

Impact of Glucocorticoid Therapy on 28-Day Mortality in Patients Having Severe Fever with Thrombocytopenia Syndrome in an Intensive Care Unit: A Retrospective Analysis

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Purpose: The high mortality rate associated with the critical stages of severe fever with thrombocytopenia syndrome (SFTS) does not have effective treatment. We aimed to evaluate the 28-day mortality and potential impact of glucocorticoid therapy in these patients.

Patients and Methods: This retrospective observational study included participants from the intensive care unit between July 2019 and April 2023. The participants were categorized into glucocorticoid (GC) and non-GC groups. Propensity score matching (PSM) was employed to ensure comparability between groups. We used Cox proportional hazard models to examine mortality risk associated with GC use, Kaplan–Meier survival analyses for overall survival, stratified Cox proportional hazard models for subgroup analyses, and likelihood ratio tests to examine interactions between subgroups.

Results: Of 218 patients with SFTS (median age, 71 years; male, 49.1%), 61.9% required mechanical ventilation, 58.3% received GC treatment, and the 28-day mortality rate was 61.5%. After PSM, there were 58 patients in each group; post-PSM analysis revealed improved 28-day mortality rates with GC treatment, particularly for patients with Glasgow coma scale (GCS) score <13 (hazard ratio [HR], 95% confidence interval [CI] for GCS score: 9–12: 0.39, 0.17–0.88, $p=0.024$ and for GCS score: 3–8: 0.09, 0.02–0.35, $p=0.001$); lactate levels >2 mmol/L (0.35, 0.15–0.83, $p=0.017$); and norepinephrine usage (0.26, 0.13–0.49, $p<0.001$). Combining antiviral (0.41, 0.22–0.78, $p=0.006$) or immunoglobulin therapy (0.22, 0.1–0.51, $p<0.001$) with GC treatment significantly decreased the 28-day mortality rates, compared with GC monotherapy.

Conclusion: Using GCs reduced the high 28-day mortality rate in the patients, especially with low GCS score, high lactate levels, norepinephrine intake, and on antiviral or immunoglobulin therapy.

Keywords: glucocorticoids, mortality, severe fever with thrombocytopenia syndrome, intensive care unit, virus infection

Introduction

Severe fever with thrombocytopenia syndrome (SFTS) is an emerging tick-borne infectious disease that affects both humans and animals and is caused by severe fever with thrombocytopenia syndrome virus (SFTSV). The SFTSV was first isolated from a patient's blood sample in Henan province in 2009.¹ The disease is endemic in several Asian countries, including China, Korea, Vietnam, Pakistan, and Japan, and has been shown to cause high mortality rates across these regions.^{1–5} The clinical manifestations of SFTSV infection mainly include fever, thrombocytopenia, leukopenia, and gastrointestinal symptoms. Although most patients with SFTSV have mild to moderate symptoms, some may experience severe complications, such as organ failure and blood clotting issues, which can quickly lead to death.⁶

Once the central nervous system is involved, the mortality rate can reach 44.7%.⁷ For critically ill patients with SFTSV, no effective drug or intervention has been shown to reduce mortality except life support.

A severe systemic inflammatory response is one of the primary characteristics of this condition.⁸ Consequently, systemic glucocorticoid (GC) therapy serves as an adjunct treatment in patients with severe SFTS in clinical settings.^{9–12} However, the effects of GCs on SFTS have been inconsistent across studies,^{9,11} suggesting the need to understand the specific circumstances that cause variations in treatment efficacy. Notably, the effect of GC therapy may depend on the severity of patient's condition.

Despite the known inconsistencies and the potential impact of patient conditions on therapy outcomes, to the best of our knowledge, no studies have specifically addressed the use of GCs in critically ill patients with SFTS in the intensive care unit (ICU). Therefore, this study aimed to evaluate the 28-day mortality and potential impact of glucocorticoid therapy in these patients.

Materials and Methods

Data Source and Study Population

This study employed a retrospective observational design, selecting patients aged ≥ 18 years with SFTS admitted to the ICU of Yantai Qishan Hospital in Yantai City from July 2019 to April 2023. This study was approved by the Ethics Committee of Qishan Hospital (202401). Informed consent was waived by ethics committee due to its retrospective design. In accordance with the guidelines set forth by the Declaration of Helsinki, this study was conducted with the utmost respect for patient confidentiality and ethical standards. Every case was meticulously confirmed in the laboratory center at Qishan Hospital. The diagnosis of SFTS was ascertained by detecting the ribonucleic acid (RNA) of the SFTSV in patients' blood samples. This was accomplished using real-time reverse transcription-polymerase chain reaction.¹³ Following the successful identification of SFTSV RNA, we accurately quantified the viral load in each sample. This rigorous approach ensured a precise and reliable diagnosis of SFTS in all examined cases. The exclusion criteria included individuals with incomplete clinical data, hematological disorders, and an ICU stay of less than 24 hours.

