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Research article

Association of gastrointestinal symptoms with mortality in patients with severe fever with thrombocytopenia syndrome

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ABSTRACT

Background: The clinical significance of gastrointestinal (GI) symptoms in patients with severe fever and thrombocytopenia syndrome (SFTS) is poorly characterized. This study aimed to determine the prevalence and effect of GI symptoms on the prognosis of patients with SFTS.
Methods: This was a retrospective multi-center cohort study that included hospitalized patients with SFTS from three institutions between October 2010 and August 2022. The risk factors for mortality and intensive care unit (ICU) admission were identified by Cox and logistic regression analyses, respectively. Kaplan-Meier curves were used to analyze the cumulative mortality risk.
Results: Among 304 patients, the median age was 62.0 years and 51.0 % of the patients were male. A total of 202 patients (66.4 %) had at least one GI symptom on admission. Diarrhea (69.8 %) and nausea (57.4 %) were the most common symptoms. Patients with GI symptoms had lower male proportion (46.0 % vs. 60.8 %, P = 0.015), higher aspartate aminotransferase (177.5 U/L vs. 118.0 U/L, P = 0.010) and lactic dehydrogenase (771.0 U/L vs. 666.5 U/L, P = 0.017) levels than that of patients without GI symptoms. However, there was no significant difference in mortality

Abbreviations: ALB, albumin; ALP, alkaline phosphatase; ALT, alanine aminotransferase; ARDS, acute respiratory distress syndrome; AST, aspartate aminotransferase; CI, confidence interval; Cr, creatinine; ECMO, extracorporeal membrane oxygenation; GGT, gamma glutamyl transpeptidase; GI, gastrointestinal; GLB, globulin; HR, hazard ratio; ICU, intensive care unit; IQR, interquartile range; Hb, hemoglobin; INR, international normalized ratio; LDH, lactate dehydrogenase; PLT, platelet; PT, prothrombin time; SFTS, thrombocytopenia syndrome; SFTSV, SFTS virus; Tbil, total bilirubin; WBC, white blood cells.

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rates (23.8 % vs. 21.6 %, P = 0.668) and ICU admission (14.4 % vs. 12.7 %, P = 0.701) between SFTS patients with and without GI symptoms. Multivariate analysis suggested that GI symptoms at admission were not associated with mortality and ICU admission.
Conclusions: GI symptoms are common in patients with SFTS. However, the presence of GI symptoms was not an independent risk factor for poor prognosis.

1. Introduction

Severe fever with thrombocytopenia syndrome (SFTS) is an emerging infectious disease caused by the SFTS virus (SFTSV), a novel phlebovirus in the Bunyaviridae family, which has recently been officially renamed the Dabie bandavirus [1,2]. SFTS was first confirmed in China in 2009 and subsequently reported in South Korea, Japan, and Vietnam [3–5]. In Missouri, United States, two patients with SFTS-like illness and thrombocytopenia were first reported in 2012 [6]. The number of confirmed cases has increased significantly in recent years. Ticks infected with SFTSV mainly transmit medium by biting human skin, and human-to-human transmission by blood or body fluids has also been reported in previous studies [7,8]. The mortality rate associated with SFTS is as high as 30 % [1,9].

The duration from SFTSV infection to symptom onset is approximately 5–14 days, which is determined by the viral load and route of infection [10]. Multiple organ dysfunction is the main characteristic of SFTS, which presents a series of manifestations, including fever, thrombocytopenia, leukopenia, bleeding tendency, liver and kidney injury, gastrointestinal (GI) symptoms, and neurologic symptoms [1,7,11,12]. The exact pathogenesis of SFTS remains unclear, although numerous studies have found that it may be a virus-triggered inflammatory storm involving numerous cytokines [13,14]. The majority of patients with severe SFTS died within two weeks of onset because of encephalitis, cardiac insufficiency, acute kidney injury, and secondary infection. Several studies have reported GI symptoms in patients with SFTS, including nausea, vomiting, abdominal pain, and diarrhea [1,7,15]. However, limited data are available in the literature regarding the prevalence and clinical significance of GI symptoms in patients with SFTS.

