Original Article

Mortality Rates in Early versus Late Intensive Care Unit Readmission

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Abstract

Background: ICU readmission is associated with poor outcomes. Few studies have directly compared the outcomes of early versus late readmissions, especially in Saudi Arabia.

Objective: To compare the outcomes between early and late ICU readmissions, mainly with regards to hospital mortality.

Methods: This retrospective study included unique patients who, within the same hospitalization, were admitted to the ICU, discharged to the general wards, and then readmitted to the ICU of King Saud Medical City, Riyadh, Saudi Arabia, between January 01, 2015, and June 30, 2022. Patients readmitted within 2 calendar days were grouped into the Early readmission group, while those readmitted after 2 calendar days were in the Late readmission group.

Results: A total of 997 patients were included, of which 753 (75.5%) belonged to the Late group. The mortality rate in the Late group was significantly higher than that in the Early group (37.6% vs. 29.5%, respectively; 95% CI: 1%–14.8%; $P = 0.03$). The readmission length of stay (LOS) and severity score of both groups were similar. The odds ratio of mortality for the Early group was 0.71 (95% CI: 0.51–0.98, $P = 0.04$); other significant risk factors were age (OR = 1.023, 95% CI: 1.016–1.03; $P < 0.001$) and readmission LOS (OR = 1.017, 95% CI: 1.009–1.026; $P < 0.001$). The most common reason for readmission in the Early group was high Modified Early Warning Score, while in the Late group, it was respiratory failure followed by sepsis or septic shock.

Conclusion: Compared with late readmission, early readmission was associated with lower mortality, but not with lower LOS or severity score.

Keywords: Early, intensive care unit, late, mortality, patient readmission, Saudi Arabia

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INTRODUCTION

The intensive care unit (ICU) is an imperative component of a healthcare facility that provides close monitoring and life-saving interventions for critically ill patients.[1] Stay in the ICU is expensive, with ICUs accounting for up to 30% of a hospital's budget, despite serving only about 5% of hospitalized patients.[1,2] Accordingly, intensivists continually monitor the readiness of patients' transfer to

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lower acuity levels of care, delicately balancing the efficient use of resources and mitigating the harms of a premature discharge from the ICU.[3] On one hand, early discharge from the ICU may reduce the risk of nosocomial infections and iatrogenic complications, alleviate the stress of the patient and their family, and free ICU beds to receive other critically ill patients.[3,4] On the other hand, prematurely discharge to a lower acuity level exposes patients to the risk of inadequate monitoring, limited availability of interventions, and delayed recognition of deterioration, all of which increases the likeliness of ICU readmission.[4,5]

Several studies have found that readmission to the ICU is associated with worse outcomes, including mortality, morbidity, and length of stay (LOS), and increased costs.[6,7] As a result, the rate of readmission, particularly within 2 calendar days, is commonly considered as one of the key performance indicators (KPI) of an ICU/critical care unit.[3,4,8] The 2-calendar-day cutoff was shown to be the optimal interval of measuring ICU readmission,[9] with an inflection point about this time between readmission due to premature discharge and the severity of the chronic illness itself.[5] Similarly, this cut-off also reflects the differentiation between readmission as a result of poor quality of care and failure to respond to treatment.[10]

The majority of studies on ICU readmission have focused on predicting the factors associated with ICU readmissions, comparing outcomes between readmitted and not readmitted patients, or both.[4-7,11] Intriguingly, few studies have compared the outcomes of patients readmitted to an ICU within and after 2 days, and even when such a comparison is reported, it is usually not the primary outcome or the main focus of the study's discussion.[12,13] This is especially the case in such studies from Saudi Arabia. Therefore, the current study was conducted to determine the differences in mortality and reasons for readmission between patients readmitted to an ICU within and after 2-calendar days in a tertiary care hospital in Saudi Arabia. We hypothesized that late readmissions would be associated with worse outcomes.

METHODS

This retrospective study included patients who were readmitted to the ICU of King Saud Medical City (KSMC), Riyadh, Saudi Arabia, between January 01, 2015, and June 30, 2022. The starting date of the study was since the patient data began being maintained electronically at the ICU of KSMC. The study was approved by the Institutional Review Board of KSMC.

