

Outcome of Early Mobilization of Critically Ill Patients: A Propensity Score Matching Trial

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Abstract

Critically ill patients are frequently immobilized which exposes them to multiple hazards particularly muscle weakness. Early mobilization of those patients was proposed few years ago and may be associated with improvement of patient's outcomes, especially reduction of ICU length of stay.

Aim: To report the results of a quality improvement project of early mobilization in a tertiary center ICU.

Method: A full detailed protocol was developed for the intervention and applied in the ICU as of January 2017. Outcomes of enrolled patients were compared to that of un-enrolled patients. The impact of the program on ICU LOS was evaluated by propensity score matching, using un-enrolled patients as controls.

Results: Propensity score matching yielded a significant impact on LOS in the form of average reduction of 8.6 days (95% CI: 3.4-13.8, $p=0.001$), the average ICU LOS of enrolled patients was significantly lower than that of un-enrolled (15.8 ± 8.2 vs. 21 ± 9 , $p=0.04$), as well as the duration of weaning trials duration (4.1 ± 2.6 vs. 7.6 ± 5.2 , $p=0.03$), there was no difference in ICU mortality ($p=0.07$).

Conclusion: Early mobilization of critically ill patients may be associated with reduced ICU LOS and weaning trial period.

Keywords: Critical care; Mobilization; Propensity

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Introduction

Patients admitted to Intensive care units (ICU) usually undergo unavoidable periods of immobilization pertaining to the nature of interventions required as part of their management [1], interventions such as mechanical ventilation (MV), sedation, along with the insertion of multiple devices to provide fluids, nutrition, vasopressors and medication or for monitoring purposes, such as central lines, endotracheal tubes, nasogastric tubes, Foley's catheters and others [2]. Immobilization of critically ill patients, although essential for the management, is not without sequel, immobilization decreases muscle strength by 20% within the first week and further 20% for every subsequent week of immobilization [3], it has been associated with ICU acquired weakness [4], in addition to atelectasis, bone demineralization, vasomotor instability, pressure ulcers, contractures and venous thromboembolism [5]. All these impacts result essentially in difficulty of weaning from MV, prolonged ICU and hospital length

of stay (LOS) which is subsequently translated in increased daily costs and resources utilization [6].

Routine physiotherapy (PT) in ICU although intended to counter such sequel, has not been determined to benefit patients [1], furthermore, study show that only 27% of ICU patients receive such service, only 6% of which are mechanically ventilated [7]. Early mobilization of critically ill and mechanically ventilated

patients was first described in 2007 by Bailey et al. [8], in their study they concluded the intervention's safety and effectiveness. Since then early mobilization of critically ill patients was studied extensively, a recent meta-analysis of 17 studies concluded its beneficial effects [9].

Aim of the Study

To report and evaluate the results of an early mobilization program for critically ill patients, as a quality improvement (QI) project.

Study Design

The early mobilization of critically ill patients program is a QI project applied in the ICU at King Saud Medical City, the largest ministry of health hospital in Saudi Arabia, with 127 operational beds, divided into surgical, medical, trauma and isolation units. It was approved by the total quality management (TQM) in our institution.

The project started by developing a protocol for the program, which is mostly based on the framework of the mobilization program devised by Priyakshi et al. [1]. In our protocol the core team consisted of critical care physician, critical care nurse, respiratory therapist, physiotherapist and patient safety and quality coordinator.

Patients in the ICU were screened daily for inclusion criteria, which were: The patient was independently able to mobilize prior to the current hospital admission (this includes patients who use a walking stick or gait aid to mobilize, but not patients who need assistance from another person or a machine such as a wheelchair), the team is able to communicate with the patient in a language that he/she understands, age 14 years or more, hemodynamically stable (mean arterial pressure [MAP] \geq 60 mmHg without vasopressors or inotropes), fully conscious, with no use of sedatives, or muscle relaxants, maintains oxygen saturation of 95% or more with FiO_2 not more than 50% whether they were mechanically ventilated or not.

Whereas the exclusion criteria were: Complete bed rest order, unstable fractures, palliative care/DNR order, active bleeding, evidence of increased intracranial pressure (by monitoring, radiological, or clinical criteria), surgically open abdomen, mechanically ventilated with PEEP more than 12, or controlled mode of ventilation of any setting, respiratory Rate \geq 40 /min, acidosis with $PH \leq 7.25$, tachycardia ≥ 130 beats/min, ongoing renal replacement therapy and ventilator dysynchrony.

