

Early Versus Late Use of Dexamethasone in Critically Ill Patients With COVID-19: A Multicenter, Cohort Study

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Keywords: COVID-19, SARS-Cov-2, dexamethasone, steroids, timing, early use, critically ill, Intensive Care Units (ICUs), 30-day mortality.

Posted Date: July 26th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-349677/v6>

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Abstract

Rationale: It is unclear whether the timing of dexamethasone initiation is associated with positive outcomes.

Objectives: To evaluate the appropriate timing of systemic dexamethasone initiation in critically ill patients with COVID-19.

Methods: A multicenter, non-interventional cohort study including adults with COVID-19 patients admitted to intensive care units (ICUs) received systemic dexamethasone between March 2020 and January 2021. Patients were divided into two groups based on the timing for dexamethasone use (early vs. late). Early use is defined as the new initiation of dexamethasone within 24 hours of ICU admission. Propensity score matching was used based on the patient's SOFA score, MV within 24 hours of ICU admission, proning status, and tocilizumab use during ICU stay.

Results: A total of 480 patients were included in the study; dexamethasone was initiated early within 24 hours of ICU admission in 367 patients. Among 202 patients matched using propensity score, 101 had received dexamethasone after 24 hours of ICU admission (1:1 ratio). The 30-day mortality (OR [95%CI]: 1.82[1.04, 3.19], $P=0.04$) and in-hospital mortality (OR [95%CI]: 1.80[1.03, 3.15], $P=0.04$) were higher in the late group. Among the non-mechanically ventilated patients, late use of dexamethasone was associated with higher odds of developing respiratory failure that required MV (OR [95%CI]: 3.8 [1.41, 10.3], $P=0.008$).

Conclusion: Early use of dexamethasone within 24 hours of ICU admission in critically ill patients with COVID-19 was associated with mortality benefits. Moreover, dexamethasone's early use might be considered a proactive measure in non-mechanically ventilated critically ill patients with COVID-19, to prevent further complications.

Introduction

In 2019, a newly discovered severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first reported in Wuhan, China.(1) Since the outbreak of this virus, more than 180,000,000 confirmed cases have been reported worldwide.(2) More than 4 million deaths occurred among the confirmed SARS-CoV-2 cases, with overall case mortality of almost 2% globally.(1) (1)The clinical presentation of COVID-19 ranges in severity from asymptomatic mild illness to severe pneumonia, leading to acute respiratory distress syndrome (ARDS) and associated with a high mortality rate.(3) Severe respiratory symptoms may increase the risk of hospitalization and intensive care unit (ICU) admission.(4) The ICU mortality rate is increased in patients admitted to the ICU and have severe acute lung injury ranging from 26% to 40%. (5, 6)

In critically ill patients with severe COVID-19, the hyperactivation of the systematic inflammatory system causes a state known as "cytokine release syndrome" (CRS).(7) This state may lead to multiple

complications such as acute respiratory distress syndrome (ARDS), septic shock, and acute kidney injury (AKI), disseminated intravascular coagulation (DIC), increasing the risk of mortality in those patients.(1, 8, 9) Currently, several variants of SARS-CoV-2 that cause COVID-19 are discovered, yet there are limited treatment options specific for COVID-19. The mainstay for the treatment of patients with moderate to severe COVID-19 is anti-inflammatory/antirheumatic medications, immune-based therapy, antiviral agents, and convalescent plasma.(10)

Given the fact that COVID-19 patients can develop a systemic inflammatory response that can lead to lung injury and multisystem organ dysfunction, CS anti-inflammatory effect can serve as a potential therapeutic option.(11, 12) The RECOVERY group multicenter, randomized, open-label trial conducted in the United Kingdom showed a significant mortality reduction at 28-days in hospitalized patients who received dexamethasone for up to 10 days compared to patients who received the standard of care.(13) This benefit was observed in patients who were mechanically ventilated or required supplemental oxygen at enrollment.(13) Moreover, a systemic review and meta-analysis including 20,197 patients with COVID-19 reported a significant reduction in mortality and ventilator-free days, the number of patients requiring mechanical ventilation for respiratory failure, and the mechanical ventilator timing.(14)

Although most previous studies showed favorable clinical outcomes and mortality benefits in patients who were initiated CS “early” in the COVID-19 treatment.(13, 15–17) the optimal timing for starting CS in critically ill patients with COVID19 is still being investigated,(18) especially dexamethasones in COVID19 critically ill patients. Since COVID-19 related lung injury and its associated hyperinflammatory and overreacting immune response occur early in ARDS presentation. We hypothesized that early initiation of dexamethasone could attenuate the inflammatory process early, leading to survival benefits and reduction in further complications. Therefore, this study aims to evaluate the appropriate timing of systemic dexamethasone initiation in critically ill patients with COVID19 and its clinical outcomes.