KSMC is the largest public hospital in the Central region of Saudi Arabia, with 1200 in-patient beds. The ICU is a 130-bed closed unit, operated round the clock by intensivists, with a patient: nurse ratio of 1:1, and with all beds being fully equipped with facilities of invasive and non-invasive monitoring and ventilation.

Inclusion and exclusion criteria

All adult patients (aged ≥18 years) who were discharged alive from the ICU to the general wards of KSMC and then readmitted to the ICU within the same hospitalization were included. Patients who died either in the ICU or general ward were discharged home or to another healthcare facility, or discharged with a Do Not Resuscitate/Do Not Admit to ICU order were excluded. In addition, patients admitted to the maternity unit were excluded, as they represent a different population, along with fast-track patients admitted for post-operative monitoring after elective surgery, as they are admitted for a short period ranging from a few hours to a maximum of 48 hours. For all patients, only the first admission to the ICU that was followed by a readmission within the same hospitalization was considered to ensure that the enrolled patients entered the study only once, and thus the independence of the data was maintained.

Data management

Data were extracted from the electronic ICU database of KSMC. The recorded data included dates of admission, discharge, readmission, and discharge following the readmission. The recorded dates allowed calculation of the ICU length of stay (LOS) of the key admission, duration spent in the ward before readmission, and LOS of the readmission. In addition, demographic data including age and gender, source of ICU admission (general ward or emergency department), whether the patients were admitted post-operatively (other than fast track), admission diagnosis, admission category (i.e., medical, surgical, or trauma), reason for readmission, and APACHE 4 score of the admission and readmission were recorded. The outcome of the readmission was recorded as a binary "alive" or "dead".

Patients who were discharged home or to other hospitals after their readmission were considered discharged alive and not followed thereafter. There were no missing key dates, as this is strictly maintained in the database; however, admission diagnosis and readmission data were missing in some cases, and for such cases, data were retrieved from the paper medical record. The database search was performed by two authors (HH and WA) who had also participated in the creation of the database and were aware of its details. The database includes specific columns for

"Readmission", and this was used to filter the patients. Both authors double-checked each other's search.

Study groups

Enrolled patients were categorized into two groups: early readmission group if the patients were readmitted within 2 calendar days (Early group), and late readmission group if the readmission occurred after 2 calendar days (Late group).

Study outcomes

The primary outcome was all-cause hospital mortality (i.e., death occurring during the readmission due to any cause and without time restriction). Secondary outcomes included readmission LOS, APACHE 4 score of readmissions, and comparisons of the top three reasons for readmission between groups. We planned *a priori* a subgroup analysis by gender, ICU admission category, post-operative admissions, admission from the emergency room (ER), COVID-19 patients, and patients discharged during the weekend, in addition to the evaluation of early readmission as a risk factor for mortality.

Statistical analysis

Continuous variables were summarized as mean ± standard deviation (SD) as well as median and interquartile range (IQR). Binary and categorical variables were summarized as frequency and percentages. Comparisons for continuous variables between groups were performed by Student *t*-test or the alternative non-parametric Wilcoxon rank sum test, according to the normality of the data determined by the Shapiro–Wilk normality test. Discrete variables were compared by Pearson's Chi-square test or Fisher's exact test if any cell in the contingency 2 × 2 table had a value of less than five. For all comparisons, *P* values were presented with the corresponding 95% confidence interval (CI) of the difference. To evaluate early readmission as a risk factor of mortality, we fitted a logistic regression model, initially entering all recorded variables, then using the backward elimination method, with only variables with *P* value < 0.1 being retained in the model, and the result were presented as odds ratio (OR) and 95% CI. With examination of the fulfillment of logistic regression assumptions, we also fitted a Bayesian logistic regression (with weakly informative priors) using the same variables retained in the original model as a sensitivity test.

As a sensitivity test for the primary outcome, we repeated the analysis of all-cause mortality using the median value of time to readmission as a cutoff between early and late readmission.

All statistical tests were two tailed and were considered statistically significant if the *P* value was <0.05 without correction for multiple testing. All statistical tests were performed using Stata® (StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC.).