Other than the exclusion criteria, there were certain safety considerations that had to be discussed among the core team members for each patient individually, in order to decide whether to exclude the patient permanently from the program or to wait for improvement (if applicable), these considerations were: Body Mass Index >40 , hemoglobin <7 g/dl, recent tracheostomy within 24 h, history of cardiac arrest/cardiopulmonary resuscitation, venous thromboembolism, multiple lines and drains and response of the patient to the previous session of mobilization if already enrolled.

The program included six levels of activities (**Table 1**) and an algorithm to move the patient up and down between these levels according to his/her response. The protocol also details the maximum duration of each session (20 min), when to interrupt a session, required instruments and material, infection control considerations and key performance indicators (KPIs) to be measured (full protocol in supplementary file). The program was officially launched on January 1st, 2017, since the program was an approved QI; no consent was required to enroll patients.

Apart from enrollment in the early mobilization program all patients were managed similarly according to our ICU protocols specific for the patient's conditions, the ICU protocols are adapted from the best available knowledge and are based on evidence-based medicine, for example the brain trauma foundation guidelines [10] for traumatic brain injury and surviving sepsis campaign guidelines [11] for septic shock.

Outcomes

The primary outcome in this report is the effect of program enrollment on the LOS in ICU, through propensity score matching of enrolled patients as compared to patients not enrolled. Secondary outcomes include: average LOS, average duration of weaning trials and ICU mortality.

Statistical Method

For the primary outcome of propensity score matching a logistic regression model was developed using enrollment in the program as the dependent variable, independent variables were age, gender, APACHE 4 score, source of ICU admission (ED or ward) and binary diagnostic general category as medical or surgical, using enter method and Hosmer Lemeshow test to evaluate goodness of fit (well fitted if $p > 0.05$), the model was used to identify variables which will be used to generate propensity scores and those are the variables with $p < 0.2$ in the logistic regression model. Propensity scores were used to match enrolled patients in the program with nearest neighbors from the control group with a maximum difference of 0.005 between matched scores, in a 1:1 ratio. Propensity score matching aims at adjusting any imbalances between the compared groups that may arise from the absence of randomization in the treatment assignment, in addition to reduction of bias and variance in the estimation of treatment effect. Results were reported as average effect of treatment. This statistical method is based on that described by Brookhart et al. [12] and has been utilized by other researchers to control for confounding factors [13].

Baseline characteristics of the study population and the secondary outcomes were summarized as mean \pm standard deviation (SD) for continuous variables and number (%) for categorical variables. Data were compared with Mann Whitney U test or chi square test as appropriate and two tailed statistical tests were considered significant if p value was < 0.05 , two data sets were provided comparing demographic and secondary outcomes before and after matching.

Stata[®] was used for the propensity score matching (Stata Corp. 2017. *Stata Statistical Software: Release 15*. College Station, TX:

Stata Corp LLC) and for the rest of the statistics SPSS® was used (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp).

Results

During the year 2017 there were 2771 admissions to our ICU, 1740 patients were excluded permanently due to exclusion criteria that were not expected to revert, the remaining 1031 patients were screened daily for possible enrollment in the early mobilization program, 218 patients were enrolled in the program, whereas 813 patients were not and served as the control group (Figure 1).

Demographic characteristics and secondary outcomes before and after matching are summarized in Table 2. Before matching, the control group had significantly fewer males (32.8%) as compared to the enrolled group (47.7%, $p=0.0001$), other demographics did not differ between groups. Similarly, there was a statistically significant difference between the average ICU LOS for the enrolled group of 15.8 ± 8.2 and that of the control group of 26.6 ± 12 ($p=0.03$), the enrolled group had an average day of weaning trials from mechanical ventilation of 4.1 ± 2.6 which was also significantly lower than that of the control group of 8.2 ± 18

($p=0.03$), ICU mortality rate of enrolled patients of 13.3% was significantly lower compared to that of the control group of 21% ($p=0.01$).

Propensity score matching resulted in 218 pairs with one enrolled and one un-enrolled patient in each pair, utilizing the variables with p value < 0.2 in the logistic regression model, which was well fitted with a Hosmer Lemeshow p value of 0.07, those variables were: age, gender, APACHE 4 score, source of ICU admission and general diagnostic category (Table 3).

Propensity score matching reduced the mean bias in the treatment effect by 40% (Figure 2), as a result, any demographic imbalances between groups did not persist between matched groups, likewise, statistically significant difference in mortality did not persist ($p=0.07$, matched groups), whereas the significant difference in ICU LOS and weaning trials duration persisted (p values 0.04 and 0.03 respectively), we did not account in our data collection or analysis for adverse events (AEs) taking place during ICU stay for any of the groups assuming that those rates would be similar since all patients were treated similarly.