Methods

Study design

This is a multicenter, non-interventional cohort study including critically ill patients aged ≥ 18 -years with COVID-19 who received dexamethasone and were admitted to the ICU from March 01, 2020, until January 31, 2021. The retrospective component included de-identified data of COVID-19 PCR positive patients admitted before the date of IRB approval (March–June 2020). The prospective component was conducted between July 1, 2020 and January 31, 2021. The study was conducted at four hospitals in Saudi Arabia: King Abdulaziz Medical City (Riyadh), King Abdulaziz University Hospital (Jeddah), King Abdullah bin Abdulaziz University Hospital (Riyadh), and King Salman Specialist Hospital (Hail). The primary site for this multicenter prospective study was King Abdulaziz Medical City (Riyadh).

Patients were diagnosed with COVID-19 using Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) nasopharyngeal and or throat swabs. Patients were considered eligible for dexamethasone according to the Saudi Ministry of Health (MOH) protocol near June 2020 for patients with confirmed

COVID-19.(19) Eligible patients were then classified into two groups based on the timing of dexamethasone initiation during ICU stay to either “early” or “late.” The definition of early versus late CS initiation is debatable in critically ill patients in general and, more specifically, in COVID-19 patients. Patients who were initiated on dexamethasone 24 hours within ICU admission were considered to have “early” CS initiation. In contrast, patients who received dexamethasone beyond that time were categorized to have “late” CS initiation. The decision of starting early versus late CS was based on the physicians’ clinical judgment. The study was approved by King Abdullah International Medical Research Center (KAIMRC) in July 2020 (Ref.# RC20/430/R).

Patient Cohort

We aimed to enroll as many patients as possible, with no predefined sample size. All included patients have received a dose of 6 mg IV once daily of dexamethasone based on MOH protocol.(13, 19) Patients were excluded if the dexamethasone was initiated prior to ICU admission, use of dexamethasone interchangeably with methylprednisolone and vice versa, the ICU length of stay (LOS) \leq one day or death within 24 hours of ICU admission, and/or labeled as "Do-Not-Resuscitate" code status within 24 hours of ICU admission (Figure 1).

Data collection

Study data were collected and managed using Research Electronic Data Capture (REDCap®) software hosted by King Abdullah International Medical Research Center (KAIMRC) ^{31,32}. We collected patients demographic data (See additional file 1), comorbidities, vital signs and laboratory tests, Acute Physiology and Chronic Health Evaluation II (APACHE II), Sequential Organ Failure Assessment (SOFA), and Nutrition Risk in Critically ill (*NUTRIC*) scores, Glasgow Coma Score (GCS), acute kidney injury, fluid balance, proning position status, the needs for mechanical ventilation (MV) and MV parameters (e.g., PaO₂/FiO₂ ratio, FiO₂ requirement) within 24 hours of ICU admission. Also, renal profile, liver function tests (LFTs), coagulation profile (i.e., INR, aPTT, fibrinogen), and inflammatory markers (CRP, procalcitonin) within 24 hours of ICU admission were collected. Tocilizumab use was recorded for the eligible patients. All patients were followed until they were discharged from the hospital or died during in-hospital stay whichever occurred first.

Outcomes

The primary endpoint was the in-hospital mortality in critically ill patients with COVID-19 in relation to the timing of dexamethasone initiation. The secondary endpoints were 30-day mortality, hospital LOS, ICU LOS, ventilator-free days, and, ICU-related complication (s) during ICU stay (i.e., AKI, liver injury, hospital-acquired pneumonia, secondary fungal infection, respiratory failure requires MV, and thrombosis or infarction).

Outcome definition (s)

Primary outcome: In-hospital mortality is defined as death occurring during the hospital stay.