RESULTS

During the study period, there were 24,308 admissions to the ICU. After applying all the exclusion criteria, 997 patients who had a first-time readmission to the ICU were included in the analysis [Figure 1]. Of these, 244 (24.5%) belonged to the early readmission group, and 753 (75.5%) to the late readmission group. Both groups were comparable with regards to age, post-operative admission, ER admissions, weekend discharges, and proportion of COVID-19 patients. The Early group had a higher proportion of males and trauma patients, and a lower proportion of medical patients compared with the Late group [Table 1].

The most common diagnosis of ICU admission for both groups was respiratory failure (18.4%), followed by ischemic stroke (12.5%) and exploratory laparotomies (9.3%) [Supplementary Figure 1]. The most common reason for readmission was respiratory failure in the Late group and Modified Early Warning Signs (MEWS) score ≥5 for the Early group [Supplementary Figure 2].

Primary and secondary outcomes

The all-cause hospital mortality rate was significantly higher in the Late group than the Early group (37.6%

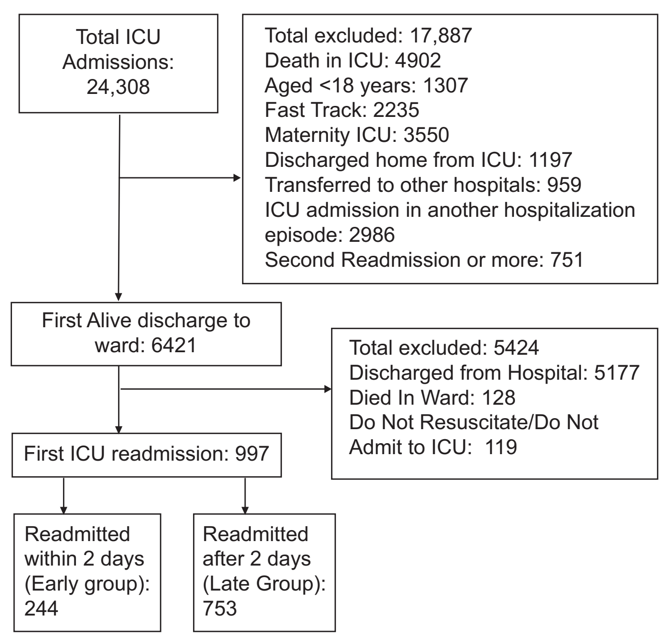


Figure 1: Flow diagram of patients' enrollment

Table 1: Demographic and clinical variables of the study groups

Variable	All (*N*=997)	Early (*n*=244)	Late (*n*=753)	95% CI of difference; *P*
Gender (male), *n* (%)	674 (67.6)	180 (73.8)	494 (65.6)	1.3–14.7; 0.02
Age (years)				
Mean±SD	51.7±21.1	50.2±21.7	52.2±20.9	−1.1–5.1; 0.2*
Median (IQR)	54 (37–66)	751.5 (35–66)	54 (37–67)	
Admission type, *n* (%)				
Medical	653 (65.5)	146 (59.8)	507 (67.3)	0.4–14.8; 0.04
Surgical	248 (24.9)	61 (25)	187 (24.8)	−6–6.9; 0.9
Trauma	96 (9.6)	37 (15.2)	59 (7.8)	2.6–12.8; 0.001
Postoperative, *n* (%)	75 (7.5)	20 (8.9)	55 (7.3)	−2.3–6.2; 0.5
ER admission, *n* (%)	696 (69.8)	160 (65.6)	536 (71.2)	−1.2–12.7; 0.1
Time to readmission (days)				
Mean±SD	11.7±13.1	1.2±0.7	15.1±13.4	12.2–15.6; <0.001*
Median (IQR)	7 (3–16)	1 (1–2)	10 (6–20)	
Weekend discharge, *n* (%)	224 (22.5)	60 (24.6)	164 (21.8)	−3.3–9.4; 0.4
COVID-19, *n* (%)	68 (6.8)	16 (6.6)	52 (6.9)	−3.9–3.8; 0.9
APACHE 4 score on admission				
Mean±SD	71.4±15.2	70.8±15	71.6±15.3	−1.4–3; 0.5
Median (IQR)	72 (61–82)	72 (61.5–81)	72 (61–82)	
Admission LOS (days)				
Mean±SD	13.4±18	13.4±17.4	13.3±18.2	−2.6–2.6; 0.4*
Median (IQR)	8 (3–16)	8 (4–17)	7 (3–16)	

*Wilcoxon rank sum test. ER – Emergency department; LOS – length of stay; CI – Confidence interval; SD – standard deviation; IQR – Interquartile range; APACHE – Acute physiology and chronic health evaluation

vs. 29.5%, 95% CI: 1%–14.8%; $P = 0.03$) [Table 2]. A post hoc visual representation of the cumulative mortality rate showed a stepwise increase in mortality across time intervals to readmission increasing by 2 days [Supplementary Figure 3].

