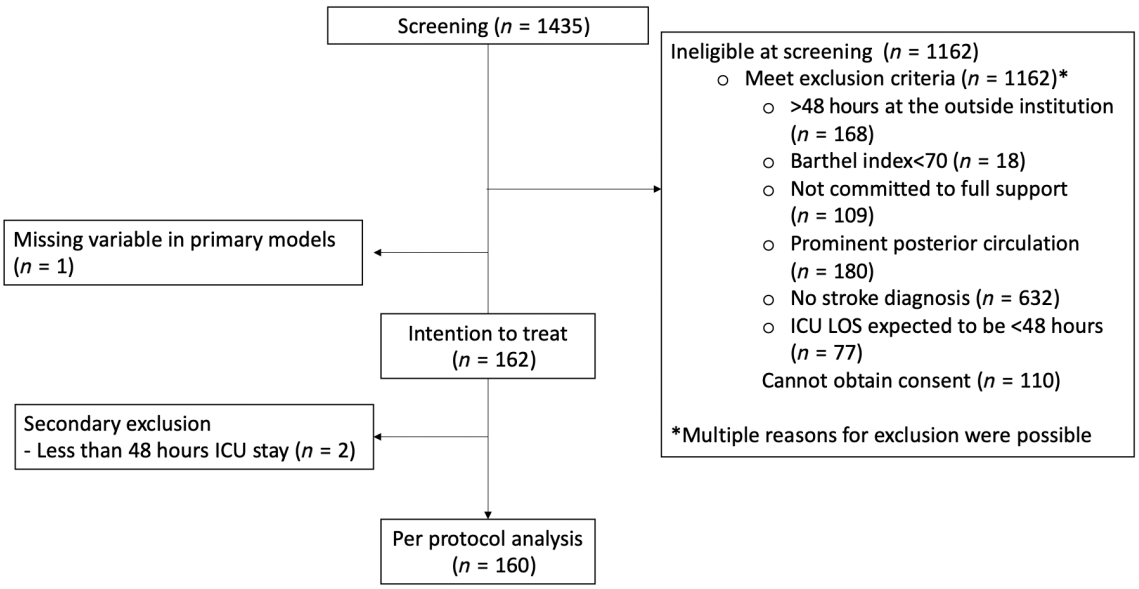

FIGURE 1 CONSORT diagram. CONSORT, Consolidated Standards of Reporting Trials; ICU, intensive care unit; LOS, length of stay.

TABLE 2 Patient characteristics.

Baseline characteristics	Low mobilization dose (mean MQS < 7.3) $N = 81$	High mobilization dose (mean MQS ≥ 7.3) $N = 81$	*p* value
Gender, female, *n* (%)	44 (54%)	39 (48%)	.43
Age, years, mean ± SD	68.3 ± 13.2	66.1 ± 15.5	.33
Body mass index, kg/m^2, mean ± SD	28.1 ± 7.1	27.4 ± 7.2	.50
Type of stroke, *n* (%)			.01
Ischemic	40 (49%)	56 (69%)	
Hemorrhagic	41 (51%)	25 (31%)	
Glasgow coma score at admission, median (IQR)	9 (7,11)	13 (10,14)	<.01
Acute physiology and chronic health evaluation II score, median (IQR)	18 (15,21)	16 (12,20)	.04
Barthel Index, mean ± SD	98.2 ± 4.9	98.7 ± 4.1	.49
% maximum of stroke severity score, mean ± SD	51.3 ± 19.4	44.2 ± 24.4	.04
Charlson comorbidity index, median (IQR)	3 (2,5)	3 (2,5)	.25
Frailty phenotype modified, median (IQR)	0 (0,1)	0 (0,1)	.65

Abbreviations: IQR, interquartile range; MQS, mobilization quantification score.

high MQS compared to patients with hemorrhagic stroke (31%; $p = .01$), but there was no significant difference in adverse discharge disposition between the two groups ($p = .39$). There were significant differences between patients with low versus high MQS with respect to admission Glasgow Coma Scale score ($p < .01$), APACHE II score ($p = .04$), and stroke severity score ($p = .04$), which were subsequently controlled for through multivariable analysis. Among the study population, 112 (69%) had hypertension, 36 (22%) had diabetes, 34 (21%) had atrial fibrillation, 24 (15%) were current smokers, 42 (32%) had a history of smoking, and 47 (29%) had dyslipidemia. Additional baseline characteristics on admission are summarized in Table 2.