Secondary outcomes :

- Ventilator-free days (VFDs) at 30 days were calculated as the following: if the patients die within 30 days of MV, the VFDs = 0, VFDs = 30 – days after MV initiation (if successfully liberated from MV) , and VFDs = 0 if the patient is on MV for >30 days.
- ICU complications:
 - a. Acute kidney injury (AKI) was defined as a sudden decrease of renal function within 48 hours, defined by an increase in absolute SCr of at least 26.5 $\mu\text{mol/L}$ (0.3 mg/dL) or by a percentage increase in SCr $\geq 50\%$ (1.5 \times baseline value) during ICU stay.(20)
 - b. Acute liver injury was defined as alanine aminotransferase (ALT) exceeding three times the upper limit of normal or double in patients with elevated baseline ALT during the ICU stay.
 - c. Secondary fungal infection was identified through the blood, urine, wound, drainage, cerebrospinal fluid (CSF), and/or respiratory cultures. The fungal growth is considered significant if the growth is \geq of 100,000 CFU/ml in sputum or endotracheal aspiration shows; bronchoalveolar lavage (BAL) shows the growth \geq of 10,000 CFU of single organism/ml for protected specimen brushes (PSBs), and $\geq 100,000$ CFU of single organism/ml for BAL fluid. Additionally, urinary cultures were considered significant if showing a growth of $\geq 100,000$ CFU/ml of no more than two species of microorganisms. Cultures were excluded if the laboratory reported them as a "contaminant sample" (21, 22)
 - d. Respiratory failure was defined as either low arterial carbon dioxide tension (PaCO_2) or hypoxemic respiratory failure ($\text{PaO}_2 < 60$ mm Hg with a normal or hypercapnic respiratory failure ($\text{PaCO}_2 > 50$ mm Hg) that requires mechanical ventilation.
 - e. Arterial/venous thrombosis was defined using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD10-CM) code (i.e., myocardial infarction (MI), ischemic stroke, pulmonary embolism, deep vein thrombosis).(23)

Statistical analysis

We presented categorical variables as number (percentage), numerical variables (continuous variables) as mean and standard deviation (SD), or median and lower quartile (Q1) and upper quartile (Q3), as appropriate. The normality assumptions were assessed for all numerical variables using a statistical test (i.e., Shapiro–Wilk test) and graphical representation (i.e., histograms and Q-Q plots). We assessed model fit using the Hosmer-Lemeshow goodness-of-fit test. No imputation was made for missing data as the cohort of patients in our study was not derived from random selection.

We compared categorical variables using the Chi-square or Fisher exact test. We compared the normally distributed continuous variables using student t-test and other non-normally distributed continuous variables with the Mann-Whitney U test. Baseline characteristics, baseline severity, and outcome variables

were compared between the two groups. Multivariate logistic and generalized linear regression were used to determine the relationship between the timing of initiation with different outcomes considered in this study. The odds ratios (OR) and incidence rate ratio (IRR) with the 95% confidence intervals (CI) were reported for the associations. We considered a *P* value of < 0.05 statistically significant, and we used SAS version 9.4 for all statistical analyses.

Propensity score matching Procedure (Proc PS match) (SAS, Cary, NC) with a 1:1 ratio were used to match patients in the early group to late group based on the patient's SOFA score, MV within 24 hours of ICU admission, proning status, and tocilizumab Use during ICU stay⁴. A greedy nearest neighbor matching method was used in patients who received early dexamethasone (control) is matched with one patient in the late group; this eventually produces the smallest within-pair difference among all available pairs with treated patients. These patients are matched only if the difference in the logits of the propensity scores for pairs of patients from the two groups is less than or equal to 0.5 times the pooled estimate of the standard deviation.

Results

Demographic and Clinical Characteristics

A total of 790 critically ill patients with COVID-19 who received dexamethasone were screened; 480 patients were included during the study period. Out of the 480 patients, 76.4 % (367 patients) received dexamethasone early within 24 hours of ICU admission. A total of 202 patients were included after propensity score matching (1:1 ratio) based on the selected criteria (Figure 1). The majority of the patients were men (70.8%), and the mean age of the patients was 62.9±15.4 years. The most common comorbidities were diabetes mellitus (60.9%), hypertension (61.4%), and dyslipidemia (19.8%); comorbidities were not significantly different between the two groups as presented in Table E1 available in the online supplement.