The mean APACHE 4 score of readmissions of the Early and Late group were 75.8 ± 10.3 and 75.8 ± 11.2, respectively (95% CI: −1.6–1.6; $P > 0.99$). Similarly, there were no significant differences between the groups regarding readmission LOS (Early group: 13.6 ± 15.9 days; Late group: 13.6 ± 16.9 days; 95% CI: −2.4–2.5; $P = 0.4$) [Table 2].

Comparison of the top three reasons for readmission in each group revealed that significantly more patients in the Early group were readmitted due to high MEWS (47.5% vs. 21.2%; 95% CI: 19.2%–33.4%, $P < 0.001$). On the contrary, compared with the Early group, a significantly higher proportion of patients in the Late group had respiratory failure (34.3% vs. 23%, respectively; 95% CI: 4.6%–17.5%; $P = 0.001$) and sepsis or septic shock (28.7% vs. 14.8%; 95% CI: 7.9%–19.3%; $P < 0.001$) [Table 2].

The logistic regression model of the risk factors of mortality on readmission initially included all variables of the study; backward elimination retained five variables with P values <0.1, of which only three variables were statistically significant. Being in the Early group was associated with a mortality OR of 0.71 (95% CI: 0.51–0.98; $P = 0.04$) [Table 3]. Two other significant risk factors were age (OR = 1.023, 95% CI: 1.016–1.03; $P < 0.001$) and LOS of the readmission (OR = 1.017, 95% CI: 1.009–1.026; $P < 0.001$). The model was well fitted (Hosmer–Lemeshow P value = 0.1) and fulfilled all the assumptions of logistic regression [Supplementary Figures 4, 5 and Supplementary Table 1].

Bayesian logistic regression of the same model with weakly informative priors supports the results of the original model, with OR of being in the Early group = 0.72 (95% credible interval: 0.51–0.98) [Supplementary Table 2].

The median (IQR) time to readmission was 7 (3–16) days. When the primary outcome was repeated using a cutoff value of 7 days between early and late readmission, similar results were obtained. There was a significant difference in terms of mortality in patients readmitted within 7 days (31.8%) and after 7 days (39.8%) (95% CI: 1.9%–14.05%; $P = 0.01$).

In the subgroup analysis [Figure 2], early readmission significantly reduced the risk of death only for medical admissions; while no significant reduction was seen in all the other subgroups, there was a trend toward reduced risk in most of the subgroups. A post hoc analysis of the COVID-19 positive subgroup revealed no difference in the primary outcome, but a significantly shorter readmission LOS for the Early group [Supplementary Table 3].

Table 2: Primary and secondary outcomes

Variable	All (*N*=997)	Early (*n*=244)	Late (*n*=753)	95% CI of difference; *P*
Readmission mortality, *n* (%)	355 (35.6)	72 (29.5)	283 (37.6)	1–14.8; 0.03
Time to readmission (days)				
Mean±SD	11.7±13.1	1.2±0.7	15.1±13.4	12.2–15.6; <0.001
Median (IQR)	7 (3–16)	1 (1–2)	10 (6–20)	
APACHE 4 score on readmission				
Mean±SD	75.8±11	75.8±10.3	75.8±11.2	−1.6–1.6; >0.99
Median (IQR)	76 (68–83)	76 (69.4–83)	76 (68–83)	
Readmission LOS (days)				
Mean±SD	13.6±16.9	13.6±15.9	13.6±15.9	−2.4–2.5; 0.4*
Median (IQR)	7 (3–18)	7 (3–18)	7 (3–17)	
Readmission mortality, *n* (%)	355 (35.6)	72 (29.5)	283 (37.6)	1–14.8; 0.03
Top three reasons for readmission, *n* (%)				
MEWS score ≥5	276 (27.7)	116 (47.5)	160 (21.2)	19.2–33.4; <0.001
Respiratory failure	314 (31.5)	56 (23)	258 (34.3)	4.6–17.5; 0.001
Sepsis/septic shock	252 (25.3)	36 (14.8)	216 (28.7)	7.9–19.3; <0.001