Primary analysis

Within the study cohort, 72 (44.4%) patients had adverse discharge disposition. Among patients with a low MQS, 55 (67.9%) had adverse discharge disposition compared to 17 (20.1%) with high MQS (Figure 2). High MQS was associated with lower odds of adverse discharge disposition (odds ratio [OR]: 0.13; 95% confidence interval [CI]: 0.06–0.26; $p < .01$). When adjusting for APACHE II, CCI, and stroke severity score, the association of high MQS with lower likelihood of adverse discharge disposition remained robust (adjusted OR [aOR]: 0.14; 95% CI: 0.06–0.31; $p < .01$).

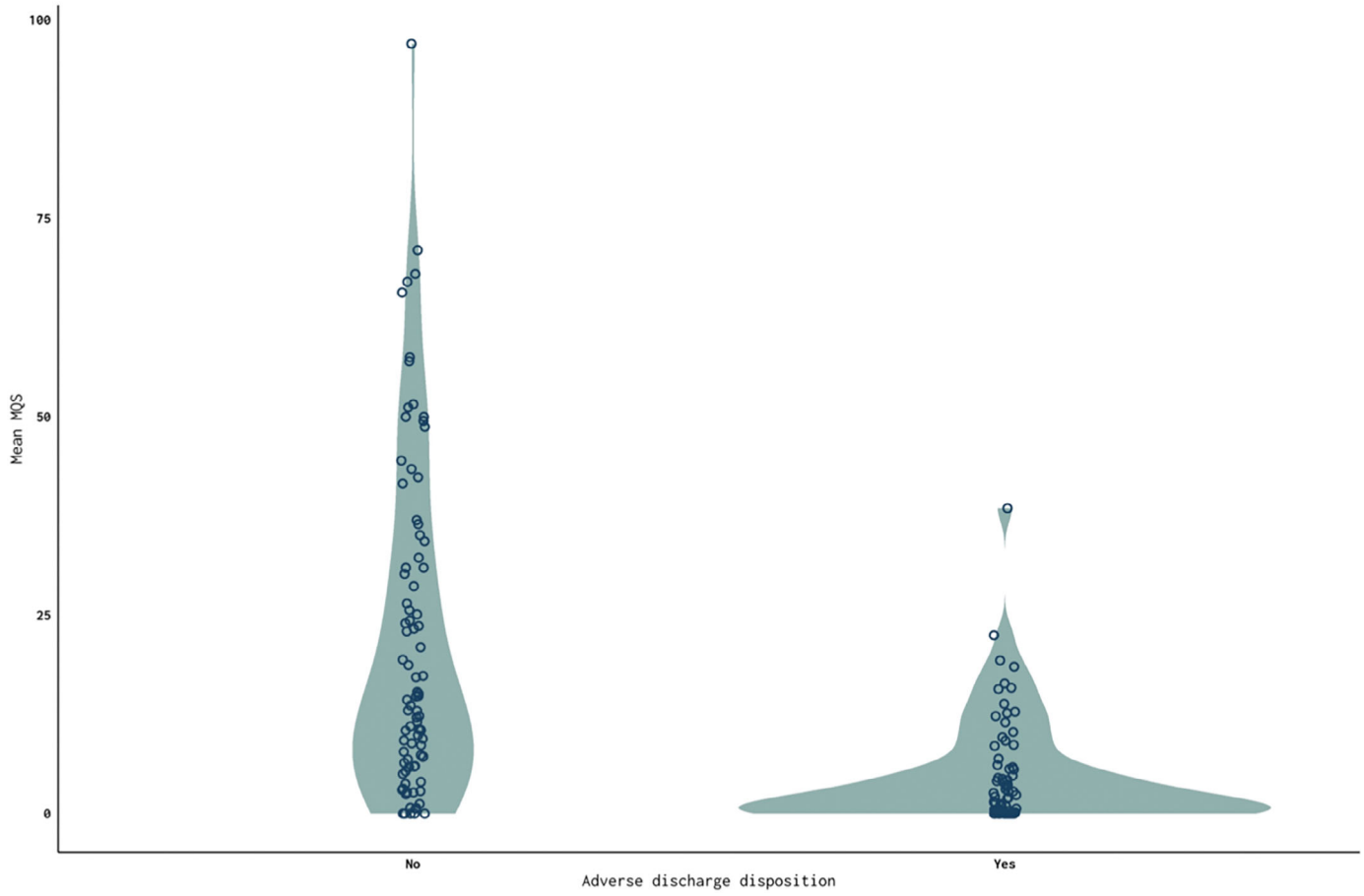

FIGURE 2 Violin plots of mean mobilization quantification score (MQS) during hospitalization for patients with and without adverse discharge disposition. Data points are jittered for improved visualization.

For the outcome adverse discharge disposition, the sensitivity/specificity of high MQS was 71% and 76% respectively, the positive predictive value was 79%, the negative predictive value was 68%, and the area under the receiver operating curve was 0.74 (95% CI: 0.66–0.81). The Hosmer—Lemeshow test yielded a chi-square of 4.42 ($p = .82$), indicating that the model did not demonstrate lack of goodness of fit. Youden Index yielded an optimal mean MQS threshold of 5.9 during critical illness as the optimal minimum dose for patients to avoid adverse discharge disposition. A generalized linear model confirmed that there was a dose–response relationship between mean MQS and discharge disposition (accuracy 0.72; 95% CI: 0.64–0.79; $p < .01$; Figure 3). The association between MQS and adverse discharge disposition was unchanged when using the optimal mean MQS threshold of 5.9, as determined by the Youden Index analysis (aOR: 0.11; 95% CI: 0.05–0.25; $p < .01$).