There was no significant difference between the two groups' baseline severity scores (i.e., APACHE II, SOFA, and NUTRIC scores), the needs for MV within 24 hours, baseline Oxygenation Index (OI), PaO₂/FiO₂ ratio, best Glasgow coma score (GCS), blood glucose level, lactic acid, platelets count, CRP, Creatine phosphokinase(CPK), ferritin, procalcitonin, D-dimer, serum creatinine and AKI within 24 hours of ICU admission after using propensity score. The median APACHE II score was 13, while the median SOFA score was 4. Additionally, the difference in tocilizumab use during ICU stay was not significant between the two groups, as shown in (Table E1).

Mortality and length of stay

The ICU mortality within 30 days in early groups was 42.6% compared with 57.4 % in the late initiation group after using propensity score matching (OR [95%CI]: 1.82 [1.04, 3.19], *P*=0.04). Additionally, the in-hospital mortality was higher by two folds in patients who received dexamethasone after 24 hours of ICU admission (OR [95%CI]: 1.80 [1.03, 3.15], *P*=0.04) (**Table 1**).

Table 1 Regression analysis of mortality and ICU length of stay after Propensity Score adjustment

Outcomes	n of outcomes/Total no-of patients			Odds Ratio (OR) (95%CI)	P-value \$
	Early	Late	P-value		
30-day mortality, n (%) Δ	43/101 (42.6)	58/101 (57.4)	0.03 ^{^^}	1.82 (1.04, 3.19)	0.04
In-hospital mortality, n (%) Δ	47/101 (46.5)	61/100 (61.0)	0.04 ^{^^}	1.80 (1.03, 3.15)	0.04
				Incidence rate ratios (IRR) (95%CI)	P-value \$
Ventilator free days, Mean (SD)	12.6 (\pm 13.3)	7.9 (\pm 11.3)	0.009 [^]	0.62 (0.38, 1.04)	0.07
ICU Length of Stay (Days), Median (Q1,Q3) &	8.0 (5.0, 14.0)	12.0 (8.0, 20.0)	0.03 [^]	1.23 (0.88, 1.71)	0.21
Hospital Length of Stay (Days), Median (Q1,Q3) &	13.5 (9.0, 23.0)	21.0 (12.0, 39.0)	0.01 [^]	1.61 (1.12, 2.31)	0.009
<p>Δ Denominator of the percentage is the total number of patients</p> <p>& Denominator is patients who survived.</p> <p>[^] Wilcoxon rank sum test is used to calculate the P-value.</p> <p>^{^^} Chi-square test is used to calculate the P-value.</p> <p>^{\$*} Propensity score adjusted negative binomial regression is used to calculate incidence rate ratio (IRR) and p-value.</p> <p>^{\$} Propensity score matched used based on patient's SOFA score, Mechanical Ventilation within 24 hours of ICU admission, Proning position status, and Tocilizumab Use during ICU stay.</p> <p>¥ Denominator of the percentage is survival.</p> <p>&^ Denominator of the percentage is patients who have respiratory failure requiring MV during ICU stay.</p>					

Table 2 Regression analysis of ICU complications during ICU admission after Propensity Score adjustment

