

Treatment of COVID-19 Patients by Glucocorticoids: Which Dose? Which Type? A Single- Center Cohort Study

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Abstract

Background

Glucocorticoids were widely used in COVID-19, but the optimal type and cumulative dose remain unclear, especially regarding short-term outcomes and adverse effects.

Objective

To investigate the association between cumulative doses of different glucocorticoids (methylprednisolone, dexamethasone, prednisolone) and clinical outcomes (mortality, hospital stay, ICU admission, and lung involvement) in hospitalized COVID-19 patients.

Methods

This single-center historical cohort study included 5,261 hospitalized patients with confirmed COVID-19 and pulmonary involvement who received at least one glucocorticoid. Cumulative steroid doses (mg) were used as continuous independent variables. Outcomes included in-hospital mortality, length of stay, ICU admission, ICU length of stay, and change in CT severity score (0–25). Multivariable logistic and linear regression models were adjusted for age, sex, baseline SpO₂ (continuous), initial CT score (continuous), and cumulative doses of remdesivir, tocilizumab, and anakinra. To address channeling bias, we performed additional sensitivity analyses, including propensity score matching and E-value calculations.

Results

Overall mortality was 6.3% in the study cohort. In multivariable analysis, a higher cumulative methylprednisolone dose was independently associated with lower mortality (OR per 100 mg increase: 0.82, 95% CI: 0.74–0.91, $p < 0.001$). Higher cumulative dexamethasone dose was associated with longer hospital stay ($\beta = 0.68$ per 10 mg, $p < 0.001$) and with less radiological improvement ($\beta = 0.42$ per 10 mg, $p = 0.031$). A higher prednisolone dose was also associated with a longer length of stay ($\beta = 0.29$ per 50 mg increase, $p = 0.009$). No glucocorticoid was independently associated with ICU length of stay after adjustment. The R^2 values for hospital stay models ranged from 0.18 to 0.31, indicating that steroid dose explained a modest but significant portion of the variance.

Conclusion

In this observational study, a higher cumulative methylprednisolone dose was associated with reduced mortality, while higher dexamethasone and prednisolone doses were associated with prolonged

hospitalization. Given the high risk of channeling bias and time-dependent confounding, these results should be interpreted strictly as hypothesis-generating. They should not be used to guide changes in clinical practice. Future randomized controlled trials directly comparing different glucocorticoid types and doses are urgently needed.

1. Introduction

The COVID-19 pandemic, caused by SARS-CoV-2, has posed unprecedented challenges to healthcare systems. While antiviral therapies were initially prioritized, it became clear that a significant portion of severe cases were driven by hyperinflammation – the "cytokine storm" – leading to ARDS and multi-organ failure(1, 2). This dysregulated immune response involves excessive IL-1 β , IL-6, and TNF- α (3, 4).

Glucocorticoids emerged as a cornerstone for moderate-to-severe COVID-19. The RECOVERY trial showed that dexamethasone 6 mg daily for up to 10 days reduced 28-day mortality in patients requiring oxygen or ventilation(1, 5). This finding was a turning point, establishing systemic corticosteroids as the standard of care for severe COVID-19 (6). Subsequent meta-analyses confirmed mortality benefit in critical illness but showed no benefit and possible harm in mild cases(7, 8).

Despite this, questions remain about the optimal agent and dosing. Methylprednisolone has higher anti-inflammatory potency and a different pharmacokinetic profile. Some observational studies and meta-analyses have suggested that methylprednisolone may offer superior outcomes compared to dexamethasone(9, 10), although a recent meta-analysis of RCTs found similar effects (11). The optimal dose also remains unclear; a network meta-analysis suggested pulse methylprednisolone was associated with the lowest mortality (12).

Glucocorticoids carry certain risks. High-dose and prolonged therapy increase the risk of secondary infections, including COVID-19-associated pulmonary aspergillosis (CAPA) (13–15). hyperglycemia, fluid retention, and other metabolic complications (16).

Given the clinical equipoise and the inherent limitations of observational data – particularly channeling bias and time-dependent confounding – real-world evidence from large cohorts is essential to generate hypotheses for future trials. This study evaluated the association between cumulative doses of different glucocorticoids and key clinical outcomes in a large cohort of hospitalized COVID-19 patients. We emphasize that our findings are exploratory and hypothesis-generating, not confirmatory or practice-changing.

2. Methods

2.1 Study Design and Setting

This was a historical cohort study conducted at a single tertiary care center (Baqiyatallah Hospital, Tehran, Iran). The study included patients admitted with COVID-19 from March 2020 to September 2022.

The study was approved by the institutional ethics committee (IR.BMSU.REC.1402.081).

2.2 Participants and Data Collection

All hospitalized patients with confirmed COVID-19 (positive PCR or typical findings on chest CT) and pulmonary involvement were screened. Data were extracted from hospital information systems, clinical records, and the PACS (picture archiving and communication system) imaging database.

Inclusion criteria:

1. Diagnosis of COVID-19 with pulmonary involvement.
2. Positive PCR or typical findings on chest CT.
3. Received at least one type of glucocorticoid.

Exclusion criteria:

1. Incomplete medical records.
2. Discharge against medical advice.
3. Transfer from another center.
4. Preexisting rheumatologic diseases, immunodeficiency, or active malignancies.
5. Received non-pharmacological treatments (e.g., ozonotherapy, hemoperfusion, plasmapheresis).
6. Received other investigational therapies (e.g., Kaletra, hydroxychloroquine, Recigen, favipiravir, COVID-19 convalescent plasma).
7. Recent use of biological agents or glucocorticoids (within six months).
8. Immunosuppressive therapy or organ transplant recipients.

2.3 Variables

Independent Variables:

Independent Variables (cumulative doses during hospitalization, in mg):

- Total methylprednisolone (continuous)
- Total dexamethasone (continuous)
- Total prednisolone (continuous)
- Total glucocorticoid dose, calculated both with and without anti-inflammatory coefficients (hydrocortisone = 1, prednisolone = 4, methylprednisolone = 5, dexamethasone = 30) (16).

Dependent Variables (Outcomes):

- In-hospital mortality (all-cause).
- Length of hospital stay (days).
- Need for ICU admission (yes/no).

- Length of ICU stay (days).
- Change in pulmonary involvement: difference in CT severity score between initial and follow-up CT (score 0–25 per lobe, converted to percentage)(17).