*Wilcoxon rank sum test. APACHE – Acute physiology and chronic health evaluation; LOS – Length of stay; CI – Confidence interval; SD – Standard deviation; IQR – Interquartile range; MEWS – Modified Early Warning Signs

Table 3: Multivariable logistic regression of mortality upon readmission

Variable	OR (95% CI)	*P*
Age (years)	1.023 (1.016–1.03)	<0.001
Postoperative	0.57 (0.32–1.006)	0.052
LOS of admission (days)	0.99 (0.98–1.001)	0.076
LOS of readmission (days)	1.017 (1.009–1.026)	<0.001
Early group	0.71 (0.51–0.98)	0.04

LOS – Length of stay; OR – Odds ratio; CI – Confidence interval

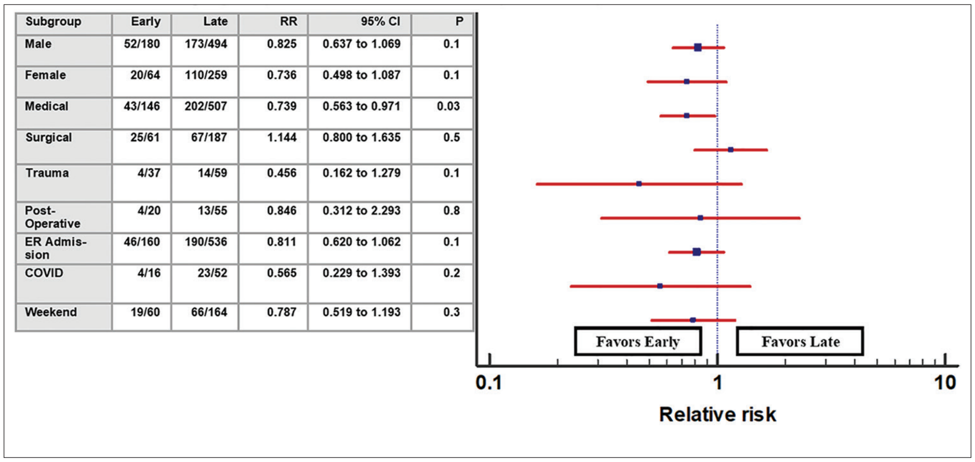
DISCUSSION

In this study of about a thousand ICU readmissions, the all-cause hospital mortality of patients readmitted within 2 days was significantly lower than those readmitted after 2 days. Both groups had similar a LOS and an APACHE 4 score upon readmission. Readmission within 2 days reduced the odds of mortality by 29% in the multivariable logistic regression, and the sensitivity tests supported these findings. The patients in the Early group were most commonly readmitted due to high MEWS, whereas respiratory failure and sepsis or septic shock were the most common reasons for readmission in the Late group.

Globally, ICU readmission are estimated to range from 2% to 25%,[14,15] and is undoubtedly associated with poor outcomes.[6,7,10] Hence, the readmission rate within 48 hours has been utilized as a KPI that reflects the quality of care provided by the ICU.[3,4] Accordingly, intensivists should carefully judge the readiness of ICU discharge, by relying on clinical skills, following institutional policies, or using prediction models and scores.[6,16] However, when readmission becomes inevitable, we believe that patients' safety should be prioritized over the KPI, and the patient should be readmitted as soon as possible. This concept is supported by our results and is mirrored by those of other studies.[12,13]