Study Definition

The study was started with patient data from the first day of ICU admission, and the worst value within 24 h was recorded. The severity of the condition was quantitatively assessed using the sequential organ failure assessment (SOFA) score. The SOFA score represents indicators of different organ functions. The Grading was conducted based on the viral load, which was categorized into three levels: low viremia ($<10^6$ copies per mL), intermediate viremia (10^6 – 10^7 copies per mL), and high viremia ($>10^7$ copies per mL).¹⁴ The definition of GC use included the administration of methylprednisolone and/or hydrocortisone. The primary outcome was 28-day mortality from ICU admission, and secondary outcomes included bleeding sites, secondary infections, mechanical ventilation, arrhythmia, continuous renal replacement therapy (CRRT), ICU stay, and hospital stay. We recorded the duration from symptom onset to ICU admission (time from symptom onset to ICU admission, T-SO-ICUA).

Statistical Analysis

Categorical variables were described as frequencies, whereas continuous variables were presented as either mean \pm standard deviation or median (range). To evaluate statistical significance, Student's *t*-test or analysis of variance was applied, as appropriate. For categorical variable comparisons, the chi-square (χ^2) test was used along with Fisher's exact test. After analyzing baseline data, the participants were categorized into GC and non-GC groups based on GC usage. Propensity score matching (PSM) was based primarily on demographic and clinical characteristics excluding vital signs and investigations, with the exception of viral load. The results were compared between the GC and non-GC groups using 1:1 matching with a caliper value of 0.02. This method successfully neutralized pre-existing disparities between the groups. Kaplan–Meier survival analysis was used to evaluate the duration from SFTS onset to mortality and subsequent comparisons between the groups. A Cox proportional hazards model was used to assess the mortality risk associated with GC treatment. Subgroup analyses were conducted using a stratified Cox proportional hazards model based on the

Glasgow coma scale (GCS) score; lactate levels; use of immunoglobulin, norepinephrine, and antiviral drugs; and partial pressure of oxygen in the alveoli/ fraction of inspired oxygen levels. Likelihood ratio tests were used to examine the interactions between the subgroups. The R statistical software (version 4.2.2, The R Foundation) was used for all statistical analyses. All tests were two-sided, and statistical significance was set at $p < 0.05$.

Results

Baseline Characteristics

Between July 2019 and April 2023, a total of 231 confirmed cases of SFTS were examined. A total of 218 patients who met the eligibility criteria were enrolled in this study (Figure 1). The median age of the cohort admitted to the ICU was 71 years (interquartile range [IQR]: 65–76 years), and 107 (49.1%) patients were male. The proportions of participants who reported smoking cigarettes and consuming alcohol were 21.1% (46/218) and 17.9% (39/218), respectively. The chronic comorbidities observed included hypertension, diabetes, coronary heart disease (CHD), and chronic obstructive pulmonary disease (COPD). These conditions were present in 57 (26.1%), 46 (21.1%), 15 (6.9%), and 5 patients (2.3%), respectively. The median of T-SO-ICUA was 7.0 days (IQR: 6.0–8.0 days). According to the viral load, the distribution of the patients in the categories of low, medium, and high viremia were 173 (79.4%), 27 (12.4%), and 18 (8.2%), respectively. The median SOFA score was 10.5 (IQR: 6.2–13.0), indicating a considerable degree of critical illness among the patients (Table 1).

A total of 127 patients (58.3%) received GC treatment in the ICU. In the unmatched cohorts, individuals who received GCs were younger (70 [64–75.5] vs 74 [66–78.5] years, $p = 0.035$) and had higher SOFA scores (12.0 [9.0–13.5] vs 7.0 [4.5–12.0], $p < 0.001$). However, factors such as sex, BMI, smoking status, T-SO-ICUA, and chronic comorbidities were not significantly different between the cohorts. After PSM, there were 58 patients in each group and there were no significant differences in the vital signs or laboratory variables between the GC and non-GC groups (Table 2).