Confounding Variables:

- Age (continuous), sex
- Baseline SpO₂ (continuous, %)
- Initial CT severity score (continuous, 0–25)
- Cumulative doses of remdesivir, Actemra (tocilizumab), and CinnoRA (anakinra)

Initial disease severity was also categorized for descriptive purposes:

- Critical: SpO₂ ≤ 88%, or requiring mechanical ventilation, or hemodynamic instability, or non-pulmonary organ failure.
- Severe: >50% lung involvement or SpO₂ < 90%.
- Moderate: SpO₂ between 90–93%.
- Mild: SpO₂ ≥ 93%.

2.4 Statistical Analysis

- Descriptive statistics (mean, SD, median, IQR) for continuous variables; frequencies/percentages for categorical variables.
- Kolmogorov-Smirnov test for normality.
- For comparisons between groups (survivors vs non-survivors, ICU vs non-ICU), Mann-Whitney U or Kruskal-Wallis tests were used.
- Spearman's rank correlation for bivariate associations between cumulative doses and continuous outcomes.
- Multivariable logistic regression for in-hospital mortality, with cumulative doses (continuous) of each glucocorticoid as independent variables, adjusted for age, sex, baseline SpO₂, initial CT score, and cumulative doses of remdesivir, Actemra, and CinnoRA.
- Multivariable linear regression for hospital stays, ICU stay, and change in CT score, with the same covariates.
- R² values were reported for all regression models to indicate the proportion of variance explained.
- Sensitivity analyses: We performed E-value calculations to assess the robustness of our findings to unmeasured confounding. Additionally, for the dexamethasone radiology finding, we made adjustments for the time from symptom onset to the first CT and between CT scans to rule out timing-related confounding.

- Time-dependent confounding was addressed by analyzing average daily dose as a secondary exposure variable, in addition to cumulative dose.

All analyses were performed using SPSS version 26 and R version 4.2. A p-value < 0.05 was considered statistically significant.

3. Results

3.1 Patient Cohort and Demographics

Of 13,135 screened patients, 7,874 were excluded, leaving 5,261 for final analysis. Reasons for exclusion are detailed in Table 1. The most common reasons were receiving other investigational drugs (e.g., hydroxychloroquine, Kaletra) or not receiving glucocorticoids.

Overall mortality was 8.5% for the entire screened population, 10% for the excluded group, and 6.3% for the study cohort ($p < 0.001$) (Figure 1).

3.2 Mortality Outcomes

In patients who died, cumulative doses of all glucocorticoids were significantly higher compared to survivors ($p < 0.001$ for all). This difference was most pronounced for dexamethasone and least for methylprednisolone. However, this likely reflects that sicker patients received higher doses (channeling bias), not that higher doses caused mortality. Figure 2 compares total glucocorticoid doses between survivors and non-survivors across severity groups.

Multivariable logistic regression (Table 2) using cumulative doses as continuous variables revealed:

- Higher cumulative methylprednisolone dose (per 100 mg) was independently associated with lower mortality (OR: 0.82, 95% CI: 0.74–0.91, $p < 0.001$).
- Higher cumulative Actemra dose (per 200 mg) (OR: 0.78, 95% CI: 0.69–0.88, $p < 0.001$) and higher CinnoRA dose (per 100 mg) (OR: 0.74, 95% CI: 0.66–0.83, $p < 0.001$) were also independently associated with lower mortality.
- Cumulative dexamethasone dose was not independently associated with mortality (OR per 10 mg: 1.04, 95% CI: 0.96–1.13, $p = 0.34$).
- Cumulative prednisolone dose and remdesivir dose showed no significant independent association with mortality.
- The model's Nagelkerke R^2 was 0.28.

Figure 3 presents a forest plot of adjusted odds ratios for mortality (per 10-mg or 100-mg increase, as specified).

E-value calculation for the methylprednisolone-mortality association (OR=0.82): The E-value was 2.18, meaning that an unmeasured confounder would need to be associated with both methylprednisolone

use and mortality with a risk ratio of at least 2.18 to fully explain away the observed association. This suggests moderate robustness but does not rule out residual confounding.

3.3 Length of Hospital Stay

Spearman's correlation showed a statistically significant positive correlation between cumulative doses of all glucocorticoids (with and without coefficients) and length of hospital stay (Figure 4). This correlation is expected and primarily reflects that patients with longer hospital stays received more medication (time-dependent confounding).

Multivariable linear regression (Table 3), adjusted for all covariates and using cumulative doses as continuous variables, showed:

- Higher cumulative dexamethasone dose (per 10 mg) was independently associated with longer hospital stay ($\beta = 0.68$, 95% CI: 0.52–0.84, $p < 0.001$).
- Higher cumulative prednisolone dose (per 50 mg) was also associated with longer stay ($\beta = 0.29$, 95% CI: 0.07–0.51, $p = 0.009$).
- Higher cumulative methylprednisolone dose was not significantly associated with hospital stay ($\beta = 0.11$ per 100 mg, 95% CI: –0.04 to 0.26, $p = 0.15$).
- The adjusted R^2 for this model was 0.31.

Figure 5 shows scatter plots for each steroid type, with regression lines and 95% CIs. Dexamethasone had the strongest correlation (Spearman's $r = 0.40$, $R^2 = 0.299$), while methylprednisolone showed no significant correlation ($r = 0.12$, $R^2 = 0.069$, $p = 0.09$).

When analyzing average daily dose instead of cumulative dose, the associations with dexamethasone and prednisolone remained significant but were attenuated (dexamethasone: $\beta = 0.41$ per 10 mg/day, $p = 0.02$; prednisolone: $\beta = 0.18$ per 50 mg/day, $p = 0.04$), suggesting that duration of therapy contributes substantially to the observed associations.

3.4 Length of ICU Stay

A positive correlation was observed between total glucocorticoid dose and ICU length of stay in critically ill patients (Figure 6; Spearman's $r = 0.25$, $p = 0.002$). However, in the multivariable linear regression model (Table 4), after adjusting for covariates, no single glucocorticoid was independently associated with ICU length of stay. The adjusted R^2 for this model was 0.14.

3.5 Change in Pulmonary Involvement (CT Severity)

The bivariate correlation analysis did not show a significant relationship between the cumulative dose of any glucocorticoid and the change in lung involvement (Figure 7; $R^2 = 0.001$, $p = 0.52$).