Outcomes	n of outcomes/Total no-of patients		P-value	Odds Ratio (OR) (95%CI)	P-value §
	Early	Late			
Respiratory Failure Required MV, n (%) §*	10/34 (29.4)	23/38 (60.5)	0.008 ^{^^}	3.8 (1.41, 10.3)	0.008
Acute kidney injury, n(%)Δ	48/101 (47.5)	43/101 (42.6)	0.48 ^{^^}	1.01 (0.63, 1.61)	0.97
Liver injury, n(%)Δ	15/101 (14.9)	8/101 (7.9)	0.12 ^{^^}	0.71 (0.33, 1.57)	0.40
Thrombosis/infarction, n(%)Δ	10/101 (9.9)	9/100 (9.0)	0.82 ^{^^}	1.14 (0.52, 2.52)	0.73
Hospital acquired pneumonia, n(%)Δ	39/101 (38.6)	45/101 (44.6)	0.39 ^{^^}	1.32 (0.83, 2.10)	0.25
Secondary fungal infection, n(%)Δ	8/67 (11.9)	9/84 (10.7)	0.81 ^{^^}	0.73 (0.34, 1.58)	0.43
				Incidence rate ratios (IRR) (95%CI)	P-value §
Ferritin level follow-up (Highest during ICU stay) , Median (Q1,Q3))Δ	1028.0 (381.4, 2026.4)	1072.0 (394.6, 2167.8)	0.68 [^]	1.18 (0.89, 1.57)	0.24
Procalcitonin level follow-up (Highest during ICU stay) , Median (Q1,Q3))Δ	0.33 (0.1, 1.4)	0.85 (1.9, 3.1)	0.04 [^]	3.91 (2.15, 7.14)	<0.0001
C-reactive protein(CRP) level follow-up (Highest during ICU stay) , Median (Q1,Q3))Δ	161.8 (61.0, 238.0)	127.5 (21.1, 258.5)	0.49 [^]	0.97 (1.32, 1.25)	0.83
D-dimer level follow-up (Highest during ICU stay) , Median (Q1,Q3))Δ	3.4 (1.1, 8.1)	4.3 (2.2, 16.5)	0.02 [^]	13.1 (5.4, 31.4)	<0.0001
Creatine phosphokinase(CPK) level follow-up (Highest during ICU stay) , Median (Q1,Q3))Δ	267.0 (91.5, 812.5)	232.5 (103.5, 708.5)	0.84 [^]	1.38 (0.99, 1.92)	0.06
<p>§* Denominator of the percentage is non-mechanically ventilated patients with 24 hours of ICU admission.</p> <p>Δ Denominator of the percentage is the total number of patients</p> <p>^{^^} Chi-square test is used to calculate the P-value.</p> <p>[^] Wilcoxon rank sum test is used to calculate the P-value.</p> <p>§ Propensity score matched used based on patient's SOFA score, Mechanical Ventilation within 24 hours of ICU admission, Proning position, and Tocilizumab Use during ICU stay.</p>					

Among survived patients who received dexamethasone, we observed a significantly longer hospital LOS in patients who received dexamethasone after 24 hours of ICU admission compared to the early initiation of dexamethasone (IRR [95%CI]: 1.61 [1.12, 2.31], $P=0.009$). Moreover, late initiation of dexamethasone was associated with significantly fewer VFD (IRR [95%CI]: 0.62 [0.38, 1.04], $P=0.07$) (Table 1).

ICU Complications during ICU stay

Among the non-MV critically ill patients with COVID-19, late initiation of dexamethasone associated with a higher odds for developing respiratory failure that required MV support (OR (95%CI): 3.8 (1.41, 10.3), $P=0.008$) as demonstrated in Table 2. Conversely, other complication during ICU stay such as hospital acquired pneumonia (OR (95%CI): 1.32 (0.83, 2.10), $P=0.25$), secondary fungal infection (OR (95%CI): 0.73 (0.34, 1.58), $p\text{-value}=0.43$), AKI (OR (95%CI): 1.01 (0.63, 1.61), $P=0.97$), liver injury (OR (95%CI): 0.71 (0.33, 1.57), $P=0.40$) and thrombosis (OR (95%CI): 1.14 (0.52, 2.52), $P=0.73$) were not statistically significant between the two groups as shown in Table 2.

Discussion

Our study aimed to assess the time of dexamethasone initiation on the clinical outcomes of critically ill patients with COVID-19. A total of 480 patients were included in the analysis; dexamethasone was initiated early in most of the included patients (76.4%). This study was started in March 2020 before releasing RECOVERY Collaborative group study results about dexamethasone use.(13) During that time, clinicians were hesitant to start dexamethasone early in all patients due to conflicting evidence about steroids. After propensity score matching using the SOFA score, MV status within 24 hours of ICU admission, proning position status, and tocilizumab use during ICU stay, we found that dexamethasone early initiation was associated with mortality benefits and shorter hospital LOS among the survived patients. Additionally, early initiation was associated with lower odds of respiratory failure that requires MV during ICU stay.

In critically ill patients with COVID-19, the dysregulated inflammatory immune response observed can be counteracted by the use of CS to down-regulate the inflammatory immune response and accelerate disease resolution.(24, 25) Although the World Health Organization (WHO) initially did not recommend using CS for COVID-19 treatment, as of September 02, 2020, the WHO and the National Institute of Health (NIH) recommended using systemic CS in critically ill patients with severe COVID-19.(26, 27) Moreover, the use of dexamethasone is recommended by the surviving sepsis guideline for patients with severe COVID-19 requiring MV and patients with refractory shock.(28) However, none of these guidelines recommend the appropriate time for CS initiation in patients with COVID-19.

