ResearchOnline@ND

The University of Notre Dame Australia
ResearchOnline@ND

IHR Papers and Journal Articles
Institute for Health Research

2021

Quantification of the negative impact of sedation and inotropic support on achieving early mobility in burn patients in ICU: A single center observational study

Lauren Bright

Lisa Van Der Lee

Dana Hince

Fiona M. Wood

Dale W. Edgar

Follow this and additional works at: https://researchonline.nd.edu.au/ihr_article

Part of the Medicine and Health Sciences Commons

This article was originally published as:
Bright, L., Van Der Lee, L., Hince, D., Wood, F. M., & Edgar, D. W. (2021). Quantification of the negative impact of sedation and inotropic support on achieving early mobility in burn patients in ICU: A single center observational study. *Burns, 47* (8), 1756-1765.

Original article available here:
10.1016/j.burns.2021.09.015

This article is posted on ResearchOnline@ND at . For more information, please contact researchonline@nd.edu.au.

THE UNIVERSITY OF NOTRE DAME AUSTRALIA

©2021. This manuscript version is made available under the CC-BY-NC-ND 4.0 International license http://creativecommons.org/licenses/by-nc-nd/4.0/

This is the accepted manuscript version of an article published as:

Bright, L., Van Der Lee, L., Hince, D., Wood, F.M., & Edgar, D.W. (2021). Quantification of the negative impact of sedation and inotropic support on achieving early mobility in burns patients in ICU: A single center observational study. *Burns, 47*(8), 1756-1765. https://doi.org/10.1016/j.burns.2021.09.015

This article has been published in its final form at:

https://doi.org/10.1016/j.burns.2021.09.015

burns xxx (2021) xxx –xxx

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/burns

Quantification of the negative impact of sedation and inotropic support on achieving early mobility in burn patients in ICU: A single center observational study

Lauren Bright [a,f], Lisa Van Der Lee [b], Dana Hince [c], Fiona M. Wood [d,e], Dale W. Edgar [a,b,c,d,e,*]

[a] School of Physiotherapy, The University of Notre Dame Australia, Fremantle, Western Australia, Australia
[b] Department of Physiotherapy, Fiona Stanley Hospital, South Metropolitan Health Service, Murdoch, Western Australia, Australia
[c] Institute for Health Research, The University of Notre Dame Australia, Fremantle, Western Australia, Australia
[d] Burn Injury Research Unit, Faculty of Health and Medical Sciences, University of Western Australia, Crawley, Western Australia, Australia
[e] Fiona Wood Foundation, Fiona Stanley Hospital, Murdoch, Western Australia, Australia
[f] Department of Physiotherapy, Calvary Public Hospital Bruce, Bruce, Australian Capital Territory, Australia

ARTICLE INFO

Article history:
Available online xxx

Keywords:
Burns
Intensive Care
Physical Therapy
Rehabilitation
Critical Care

ABSTRACT

Introduction: Early rehabilitation for burns survivors in the intensive care unit (ICU) is arguably more challenging than the general population. Early achievement of functional verticality milestones (FVMs) has the potential to ameliorate the detrimental effects of bed rest and immobility observed in ICU patients and reduce healthcare costs. However, the time to achieving FVMs after burn injury is influenced by factors such as sedation practices, cardiovascular stability, mechanical ventilation, acute skin reconstruction and length of stay (LOS) during the acute intensive care period.

Objectives/Aims: The aims of this study were to identify the association between early achievement of FVMs and factors influencing cessation of bedrest in adult patients with burns receiving ICU care, and to explore barriers to achievement of FVMs as recorded by clinicians.

Methods: A 5-year retrospective observational cohort study was conducted. The digital medical records were reviewed for each case to explore episodes of FVMs and patient factors which may contribute to persistent bed rest, such as use of infused sedative and/or inotropic medication, mechanical ventilation, burn surgery, total body surface area (TBSA), ICU length of stay and pre-ICU practices. Logistic regression was used to examine the association between FVM achievement and treatment and injury factors in ICU survivors.

Results: The total sample available for analysis included 64 patients. When sedation/agitation score was within recommended limits, odds of achieving FVMs was 21 times greater than periods outside those limits. When deep sedatives were infused, the odds of achieving FVMs decreased by 87% compared to periods when there was no infusion of these medications. In

* *Corresponding author at*: State Adult Burn Unit, Fiona Stanley Hospital, Murdoch, Western Australia, Australia.
E-mail address: dale.edgar@health.wa.gov.au (D.W. Edgar).
https://doi.org/10.1016/j.burns.2021.09.015
0305-4179/© 2021 Elsevier Ltd and ISBI. All rights reserved.

addition, the odds of achieving FVMs was reduced by 13% for each increase of 1 mL/h in the daily maximum noradrenaline dose.
Discussion and Conclusion: Maintaining sedation and agitation scores within the optimal range, and minimising sedative infusion and inotropic support enhances the likelihood of early and frequent mobilization in patients with burns admitted to ICU. Additional barriers identified were mechanical ventilation, burns surgery, pre-ICU practices and ICU length of stay. The challenge for clinicians moving forward is to determine how these factors may be modified to increase early mobilization of burn patients in ICU.
© 2021 Elsevier Ltd and ISBI. All rights reserved.

1. Introduction

Early rehabilitation, commencing in the intensive care unit (ICU), is vital to positively influencing the long-term functional independence and quality of life of survivors of severe burns [1]. The benefits of early mobilization for critical care patients are well documented in the literature however evidence is sparse regarding burn-specific rehabilitation in ICU.

Prolonged bedrest during ICU admission has been associated with reduced muscle strength, orthostatic intolerance and reduced cardiac function [2]. In addition, there are multiple factors which may contribute to delay in mobilization in the ICU burns population [3]. These can include burn size and location; airway involvement; increased risk of sepsis; marked fluid shifts and preponderance to hypovolaemic shock [4]; and, skin grafting surgery [5].