This study aimed to describe the prevalence and distribution of GI symptoms and to investigate the potential association between the presence of GI symptoms and the prognosis of patients with SFTS.

2. Methods

2.1. Study population

This retrospective cohort study included consecutive patients with SFTS from three medical institutions in China between October 2010 and August 2022. The diagnosis of SFTS was based on venous blood testing for SFTSV RNA. Patients with incomplete clinical data were excluded from analysis. This study was approved by the ethics committee of Nanjing Drum Tower Hospital (approval number: 2022-238-02) and the protocol was conducted in accordance with the Declaration of Helsinki. The requirement for informed consent was waived by the ethics committee because of its retrospective design.

2.2. Data acquisition

Demographic data, medical history, therapy regimens, and laboratory data were retrospectively collected using a standard data collection form. Laboratory parameters and clinical information, including viral symptoms (fever, cough, headache, muscle ache, fatigue, and sore throat) and GI symptoms, were collected from the electronic medical record system. The presence of at least one of the following symptoms was identified as a positive GI symptom at admission and during hospitalization: nausea, vomiting, abdominal pain, diarrhea, constipation, and hematochezia.

2.3. Follow-up and definition

All patients with SFTS were followed-up from admission to discharge or death, and laboratory tests were monitored approximately every three days. The primary outcome was death, and the secondary outcome was intensive care unit (ICU) admission during hospitalization. The follow-up time of the survivors was calculated from the date of admission to discharge, and the duration of death was calculated from the date of admission to the date of death. The diagnoses of respiratory failure, acute respiratory distress syndrome (ARDS), renal injury, liver injury, and shock were based on corresponding guidelines [16–19].

2.4. Statistical analysis

Continuous variables are summarized as median and interquartile range (IQR), and categorical variables are summarized as frequencies and proportions. To compare the differences between groups, independent-group Student's t-tests or the Mann-Whitney U tests were used for continuous variables with and without normal distribution, and the chi-squared test was used for categorical variables. Cox regression analysis was conducted to identify the risk factors for mortality, and risk factors for ICU admission were identified using logistic regression analysis. The presence or absence of GI symptoms and the number of GI symptoms were included in

the multivariate analysis, and the remaining variables ($P < 0.05$) in the univariate analysis were selected for multivariate analysis by input step. The cumulative incidence of mortality was estimated using Kaplan-Meier survival analysis. All statistical analyses were performed using the SPSS software (version 23.0; IBM Corporation, Armonk, NY, USA) and R software version 4.1.3 (R Foundation, Vienna, Austria; www.R-project.Org). Statistical significance was set at $P < 0.05$.

3. Results

3.1. Clinical features of study population

A total of 309 patients hospitalized with SFTS were identified during the study period. Due to the lack of clinical data, five patients were excluded, and 304 patients were eventually included in this study. The clinical features of the study population are summarized in Table 1. The median age of the patients was 62.0 years and approximately half of the patients were male (51.0 %). The median time from symptom onset to admission was 7.0 days. Nearly half of patients (46.4 %) had other chronic diseases. The most common viral symptoms on admission were fever (99.3 %) and fatigue (79.6 %). Two hundred and two patients (66.4 %) had GI symptoms at admission, including nausea (38.2 %), vomiting (26.0 %), abdominal pain (19.1 %), diarrhea (46.4 %), constipation (3.6 %), and hematochezia (3.0 %). Regarding laboratory tests, the median levels of white blood cells (WBC), platelets (PLT), alanine

Table 1
Comparison of clinical demographics and characteristics of SFTS patients with and without gastrointestinal symptoms at admission.