In our study, early dexamethasone initiation was associated with a significant reduction in 30-day mortality and in-hospital mortality. The majority of these patients received MV within 24 hours of ICU admission. The result of our study is consistent with the RECOVERY trial finding showing that the use of

dexamethasone was associated with lower 28-day mortality among patients who received respiratory support.(13) However, in the RECOVERY trial, the median time for dexamethasone initiation since symptoms onset was 8 (5-13) days.(13) Suggesting that the benefit of dexamethasone in patients with COVID-19 is noticeable receiving dexamethasone more than seven days post-symptoms onset.(13) Also, the RECOVERY trial did not investigate if early dexamethasone initiation is different from just initiating dexamethasone at any given point in terms of hospital length of stay (LOS), ICU LOS, and MV duration.

Several meta-analyses and systemic reviews reported a significant reduction in the mortality rates in patients with COVID-19 receiving CS compared to standard care only.(14, 29) However, none of the studies included in the meta-analyses assessed the mortality benefit of early or late CS initiation.(14, 29) On the other hand, an observational retrospective study including 615 patients with COVID-19 found that starting CS at > 72 hours from admission associated with significant mortality reduction (HR 0.56, 95% CI 0.38–0.82; $p = 0.003$) compared to that early start of CS (within 24 hours).(30) The mortality benefit was evident in patients who were initiated on CS at > 7 days of symptom onset. (30) It is noteworthy that most of the study patients received methylprednisolone (87%).(30).The present study found shorter hospital LOS and longer VFD in the early group. Similarly, the study by Monedero et al. found that early CS use in critically ill COVID19 patients was associated with shorter MV duration and less ICU LOS compared to delayed or no use of CS.(16)

Besides the mortality benefits that were observed in these studies, limited studies investigated the impact of late CS initiation on respiratory failure that required MV. Our study found that early initiation of dexamethasone was associated with a lower odds of respiratory failure that required MV. That could be related to dexamethasone's prolonged and potent effect, which can mediate downregulation of systemic and pulmonary inflammation, restore homeostasis, and enhance disease resolution. Even though the NIH guideline recommends using CS in severely ill COVID-19 patients who require MV based on the evidence of the RECOVERY trial results (13, 26), our study demonstrated lower odds of developing respiratory failure in non-MV patients. Monedero et al. reported a lower MV rate in the early steroids group in parallel to our findings.(16) However, in that study, the cutoff of early initiation of CS was at 48 hours from ICU admission while including patients who were started on CS before ICU admission.(16)

We believe that our multicenter prospective cohort study is one of the first studies to highlight the appropriate time of dexamethasone initiation and its effects on the clinical outcomes of critically ill patients with COVID-19. It is prospective design allows to prospectively explore the association between the time of dexamethasone therapy initiation in COVID19 patients with ICU mortality. Additionally, it had a predefined cutoff margin of early vs. late initiation time, and it assessed several important clinical outcomes in the final analysis. Nevertheless, we also determined some limitations to our study. First, the observational nature of the study design limits the exclusion of missing data of some variables. Second, despite propensity score matching, some residual confounding factors are still possible. Lastly, there was a dynamic change in the national and international COVID-19 management guidelines as more evidence emerged, affecting the general practice.

Conclusion

Early use of dexamethasone within 24 hours of ICU admission in COVID-19 critically ill patients was associated with reduced mortality. Moreover, this approach might be considered a proactive measure in the non-MV critically ill patients with COVID-19 to prevent further complications. This study reinforces previous reports' findings of the mortality benefit of CS in critically ill patients with COVID-19. Further randomized clinical and interventional studies are needed to confirm the optimal timing for CS initiation, and its benefit in non-MV COVID-19 critically ill patients.

Declarations

Acknowledgements

Not applicable.

Author contributions

All authors contributed to data collections, analysis, drafted, revised, and approved the final version of the manuscript.

Funding

None.

Availability of data and material

The datasets used and/or analyzed during the current study are available from corresponding author on reasonable request.

Ethics approval and consent to participate

The study was approved in July, 2020 by King Abdullah International Medical Research Center Institutional Review Board, Riyadh, Saudi Arabia (Reference No: RC20/430/R).