The concomitant pro-inflammatory processes associated with critical illness and burn wound healing contribute to ICU-acquired weakness[6]. Early mobilization is associated with reduced effects of ICU acquired weakness and improved function and quality of life [1,3] in the general ICU population. However, there is limited evidence regarding best ICU mobilization practices, and barriers to early mobilization, for patients with burns.

Severe burns result in significant pain and suffering. Whilst utilisation of sedation and analgesia in the burns population is integral to management, use has been associated with an extended period of mechanical ventilation, bed rest, and increased length of stay (LOS) [7]. Deeply sedated patients with burns may also have greater risk of ICU acquired weakness due to the compounding effects of systemic inflammatory response syndrome, and prolonged enforced bedrest [6]. Sedation and prolonged mechanical ventilation increase the risk of ventilator-associated pneumonia, which is also associated with poorer outcomes [8,9]. However, intubation is necessary and life-saving in the context of large burns, airway involvement and/or sepsis and therefore adequate sedation is necessary to avoid unplanned extubation [8].

Severe burn injuries cause a systemic inflammatory response, and inotropic support may be necessary [11] to prevent cardiovascular dysfunction from shock and to maintain vital organ perfusion [12]. However, the side effect of inotropic support used in this fashion is reduced skin perfusion, and thus is likely to have a negative impact on healing capacity and skin graft adherence in the burn injury context. Thus, there may be additional benefits to burn and skin injured patients in relation to down titration of inotropic support, provided cardiovascular targets for end-organ perfusion can be maintained.

Clinicians often use the rate of inotropic infusion as an indicator of cardiovascular instability. There is limited evidence and anecdotal variability in clinical practice regarding the optimal safe range of inotrope levels to enable mobilization or achieving a functional vertical position in the ICU cohort [13,14], and no specific guidance in this area for those with burns. If patients have a higher rate of infusion, clinicians may overcautiously withhold mobilization and verticality events, potentially causing delay in recovery of physical function.

Along the recovery trajectory of critical illness, functional vertical milestones (FVMs) are progressively achieved during the rehabilitation process to regain physical function [15]. These milestones are achieved with varying degrees of physical assistance according to the patient's stability and capacity.

The primary aim of the study was to quantify the associations between achievement of FVMs and factors influencing cessation of bedrest in adult patients with burns undergoing ICU care. The secondary aim was to explore barriers to achievement of FVMs as recorded by clinicians. We hypothesised that for burn patients in ICU, increased sedation, or agitation, and inotrope infusion rates during usual working hours are associated with reduced odds of achieving FVMs during the ICU stay.

2. Methods

A retrospective observational cohort study of all adult burns admissions at the Fiona Stanley Hospital (FSH) quaternary level ICU over a four-year period (February 2015 to April 2019), was conducted. Subjects were excluded from the study if death occurred, or comfort care was instigated during their ICU stay. Readmission episodes to ICU were excluded from the statistical analyses.

2.1. *Data Collection*

Data was extracted from the digital medical records for each subject using a purpose designed audit tool developed and maintained in Microsoft Excel. The audit tool (see Suppl Appendix A) incorporated clinical information related to demographics, the burn injury, achievement of FVMs, clinician documented barriers, and factors related to ICU and burn management likely to influence the need for bedrest. The audit tool was developed with input from expert clinicians from ICU and burns specialties and feedback was sought to establish face validity. The audit tool was then piloted on a small number of cases, with modifications made in consultation with experts to improve rigour.

Data regarding each variable of interest was extracted from the medical record using the audit tool for each subject for each ICU stay day. The timeframe between 0800−1700 represents normal daytime working hours in ICU, when physical therapy is provided to actively engage patients in rehabilitation activities to achieve FVMs. Therefore, this timeframe was chosen to audit achievement of FVMs and use of infused medications, such as sedatives and inotropes which may influence achievement of FVMs.

2.1.1. *Functional verticality milestones (FVMs)*

For the purpose of this study, FVMs were defined as: sitting on the edge of the bed, standing either at the bedside or with the use of a tilt table, marching on the spot, bed-to-chair step transfers, and ambulation, with varying degrees of physical assistance provided from staff according to patient needs. Data regarding the achievement of FVMs for each ICU stay day, the date which each FVM was first achieved in ICU, and the level of manual assistance to achieve FVMs were collected from the physiotherapy documentation for each subject. It was also recorded from physiotherapy documentation when FVMs had been achieved with nursing assistance or independently.

2.1.2. *Richmond Agitation-Sedation Scale (RASS)*

The Richmond Agitation-Sedation Scale (RASS) [16], is a reliable and valid tool to detect change in conscious status. It provides an objective assessment of sedation and agitation levels and correlates with dosage of sedative and analgesic medications [16]. It can be used to facilitate patient-centered titration of sedation, as it also incorporates assessment of pain levels which can precipitate agitation or delirium [10]. The RASS was collected for each patient as a part of routine ICU nursing observations. Expert consensus indicated a RASS score between −2 and +2 is indicative of a conscious state most amenable to mobilization of ICU patients [14]. Therefore, minimum and maximum RASS scores during daytime working hours for each subject's ICU stay day were audited into two categories; one category representing the desired range for mobilization between −2 (light sedation) and +2 (agitation), and another category for scores falling outside the desirable range for mobilization, i.e. scores less than −2 representing unrousable to moderate sedation, or scores greater than 2 representing very agitated to combative (see Suppl Appendix B).