Variables	All patients (n = 304)	GI symptoms (n = 202)	No GI symptoms (n = 102)	P value
Age (yr)	62.0 (52.0, 70.0)	61.0 (51.0, 70.3)	64.0 (52.8, 70.3)	0.577
Male (%)	155 (51.0)	93 (46.0)	62 (60.8)	0.015
Smoking (%)	49 (16.1)	27 (13.4)	22 (11.8)	0.066
Drinking (%)	37 (12.2)	25 (12.4)	12 (11.8)	0.878
Comorbidities				
Any (%)	141 (46.4)	91 (45.0)	50 (49.0)	0.512
Hypertension (%)	82 (27.0)	55 (27.2)	27 (26.5)	0.888
Type 2 diabetes (%)	32 (10.5)	20 (9.9)	12 (11.8)	0.617
Chronic liver diseases (%)	36 (11.8)	20 (9.9)	16 (15.7)	0.140
Chronic lung diseases (%)	10 (3.3)	8 (4.0)	2 (2.0)	0.356
Cardiovascular disease (%)	10 (3.3)	6 (3.0)	4 (3.9)	0.661
Chronic kidney disease (%)	3 (1.0)	1 (0.5)	2 (2.0)	0.222
Cancer (%)	11 (3.6)	7 (3.5)	4 (3.9)	0.841
Time from symptom onset to admission (days)	7.0 (5.0, 9.0)	7.0 (5.0, 9.0)	7.0 (5.0, 10.0)	0.839
Viral symptoms				
Fever (%)	302 (99.3)	201 (99.5)	101 (99.0)	0.621
Cough (%)	73 (24.0)	54 (26.7)	19 (18.6)	0.118
Headache (%)	64 (21.1)	48 (23.8)	16 (15.7)	0.103
Muscle ache (%)	99 (32.6)	68 (33.7)	31 (30.4)	0.566
Fatigue (%)	242 (79.6)	166 (82.2)	76 74.5)	0.117
Sore throat (%)	12 (3.9)	8 (4.0)	4 (3.9)	0.987
Gastrointestinal symptoms				
Nausea (%)	116 (38.2)	116 (57.4)	–	–
Vomiting (%)	79 (26.0)	79 (39.1)	–	–
Abdominal pain (%)	58 (19.1)	58 (28.7)	–	–
Diarrhea (%)	141 (46.4)	141 (69.8)	–	–
Constipation (%)	11 (3.6)	11 (5.4)	–	–
hematochezia (%)	9 (3.0)	9 (4.5)	–	–
Laboratory tests				
WBC ($\times 10^9$/L)	3.2 (1.9. 5.4)	3.2 (1.8, 5.5)	3.3 (2.0. 5.2)	0.655
Neutrophil ($\times 10^9$/L)	1.8 (0.9, 3.6)	1.9 (0.9, 3.7)	1.7 (1.0, 3.5)	0.949
Lymphocyte ($\times 10^9$/L)	0.9 (0.5, 1.3)	0.9 (0.5, 1.4)	0.8 (0.5, 1.2)	0.268
Hb (g/L)	129.0 (117.0, 141.0)	130.0 (117.8, 141.0)	129.0 (115.0, 144.3)	0.990
PLT ($\times 10^9$/L)	49.0 (34.0, 73.8)	48.5 (33.0, 73.0)	49.0 (35.8, 78.3)	0.365
ALT (U/L)	76.1 (46.2, 139.6)	82.1 (47.6, 143.3)	68.9 (41.9, 123.3)	0.106
AST (U/L)	157.3 (79.7, 347.8)	177.5 (86.7, 402.5)	118.0 (73.1, 263.2)	0.010
ALP (U/L)	70.1 (55.0, 107.4)	69.7 (55.4, 107.2)	71.4 (53.8, 108.6)	0.686
GGT (U/L)	58.6 (27.2, 143.7)	58.3 (30.1, 145.2)	59.1 (24.8, 142.0)	0.322
Tbil (μmol/L)	9.9 (6.9, 17.5)	9.9 (6.9, 16.9)	10.2 (6.8, 19.0)	0.503
LDH (U/L)	734.0 (463.5, 1353.5)	771.0 (520.0, 1473.3)	666.5 (393.3, 1003.5)	0.017
ALB (g/L)	33.0 (30.1, 35.9)	32.7 (29.9, 35.6)	34.0 (30.6, 36.0)	0.127
GLB (g/L)	25.4 (22.1, 30.0)	26.0 (22.6, 30.2)	24.2 (21.0, 28.8)	0.057
Cr (μmol/L)	62.0 (49.0, 83.0)	61.5 (48.8, 85.5)	63.0 (50.0, 79.8)	0.927
PT (s)	11.5 (10.7, 12.4)	11.4 (10.7, 12.4)	11.5 (10.7, 12.5)	0.835
INR	1.0 (1.0, 1.1)	1.0 (1.0, 1.1)	1.0 (1.0, 1.1)	0.495