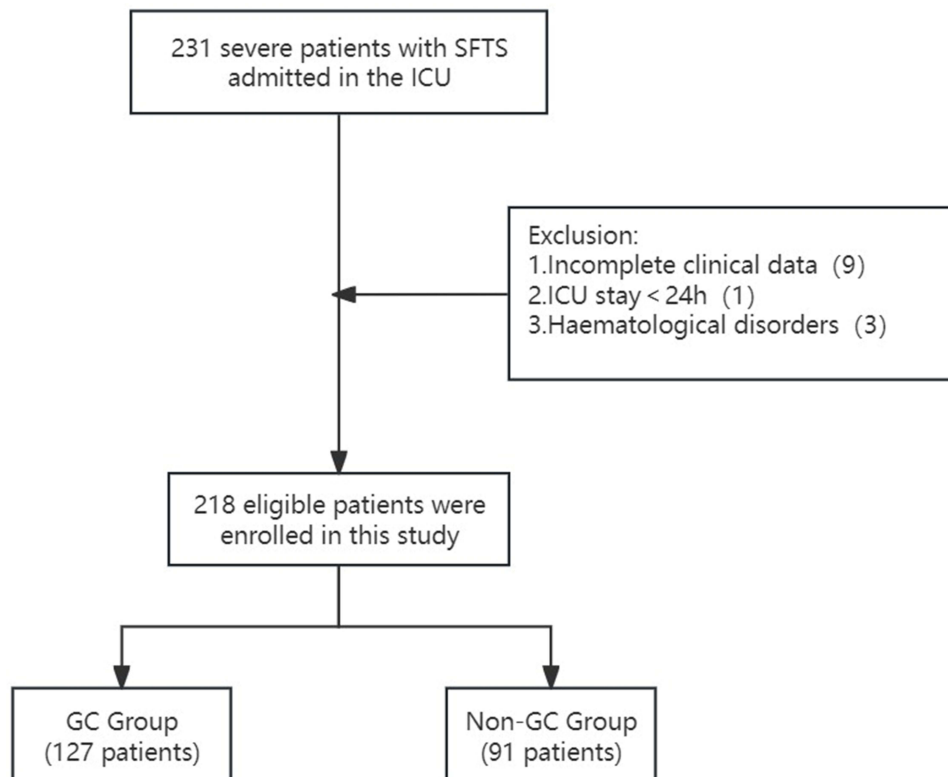


Figure 1 Flow chart of the study.

Abbreviations: SFTS, severe fever with thrombocytopenia syndrome; GC, glucocorticoid; ICU, intensive care unit.

Table 1 Clinical Characteristics of Patients with SFTS in the Non-GC and GC Groups in the Original and Matched Cohorts

Variable	Original Cohort				Matched Cohort		
	Total (n=218)	Non-GC (n=91)	GC (n=127)	p	Non-GC (n=58)	GC (n=58)	p
Age (years), median (IQR)	71.0 (65.0–76.0)	74.0 (66.0–78.5)	70.0 (64.0–75.5)	0.035	71.0 (65.2–78.8)	71.0 (65.0–76.0)	0.478
Male, n (%)	107 (49.1)	41 (45.1)	66 (52)	0.314	30 (51.7)	26 (44.8)	0.457
BMI (kg/m ²), median (IQR)	25.0 (23.4–25.8)	24.8 (23.2–25.5)	25.0 (23.6–25.9)	0.355	25.0 (23.9–25.8)	24.8 (23.0–26.0)	0.568
Smoking, n (%)	46 (21.1)	17 (18.7)	29 (22.8)	0.459	13 (22.4)	10 (17.2)	0.485
Alcohol consumption, n (%)	39 (17.9)	10 (11)	29 (22.8)	0.024	10 (17.2)	10 (17.2)	1
SOFA score, median (IQR)	10.5 (6.2–13.0)	7.0 (4.5–12.0)	12.0 (9.0–13.5)	< 0.001	10.0 (6.0–13.0)	9.5 (7.0–12.0)	0.468
Viral load n (%)				< 0.001			0.543
Low	173 (79.4)	85 (93.4)	88 (69.3)		52 (89.7)	48 (82.8)	
Medium	27 (12.4)	5 (5.5)	22 (17.3)		5 (8.6)	8 (13.8)	
High	18 (8.3)	1 (1.1)	17 (13.4)		1 (1.7)	2 (3.4)	
T-SO-ICUA, median (IQR)	7.0 (6.0–8.0)	7.0 (6.0–8.5)	7.0 (5.5–8.0)	0.750	7.0 (6.0–8.0)	7.0 (6.0–9.0)	0.573
Chronic comorbidity, n (%)							
Diabetes, n (%)	46 (21.1)	17 (18.7)	29 (22.8)	0.459	16 (27.6)	13 (22.4)	0.520
Hypertension, n (%)	57 (26.1)	23 (25.3)	34 (26.8)	0.804	15 (25.9)	12 (20.7)	0.510
CHD, n (%)	15 (6.9)	6 (6.6)	9 (7.1)	0.887	4 (6.9)	4 (6.9)	1
COPD, n (%)	5 (2.3)	4 (4.4)	1 (0.8)	0.163	1 (1.7)	1 (1.7)	1

Abbreviations: SFTS, severe fever with thrombocytopenia syndrome; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; SOFA, sequential organ failure assessment; T-SO-ICUA: time from symptom onset to ICU admission; BMI, body mass index; GC, glucocorticoid; IQR, interquartile range.

Clinical Outcomes with Propensity Score-Matched Cohorts

In our study of 218 patients, we observed a 28-day mortality rate of 61.5% (134 patients), mechanical ventilation in 61.9% (135 patients), CRRT in 21.1% (46 patients), median ICU stay of 4.0 days (range: 2.0–9.8 days), and median hospital stay of 8.0 days (range: 4.0–16.8 days). Complications, such as bleeding sites, secondary infections, and arrhythmias, are detailed in [Table 3](#). Further analyses before PSM indicated that the GC group had higher rates of mortality (68.5% vs 51.6%; $p=0.012$), secondary infections (68.5% vs 51.6%; $p=0.012$), mechanical ventilation (79.5% vs 37.4%; $p<0.001$), CRRT (31.5% vs 6.6%; $p<0.001$), and arrhythmias (49.6% vs 35.2%; $p=0.034$) than the non-GC group did, highlighting the potential risks associated with GC treatment.