2.1.3. *Infused sedatives*

For each day in ICU, the use of infused sedative medications (propofol, midazolam, dexmedetomidine, clonidine, fentanyl, ketamine, remifentanil, ketamine/midazolam, tramadol, and other opioid derivatives with sedative effects) during daytime working hours was recorded, and whether sedative infusion and achievement of FVMs occurred simultaneously for each subject. Sedative use was divided into three categories for each subject: deep sedatives (propofol and midazolam); lighter sedatives appropriate for non-mechanically ventilated patients (clonidine and dexmedetomidine); and opioid derivatives used predominately for analgesia, but which also have central nervous system depressant effects (fentanyl, ketamine, remifentanil, ketamine/midazolam, tramadol).

2.1.4. *Infused inotropes*

The use and rates of infused inotropes (noradrenaline, metaraminol and dobutamine) were recorded for each subject's ICU stay days. Maximum and minimum dosages, calculated using drug concentration and infusion rates, were collected during daytime working hours. Episodes of simultaneous inotrope infusion and achievement of verticality task were also collected.

2.1.5. *Mechanical ventilation, surgery, TBSA, length of stay, pre-ICU and transport practices*

Use and duration of mechanical ventilation, as well as episodes of burns surgery during ICU admission were collected for each subject. In addition, episodes of burns surgery occurring prior to ICU were collected for those patients who were admitted to ICU from the burns ward. Wound total body surface area (TBSA) was collected for each subject. Data regarding ICU and hospital LOS were also collected for each subject. Data regarding mode of transport to Fiona Stanley Hospital (FSH) ICU was also collected for each subject.

2.1.6. *Barriers to functional vertical milestones*

Data was collected regarding the recorded barriers to achieving FVMs as documented in the medical record by the treating physical therapists.

2.2. *Data Analysis*

Quantitative analyses were completed using StataMP 14 for Windows (StataCorp 2015, College Station, TX). Descriptive statistics, using frequency and percentages were used to describe all categorical variables. Median, interquartile range [IQR] and minimum/maximum were used to describe ICU LOS, hospital LOS, number of staff utilised to achieve FVM, duration of mechanical ventilation and maximum/minimum RASS scores during usual working hours. These variables are described at both the patient level and the day level where relevant. TBSA was managed in the analysis in the following categories: <20%, 20−≤40% and >40%. Median time to the first instance of each FVM (in days) and 95% confidence intervals (95% CI) were estimated using Kaplan-Meier estimates given that data were right censored (not all patients achieved a FVM prior to being discharged from the ICU). Given specific times were not available for each FVM, ICU admission time was considered time zero (0), with the first day of admission designated day one (1).

Mixed model logistic regression was used to assess the association between predictors treated as fixed effects (maximum/minimum RASS during working hours [within/outside optimal range], propofol or midazolam infusion during working hours [yes/no], dexmedetomidine or clonidine infusion during working hours [yes/no], opioid analgesia during working hours [yes/no], inotrope infusion on day [yes/no], noradrenaline infusion on day [yes/no], maximum rate of noradrenaline infusion during working hours and the achievement of FVM for each day of ICU admission. The analysis was conducted for factors and data categorised at the day level in order to investigate the time varying nature of the predictors of interest. A random effect for participant was included to accommodate for the correlation between days within person. Multivariable models included TBSA or mechanical ventilation, separately, in the models described above to investigate potential confounding. Finally, in order to investigate the combined impact of ventilation, inotropes and maximum RASS category on achieving an FVM, we estimated the probability of achieving a FVM based on a mixed logistic regression model. Statistical significance was set at $p < 0.05$.

2.3. *Ethics*

Ethics approval and a waiver of consent for this study was granted by the Human Research and Ethics Committee (HREC) of The University of Notre Dame Australia (019027F). The study was approved as per the South Metropolitan Health Service (SMHS) Governance, Evidence, Knowledge and Outcome (GEKO) assessment as a quality improvement activity (ref 28299).

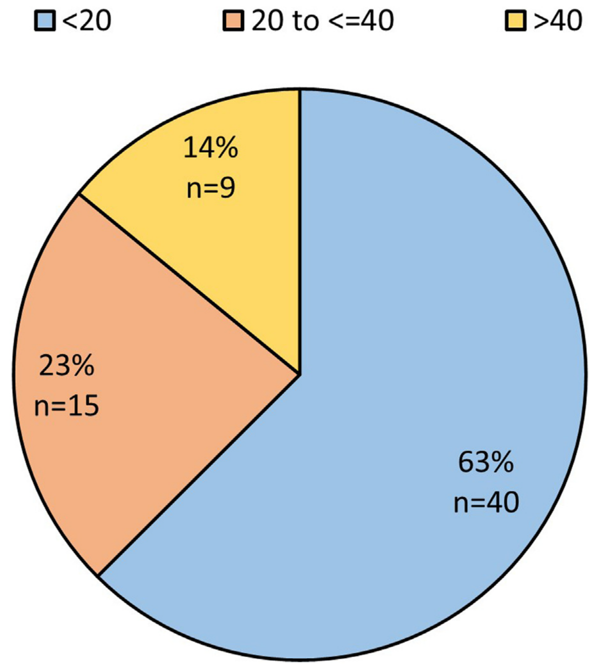

Fig. 1 – Distribution of TBSA by category (n = 64).

3. Results

3.1. *Overview of cohort*

Between February 2015 and April 2019, 70 patients with burns were admitted to FSH ICU. Six (6) patients were provided with comfort care from admission and thus, data were collected for the 64 subjects who fit the inclusion criteria for this study, with related and recorded data for events over a total of 529 days of ICU stay. Males constituted 70% (n = 45) of the study sample. Demographic data and clinical characteristics are presented in Table 1. Burn wound TBSA distribution is shown in Fig. 1. Included patients had a higher incidence of face, neck, head and upper limb burns compared to lower limb and trunk burns (see Table 4 in Suppl Appendix C).