ALB, albumin; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Cr, creatinine; GGT, gamma glutamyl transpeptidase; GI, gastrointestinal; GLB, globulin; Hb, hemoglobin; INR, international normalized ratio; LDH, lactate dehydrogenase; PLT, platelet; PT, prothrombin time; Tbil, total bilirubin; WBC, white blood cells.

aminotransferase (ALT), aspartate aminotransferase (AST), serum creatinine (Cr), and prothrombin time (PT) were 3.2 × 10^9/L, 49.0 × 10^9/L, 76.1 U/L, 157.3 U/L, 62.0 μmol/L and 11.5 s, respectively.

Compared to patients without GI symptoms at admission, patients with GI symptoms had a lower proportion of male (46.0 % vs. 60.8 %, P = 0.015). However, age, comorbidities, and viral symptoms were comparable between patients with and without GI symptoms. In addition, patients with GI symptoms had higher levels of AST (177.5 U/L vs. 118.0 U/L, P = 0.010) and lactate dehydrogenase (LDH) (771.0 U/L vs. 666.5 U/L, P = 0.017) than those of patients without GI symptoms, while other laboratory parameters were comparable between these two groups (Table 1).

3.2. Treatment, complications, and outcomes

Oxygen therapy was required in 115 (37.8 %) patients, and the proportions of patients who received invasive mechanical ventilation and noninvasive mechanical ventilation were 9.9 % and 6.3 %, respectively. Most patients (92.1 %) received ribavirin antiviral therapy, and 72.7 % of patients received empirical antibiotic therapy. Moreover, 28.9 % and 39.8 % of patients were treated with corticosteroids and gamma globulin, respectively. Common complications included liver injury (72.7 %), renal injury (16.8 %), respiratory failure (15.1 %), shock (10.5 %), and ARDS (6.6 %) during disease course. A total of 70 (23.0 %) patients died and 42 (13.8 %) were admitted to the ICU in the present study. The median hospitalization was 10.0 days (Table 2).

Regarding treatment regimens, complications, and outcomes, the proportion of noninvasive mechanical ventilation (7.4 % vs. 3.9 %, P = 0.040) and renal injury (20.3 % vs. 9.8 %, P = 0.021) were higher in patients with GI symptoms. However, other treatment regimens, complications, and outcomes were comparable between the patients with and without GI symptoms (Table 2).

3.3. Association of GI symptoms with mortality and ICU admission

Cox regression analysis was conducted to identify risk factors for mortality (Table 3). In univariate analysis, age, WBC, PLT, ALT, LDH, ALB, Cr, PT, use of corticosteroids, and gamma globulin were associated with mortality. However, neither the presence of GI symptoms nor the number of GI symptoms at admission were risk factors for mortality after adjusting for confounding factors in multivariate analysis. In addition, LDH, Cr, PT, use of corticosteroids, and gamma globulin were associated with ICU admission in the univariate analysis, whereas GI symptoms at admission were not associated with ICU admission in the multivariate analysis (Table S1).

3.4. Comparison of mortality risk between patients with and without GI symptoms

The median follow-up periods of patients with and without GI symptoms at admission were 10.0 days. A total of 48 (23.8 %) and 22 (21.6 %) patients were deceased in patients with and without GI symptoms died, respectively (P = 0.668). Kaplan–Meier analysis demonstrated that the cumulative incidence of mortality was comparable in patients with and without GI symptoms (P = 0.749) (Fig. 1), and similar results were observed in different subgroups of age (Fig. 2A-D) and sex (Fig. 2E-F). Further analysis revealed that mortality risk increased gradually with age in patients with and without GI symptoms (Table 4). However, there was no significant difference in the mortality rates between patients with and without GI symptoms in the different age subgroups (Table 4). The rates of ICU admission were also comparable between patients with and without GI symptoms in different age subgroups (Table S3).

Table 2
Comparison of treatment, complications, and outcomes of SFTS patients with and without gastrointestinal symptoms at admission.