Participants' confidentiality was strictly observed throughout the study by using anonymous unique serial number for each subject and restricting data only to the investigators. Informed consent was not required due to the research's method as per the policy of the governmental and local research center.

Consent for publication

Not applicable.

Competing interests

No author has a conflict of interest in this study.

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Figures

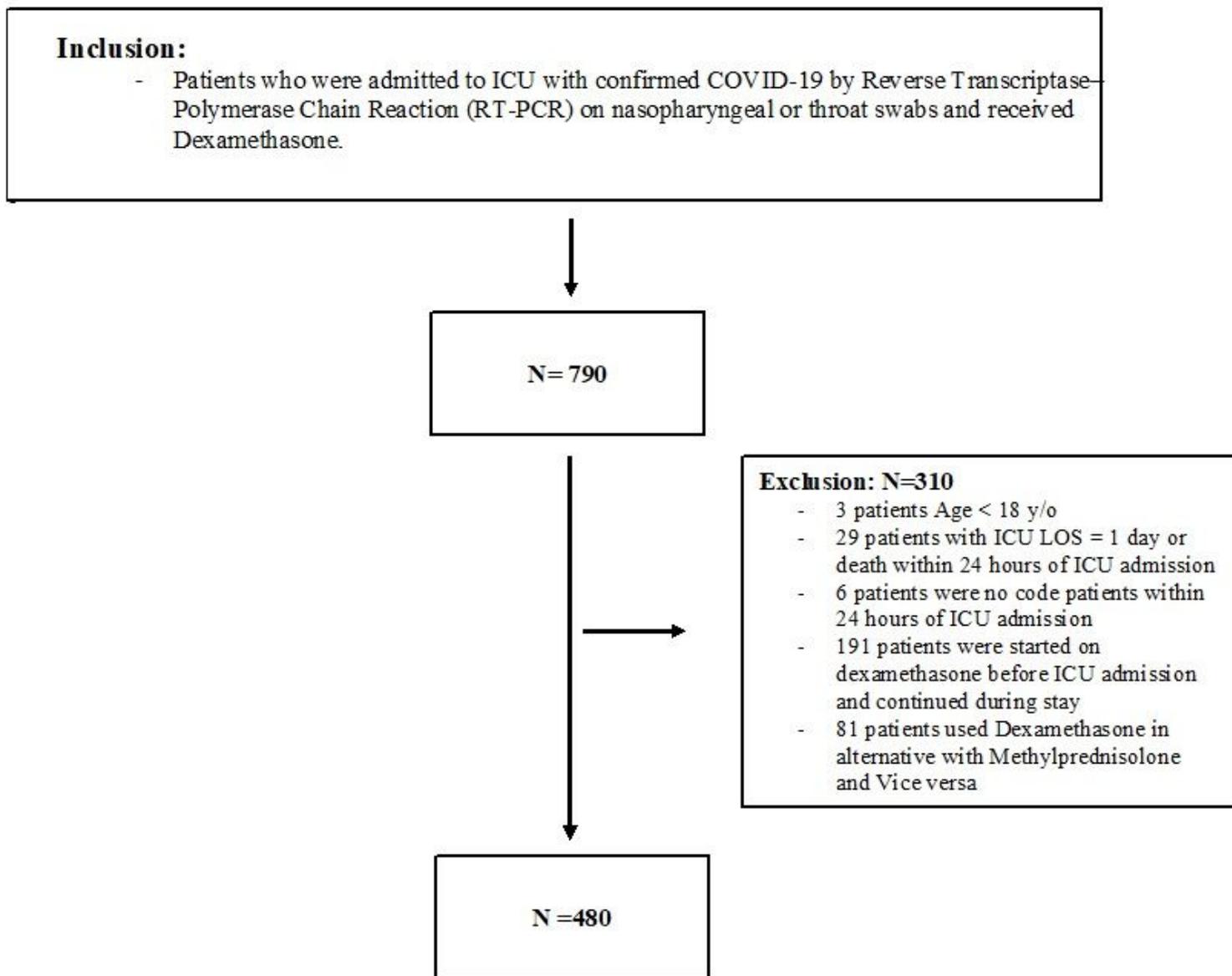


Figure 1

Flow diagram showing patients recruited with COVID-19 who received dexamethasone COVID-19= Coronavirus disease, ICU=intensive care unit, LOS=length of stay

Supplementary Files

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