In the multivariable linear regression model (Table 5), adjusted for all covariates, including baseline SpO₂ and initial CT score:

- Higher cumulative dexamethasone dose (per 10 mg) was the only variable significantly associated with less radiological improvement (i.e., higher CT score at follow-up, indicating worse or persistent lung involvement) ($\beta = 0.42$ per 10 mg, 95% CI: 0.04–0.80, $p=0.031$).
- No other glucocorticoid showed a significant association.
- The adjusted R² for this model was 0.19.

Sensitivity analysis (additional adjustment for the time from symptom onset to the first CT and the interval between CT scans) did not materially change this finding ($\beta=0.39$, $p=0.045$), suggesting that the association was not explained by timing differences. However, this paradoxical finding should be interpreted with extreme caution, as it may reflect residual confounding by indication (sicker patients receiving higher dexamethasone doses) or chance.

3.6 Summary of Key Findings

- Higher cumulative methylprednisolone dose → Associated with lower mortality (OR per 100 mg: 0.82, $p<0.001$)
- Higher cumulative dexamethasone dose → Associated with longer hospital stay ($\beta=0.68$ per 10 mg, $p<0.001$) and with less radiological improvement ($\beta=0.42$ per 10 mg, $p=0.031$)
- Higher cumulative prednisolone dose → Associated with longer hospital stay ($\beta=0.29$ per 50 mg, $p=0.009$)
- No glucocorticoid was independently associated with ICU stay duration after adjustment
- Actemra and CinnoRA (cumulative doses) were also associated with lower mortality

4. Discussion

This large single-center cohort study provides real-world evidence on the association between cumulative glucocorticoid doses and clinical outcomes in COVID-19. The key findings are: 1) a higher cumulative methylprednisolone dose was independently associated with reduced mortality; 2) higher cumulative dexamethasone and prednisolone doses were independently associated with prolonged hospital stay; and 3) a higher cumulative dexamethasone dose was paradoxically associated with less radiological improvement.

4.1 Mortality Benefit – Association, Not Causation

The mortality benefit seen with methylprednisolone aligns with major trials (1, 5, 7, 8) and recent meta-analyses suggesting methylprednisolone may be preferred in severe cases (9, 10). In critical patients, survivors received higher methylprednisolone doses than non-survivors (Fig. 2), suggesting a dose-

dependent protective effect. A network meta-analysis also found that pulse methylprednisolone was associated with the lowest 28-day mortality (12).

The superior anti-inflammatory potency of methylprednisolone (5× hydrocortisone vs. 4× for prednisolone and 30× for dexamethasone) (16) may explain its enhanced efficacy in severe disease.

However, we must emphasize that this is an observational study. The association between higher methylprednisolone dose and lower mortality may be confounded by indication – for example, clinicians may have chosen methylprednisolone for patients they judged to have a better prognosis, or used it earlier in the disease course. The E-value of 2.18 suggests moderate robustness but does not rule out residual confounding. Thus, our findings should be considered hypothesis-generating rather than practice-changing.

4.2 Prolonged Hospital and ICU Stays

The positive correlation between higher glucocorticoid doses and longer hospital stay is concerning. In the adjusted linear regression, dexamethasone ($\beta = 0.68$ per 10 mg) and prednisolone ($\beta = 0.29$ per 50 mg) were independent predictors of longer stays.

Several explanations exist:

1. **Channeling Bias and Time-Dependent Confounding (most likely):** Sicker patients with more protracted disease received higher and longer steroid doses. Despite adjustment for baseline SpO₂ and initial CT score, residual confounding cannot be excluded. **The attenuation of associations when using average daily dose instead of cumulative dose supports this interpretation.**
2. **Drug-Induced Morbidity:** High-dose steroids cause hyperglycemia, fluid retention, and immunosuppression, leading to secondary infections (bacterial or fungal) that delay recovery (13, 14). The RECOVERY trial found that higher-dose corticosteroids (20 mg dexamethasone) did not reduce mortality compared to standard low-dose (18), and low-dose dexamethasone was associated with increased non-COVID infections(19).
3. **Duration of Effect:** Cumulative dose is a function of both daily dose and duration. Patients with longer disease courses require more medication and thus have longer stays.

Interestingly, no drug was independently associated with ICU stay duration. This suggests that once patients are admitted to the ICU, disease severity and other factors (e.g., ventilator settings, organ support) may override the effect of glucocorticoid dose.

4.3 Paradoxical Radiological Finding – Dexamethasone and Worse CT Scores

The most intriguing and concerning finding is that a higher cumulative dexamethasone dose was independently associated with less radiological improvement ($\beta = 0.42$ per 10 mg, $p = 0.031$). This finding persisted after a sensitivity analysis that adjusted for the timing of CT scans.

Possible explanations:

1. **Resistant Inflammation:** Patients with more severe, progressive disease may receive higher doses of dexamethasone, and their lung involvement continues to worsen despite treatment.
2. **Immunosuppression and viral persistence:** Higher dexamethasone doses may suppress the immune response to the point where viral replication continues, leading to persistent lung damage.
3. **Metabolic Effects:** Dexamethasone's longer half-life and stronger mineralocorticoid effects may contribute to fluid retention and pulmonary edema, mimicking worsening lung involvement on CT (16).
4. **Secondary Infections:** Immunosuppression may increase the risk of CAPA, which can cause new infiltrates (13, 15).

This finding is novel and should be interpreted with extreme caution. It is a single-center, observational finding and may be entirely due to unmeasured confounding. It should serve as a hypothesis for future prospective studies, not as a basis for changes in clinical practice.

4.4 Clinical Implications – Cautious and Hypothesis-Generating

Given the observational nature of this study and the high risk of bias, we cannot make any clinical recommendations based on these findings. Instead, we suggest:

- The association between methylprednisolone and improved mortality warrants confirmation in randomized controlled trials
- The association between higher dexamethasone doses and prolonged hospitalization requires further investigation with time-dependent analyses
- Clinicians should continue to follow evidence-based guidelines from randomized trials (such as RECOVERY) for glucocorticoid use in COVID-19
- Patients receiving high-dose or prolonged glucocorticoid therapy should be closely monitored for secondary infections, particularly CAPA.(13, 15).

4.5 Limitations – Explicit and Comprehensive

1. **Observational design and channeling bias:** The most important limitation. Sicker patients received higher doses and different steroids. Despite rigorous adjustment, residual confounding is likely. E-value calculations suggest moderate but not complete robustness to unmeasured confounding.
2. **Time-dependent confounding:** Cumulative dose is inherently correlated with length of stay. Our sensitivity analysis using the average daily dose partially addressed this, but it cannot fully eliminate it.
3. **No true control group:** We compared doses rather than the presence/absence of steroids. This partially addresses the issue but does not eliminate confounding.