Variables	All patients (n = 304)	GI symptoms (n = 202)	No GI symptoms (n = 102)	P value
Treatment				
Oxygen therapy (%)	115 (37.8)	84 (41.6)	31 (30.4)	0.057
Noninvasive mechanical ventilation (%)	19 (6.3)	15 (7.4)	4 (3.9)	0.040
Invasive mechanical ventilation (%)	30 (9.9)	21 (10.4)	9 (8.8)	0.664
Blood purification (%)	17 (5.6)	14 (6.9)	3 (2.9)	0.153
ECMO (%)	2 (0.7)	2 (1.0)	0	0.313
Use of corticosteroid (%)	88 (28.9)	59 (29.2)	29 (28.4)	0.888
Use of gamma globulin (%)	121 (39.8)	87 (43.0)	34 (33.3)	0.102
Use of ribavirin (%)	280 (92.1)	183 (90.6)	97 (95.1)	0.169
Antibiotic therapy (%)	221 (72.7)	146 (72.3)	75 (73.5)	0.817
Complications				
Respiratory failure (%)	46 (15.1)	34 (16.8)	12 (11.8)	0.244
ARDS (%)	20 (6.6)	16 (7.9)	4 (3.9)	0.184
Renal injury (%)	51 (16.8)	41 (20.3)	10 (9.8)	0.021
Liver injury (%)	221 (72.7)	154 (76.2)	67 (65.7)	0.051
Shock (%)	32 (10.5)	23 (11.4)	9 (8.8)	0.492
Outcomes				
Admission to ICU (%)	42 (13.8)	29 (14.4)	13 (12.7)	0.701
Death (%)	70 (23.0)	48 (23.8)	22 (21.6)	0.668
Days of Hospitalization (days)	10.0 (7.0, 14.0)	10.0 (7.0, 14.0)	10.0 (7.0, 13.0)	0.956

ARDS, acute respiratory distress syndrome; ECMO, extracorporeal membrane oxygenation; GI, gastrointestinal; ICU, intensive care unit.

Table 3
Multivariate analysis of risk factors for mortality in SFTS patients.

			Model-1		Model-2	
	Univariate		Multivariate		Multivariate	
	HR (95 % CI)	P value	HR (95 % CI)	P value	HR (95 % CI)	P value
Age (yr)	1.040 (1.018, 1.063)	<0.001	1.047 (1.021, 1.073)	<0.001	1.048 (1.022, 1.075)	<0.001
Male	0.840 (0.524, 1.346)	0.469				
Hypertension	1.394 (0.848, 2.291)	0.191				
Type 2 diabetes	0.772 (0.334, 1.783)	0.544				
Gastrointestinal symptoms						
no	reference		reference			
yes	1.085 (0.655, 1.798)	0.752	1.140 (0.645, 2.013)	0.652		
Gastrointestinal symptoms						
0	reference				reference	
1-2	1.072 (0.623, 1.846)	0.802			0.989 (0.529, 1.847)	0.972
≥3	1.111 (0.583, 2.117)	0.748			1.476 (0.734, 2.971)	0.275
WBC ($\times 10^9$/L)	1.075 (1.022, 1.131)	0.005	1.023 (0.955, 1.096)	0.519	1.025 (0.957, 1.097)	0.485
PLT ($\times 10^9$/L)	0.987 (0.978, 0.997)	0.008	0.997 (0.988, 1.006)	0.491	0.997 (0.988, 1.006)	0.503
ALT (U/L)	1.001 (1.000, 1.002)	0.009	0.998 (0.995, 1.000)	0.082	0.998 (0.995, 1.001)	0.120
LDH (U/L)	1.001 (1.000, 1.001)	<0.001	1.001 (1.000, 1.001)	<0.001	1.001 (1.000, 1.001)	<0.001
ALB (g/L)	0.877 (0.826, 0.933)	<0.001	0.975 (0.917, 1.037)	0.429	0.974 (0.917, 1.035)	0.397
GLB (g/L)	0.987 (0.954, 1.021)	0.436				
Cr (μmol/L)	1.006 (1.003, 1.008)	<0.001	1.000 (0.998, 1.004)	0.613	1.001 (0.998, 1.004)	0.507
PT (s)	1.131 (1.079, 1.185)	<0.001	1.125 (1.058, 1.195)	0.011	1.117 (1.050, 1.187)	<0.001
Use of corticosteroid (%)	2.734 (1.703, 4.390)	<0.001	1.912 (1.147, 3.186)	0.013	2.081 (1.228, 3.526)	0.006
Use of gamma globulin (%)	1.774 (1.103, 2.854)	0.018	1.204 (0.715, 2.028)	0.485	1.185 (0.702, 2.000)	0.526