In an analysis examining the effect of mean duration of mobilization on adverse discharge disposition, high mean duration of mobilization (mean duration >41 minutes per day) was associated with lower odds of adverse discharge disposition (OR: 0.11, 95% CI: 0.05–0.23; $p < .01$) compared to low mean duration of mobilization (mean duration ≤41 minutes per day). This relationship was maintained when controlling for APACHE II, CCI, and stroke severity (aOR: 0.11, 95% CI: 0.05–0.25; $p < .01$). Patients who achieved a level of ≥ 5 or greater on the modified ICU mobility scale (active stand or step-shuffle to the chair at minimum) at any point during their ICU admission had lower odds of adverse discharge disposition compared to patients whose maximum mobilization level was < 5 during the course of their ICU stay (OR: 0.14, 95% CI: 0.07–0.29; $p < .01$). This finding remained robust when controlling for APACHE II, CCI, and stroke severity (aOR: 0.18, 95% CI: 0.08–0.40; $p < .01$).

Adverse event rates

Among patients included in our cohort, two (1.2%) had falls (one with low mean MQS versus one with high mean MQS), three (1.9%) experienced angina (one with low mean MQS versus two with high mean MQS), three (1.9%) had a myocardial infarct (three with low mean MQS versus none with high mean MQS), four (2.5%) had deep venous thrombosis (three with low