3.1.1. *Mechanical ventilation*

For Seventy-two percent of subjects (n = 46) were mechanically ventilated during ICU admission, and for 67% of subjects (n = 43; mechanical ventilation was recorded 63% [n = 335] of total ICU days) during waking hours. When subjects were mechanically ventilated, in 48% (n = 22) this was <24 hours. Three subjects (5%) underwent prolonged mechanical ventilation via a tracheostomy impacting a combined total of 71 (13%) of the studied total of ICU days. Verticality was achieved on 39% (n = 28/71) of the days when tracheostomies were inserted, with all three patients ambulating on at least one occasion whilst mechanically ventilated. Patients who were mechanically ventilated at some point during their ICU stay were *not* intubated for a cumulative total of 132 (25%) of the studied ICU days. Of the mechanical ventilation free days, FVMs were achieved on 46.2% (n = 61) of these days.

3.1.2. *Acute surgery*

Burns surgery occurred during ICU admissions for 39% subjects (25 of 64). In addition, 14 subjects transferred from the ward into ICU and seven (50%) of those had surgery prior to their ICU admission. Surgeries affected the capacity to ambulate in ICU on 10.8% (n = 57) of the total studied days of ICU admission (n = 529). As expected, no patients achieved a FVM on the day of surgery.

Table 1 – Demographic data and clinical characteristics.

	Median	25th percentile	75th percentile	Range (min−max)
Age (in years)	40.5	30.4	54.2	19.3−88.8
TBSA (%)	14.5	5.75	24.9	0.01−73.7
ICU LoS (days)	2.5	1.3	6.3	0.3−78.0
FSH LoS if survived FSH admission (days)	19	10	40	1−234
Duration of mechanical ventilation[a] (days)	1.3	0.5	6.4	0.1−50.5
Duration of mechanical ventilation via tracheostomy (in days)	20.2	13.8	33.8	13.8−33.8

[a] Including one (1) subject who was re-intubated during ICU admission.

Please cite this article in press as: L. Bright, et al., Quantification of the negative impact of sedation and inotropic support on achieving early mobility in burn patients in ICU: A single center observational study, Burns (2021), https://doi.org/10.1016/j.burns.2021.09.015

3.1.3. Pre-ICU practices

Over two thirds (66%, n = 42) of subjects were transported to hospital via Royal Flying Doctor Service (RFDS), helicopter or St John Ambulance (SJA). Of these subjects, 88% (n = 37) were admitted directly to ICU, with 86.5% (n = 32) receiving mechanical ventilation for, or during transport. Fourteen (14) patients who were transferred to the ICU from the burns center or transported from other metropolitan hospitals for escalation or specialised care and mechanical ventilation in the ICU.

3.2. Achievement of functional verticality milestones

Functional verticality milestones and median time (days) taken to achieve each task is presented in Table 2. At least one episode of verticality was achieved for 73% (n = 47) of subjects (92% (n = 487) ICU days) over the course of ICU admission. The median (IQR) number of times per admission that verticality was achieved was one (1) [0-2] times. Of the seven (7) subjects that stood using a tilt-table, two patients did not achieve a more advanced FVM prior to ICU discharge. A median of 2 (IQR 2–3, range 1–5) staff members were engaged to assist for the achievement of FVM tasks. Less than 5% (n = 3) of subjects achieved their first FVM without the assistance of a physical therapist and there were six (6) occasions when an FVM was achieved without the physical therapist instigating the task. There was no infusion of deep sedatives or inotropes on the days that FVMs were achieved either independently or with the assistance of nursing staff.

Episodes of FVMs were not recorded for 26.6% (n = 17) of the cohort and their cumulative LOS in ICU represented 42 (8%) of recorded days. Of the complete bedrest sub-group who did not record a FVM during their ICU stay, 23.5% (n = 4; present in ICU for 1.7% (n = 9) of the total studied days) were not mechanically ventilated at any stage during ICU admission and 58.8% (n = 10; admitted for 6% (n = 30) of total ICU days) were mechanically ventilated for <24 hours during their ICU admission. In addition, six (6) of the subjects that did not achieve verticality had an ICU LOS < 24 hours. Of note, the minimum time (in days) to first achievement of an FVM whilst utilising a tilt table was seven (7) days. The maximum time (in days) to first achievement of sitting on the edge of the bed and standing was 25 and 53 days respectively.

3.3. Effect of sedation

On 64% of the total studied days, subjects were at least lightly sedated (RASS −2, lightly sedated, or lower) during working hours. Median (IQR) for maximum RASS was 0, alert and calm (range 0 to −3, moderate sedation) and minimum RASS was −3 (−4, deep sedation, to −1, drowsy) during working hours. Verticality was achieved on 24% (n = 29) of the days where no RASS score was recorded during working hours, equivalent to FVM being achieved on 13% (n = 67/529) of the total studied ICU days. Table 3 outlines the associations between maximum and minimum RASS scores during working hours and the achievement of a FVM on the same day.

The unadjusted odds of achieving verticality was 21 (95% CI 7.6–59.0) times greater on days where maximum RASS was in the −2 to 2 range, compared to outside this range, but was reduced to 13.5 (95% CI 4.7–38.7) following adjustment for mechanical ventilation (Table 3). On two days, FVMs were achieved with a maximum RASS less than −2 (light sedation), and on 99 days FVMs were achieved within a range of −2 (light sedation) and 2 (agitation). Two subjects achieved verticality with a maximum RASS score of 3 or 4 (very agitated or combative respectively) during working hours (1% (n = 6/462) ICU days). The outcomes for minimum RASS during working hours confirmed the direction of the associations with sedation practices, while exhibiting smaller magnitude co-efficients (Table 3 and Fig. 2). There were 17 days (4%) when a FVM was achieved with a minimum RASS range during working hours of −5 (unarousable) to −3 (moderate sedation), and 85 days (18%) where a FVM was achieved within a range of −2 (light sedation) and 2 (agitated). One subject achieved verticality with a minimum RASS score of 3 (very agitated).