The primary outcome of effect of treatment was an estimated reduction of ICU LOS of 8.6 days (95% CI: 3.4-14.8, $p=0.001$).

Table 1 Mobilization program levels of activities.

Phase	Activities Included
0	Passive range of movement of 4 limbs (PROM)
1	Active range of movement, flexion/extension against resistance
2	Sitting on the edge of bed (SOEOB), supported or not.
3	Stand, and sit out of bed (S-SOEB)
4	Stand, March on spot (MOS)
5	Ambulating, with or without assistance.

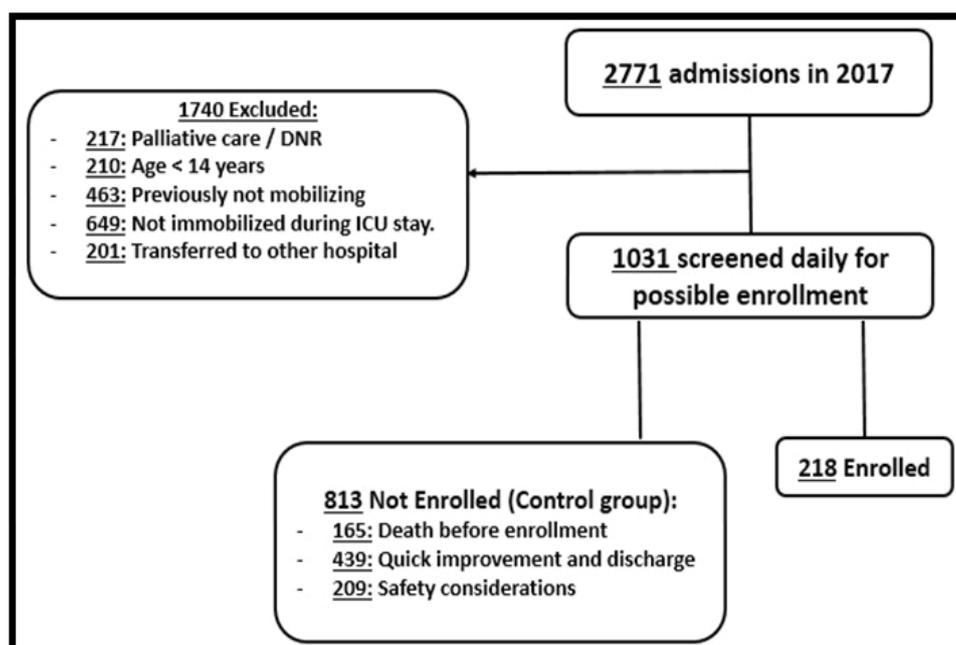


Figure 1 Patients enrolment.

Table 2 Demographics and secondary outcomes.

	All Patients			Matched Patients		
	Enrolled (n=218)	Not Enrolled (n=813)	P	Enrolled (n=218)	Not Enrolled (n=218)	P
Age (mean ± SD)	46.5 ± 16.3	49.9 ± 19	0.4	46.5 ± 16.3	45.7 ± 18	0.6
Males (n, %)	104 (47.7%)	267 (32.8%)	0.0001	104 (47.7%)	97 (44.5%)	0.6
APACHE 4 score (mean ± SD)	82.3 ± 25.7	81 ± 24.6	0.7	82.3 ± 25.7	83 ± 25	0.7
Source of admission: ED (n, %)	128 (58.7%)	459 (56.5%)	0.6	128 (58.7%)	129 (59.2%)	0.99
Diagnosis category: Medical (n, %)	147 (67.4%)	618 (76%)	0.01	147 (67.4%)	146 (67%)	0.99
ICU LOS (mean ± SD)	15.8 ± 8.2	26.6 ± 12	0.03	15.8 ± 8.2	21 ± 9	0.04
Weaning Trials Duration (mean ± SD)	4.1 ± 2.6	8.2 ± 18	0.02	4.1 ± 2.6	7.6 ± 5.2	0.03
ICU mortality (n, %)	29 (13.3%)	171 (21%)	0.01	29 (13.3%)	44 (20.2%)	0.07

Table 3 Logistic regression model.