4. **Single-center study:** Limits generalizability.
5. **Incomplete data:** Follow-up CT scans, serial inflammatory markers, and oxygen saturation were not available for all patients.
6. **Concurrent immunomodulators:** The use of Actemra and CinnoRA adds complexity; although we adjusted for their doses, interaction effects cannot be fully ruled out.
7. **Non-standardized protocols:** Dosing and duration were at the physician's discretion, leading to significant practice variation.
8. **Cumulative dose as a measure:** Cumulative dose combines daily dose and duration, which may have different biological effects. Our sensitivity analysis partially disentangled these effects
9. R^2 values were modest (0.14–0.31), indicating that steroid doses explain only a fraction of the variance in outcomes.

5. Conclusion

In this large observational cohort study of COVID-19 patients, a higher cumulative methylprednisolone dose was independently associated with lower mortality (OR per 100 mg: 0.82, $p < 0.001$), along with Actemra and CinnoRA. However, higher cumulative doses of dexamethasone and prednisolone were independently associated with prolonged hospital stays. Paradoxically, a higher cumulative dexamethasone dose was associated with less radiological improvement, suggesting that its benefit may not be mediated through prevention of lung opacification, or that the dose-response relationship is more complex than previously thought.

Given the observational nature of the study and the high risk of channeling, time-dependent, and residual confounding, these findings should be interpreted strictly as hypothesis-generating. They do not warrant any immediate change in clinical practice.

We strongly caution readers and clinicians against using these results to guide treatment decisions. Evidence from randomized controlled trials (particularly the RECOVERY trial) should continue to inform clinical practice.

Future research priorities include:

1. Randomized controlled trials directly comparing methylprednisolone and dexamethasone at different cumulative dose ranges
2. Studies using time-dependent analyses are better to disentangle the effect of dose from the duration of illness
3. Prospective studies investigating the paradoxical radiological finding with dexamethasone
4. Long-term follow-up studies to assess glucocorticoid-related adverse effects

Abbreviations

ARDS

acute respiratory distress syndrome
CAPA
COVID-19-associated pulmonary aspergillosis
COVID-19
coronavirus disease 2019
CT
computed tomography
ICU
intensive care unit
IRB
Institutional Review Board
PACS
picture archiving and communication system
PCR
polymerase chain reaction
SARS-CoV-2
severe acute respiratory syndrome coronavirus 2
SpO₂
peripheral oxygen saturation.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Institutional Review Board of Baqiyatallah University of Medical Sciences, Tehran, Iran (approval code: IR.BMSU.REC.1402.081), and was conducted in accordance with the Declaration of Helsinki. The requirement for informed consent to participate was waived by the Institutional Review Board because of the retrospective nature of the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

Behzad Einollahi, Mohammad Ahmadi, and Seyed Javad Davari-Sani conceived and designed the study. Behzad Einollahi and Seyed Javad Davari-Sani supervised the research project. Mohammad Ahmadi, Mohammad Reza Einollahi, Mehrdad Niazzadeh, Mostafa Karbalaie, Arefeh Haji Shah Valadi, and Ali Jalali were responsible for data acquisition, curation, and validation. Mohammad Ahmadi, Mohammad Reza Einollahi, Mehrdad Niazzadeh, and Mostafa Karbalaie performed the statistical analyses and data interpretation. Mohammad Ahmadi and Seyed Javad Davari-Sani drafted the initial manuscript. All authors critically revised the manuscript for important intellectual content and approved the final version. Seyed Javad Davari-Sani is the guarantor of the study and takes full responsibility for the integrity of the data and the accuracy of the analysis.

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The authors have no acknowledgments to declare.

Data Availability

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

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Tables

Table 1: Patient Disposition and Exclusion Criteria

Reason for Exclusion	n (%)
Not receiving glucocorticoids	3,200
Participating in other clinical trials	1,875
Received hydroxychloroquine	3,890
Received Kaletra	1,236
Received Recigen	986
Received favipiravir	458
Received Soodak	432
Received COVID-19 plasma	375
Received other investigational therapies	375

Baseline characteristics of the study cohort (n=5,261):

Characteristic	Value
Mean age (years)	53.7 ± 15.0
Female sex	39.6%
Mean hospital stay (days)	6.6 ± 3.9
ICU admission required	22.2%
Disease severity (categorized):	
– Mild	0% (all had pulmonary involvement)
– Moderate	42.5%
– Severe	50.6%
– Critical	6.9%
Received remdesivir	67.5%
Received CinnoRA (anakinra)	56.7%
Received Actemra (tocilizumab)	10.7%
Mean baseline SpO₂ (%)	91.4 ± 4.2
Mean initial CT severity score (0-25)	14.6 ± 5.1

Table 2: Multivariable Logistic Regression for in-Hospital Mortality (with cumulative doses as continuous variables)

Variable	OR (per specified unit increase)	95% CI	P-value
Methylprednisolone (per 100 mg)	0.82	0.74 – 0.91	<0.001
Dexamethasone (per 10 mg)	1.04	0.96 – 1.13	0.34
Prednisolone (per 50 mg)	1.06	0.94 – 1.20	0.35
Actemra (per 200 mg)	0.78	0.69 – 0.88	<0.001
CinnoRA (per 100 mg)	0.74	0.66 – 0.83	<0.001
Remdesivir (per 500 mg)	0.95	0.84 – 1.08	0.42
Age (per year)	1.04	1.02 – 1.06	<0.001
Baseline SpO ₂ (per 1%)	0.89	0.86 – 0.92	<0.001
Initial CT score (per 1 point)	1.12	1.07 – 1.17	<0.001
Nagelkerke R²	0.28		

Table 3: Multivariable Linear Regression for Hospital Stay Length (days)

Variable	β Coefficient	95% CI	P-value	Partial R ²
Dexamethasone (per 10 mg)	0.68	0.52 – 0.84	<0.001	0.12
Prednisolone (per 50 mg)	0.29	0.07 – 0.51	0.009	0.03
Methylprednisolone (per 100 mg)	0.11	–0.04 – 0.26	0.15	0.01
Actemra (per 200 mg)	0.08	–0.06 – 0.22	0.27	0.005
CinnoRA (per 100 mg)	0.06	–0.08 – 0.20	0.40	0.003
Remdesivir (per 500 mg)	–0.10	–0.25 – 0.05	0.19	0.007
Age (per year)	0.04	0.02 – 0.06	<0.001	0.04
Baseline SpO ₂ (per 1%)	–0.12	–0.18 – –0.06	<0.001	0.03
Initial CT score (per 1 point)	0.09	0.04 – 0.14	0.001	0.02
Adjusted R² (full model)	0.31			