ALB, albumin; ALT, alanine aminotransferase; CI, confidence interval; Cr, creatinine; GI, gastrointestinal; GLB, globulin; HR, hazard ratio; LDH, lactate dehydrogenase; PLT, platelet; PT, prothrombin time.

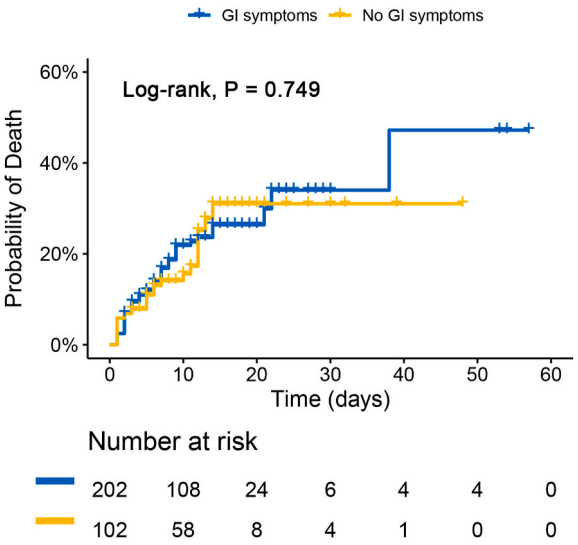

Fig. 1. The cumulative mortality of patients with and without gastrointestinal symptoms.

3.5. Comparison of clinical features and outcomes of patients with and without GI symptoms during hospitalization

GI symptoms occurred in 233 (76.6 %) of the 304 patients during hospitalization. Compared to patients without GI symptoms during hospitalization, patients with GI symptoms had a lower proportion of male (45.1 % vs. 70.4 %, $P < 0.001$). However, other clinical features and outcomes, including demographics, therapy regimens, and laboratory data, were comparable between the patients with and without GI symptoms (Table S2). In addition, mortality risk and ICU admission rate also gradually increased with age in patients with and without GI symptoms during hospitalization. However, there was no significant difference in mortality risk and ICU admission rate between the two groups in the different age subgroups (Table 4 and S3).