Following PSM, we compared the clinical outcomes between the GC and non-GC groups ([Table 3](#)). The GC group demonstrated a significantly lower 28-day mortality rate compared to the non-GC group (31% vs 51.7%; $p=0.024$). The GC group exhibited significantly higher rates of secondary infections (77.6% vs 51.7%, $p=0.004$) and a greater likelihood of requiring CRRT (27.6% vs 10.3%, $p=0.018$) than the non-GC group did. Additionally, compared with the non-GC group, the GC group experienced longer ICU stays (12.0 days [range: 6.0–16.8] vs 4.0 days [range: 2.0–7.8], $p<0.001$) and hospital stays (17.5 days [range 14.0–24.5] vs 7.0 days [range 3.0–14.0], $p<0.001$), suggesting the association of complex outcomes with GC treatment. The post-PSM analysis further elucidated survival differences between the groups ([HR] 0.42, 95% confidence interval [CI]: 0.24–0.76, $p=0.004$), as shown in [Figure 2](#).

Table 2 Vital Signs and Lab Results of SFTS Patients in Non-GC and GC Groups in the Original and Matched Cohorts

Variables	Original Cohort				Matched Cohort			
	Total (n = 218)	Non-GC (n = 91)	GC (n = 127)	p	Total (n = 116)	Non-GC (n = 58)	GC (n = 58)	p
Vital sign								
MBP, median (IQR)	88.7 (79.0, 97.9)	90.3 (82.2, 103.0)	88.0 (76.8, 97.2)	0.138	89.5 (81.9, 100.3)	90.2 (82.3, 103.6)	89.3 (78.9, 97.0)	0.436
Heart rate, median (IQR)	84.0 (74.0, 100.0)	82.0 (74.5, 101.0)	85.0 (73.5, 100.0)	0.84	84.0 (75.0, 100.0)	85.5 (75.2, 104.2)	83.0 (75.2, 100.0)	0.488
Respiratory rate, median (IQR)	23.0 (20.0, 29.0)	21.0 (19.0, 28.0)	25.0 (20.0, 29.5)	0.006	23.0 (19.8, 29.0)	22.5 (19.0, 28.0)	24.5 (20.0, 29.0)	0.121
Temperature on admission, median (IQR)	37.0 (36.6, 37.8)	37.0 (36.6, 38.0)	36.9 (36.6, 37.6)	0.822	37.0 (36.7, 38.0)	37.1 (36.8, 38.0)	37.0 (36.7, 38.1)	0.784
Maximum temperature, median (IQR)	38.9 (38.5, 39.2)	38.8 (38.5, 39.0)	39.0 (38.5, 39.2)	0.074	38.9 (38.5, 39.2)	38.8 (38.5, 39.2)	39.0 (38.5, 39.2)	0.659
Laboratory variable								
WBC, median (IQR)	4.2 (2.1, 6.9)	4.1 (2.2, 6.9)	4.3 (2.1, 7.1)	0.896	4.2 (2.2, 6.9)	4.3 (2.2, 7.8)	4.2 (2.2, 6.2)	0.444
Hemoglobin, median (IQR)	132.0 (114.2, 145.0)	130.0 (112.0, 147.0)	133.0 (116.0, 144.0)	0.965	131.5 (116.0, 144.0)	130.5 (111.5, 149.0)	132.5 (120.2, 139.0)	0.868
Platelet count, median (IQR)	44.0 (31.2, 62.0)	44.0 (31.0, 64.5)	44.0 (32.0, 60.0)	0.652	43.0 (30.0, 59.2)	40.5 (30.0, 58.5)	46.5 (30.5, 59.0)	0.456
Lymphocyte count, median (IQR)	0.8 (0.5, 1.4)	0.9 (0.5, 1.4)	0.7 (0.5, 1.4)	0.484	0.8 (0.5, 1.3)	0.9 (0.5, 1.4)	0.7 (0.4, 1.2)	0.356
PH, median (IQR)	7.4 (7.3, 7.4)	7.4 (7.4, 7.5)	7.4 (7.3, 7.4)	0.005	7.4 (7.4, 7.4)	7.4 (7.4, 7.4)	7.4 (7.3, 7.5)	0.576
Lactate, median (IQR)	1.9 (1.2, 3.3)	1.7 (1.2, 2.9)	1.9 (1.3, 3.5)	0.081	1.7 (1.2, 2.7)	1.7 (1.2, 2.9)	1.6 (1.1, 2.5)	0.615
PaO ₂ /FiO ₂ , median (IQR)	221.0 (157.5, 287.0)	233.0 (190.8, 362.2)	203.0 (139.0, 254.0)	< 0.001	225.5 (166.0, 301.5)	221.0 (166.0, 298.0)	236.0 (168.0, 306.0)	0.956
ALT, median (IQR)	117.3 (59.3, 197.9)	103.7 (50.5, 181.3)	125.1 (74.6, 214.7)	0.02	113.8 (54.5, 175.1)	131.6 (51.9, 182.5)	102.9 (60.5, 155.7)	0.337
Total bilirubin, median (IQR)	12.1 (8.6, 19.4)	11.4 (7.5, 18.3)	12.4 (9.1, 22.4)	0.113	11.3 (8.0, 17.6)	12.1 (8.3, 20.0)	11.2 (8.0, 16.1)	0.487
Albumin, mean ± SD	27.3 ± 4.3	27.4 ± 5.0	27.3 ± 3.7	0.894	27.3 ± 4.3	27.0 ± 5.2	27.7 ± 3.1	0.401
Creatinine, median (IQR)	79.9 (59.3, 127.2)	70.8 (57.2, 121.0)	84.2 (62.1, 132.2)	0.13	75.0 (59.0, 120.8)	91.2 (62.2, 204.0)	70.5 (56.2, 91.4)	0.008
Sodium, median (IQR)	135.6 (132.0, 139.0)	135.9 (132.6, 139.0)	135.4 (131.7, 138.9)	0.384	135.4 (132.4, 139.0)	135.4 (132.7, 139.0)	135.3 (132.0, 139.0)	0.611
Calcium, mean ± SD	1.9 ± 0.2	1.9 ± 0.2	1.9 ± 0.2	0.848	1.9 ± 0.2	1.9 ± 0.2	1.9 ± 0.2	0.636
PT, median (IQR)	13.1 (12.3, 14.2)	12.8 (12.1, 13.9)	13.3 (12.5, 14.4)	0.007	12.9 (12.3, 13.8)	12.9 (12.2, 14.0)	12.9 (12.4, 13.5)	0.732
DD, median (IQR)	3.4 (2.1, 7.5)	3.4 (1.6, 5.3)	3.5 (2.5, 10.0)	0.009	3.0 (1.9, 6.3)	3.4 (1.8, 5.1)	2.8 (2.0, 7.5)	0.406
Blood sugar, median (IQR)	10.2 (7.0, 14.7)	8.9 (6.6, 12.2)	10.9 (7.6, 15.7)	0.006	10.8 (7.3, 14.7)	10.6 (7.1, 14.5)	11.0 (7.4, 15.1)	0.714