Table 4: Multivariable Linear Regression for ICU Stay Length (days)

Variable	β Coefficient	95% CI	P-value
Dexamethasone (per 10 mg)	0.21	-0.32 – 0.74	0.44
Prednisolone (per 50 mg)	0.98	-0.65 – 2.61	0.24
Methylprednisolone (per 100 mg)	-0.04	-0.58 – 0.50	0.88
Actemra (per 200 mg)	-0.06	-0.84 – 0.72	0.88
CinnoRA (per 100 mg)	-0.11	-0.97 – 0.75	0.80
Remdesivir (per 500 mg)	0.54	-0.45 – 1.53	0.28
Age (per year)	0.03	-0.02 – 0.08	0.24
Baseline SpO ₂ (per 1%)	-0.14	-0.26 – -0.02	0.02
Initial CT score (per 1 point)	0.12	0.01 – 0.23	0.03
Adjusted R² (full model)	0.14		

Table 5: Multivariable Linear Regression for Change in CT Severity Score (improvement = positive value)

Variable	β Coefficient	95% CI	P-value
Dexamethasone (per 10 mg)	-0.42	-0.80 – -0.04	0.031
Prednisolone (per 50 mg)	-0.28	-0.61 – 0.05	0.10
Methylprednisolone (per 100 mg)	-0.22	-0.52 – 0.08	0.15
Actemra (per 200 mg)	-0.07	-0.41 – 0.27	0.69
CinnoRA (per 100 mg)	-0.11	-0.44 – 0.22	0.51
Remdesivir (per 500 mg)	0.02	-0.32 – 0.36	0.91
Age (per year)	-0.02	-0.05 – 0.01	0.19
Baseline SpO ₂ (per 1%)	0.08	0.01 – 0.15	0.03
Initial CT score (per 1 point)	-0.15	-0.22 – -0.08	<0.001
Adjusted R² (full model)	0.19		

Figures

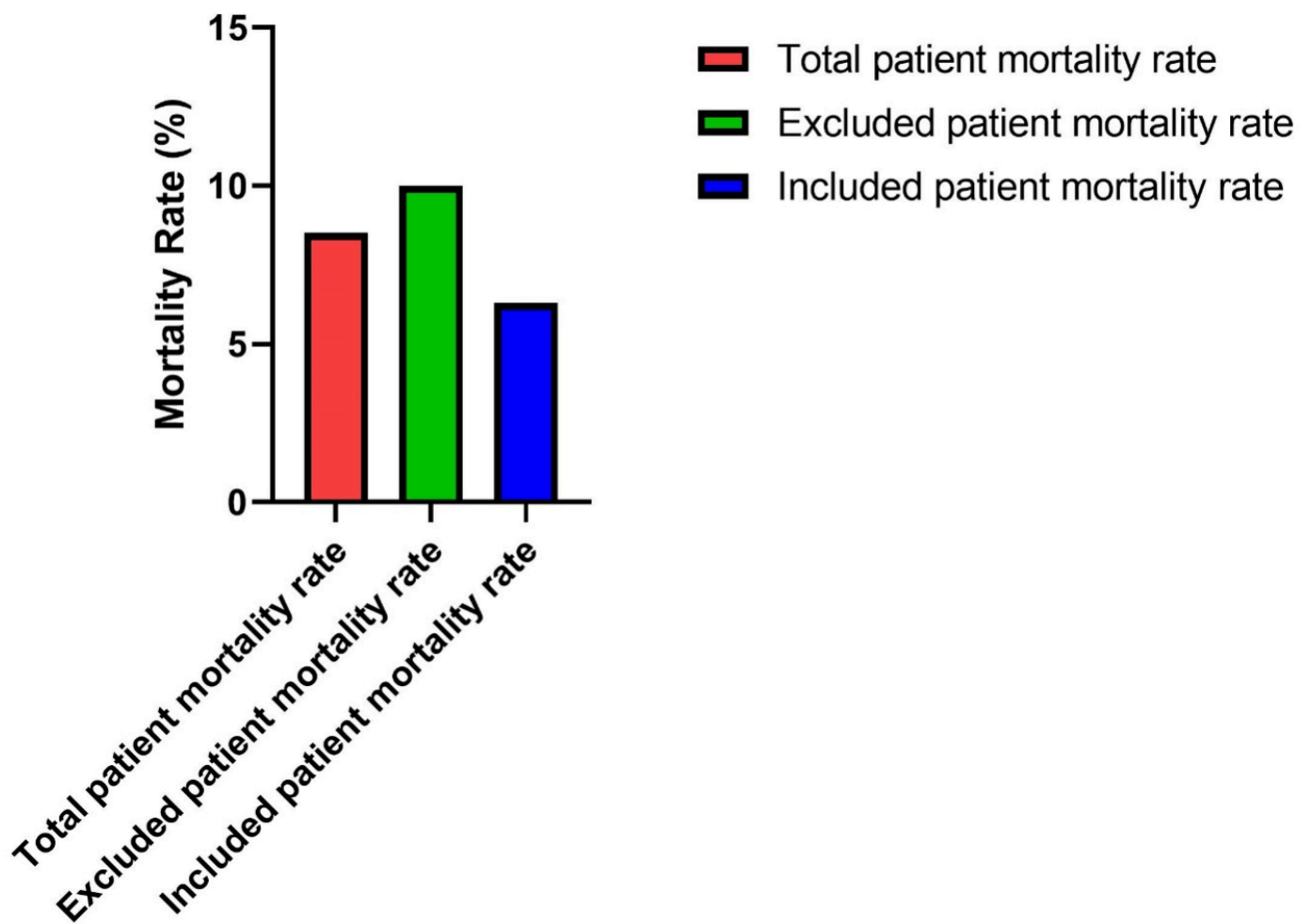


Figure 1

Mortality rates in total, excluded, and included patient populations. Overall mortality was 8.5% in all patients, 10% in excluded patients, and 6.3% in the final study cohort ($p < 0.001$).