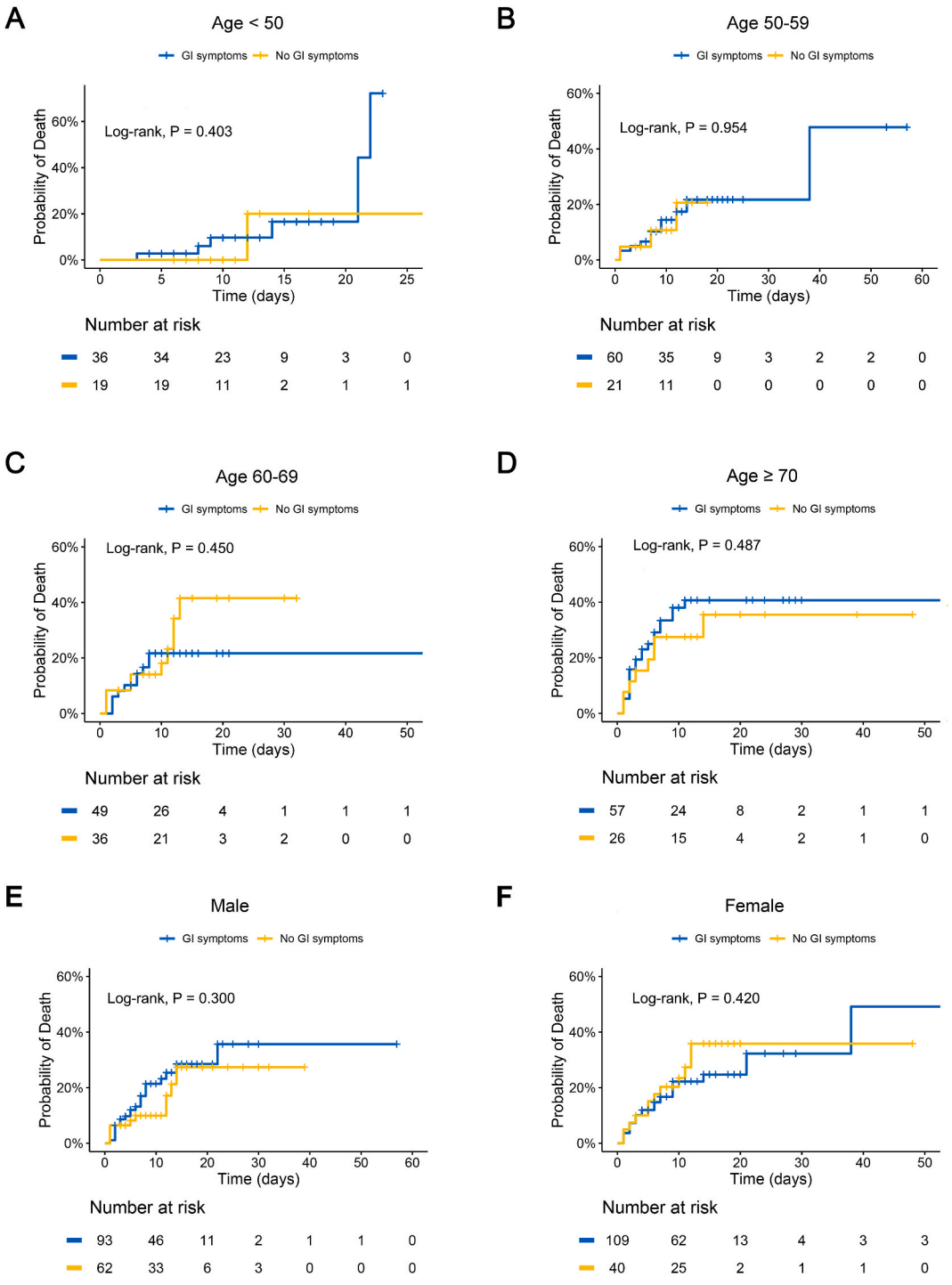

Fig. 2. The cumulative mortality of patients with and without gastrointestinal symptoms in different age (A–D) and sex (E, F).

4. Discussion

This multi-center cohort study showed that more than two-thirds of patients with SFTS had at least one GI symptom during the disease course, and diarrhea was the most prevalent GI symptom, followed by nausea and vomiting. However, the presence of GI symptoms or number of GI symptoms at admission was not associated with the risk of mortality and ICU admission. Our results suggest that, although GI symptoms are highly prevalent in patients with SFTS, they have no significant association with clinical outcomes.

Table 4
Mortality rates stratified by age and gastrointestinal symptoms at admission and disease course.

Age stratification	No GI symptoms		GI symptoms		P value
	Number	Mortality (%)	Number	Mortality (%)	
Admission					
< 50 yr	19	5.3	36	16.7	0.228
50–59 yr	21	14.3	60	18.3	0.673
60–69 yr	36	27.8	49	20.4	0.429
≥ 70 yr	26	30.8	57	36.8	0.590
Course of disease					
< 50 yr	15	6.7	40	15.0	0.409
50–59 yr	16	18.8	65	16.9	0.863
60–69 yr	24	29.2	61	21.3	0.442
≥ 70 yr	16	43.8	67	32.8	0.411

GI, gastrointestinal.