Abbreviations: SFTS, severe fever with thrombocytopenia syndrome; GC, glucocorticoid; WBC, white blood cells; ALT, alanine aminotransferase; PT, prothrombin time; DD, d-dimer; MBP, mean blood pressure; IQR, interquartile range; SD, Standard deviation; PaO₂/FiO₂, partial pressure of oxygen in the alveoli/ fraction of inspired oxygen.

Table 3 Clinical Outcomes of Patients with SFTS in the Non-GC and GC Groups in the Original and Matched Cohorts

Variables	Original Cohort				Matched Cohort			
	Total (n = 218)	Non-GC (n = 91)	GC (n = 127)	p	Total (n = 116)	Non-GC (n = 58)	GC (n = 58)	p
Primary outcome								
28-day mortality, n (%)	113 (51.8)	34 (37.4)	79 (62.2)	< 0.001	48 (41.4)	30 (51.7)	18 (31)	0.024
Secondary outcome								
Bleeding site, n (%)								
Digestive tract, n (%)	23 (10.6)	8 (8.8)	15 (11.8)	0.474	12 (10.3)	6 (10.3)	6 (10.3)	1
Nasal and oral mucosa, n (%)	62 (28.4)	19 (20.9)	43 (33.9)	0.036	36 (31.0)	17 (29.3)	19 (32.8)	0.688
Respiratory tract, n (%)	14 (6.4)	4 (4.4)	10 (7.9)	0.302	8 (6.9)	4 (6.9)	4 (6.9)	1
Brain, n (%)	4 (1.8)	0 (0)	4 (3.1)	0.142	2 (1.7)	0 (0)	2 (3.4)	0.496
Secondary infection, n (%)	134 (61.5)	47 (51.6)	87 (68.5)	0.012	75 (64.7)	30 (51.7)	45 (77.6)	0.004
Mechanical ventilation, n (%)	135 (61.9)	34 (37.4)	101 (79.5)	< 0.001	73 (62.9)	32 (55.2)	41 (70.7)	0.084
CRRT, n (%)	46 (21.1)	6 (6.6)	40 (31.5)	< 0.001	22 (19.0)	6 (10.3)	16 (27.6)	0.018
Arrhythmia, n (%)	95 (43.6)	32 (35.2)	63 (49.6)	0.034	50 (43.1)	22 (37.9)	28 (48.3)	0.261
ICU stay days, median (IQR)	4.0 (2.0, 9.8)	4.0 (2.0, 6.5)	4.0 (2.0, 10.5)	0.073	7.0 (3.0, 13.2)	4.0 (2.0, 7.8)	12.0 (6.0, 16.8)	<0.001
Hospital stay days, median (IQR)	8.0 (4.0, 16.8)	10.0 (4.0, 15.5)	7.0 (4.0, 17.0)	0.663	14.0 (5.0, 20.2)	7.0 (3.0, 14.0)	17.5 (14.0, 24.5)	<0.001

Abbreviations: SFTS, severe fever with thrombocytopenia syndrome; GC, glucocorticoid; CRRT, continuous renal replacement therapy; IQR, interquartile range; ICU, intensive care unit.