3.3.1. Sedative infusion

All sedatives were associated with at least a 63% reduction (unadjusted) in the odds of successfully achieving a FVM, with adjustment for mechanical ventilation reducing the magnitude of this relationship (see Table 3).

Table 2 – Recorded achievement of at least one FVM during ICU admission and time to first event if achieved (n = 64).

	Achievement of FVM[c] during ICU[d] admission n (%)	Time (days) to achieve FVM[f] Median (95% CI[e])
SOEOB[a]	42 (65.6)	4 (3 – 8)
Standing	37 (57.8)	4 (3 – 12)
MOS[b]	18 (28.1)	22 (12 – 37)
Step Transfer	19 (29.7)	22 (16 – 37)
Walking	27 (42.2)	9 (5 – 30)
Tilt Table	7 (10.9)	24 (19 – 35)

[a] SOEOB = sitting on edge of bed.
[b] MOS = marching on the spot.
[c] FVM = functional verticality milestone.
[d] ICU = intensive care unit.
[e] 95% CI = 95% confidence interval for Kaplan–Meier estimate of median time to FVM.
[f] Day 1 = day of admission to ICU.

Table 3 – Episodes of achieved verticality during work hours and odds ratios (95% CI) for FVM's occurring when sedative and inotrope infusions were present.

		FVM achieved [days (%)]	FVM not achieved [days (%)]	OR unadjusted (95% CI)	p	OR adjusted for TBSA (95% CI)	p	OR adjusted for mechanical ventilation (95% CI)	p
Sedation Scores									
Maximum RASS (Working hours) (N = 411)	−2 to 2	99 (96%)	166 (54%)	21.17 (7.60-58.97)	<0.001	19.95 (7.60-58.97)	<0.001	13.51 (4.72-38.67)	<0.001
	Outside	4 (4%)	142 (46%)						
Minimum RASS (Working hours) (N = 411)	−2 to 2	85 (82%)	113 (37%)	8.15 (4.66-4.25)	<0.001	7.86 (4.48-13.79)	<0.001	5.11 (2.58-10.12)	<0.001
	Outside	18 (18%)	195 (63%)						
Sedative Infusion									
Propofol or midazolam (Working hours) (N = 503)	Yes	29 (22%)	253 (68%)	0.13 (0.08-0.21)	<0.001	Insufficient data		0.20 (0.10-0.40)	<0.001
	No	102 (78%)	119 (22%)						
Dexmedetomidine or clonidine (Working hours) (N = 503)	Yes	18 (14%)	108 (29%)	0.37 (0.21-0.66)	0.001	0.38 (0.22-0.66)	<0.001	0.56 (0.31-1.02)	0.060
	No	113 (86%)	264 (71%)						
Opioid analgesia (Working hours) (N = 503)	Yes	76 (58%)	311 (84%)	0.27 (0.17-0.42)	<0.001	0.30 (0.19-0.48)	<0.001	0.61 (0.35-1.04)	0.067
	No	55 (42%)	61 (16%)						
Noradrenaline infusion									
Noradrenaline on day (N = 529)	Yes	31 (23%)	190 (48%)	0.27 (0.16-0.47)	<0.001	0.30 (0.17-0.54)	<0.001	0.21 (0.14-0.33)	<0.001
	No	101 (77%)	207 (52%)						
Maximum rate noradrenaline infusion (Working hours) (N = 526)				0.87 (0.81 to 0.94)	<0.001	0.88 (0.82-0.95)	0.001	0.89 (0.84-0.95)	<0.001

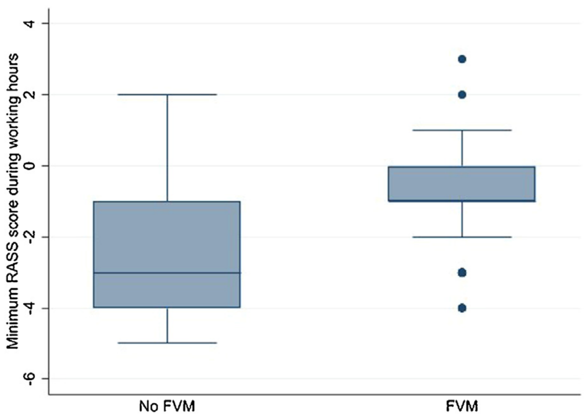

Fig. 2 – Box plot of minimum RASS during working hours on the days when FVMs were and were not achieved (n = 411 due to missing data).

For the 503 (95%) ICU days with data confirming sedative use, subjects achieved a FVM on the same day as deep sedative infusion on 6% (n = 29) of days. A FVM was achieved on the same day as light sedative infusion and infusion of opioid analgesia on approximately 4% (n = 18) and 15% (n = 76) of days respectively.

For four subjects, there were 11 days where FVM occurred with simultaneous propofol infusion. On nine of these episodes (82%), the subject was mechanically ventilated. Two of these subjects (50%) had a tracheostomy in situ. Tasks achieved included sitting on the edge of the bed (4 episodes) and standing with tilt-table (7 episodes). Median (IQR) assistance to achieve the FVM was four staff (4–4), ranging from 2 to 5 staff.

3.4. *Effect of Inotropes*

Half of subjects (51.5%, n = 33) were receiving inotrope infusions during their ICU stay (present on 231 (44%) of the total studied ICU days). The types of inotropes received were: noradrenaline (221 of total studied ICU days, 41.8%), metaraminol (15 ICU days, 2.8%) and dobutamine (4 ICU days, 0.8%). Due to the small subgroup size, it was not viable to analyse the association between metaraminol and dobutamine infusion and the achievement of FVMs using logistic regression. In the analysis, the maximum rate of noradrenaline infusion was associated with reduced odds of achieving a FVM at the $p < 0.05$ level, with adjusted and unadjusted estimates of 11 to 13% reduction (Table 3).