Several factors may explain the lower mortality of early readmitted patients. Generally, patients who were readmitted within 2 days must have had a shorter period of interruption of the critical care management and intensive monitoring, and their deterioration was recognized in a timely fashion to allow proper resuscitation. Specifically, in our study, the ICU deploys a rapid response team (RRT) composed of a critical care physician, nurses, and respiratory therapist that regularly follows all patients discharged from the ICU for 48 hours, and as a result, timely identify deteriorating patients. From another perspective, late readmissions should not be considered as suboptimal ICU care, but rather a failure to respond to treatment due to the severity and complexity of the patients' disease,[10] and thus the consequent deterioration and higher mortality are unavoidable. This difference could be seen in our results regarding the reasons for readmission in both groups. The Early group were mainly readmitted due to high MEWS, possibly due to the interrupted critical care support such as vasopressors or intravenous fluids, and such an interruption would quickly lead to deterioration and readmission. The main reasons for readmission in the Late group were respiratory failure and sepsis or septic shock, both of which would require time to develop, and reflect either a new event, such as infection, or unresponsiveness to management.

Intriguingly, despite similar APACHE 4 scores upon readmission, the mortality rates in the two groups differed significantly. This may indicate that the management during readmission may have been different; for example, the application of noninvasive ventilation before readmission, endo-tracheal intubation and its timing, and the use of vasopressors. This information was lacking in our study but should be investigated in future research. Nonetheless,



Subgroup	Early	Late	RR	95% CI	P
Male	52/180	173/494	0.825	0.637 to 1.069	0.1
Female	20/64	110/259	0.736	0.498 to 1.087	0.1
Medical	43/146	202/507	0.739	0.563 to 0.971	0.03
Surgical	25/61	67/187	1.144	0.800 to 1.635	0.5
Trauma	4/37	14/59	0.456	0.162 to 1.279	0.1
Post-Operative	4/20	13/55	0.846	0.312 to 2.293	0.8
ER Admis-sion	46/160	190/536	0.811	0.620 to 1.062	0.1
COVID	4/16	23/52	0.565	0.229 to 1.393	0.2
Weekend	19/60	66/164	0.787	0.519 to 1.193	0.3

Figure 2: Subgroup analysis of relative risk of ICU mortality between groups

it should be noted the RRT in our hospital manages all readmissions, and thus we may expect consistency in the management of readmissions. The structure and activities of our RRT were previously published.[17]

This study has the strength of a sizable cohort, and novelty in the Saudi population. It may trigger further investigations as well as considerations of policy changes. Further investigations could classify patients as early or late readmissions based on the actual days since readmission was requested by the treating team in the ward rather than counting days since discharge from the ICU, as the patient may have not needed readmission during the entire duration of stay in the ward. Policymakers may consider adopting our experience of following patients discharged from the ICU for 48 hours by the RRT, as this aids in the early recognition of deterioration, and thus early readmission, which was shown to have better outcomes in the current study. Early readmission of patients in need should be prioritized over the KPI of readmission rate for the sake of patients' safety.

Our study is subject to several limitations, including the inherent limitations of a retrospective study design. Both groups in our study had some demographic and clinical differences, in addition to unbalanced group sizes, and while the optimal solution for those imbalances – randomization – is not possible, other analytical methods, such as propensity matching, may have strengthened the analysis. Our study included a mix of cases that may have influenced the overall outcome, as can be seen in the lower relative risk of death for the early readmitted medical patients, but not for surgical or trauma patients. This was a single-center study reflecting the practice in our hospital only, and its results may not be generalized to all centers in Saudi Arabia. Further, >2000 patients were excluded because the LOS in the ICU was <48 hours, and if included, the results may have been different. We included all eligible patients within a predefined time frame; however, the included number of patients may not have been enough to provide sufficient power to detect the primary outcome, accordingly, our results should be interpreted with caution.

CONCLUSION

In this study, early readmission to ICU was associated with lower mortality compared with late readmission, but there were no differences in the LOS or severity score across both groups. Reasons for readmission differ between the early and late readmissions. Early readmission may be most beneficial to medical patients, rather than surgical or trauma patients.

Ethical considerations

This study was approved by the local Institutional Review Board of King Saud Medical City, Riyadh (H1RI-04-Aug22-01). The study was approved with a waiver of consent in view of its retrospective design, and generally follows research subjects' protection guidelines highlighted by the Declaration of Helsinki, 2013.

Data availability statement

The datasets generated and/or analyzed during the current study are not publicly available but are available from the corresponding author on reasonable request.