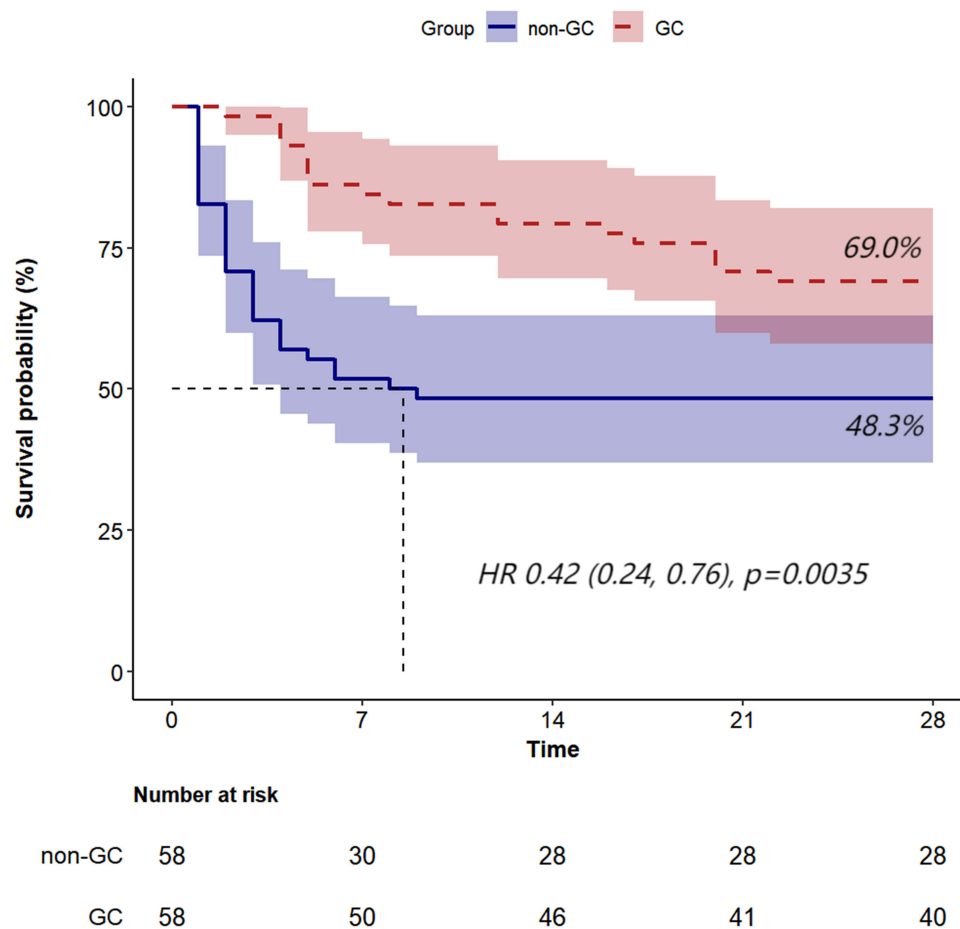


Figure 2 Kaplan–Meier survival plots differentiated by the administration of glucocorticoids. The survival curves of 58 patients with severe fever with thrombocytopenia syndrome who received glucocorticoids (illustrated using the red dashed line) compared with those of a matched group of 58 individuals who did not receive corticosteroid therapy (shown using the blue solid line).

Subgroup Analyses

We conducted stratified and interaction analyses to examine the stability of the effect of GC treatment on 28-day mortality across different subgroups. Stratification using the GCS score, lactate levels, and use of immunoglobulin, norepinephrine, and antiviral drugs yielded consistent results (Figure 3). Significant improvements in the 28-day mortality rates with GCs were observed when the GCS score was below 13 (GCS score: 9–12, HR: 0.39, 95% CI: 0.17–0.88, $p=0.024$; GCS score: 3–8, HR: 0.09, 95% CI: 0.02–0.35, $p=0.001$), lactate levels exceeded 2 mmol/L (HR: 0.35, 95% CI: 0.15–0.83, $p=0.017$), and norepinephrine (HR: 0.26, 95% CI: 0.13–0.49, $p<0.001$) was used. Combining antiviral (HR: 0.41, 95% CI: 0.22–0.78, $p=0.006$) or immunoglobulin therapy (HR: 0.22, 95% CI: 0.1–0.51, $p<0.001$) with GC treatment significantly decreased the 28-day mortality rates, in contrast to GC monotherapy, which showed no such effect.