Of 132 days that a FVM was achieved, inotrope infusion coincided on the same day as achievement of a FVM 33 times (25.0%). Subjects achieved a FVM with simultaneous inotrope infusion on 17.2% of days (n = 22). The highest noradrenaline infusion rate, during working hours on a day that simultaneous verticality was achieved, was 10 mL/hr. The most complex FVM achieved with simultaneous noradrenaline infusion were (% studied days with inotropes confirmed; count): sitting at the edge of the bed (9.4%; n = 17); standing

(4.7%, n = 4); marching on the spot or walking (1.6%, n = 2); standing with tilt-table (4.7%, n = 6).

3.5. *Barriers to functional vertical milestones*

For 529 ICU stay days, FVMs were achieved on 132 days (25.0%). The cumulative impact of ICU interventions was a primary barrier to achieving verticality in ICU. Table 4 displays the probability of achieving a FVM as a function of the combination of mechanical ventilation, presence of inotropic infusion and maximum RASS score outside the desired range, based on a mixed effects logistic model. Not surprisingly, the highest chance of achieving a FVM was 56 % (95% CI 46–65%) on days where patients were not ventilated, had no inotropes and were within the −2 to 2 RASS range. The probability of achieving a FVM was 10% or lower for all categories including a RASS score outside the range, with 0% chance included in the 95% CI for three of the states described (see Table 4).

In addition to the primary factors studied, there were twenty-nine (29) patients who had an ICU LOS < 48 hours. In the group that had an ICU LOS of less than 24 hours (n = 12 patients), a FVM was recorded for six (6) subjects. The median (IQR) number of persons to achieve FVMs whilst mechanically ventilated was 3 (2.5–3.5) staff members, ranging from 2 to 5. The most frequently recorded barriers to mobilization in the daily medical records, were post-operative orders (10.2%, n = 54 days), sedation (9.1%, n = 48 days), no PT session (7.4 %, n = 39 days), cardiovascular instability (5.7%, n = 30 days) and patient declined to participate in therapy (4.2%, n = 22 days). A specific barrier on days when a FVM was not achieved was not recorded for 35.3% of days (n = 187 days).

4. Discussion

This is the first study to quantify the relationship between host, injury and intervention factors which influence the duration of bed rest and the achievement of functional vertical milestones for patients with burns in ICU.

In this study, almost 73% of subjects achieved a FVM, either with or without physical therapist facilitation. Of the subjects who did not achieve verticality, 82% were either not ventilated or were not mechanically ventilated for greater than 24 hours. Further, a large proportion of burn patients did not mobilise in ICU despite being ventilated for a short period of time (<24 hours). It was likely that this subgroup of subjects had such a short ICU stay that there was not sufficient time for mobilization to occur prior to ICU discharge. This highlights the challenges of long duration pre-hospital transfers in Western Australia where intubation and mechanical ventilation may have been performed as a precaution in concern for maintaining airway patency during early fluid resuscitation and transport, while a short ICU admission suggests that airway involvement may not have been significant enough to prolong intubation once in ICU.

The negative impact of mechanical ventilation on mobilization practices in ICU has been established [14,17]. However, this study found that although 30% of subjects admitted to ICU with burns were not mechanically ventilated, mobilization rates were low and occurred in less than half (46%) of days following extubation. This suggests that factors other than the presence of mechanical ventilation are influencing mobilization rates and achievement of functional verticality in this complex ICU cohort. The odds of achieving a FVM in the presence of infused sedatives was still 80% less compared with no sedative infusion, and 57% less in the presence of noradrenaline, even after accounting for mechanical ventilation. In addition, the presence of sedation, cardiovascular instability and reduced patient willingness were identified as barriers to performing mobilization by treating staff. Further research is warranted to explore modifiable barriers and enablers of early mobilization of patients with burns in ICU, to gain better understanding of how early mobilization of burn patients in ICU can be facilitated. Further understanding into whether early mobilization and achievement of FVMs in ICU translates to improvements in patient-centered outcomes, such as functional recovery and quality of life is imperative to justify the significant staff resources to effect FVM's in this complex ICU cohort.

Studies [3,18] have investigated the effect of active mobilization in general ICU cohorts, however it is important to consider the potential positive benefits of passive modes of achieving FVMs, including the use of tilt-table to achieve standing as a means to access the theoretical benefits of

Table 4 – The probability of achieving an FVM as a function of the combination of mechanical ventilation (yes or no), inotropes (yes or no) and maximum RASS score (inside or outside range) status.

Mechanical ventilation	Inotropes	Max RASS[a]	Number of days in category	Predicted probability of achieving an FVM (95% CI)
No	No	−2 to 2	87	0.56 (0.46–0.65)
Yes	No	−2 to 2	86	0.39 (0.26–0.51)
No	Yes	−2 to 2	37	0.31 (0.22–0.39)
Yes	Yes	−2 to 2	60	0.18 (0.10–0.26)
Yes	No	Outside range	50	0.05 (-0.004 to 0.11)
No	Yes	Outside range	4	0.04 (0.0002–0.07)
Yes	Yes	Outside range	104	0.02 (-0.0004 to 0.04)
No	No	Outside range	4	0.10 (-0.001 to 0.19)

[a] n = 123 days with missing RASS scores.

Please cite this article in press as: L. Bright, et al., Quantification of the negative impact of sedation and inotropic support on achieving early mobility in burn patients in ICU: A single center observational study, Burns (2021), https://doi.org/10.1016/j.burns.2021.09.015

reducing horizontal states and mitigate adverse events of immobilization, such as orthostatic hypotension, contracture and decreased arousal [19]. This study demonstrated that achievement of FVMs, such as SOEOB or tilt-table standing in this study during the infusion of sedatives was staffing resource intensive, with assistance of 4 or more staff members to assure safety.