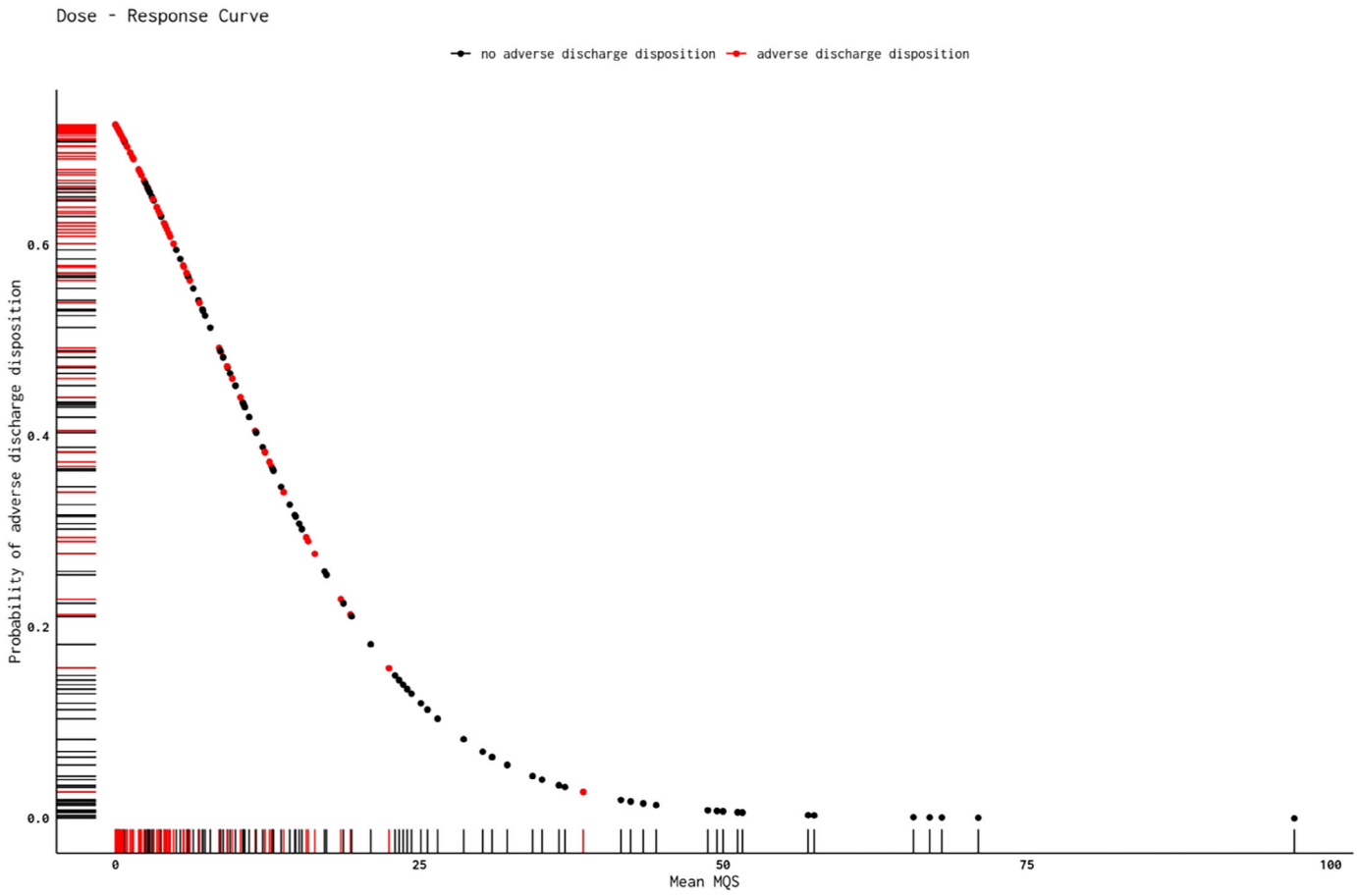

FIGURE 3 Dose response relationship between mean mobilization quantification score (MQS) during hospitalization and probability of adverse discharge disposition.

mean MQS versus one with high mean MQS), and nine (5.6%) experienced pulmonary embolism (six with low mean MQS vs. three with high mean MQS).

DISCUSSION

In this international, multicenter observational trial, we found that mobilization dose in the ICU in patients after stroke varies when adjusting for stroke severity, comorbidities, and other predictors of receiving a high dose of mobilization therapy. High mobilization dose was associated with a lower risk of losing the ability to live independently after hospital discharge. This relationship was maintained when adjusting for stroke severity, comorbidities and study center. Benefits were seen in both short-term (ICU LOS, hospital LOS, and discharge destination) and long-term outcomes (90-day functional status and mortality). Importantly, we assessed the optimal dose of mobilization and found that a mean MQS of 5.9, which is equal to walking in place for approximately 5 minutes daily, or sitting stationary in a chair for 1.5 hours daily, was the optimal minimum dose for patients to avoid adverse discharge disposition.