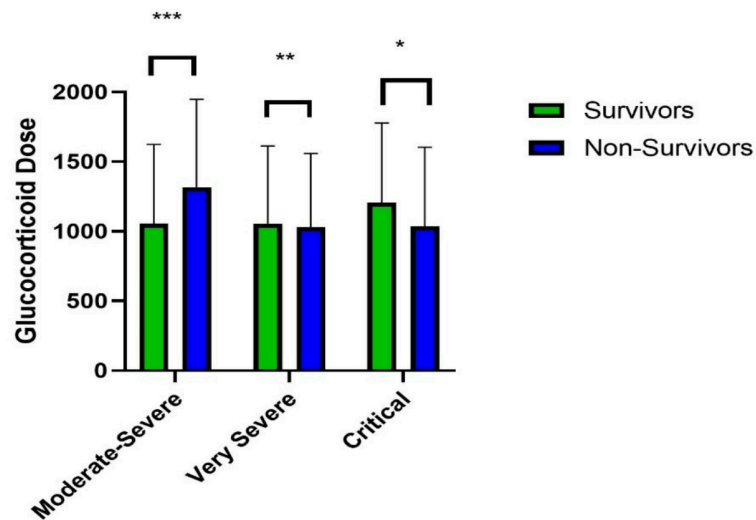


Figure 2

Comparison of total glucocorticoid dose (with anti-inflammatory coefficient) between survivors and non-survivors by disease severity. Data are presented as mean dose in milligrams (mg) of glucocorticoid equivalent. Error bars represent standard deviation. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

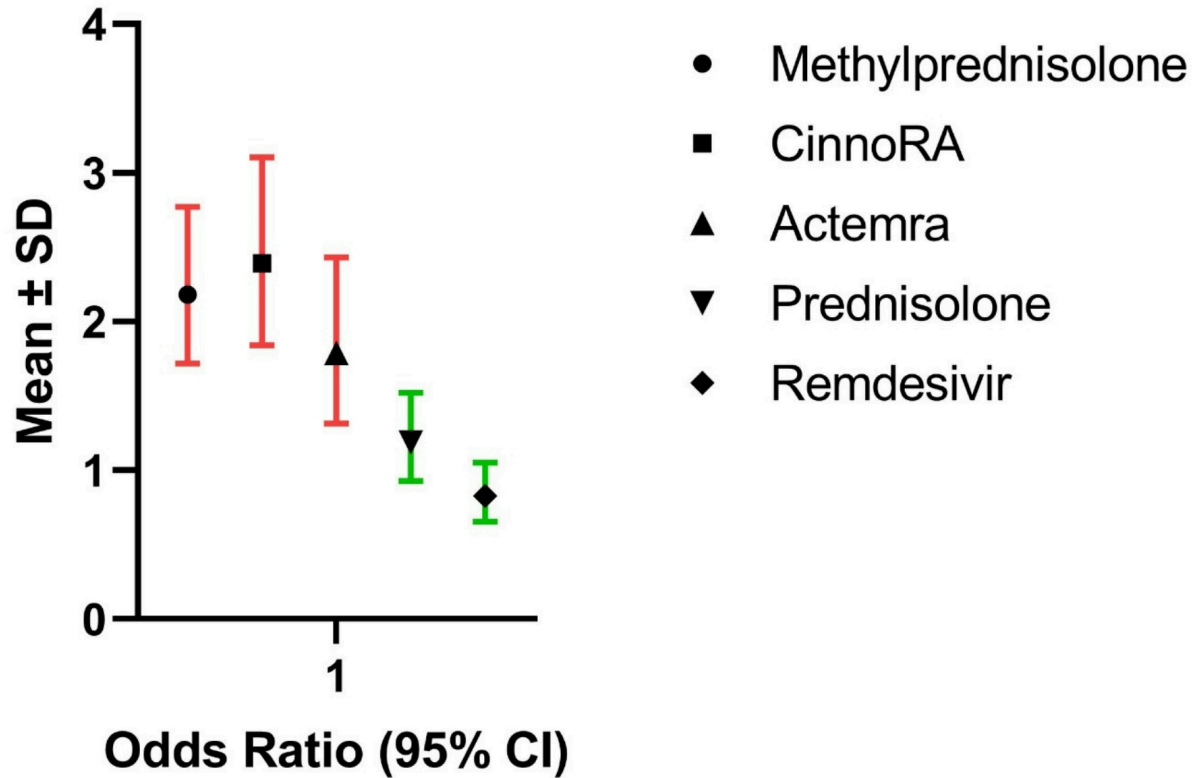


Figure 3

Forest plot showing odds ratios for in-hospital mortality. Methylprednisolone, CinnoRA, and Actemra were significantly associated with reduced mortality, while Prednisolone and Remdesivir showed no significant effect. Error bars represent 95% confidence intervals. The reference line at OR = 1.0 indicates no effect.