In this cohort, the use of tilt-table was infrequent, which is consistent with another study in general ICU patients [20]. In this cohort, the minimum time to achieve FVM using tilt table was seven (7) days into ICU admission, which may reflect the time needed to achieve medical stabilisation of the airway, cardiovascular and respiratory systems, and ensure adequate airway protection in the context of upper airway oedema, to enable safe mobilization to occur. Staff factors, such as confidence of therapists and nurses in mobilising patients with burns, and availability of staffing resources to assist may also be factors influencing the time to achieve FVMs for burn patients in ICU and further research to explore this is warranted.

Expert consensus on the safety criteria for active mobilization of general ICU patients while mechanically ventilated recommends use of the RASS score to determine patient suitability for mobilization from a neurological perspective [14]. Experts concurred that out of bed exercise during invasive mechanical ventilation, via endotracheal tube or tracheostomy is safe when RASS scores are between −2 (lightly sedated) or +2 (agitated) [14]. However, specific guidance is not available in the context of an ICU burn population, who have complex and unique challenges such as marked fluid shiftsand/or deteriorating airways due to oedema which involves additional consideration to ensure safety during mobilization. The findings of this study are consistent with the expert recommendations, where the odds of achieving a FVM is greatest when maximum RASS during working hours was within the range of −2 to +2. This study reinforced that the greatest likelihood of FVM completion arises when sedation levels are optimized, and physical therapists coordinate ambulatory manoeuvres with the medical and nursing team to facilitate achievement of FVMs. An Australian study showed that inadequate or over sedation was implied as contraindications to mobilization in 61% of patient-physical therapist interactions [17]. These findings were confirmed in this study, with RASS scores during work hours reported to be outside the optimal range for safe mobilization in over a third of ICU stay days.

Patients often receive sedation in the presence of an endotracheal tube when mechanical ventilation is necessary. These precautionary measures are taken to ensure patient tolerance of the invasive tube to secure and maintain airway patency in the context of upper airway swelling, and/or inhalation injury, and/or sepsis. This may result in deeper sedation to protect the airway to ensure adequate ventilation and oxygenation for vital organ function. In collaboration with ICU medical and nursing staff, there may be scope for active reduction of sedation to facilitate a RASS score within the desired range to facilitate mobilization in burn patients in ICU. However, further research in this area is indicated to explore the feasibility of performing this in the clinical setting and whether this translates to improvements in earlier mobilization and achievement of functional outcomes for burn patients.

Scant evidence exists regarding safe levels of inotropic support for mobilization of ICU patients [14], and thus, there is a distinct lack of effective guidance for the same in burn patients. The results of this study indicated that infusion of noradrenaline during a day in ICU, reduced the odds of achieving a FVM on that day. Furthermore, the odds of achieving a FVM reduces for every 1 unit increase in dosage of noradrenaline (i.e. 2 mL/h noradrenaline = 2× greater risk of failing to achieve a FVM). These findings are clinically relevant, as only eight FVMs were achieved with minimum noradrenaline infusion on day greater than 5 mL/h.

Simultaneous noradrenaline infusion was present during a FVM on 17% (n = 22) of the days that a FVM was achieved (n = 132). The highest minimum noradrenaline infusion rate was 10 mL/h on a day when a FVM was achieved, which suggests that some physical therapists are confident to mobilise patients with inotrope infusions. Noradrenaline rate is titrated by the attending nurse to maintain mean arterial pressure (MAP) within the target range, to ensure adequate perfusion of vital organs, both at rest and with mobilization. Therefore, whilst reducing noradrenaline infusion rates may not be in the scope of physical therapy practice, there is opportunity for multidisciplinary collaboration for the development of more comprehensive, patient-centered guidelines regarding safe mobilization practices with simultaneous inotrope infusion. Future studies are indicated to investigate safe limits for mobilization of ICU patients on inotropes, including those with burns, and whether early mobilization with the presence of infused inotropes translates to improved patient outcomes.

The often infrequent and sporadic nature of burns admissions to ICU at the FSH, and considerable variation and complexity that exists within this cohort present challenges in maintaining proficiency amongst rotating ICU physical therapy staff. Champions within the intensive care and burns teams are useful to facilitate early mobilization of these complex ICU patients. Further research is warranted to investigate whether it is feasible to modify sedation practices in this patient cohort, in order to achieve early goal directed mobilization, as has been demonstrated in the general ICU cohort [21]. Investigation of staff perceptions of barriers and enablers to mobilization in the ICU burns cohort is also warranted.

Recruitment of a larger sample size through a multi-center study would enable sufficient power to determine the relationship between predictors and time taken to achieve FVMs. Further research is indicated to investigate whether achievement of FVMs whilst in ICU impacts on long term function and quality of life.

4.1. *Limitations*

This was a retrospective study, therefore there was no control over the quality or detail of the recorded data available, though medical notes in ICU and the burn center had been digitised for the majority of the cohort and more legible than other formats. Generalizability may be limited due to the size and potentially unique casemix of the sample, and the single-center design.

The sample size also precluded more complex multivariable analysis for fear of overfitting statistical models. Some data was only applicable in subgroups of patients, further reducing the feasibility of assessing the impact of factors such as surgery, pre-ICU and transport practices and short ICU LOS. Therefore, future prospective observational research should be conducted, with multi-center design to allow greater sample sizes and increased generalizability of findings to a wider range of burn severity. The findings of this study are likely to have been affected by other confounding factors such as: pre-hospital transport practices which may affect the threshold and incidence of mechanical ventilation [22] and therefore sedation practices; burn location and depth; presence of delirium, sepsis and co-morbidities; presence of airway oedema; and reduced physical therapy staffing levels on weekends, which could have influenced opportunities for mobilization of burn patients in ICU.