Discussion

In our investigation, we documented a mortality rate of 61.5% among patients with SFTS, the highest mortality rate ever reported. This finding underscores the pioneering nature of our research, as it represents the first comprehensive analysis of data from critically ill patients in an ICU setting. Our study not only highlights the acute challenges faced in managing severe SFTS cases but also sets a critical benchmark for future research and underscores the urgent need for enhanced clinical strategies in the ICU.

This study showed a balanced sex ratio, a median ICU admission duration of 7 days, and high SOFA scores. Older individuals were found to have an increased risk of mortality, a finding that aligns with those from prior research.^{10,15,16}

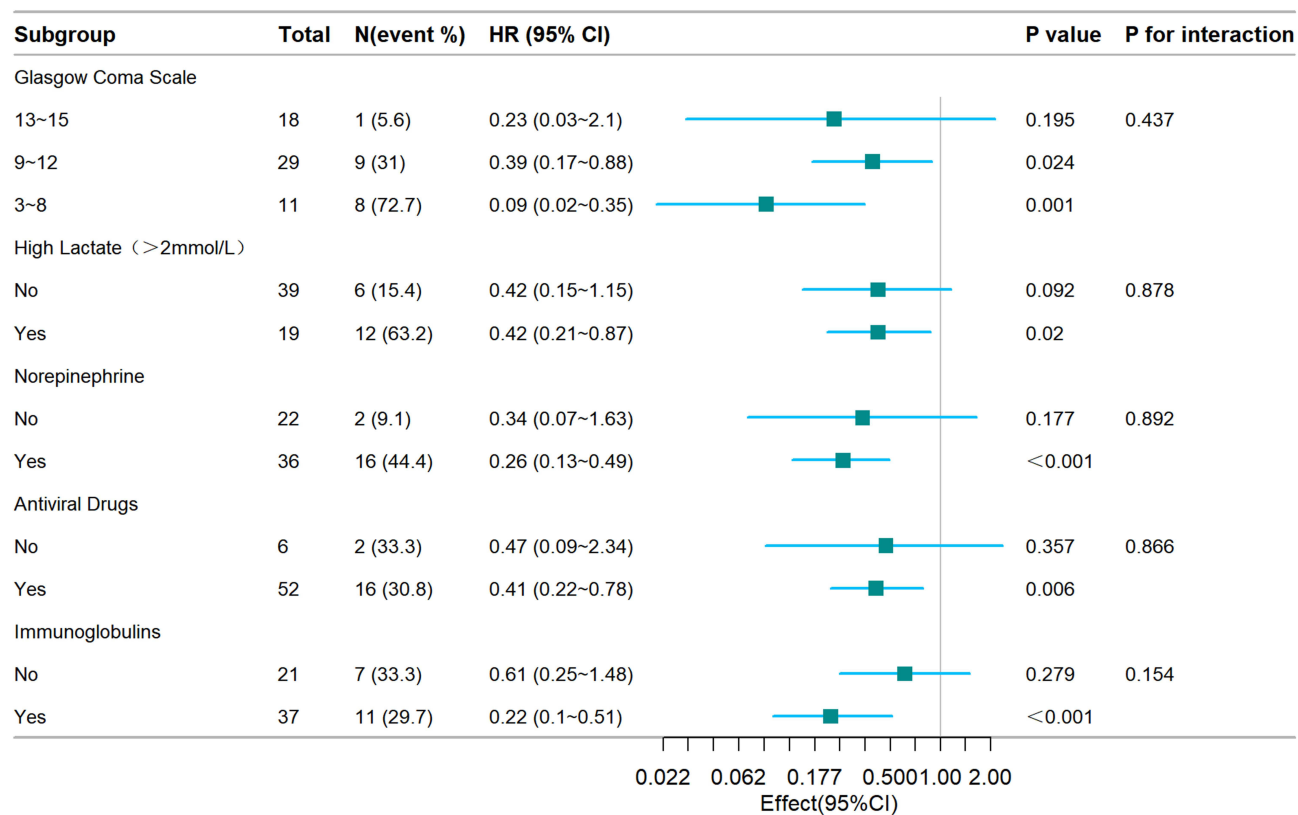


Figure 3 Stratified analyses of the associations between GC use and 28-day mortality.
Abbreviations: GC, glucocorticoid; HR, hazard ratio; CI, confidence interval.

High SOFA scores in ICU patients indicate poor organ function and are associated with a higher mortality risk.¹⁷ This study supports the idea that the severity of organ dysfunction, as measured using SOFA scores, is a key factor in determining outcomes in critically ill patients, including those with severe systemic inflammatory responses such as SFTS. When considering corticosteroid therapy in critically ill patients with SFTS, the effects of organ function on treatment effectiveness and patient survival must be considered.