Peer review

This article was peer-reviewed by two independent and anonymous reviewers.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Variable inflation factors (multicollinearity diagnostic)

Variable	VIF	1/VIF
LOS of readmission	1.03	0.968
LOS of admission	1.03	0.972
Age	1.02	0.985
Postoperative	1	0.996
Early group	1	0.998
Mean VIF	1.02	

No VIF >4. VIF – Variable inflation factor; LOS – Length of stay

Supplementary Table 2: Bayesian logistic regression

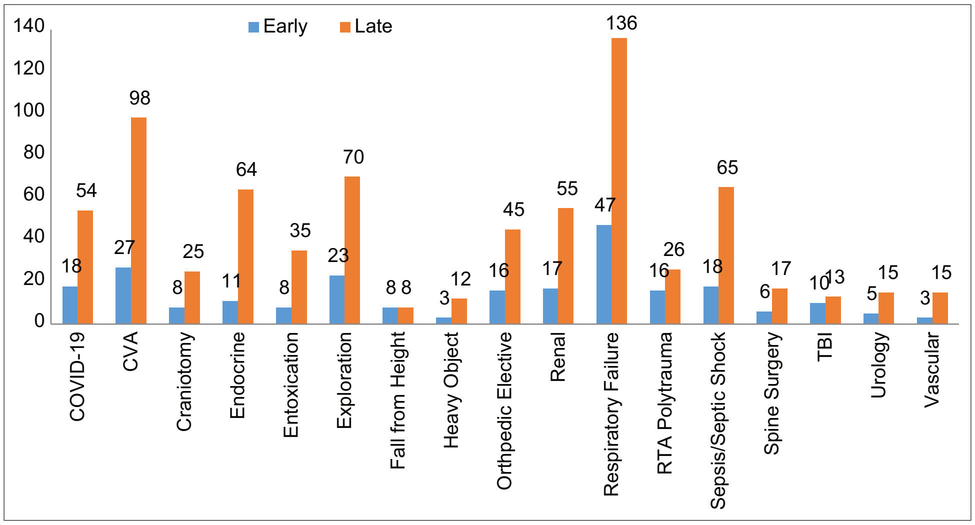
Variable	OR	Equal-tailed 95% credible interval
Age (years)	1.023718	1.017481–1.030217
Postoperative	0.6463301	0.4124817–0.9415742
LOS of admission (days)	0.9923546	0.984093–1.000665
LOS of readmission (days)	1.017402	1.00957–1.026088
Early Group	0.7171702	0.5063335–0.9800059

Using weakly informative priors (rstanarm) package in R studio.
LOS – Length of stay, OR – Odds ratio

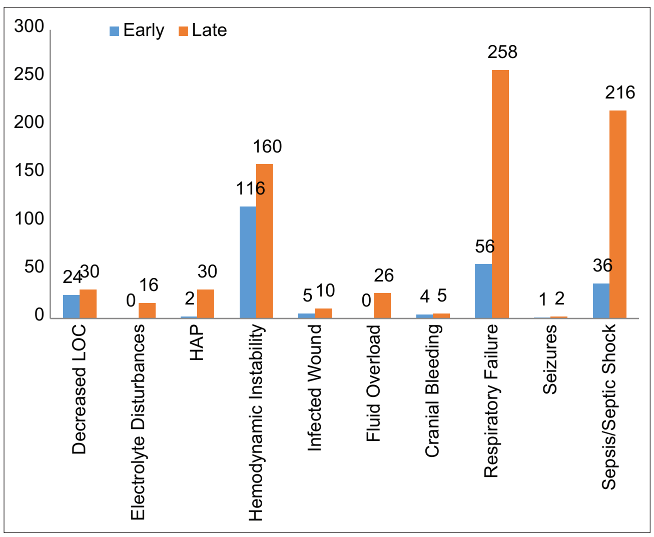
Supplementary Table 3: *Post hoc* analysis of study outcomes for COVID-19 positive group

Variable	All (*n*=68)	Early (*n*=16)	Late (*n*=52)	95% CI of difference; *P*
All-cause hospital mortality, *n* (%)	27 (39.7)	4 (25)	23 (44.2)	−5.9–44.4; 0.1
Readmission LOS	7.21±8.27 4.5 (2–7)	5.6±6.3	7.7±8.8	−2.7–6.8; 0.3*
Time to readmission	10.8±11.3 6 (3–1)	1.4±0.6	13.7±11.5	6.5–18; <0.001*
APACHE IV of readmission	77.3±12 79 (69.25–84)	72.4±13.4	78.9±11.2	−0.2–13.1; 0.06
Reasons for readmission (respiratory failure), *n* (%)	68 (100)	16 (100)	16 (100)	-