5. Conclusion

This novel study explored barriers to early mobilization of burn patients in a tertiary ICU and quantified the negative impact of infused sedatives and inotropes on achievement of functional vertical milestones. Thus, where early ambulation is desired, burn clinicians in ICU are encouraged to proactively titrate sedative infusions to the optimum RASS range and develop local conversations to confirm the parameters to progress verticality in the presence of inotropic infusions.

Conflict of Interest

None.

Acknowledgements

The authors would like to thank and acknowledge the FSH Physiotherapy Department and the ICU and Burns Physiotherapy teams for supporting this study.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.burns.2021.09.015.

REFERENCES

[1] Deng H, Chen J, Li F, Li-Tsang C, Liu Q, Ma X, et al. Effects of mobility training on severe burn patients in the BICU: a retrospective cohort study. Burns 2016;7:1404–12.
[2] Lorello DJ, Peck M, Albrecht M, Richey KJ, Pressman MA. Results of a prospective randomized controlled trial of early ambulation for patients with lower extremity autografts. Journal of Burn Care and Research 2014;5:431–6.
[3] Tipping CJ, Harrold M, Holland A, Romero L, Nisbet T, Hodgson CL. The effects of active mobilization and rehabilitation in ICU on mortality and function: a systematic review. Intensive Care Med 2017;2:171–83.
[4] Snell JA, Loh NW, Mahambrey T, Shokrollahi K. Clinical review: the critical care management of the burn patient. Crit Care (London, England) 2013;5:241.
[5] Parry I, Sen S, Palmieri T, Greenhalgh D. Current trends in practice for early mobility with the burn population. Journal of Burn Care & Research 2019;1:29–33.
[6] Witteveen E, Wieske L, Verhamme C, Schultz J, van Schaik IN, Horn J. Muscle and nerve inflammation in intensive care unit-acquired weakness: a systematic translational review. Journal of the Neurological Sciences 2014;1:15–25.
[7] Trupkovic T, Kinn M, Kleinschmidt S. Analgesia and sedation in the intensive care of burn patients. Journal of Intensive Care Medicine 2011;6:397–407.
[8] Kiekkas P, Aretha D, Panteli E, Baltopoulos GI, Filos KS. Unplanned extubation in critically ill adults: clinical review. Nurs Crit Care 2013;3:123–34.
[9] Li Bassi . Causes of secretion retention: patient factors, ventilation, devices, drugs. Curr Respir Med Rev 201410:, doi:http://dx.doi.org/10.2174/1573398x10666141126221255.
[10] Ely EW, Truman B, Shintani A, Thomason JWW, Wheeler AP, Gordon S, et al. Monitoring sedation status over time in ICU patients: reliability and validity of the Richmond Agitation-Sedation Scale (RASS). JAMA 2003;22:2983–91.
[11] Bangash MN, Kong M, Pearse RM. Use of inotropes and vasopressor agents in critically ill patients. British Journal of Pharmacology 2012;7:2015–33.
[12] Jeschke MG, Kamolz L, Sjöberg F, Wolf SE. 1. Aufl. ed. Handbook of Burns, Vol 1. Vienna: Springer Verlag, Wien; 2012.
[13] Hanekom S, Gosselink R, Dean , van Aswegen H, Roos R, Ambrosino N, et al. The development of a clinical management algorithm for early physical activity and mobilization of critically ill patients: synthesis of evidence and expert opinion and its translation into practice. Clinical Rehabilitation 2011;9:771–87.
[14] Hodgson CL, Stiller K, Needham DM, Tipping CJ, Harrold M, Baldwin CE, et al. Expert consensus and recommendations on safety criteria for active mobilization of mechanically ventilated critically ill adults. 2014.
[15] Hodgson C, Needham D, Haines K, Bailey M, Ward A, Harrold M, et al. Feasibility and inter-rater reliability of the ICU mobility scale. Hear Lung J Acute Crit Care 201443:, doi:http://dx.doi.org/10.1016/j.hrtlng.2013.11.003.
[16] Sessler CN, Gosnell MS, Grap MJ, Brophy GM, O'Neal PV, Keane KA, et al. The richmond agitation-sedation scale: validity and reliability in adult intensive care unit patients. American Journal of Respiratory and Critical Care Medicine 2002;10:1338–44.
[17] Capell EL, Tipping CJ, Hodgson CL. Barriers to implementing expert safety recommendations for early mobilization in intensive care unit during mechanical ventilation: a prospective observational study. Australian Critical Care 2019;3:185–90.
[18] Gosselink R, Bott J, Johnson M, Dean E, Nava S, Norrenberg M, et al. Physiotherapy for adult patients with critical illness: recommendations of the European Respiratory Society and European Society of Intensive Care Medicine Task Force on physiotherapy for critically ill patients. Intensive Care Med 200834:, doi:http://dx.doi.org/10.1007/s00134-008-1026-7.
[19] Chang AT, Boots R, Hodges PW, Paratz J. Standing with assistance of a tilt-table in intensive care: a survey of Australian physiotherapy practice. Australian Journal of Physiotherapy 2004;1:51–4.

[20] Berney S, Haines K, Denehy L. Physiotherapy in critical care in Australia. Cardiopulmonary physical therapy journal 2012;1:19–25.

[21] Hodgson CL, Bailey M, Bellomo R, Berney S, Buhr H, Denehy L, et al. A binational multicenter pilot feasibility randomized controlled trial of early goal-directed mobilization in the ICU. Crit Care Med 201644:, doi:http://dx.doi.org/10.1097/CCM.0000000000001643.

[22] Oscier C, Emerson B, Handy JM. New perspectives on airway management in acutely burned patients. Anaesthesia 2014;2:105–10.

REFERENCE TO SOFTWARE

StataCorp LP. Stata Statistically Software: Release 14 2015. iMDsoft Australia. Metavision Clinical Information System 2019. Core Medical Solutions. BOSSnet DMR 2019. Microsoft Excel.