Mobilization represents a promising therapy to reduce ICU-acquired muscle weakness.[26,27] ICU-acquired muscle weakness has been shown to increase mortality and prolong illness.[6,28–30] However, studies have found heterogeneous results when assessing the impact of mobilization on outcomes. The AVERT study[9] raised the concern for possible harm in patients who were mobilized very early (within 24 hours); however, a post hoc analysis revealed that patients who were mobilized in shorter, more frequent sessions had more favorable outcomes.[10]

There was no mobilization-induced harm detected in our study sample of ICU patients with stroke, as assessed by reported adverse events. Given the potential harm identified in overmobilizing patients in the non ICU-setting, identifying an optimal mobilization dose is critical.[9] The authors of the AVERT trial noted that the harmful effects of early mobilization after stroke seen in their study may have been due to changes in blood pressure, inhibition of penumbral tissue reperfusion, or increased rebleeding in the case of patients with hemorrhagic stroke. Ensuring patients are hemodynamically stable (no significant orthostatic blood pressure or pulse variability when mobilized) prior to the initiation of mobilization may help to prevent these complications.

Two important factors that differ across studies of mobilization are the initiation time point and the nature of the mobilization interventions; the definition of early mobilization has yet to be standardized. In previously published literature, early mobilization has been used to define mobilization within a specific threshold of hours or days post injury or to quantify all ICU-specific mobilization in comparison to mobilization in the outpatient or rehabilitation setting.[9] Furthermore, the specific types of mobilization practices vary substantially. Some studies require early mobilization to be protocol driven and goal directed, whereas others consider mobilization to be any facilitated passive or active movement.[13,19,31,32] We chose to approach this issue broadly, including all mobilization that encompassed both lower-level activity (ie, passive range of motion in bed) and higher-level activity (eg, ambulating) that was part of the nursing and PT-directed treatment plan.

The precise mechanism of action by which mobilization is linked to improved outcomes is unclear among neurocritical care patients; however, it is believed that these benefits are mediated by both a reduction in immobility-related complications and the promotion of neuroplasticity during a critical recovery window. ICU-acquired immobility has been linked to increased intramuscular fat, decreased cardiovascular reserve, and muscle atrophy.[33] Although additional studies are needed to determine whether mobilization can prevent these immobility-related complications, previous research suggests that early mobilization has the potential to do so.[19,34–38] The critical sensitive period represents a window of heightened neuroplasticity after stroke,[39] during which mobilization may improve outcomes by means of enhanced neuroplasticity.[40]

In adjusted analyses controlling for APACHE II, CCI, and stroke severity, high mobilization dose reduced adverse discharge disposition rates and improved 90-day outcomes. Although the dose of mobilization applied varied across centers, the association between high mobilization dose and lower risk of adverse discharge disposition was independent of center geography and local standards of care. The mean MQS was higher when the propensity score, which accounted for several clinical variables as well as the individual enrollment centers, was high. This study demonstrates that routine mobilization therapy led by nursing and PT is feasible in patients with acute stroke across hospitals in the United States and Europe. Prior studies have demonstrated that both the dose and timing of mobilization are important to optimize the rehabilitative benefit.[19,41] This study builds upon prior research by employing a novel metric of quantifying dose and timing of mobilization into a composite metric as well as further demonstrating an association between mobilization dose and outcomes.

Study limitations

Our study was subject to the challenges inherent in a prospective observational study. We used a combined MQS that included nursing-led and PT-directed mobilization. Although this approach enabled us to analyze composite mobilization, there may be benefit in looking at these exposures independently. The MQS has several benefits over other scales, including the combination of duration and intensity in a single score. We intentionally included patients with both ischemic and hemorrhagic stroke to increase generalizability of our study; however, there may be subgroups within these populations that benefit from different doses more than others. We also did not analyze our patient population by therapeutic intervention and so cannot make comments about whether various therapies prior to ICU admission affect these findings. Despite these limitations, our study has several notable strengths. Our prospective study was clinically pragmatic and included multiple centers across three countries capturing highly detailed mobilization data. We present granular data for mobilization measures and outcomes and collect total mobilization from a range of providers, allowing for a complete calculation of mobilization dose encompassing both mobilization type and duration.

CONCLUSION

This observational study identified the potential benefits of early mobilization in an inclusive population of patients in the ICU with ischemic and hemorrhagic stroke. We found that both the duration and intensity of mobilization may be important contributors to outcome, lending support to the increased use of mobilization in the ICU setting. Although this practice is generally considered safe, additional studies are needed to evaluate whether there are specific subgroups that may benefit most from mobilization. Mobilization in the ICU offers a promising intervention to improve both short and long-term outcomes in critically ill patients after stroke.

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DISCLOSURES

None.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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