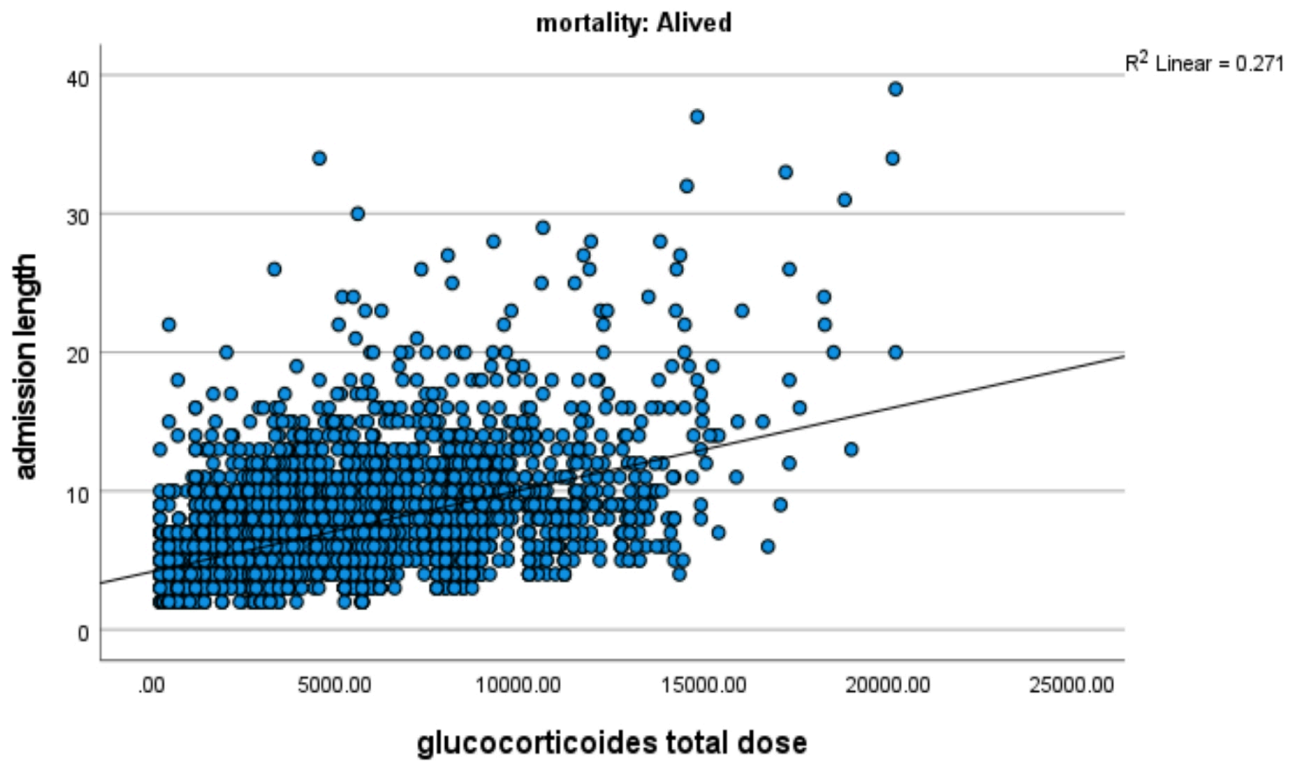


Figure 4

Scatter plot showing the positive correlation between total glucocorticoid dose and hospital stay length in survivors ($R^2 = 0.271$, $p < 0.001$).

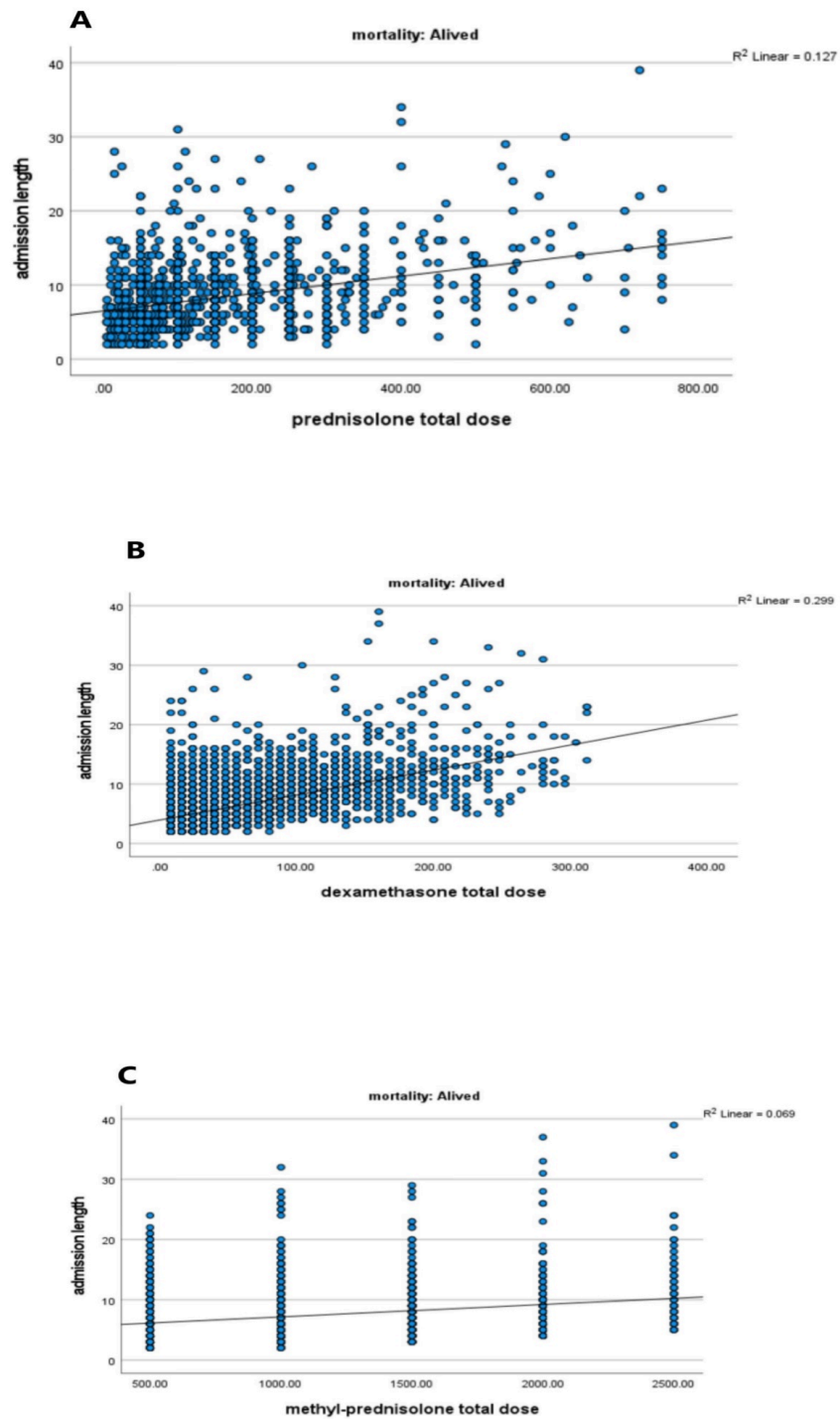


Figure 5

Scatter plots showing correlations between cumulative doses of specific glucocorticoids and hospital stay length in surviving patients. **(A)** Prednisolone dose versus hospital stay length ($R^2 = 0.127$, $p = 0.007$). **(B)** Dexamethasone dose versus hospital stay length ($R^2 = 0.299$, $p < 0.001$). **(C)** Methylprednisolone dose versus hospital stay length ($R^2 = 0.069$, $p = 0.09$). Each point represents an individual patient. The blue line represents the linear regression line with 95% confidence interval

(shaded area). Dexamethasone showed the strongest correlation with prolonged hospitalization, while methylprednisolone showed the weakest and non-significant correlation.