SFTS is a serious infectious disease with high mortality rate. According to previous studies, the highest mortality rate is 30 % in some regions [1,20]. Most patients with SFTS have fever, thrombocytopenia, renal and liver injury, myocarditis, arrhythmia, and meningoencephalitis [10]. Multiple organ dysfunction is the main cause of death in many cases, and the average time from symptom onset to death is approximately nine days [21]. The presence of neurological symptoms, older age, high levels of AST and LDH, activated partial thromboplastin time, and SFTS virus load have been demonstrated to be risk factors for poor prognosis [7,22,23]. GI symptoms are one of the most common clinical manifestations in patients with SFTS. This study found that 66.4 % and 76.6 % of the patients had at least one GI symptom at admission and during hospitalization, respectively. Diarrhea and nausea were the two most common GI symptoms, which is consistent with previous reports [10]. Nevertheless, few studies have specifically investigated the association between GI symptoms and clinical prognoses. Our findings showed that there was no difference in clinical features and prognosis between patients with and without GI symptoms. A similar study from South Korea reported that approximately 94 % of patients with SFTS had GI symptoms, whereas the GI symptom frequency was comparable between patients who survived and those with fatal outcomes [15]. However, this study included only 35 patients and the sample size was very small. A meta-analysis of 3011 patients with SFTS revealed that GI symptoms were not associated with mortality [24]. However, this study only evaluated the relationship between mortality and the presence of GI symptoms, while our study not only showed an association between death and GI symptoms but also compared clinical features, including symptoms, laboratory tests, and comorbidities between these two groups. Moreover, we compared ICU admission between patients with and without GI symptoms.

The pathogenesis of GI symptoms associated with SFTS has not been completely elucidated and may be associated with inflammatory storms triggered by a series of cytokines, including interleukin 1 (IL-1), IL-6, IL-10, TGF-β, granulocyte colony stimulating factor, interferon-γ-inducible protein, and monocyte chemotactic protein 1 [13,14,25]. Inflammatory cytokines play an important role in the course of viral diseases and target multiple organs, leading to multiple organ dysfunction, including in the digestive system [13,26]. In addition, SFTSV inhibits host immune function, which can increase the possibility of secondary infections [11]. Thus, intestinal infections may play an important role in the pathogenesis of GI symptoms in patients with SFTS. Dysregulation of the gut microbiota may also contribute to the development of GI symptoms. A small sample size study reported by Xu et al. revealed that gut microbiota diversity and fecal microbial composition were significantly changed in patients with SFTS compared with healthy controls [27]. Changes in the gut microbiota may be associated with systemic inflammatory storms that trigger inflammatory responses in the intestinal tract [27]. However, these results need to be confirmed by studies with larger sample sizes.

This study had several limitations. First, it was a retrospective study. GI symptoms were collected from medical records and might be somewhat subjective, which might have led to bias in our results. Second, the association between GI symptoms and SFTSV load was not analyzed because of the lack of quantitative virus levels. Third, the duration of GI symptoms was unclear in this study, and the association between prognosis and duration of GI symptoms needs to be confirmed. Fourth, only hospitalized patients were included in this study, whereas mild patients in the outpatient department were not included. Thus, potential selection bias may exist. Fifth, the recovery of GI symptoms after discharge for survivors remains unclear owing to the absence of long-term follow-up data.

In conclusion, this study found that GI symptoms are highly prevalent in patients with SFTS. However, the presence of GI symptoms did not increase the risk of death or ICU admission. Thus, our results suggest that GI symptoms are not associated with prognosis in patients with SFTS. Further prospective multicenter studies with larger sample sizes are required to confirm our findings and investigate the mechanisms underlying the different clinical manifestations of SFTS.

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Data availability statement

The data supporting the study findings are available upon reasonable request from the corresponding authors (Chao Wu and Rui Huang).

CRediT authorship contribution statement

Qun Zhang: Writing – original draft, Data curation. **Jian Wang:** Writing – original draft, Formal analysis, Conceptualization. **Shaoqiu Zhang:** Writing – original draft, Data curation. **Huali Wang:** Data curation. **Zhiyi Zhang:** Data curation. **Yu Geng:** Data curation. **Yifan Pan:** Data curation. **Bei Jia:** Data curation. **Yali Xiong:** Data curation. **Xiaomin Yan:** Data curation. **Jie Li:** Data curation. **Chao Wu:** Writing – review & editing, Conceptualization. **Rui Huang:** Writing – review & editing, Conceptualization. **Xiaoli Zhu:** Writing – review & editing, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e37907.

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