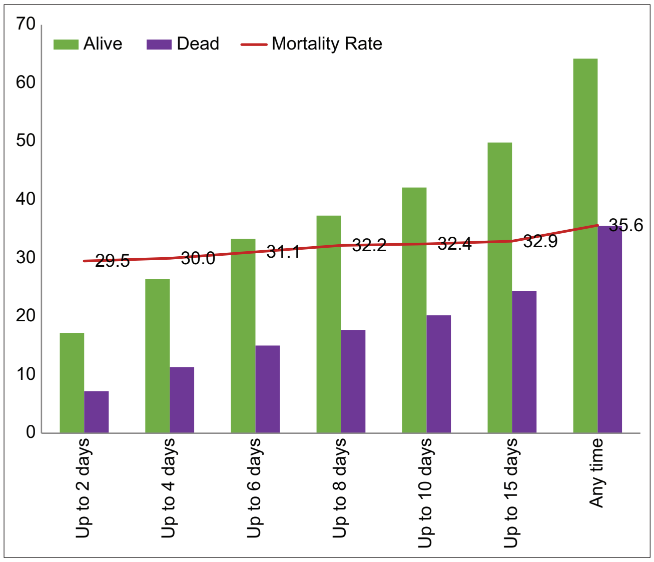
*Wilcoxon rank sum test (due to nonnormal distribution of data).
LOS – Length of stay; APACHE – Acute physiology and chronic health evaluation; CI – Confidence interval



Supplementary Figure 1: Admission diagnoses by group



Supplementary Figure 2: Reasons for readmission by group

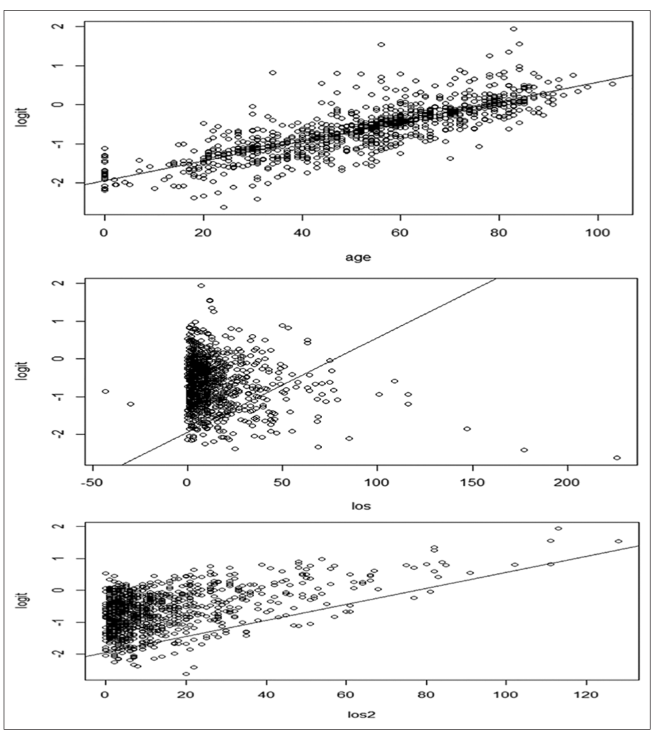


Supplementary Figure 3: Cumulative mortality by time to readmission

Correlation matrix of coefficients of regress model

e(V)	Age	PostOp	LOS	LOS2	Early	_cons
Age	1.0000					
PostOp	0.0527	1.0000				
LOS	0.0652	0.0085	1.0000			
LOS2	-0.0893	0.0222	-0.1564	1.0000		
Early	0.0394	-0.0124	0.0016	-0.0025	1.0000	
_cons	-0.8454	-0.1476	-0.2689	-0.1654	-0.2256	1.0000

Supplementary Figure 4: Logistic regression model absence of multicollinearity



Supplementary Figure 5: Linearity of continuous predictors and logit (outcome)