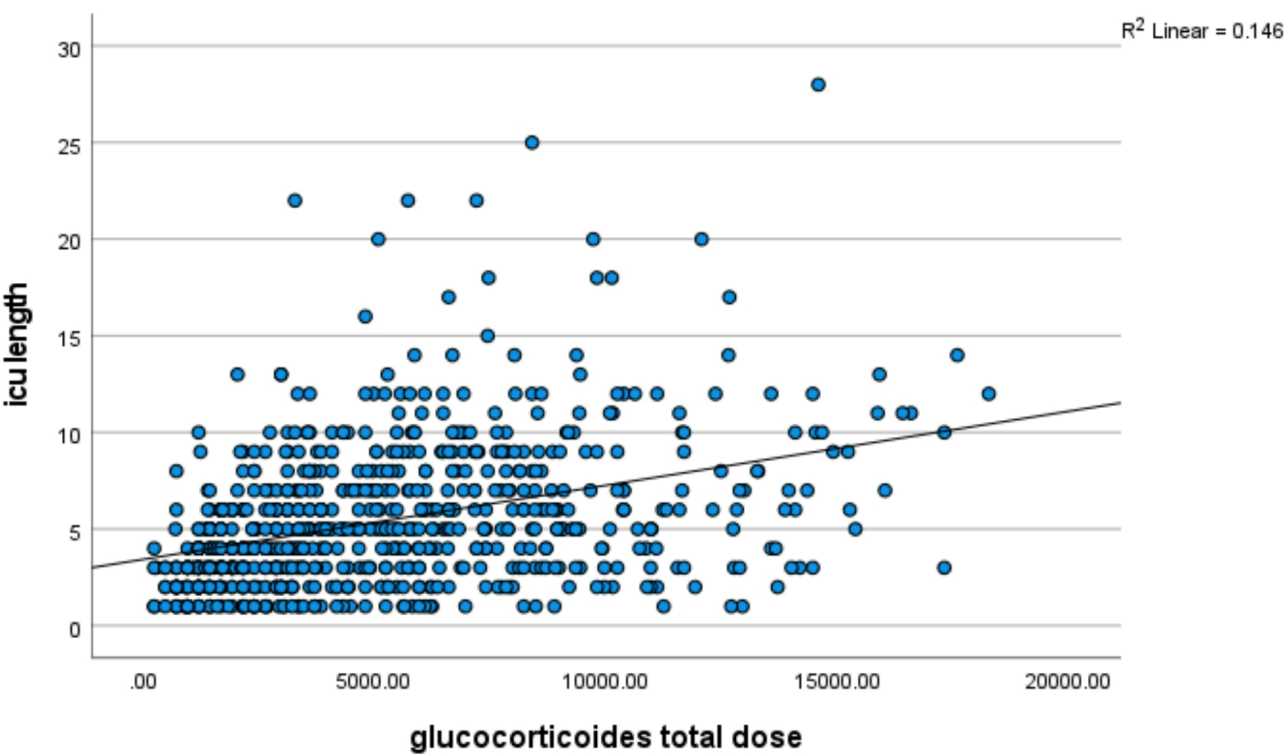


Figure 6

Correlation between total glucocorticoid dose and ICU stay length ($R^2=0.146$, $p=0.002$).

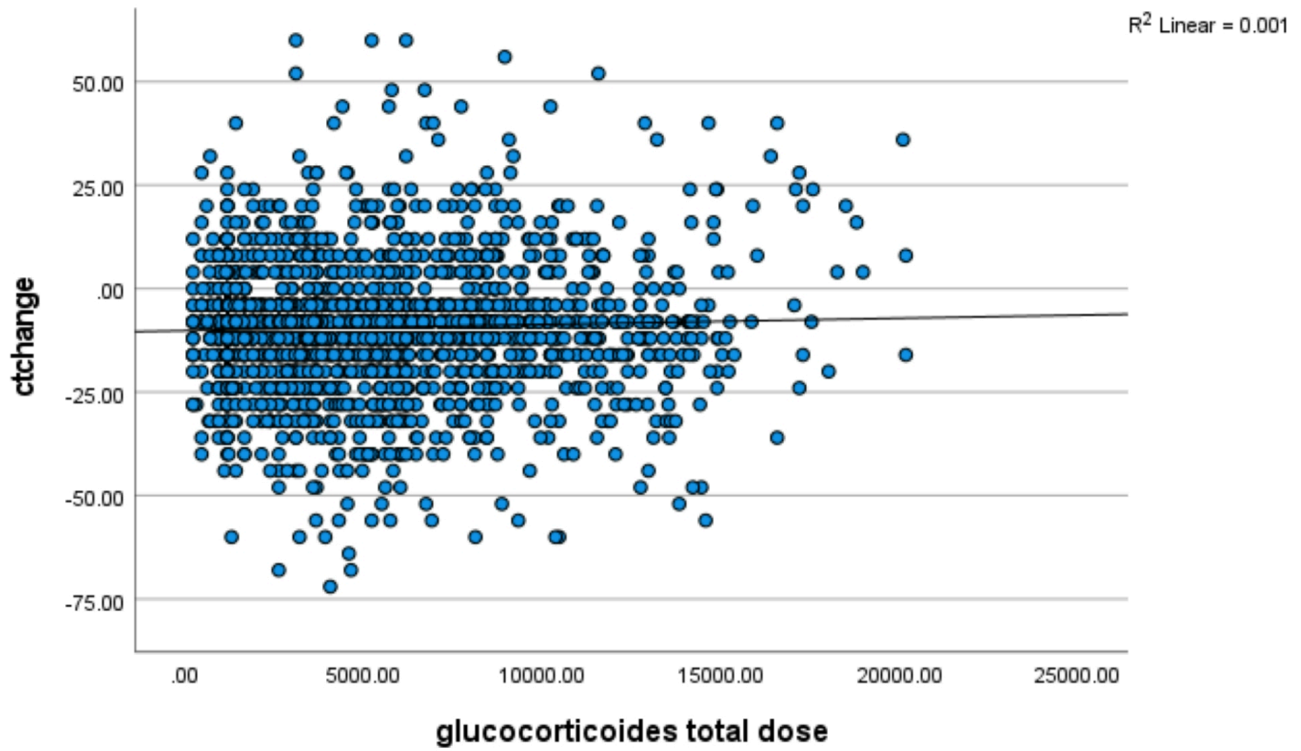


Figure 7

Correlation between total glucocorticoid dose and change in pulmonary involvement ($R^2=0.001$, $p=0.52$).