A comparison between the GC and non-GC groups revealed that patients treated with GCs were younger and had higher SOFA scores. Although the benefits of GC use are inconclusive, GCs are often administered to patients with severe clinical conditions. However, after performing PSM, we observed that GCs lowered the 28-day mortality rate in ICU patients. Patients with lower GCS scores and higher lactate levels and those receiving vasopressors exhibited significantly better outcomes with GCs. This suggests that the effects of GCs are more pronounced in critically ill patients in the ICU with severe conditions.⁹ Case reports have demonstrated that methylprednisolone is effective in treating patients with SFTS complicated by encephalopathy. In such patients, disturbance of consciousness is suggested to be an indirect consequence of the cytokine storm induced by SFTSV infection.¹⁸ The underlying pathophysiological mechanisms contributing to the unfavorable outcomes in patients with SFTS likely involve a cytokine storm associated with hemophagocytic syndrome, bleeding tendencies due to thrombocytopenia, disseminated intravascular coagulation, and multiple organ system dysfunction.⁸ Thrombocytopenia caused by SFTSV infection is an immune response.¹⁹ GCs may also play a role in immune responses. For patients with severe diseases caused by emerging viruses, for which there are no specific drugs, such as coronavirus disease 2019, GCs have been shown to be effective, even reducing the 28-day mortality rates.^{20,21}

The use of GCs for the treatment of SFTS is controversial, with clinical trials across various countries documenting their negative effects.^{9,11} Corticosteroid treatment can lead to serious side effects, such as osteoporosis, adrenal suppression, cardiac problems, and high blood sugar levels.²² Additionally, the immunosuppressive properties of GCs

pose significant risks.²³ In a single-center retrospective cohort study,¹⁰ GC treatment did not affect the fatality rate in patients with SFTS but increased the risk of secondary infections. Several studies^{24,25} have identified a significant link between SFTS and invasive pulmonary aspergillosis, with complication rates between 20% and 31.9%. This might explain the beneficial effects of antiviral drugs or immunoglobulins observed in this study. However, the administration of GCs in patients with SFTS requires careful consideration. Research indicates that while glucocorticoids are not advisable for mild cases, they may benefit patients with severe SFTS; however, these studies did not include ICU patients.¹²

Regarding the strengths of this study, this is the first cohort study on the prognosis of patients with SFTS in the ICU using GCs. Additionally, in contrast to previous studies, we conducted a rigorous evaluation by incorporating the SOFA scores and viral load into the PSM. This methodological approach effectively addressed significant confounding variables, thus providing strong evidence regarding the use of GCs in critically ill patients. Moreover, the efficacy of corticosteroid administration was investigated through stratification of patient situations by analyzing a broader patient cohort.

Our study has some limitations. This was a retrospective cohort study conducted at a single hospital. Although historical data may lack accuracy and completeness and may be subject to selection and information biases, we addressed these issues by applying PSM and the Cox regression model. The PSM was performed based on baseline and clinical characteristics, excluding the vital signs or investigations, with the exception of viral load. Following the reduction in sample size due to the matching process, the likelihood of committing a Type II error in our conclusions is heightened. This article focuses only on four common comorbidities and does not analyse additional comorbidities. Although the findings are promising, they need to be validated by prospective, randomized controlled trials before being widely implemented in clinical practice. Furthermore, patients who were administered GCs on the first day of ICU admission were included in the experimental group. We did not specify the corticosteroid types and dosages, nor did we include subsequent dose adjustments in our analysis. Therefore, future studies should investigate the relationship between corticosteroid therapy duration, dosage, and SFTS outcomes.

Conclusion

Patients with SFTS exhibit a heightened 28-day mortality rate, whereas the administration of GCs decreases the ICU mortality rates. This effect was most pronounced in individuals with low GCS scores, elevated lactate levels, norepinephrine support, and on antiviral or immunoglobulin therapy. These findings suggest a potential avenue for improving outcomes in patients with severe SFTS by identifying high-risk individuals and implementing targeted GC therapy in the ICU.

Abbreviations

SFTS, severe fever with thrombocytopenia syndrome; GC, glucocorticoid; PSM, propensity score matching; GCS, Glasgow coma scale; HR, hazard ratio; CI, confidence interval; SFTSV, severe fever with thrombocytopenia syndrome virus; ICU, intensive care unit; CRRT, continuous renal replacement therapy; T-SO-ICUA, time from symptom onset to ICU admission; SOFA, sequential organ failure assessment; BMI, body mass index; IQR, interquartile range.

Data Sharing Statement

The datasets presented in the current study are available from our database in-hospital system. The raw data required to reproduce the above findings cannot be shared at this time online as the data also forms part of an ongoing study.

Ethics Approval and Informed Consent

This study was approved by the Ethics Committee of Qishan Hospital (202401). Informed consent was not required as this was a retrospective observational study. In accordance with the guidelines set forth by the Declaration of Helsinki, this study was conducted with the utmost respect for patient confidentiality and ethical standards. Although patient consent to review medical records was not required by the Ethics Committee of Qishan Hospital, we have implemented strict measures to ensure that all patient data remains confidential and secure. All personal identifiers have been removed or anonymized to protect patient privacy, and the data will be used solely for the purpose of this study.

Consent for Publication

All authors gave their consent for publication.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The author(s) report no conflicts of interest in this work.

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