Variable	Odds Ratio	95% CI	p
Age	0.9893	0.9698 to 1.0092	0.1906
Gender: Female	0.5016	0.2386 to 1.0543	0.0687
APACHE 4	0.9992	0.9841 to 1.0146	0.1206
Source of Admission: Ward	0.8982	0.8236 to 1.1045	0.1796
Diagnosis: Surgical	2.2883	1.0627 to 4.9277	0.0344

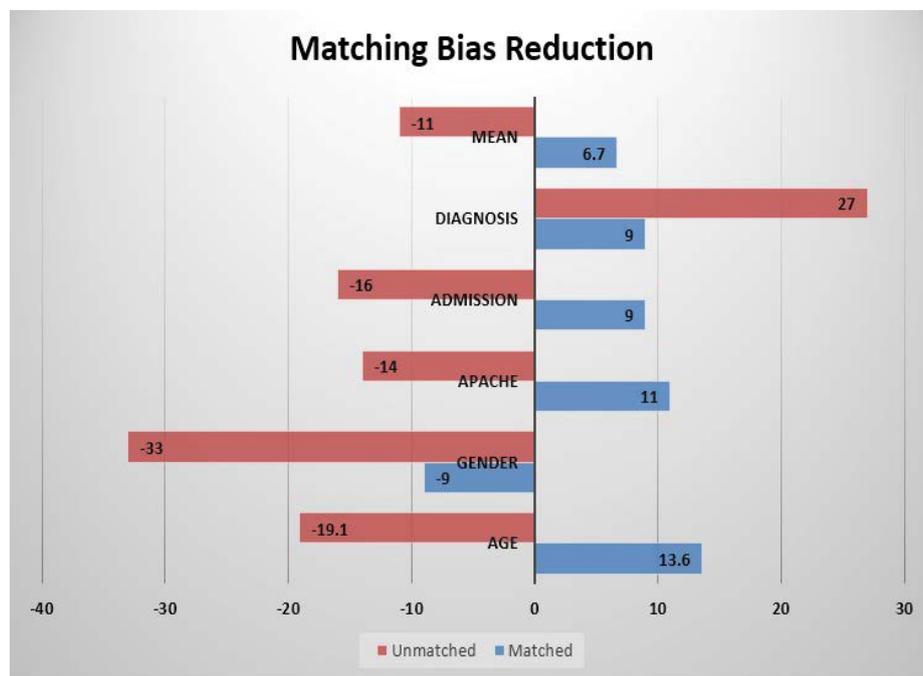


Figure 2 Propensity score matching reduction of bias.

Discussion

of our study provide statistical evidence that enrollment in the early mobilization program may significantly reduce LOS in ICU by 8.6 days, despite the fact that no causal relationship can be established based on statistics alone, these results clearly indicate that early mobilization of critically ill patients is associated with reduced LOS, similarly, as a secondary outcome in our study after

matching average ICU LOS was significantly lower in the enrolled group (p=0.04) as well as the duration of weaning trials (p=0.03), ICU mortality, however, was not different between both matched groups (p=0.07) despite being numerically lower in the enrolled group. To our knowledge no previous study used propensity score matching to evaluate the impact of early mobilization on ICU LOS, however, this impact was studied by many researchers in

different designs, several similar QI projects reported significant reduction of LOS for enrolled patients [7,14,15], whereas others failed to demonstrate that [16]. Likewise, reduction of median ICU LOS for the enrolled group was reported in a randomized controlled trial [1]. The aforementioned study in accordance with our study reported a significant difference in weaning days between both groups [1]. That study by Priyakshi et al. [1] as well as others report more ventilator free days for enrolled patients, which may correlate to fewer weaning trial days [17].

ICU mortality was not significantly different between matched groups, it is not a frequent measure in similar studies, however, a similar finding was reported by a controlled trial on stroke patients [18] and in a prospective trial the mortality rate of the enrolled patients was a very close to ours 18.8%, but there was no comparison group [19].

Regardless of the different measured outcomes of effectiveness, many published literature reviews and meta-analyses, although were not able to conclusively confirm benefit, yet they all concluded the feasibility, safety, potential beneficial effect and cost effectiveness of early mobilization of critically ill patients [2,9,19,20].

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Conclusion

Early mobilization programs for critically ill patients may be associated with reduction of ICU LOS and weaning trial period.

Limitations

Although propensity score matching was designed to perform similar to randomized control trials (RCT) using retrospective data, yet it can't have the same strength of an RCT as scientific evidence. The number of enrolled patients in our program (218) was lower than that reported in most studies on the topic, we did not account for AEs taking place during ICU stay which may prolong ICU LOS or affect outcomes, our report does not include any follow up measures after ICU discharge, such as hospital LOS, or qualitative measures of the patient's lives after hospital discharge, such as return to work or level of assistance rating, finally, the variables used to generate propensity scores were few and general, when there are far more predictors of patient's outcome in ICU.

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