

# Characteristics and Outcomes of Frail Patients with Suspected Infection in Intensive Care Units: A Descriptive Analysis From A Multicenter Cohort Study

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# Abstract

**Background:** Frailty is associated with morbidity and mortality in patients in intensive care units (ICUs). However, the characteristics of frail patients with suspected infection, including sepsis, remain unclear. We aimed to investigate the characteristics and outcomes of frail patients with suspected infection in ICUs.

**Methods:** This is a secondary analysis of a multicenter cohort study conducted by 22 ICUs in Japan. Adult patients ( $\geq 16$  years) with newly suspected infection from December 2017 to May 2018 were included. We compared baseline patient characteristics and outcomes between three frailty groups based on the Clinical Frailty Scale (CFS) score: fit (score 1–3), vulnerable (score 4), and frail (score 5–9). We conducted subgroup analysis of patients with sepsis defined based on Sepsis-3 criteria. We also produced Kaplan–Meier survival curves for 90-day survival.

**Results:** We enrolled 650 patients with suspected infection, including 599 (92.2%) patients with sepsis. Patients with a median rating of 3 (3–5) on the CFS were included: 337 (51.8%) were fit, 109 (16.8%) were vulnerable, and 204 were (31.4%) frail. Comorbidities were more common in frail and vulnerable patients than in fit patients. The Sequential Organ Failure Assessment scores for fit, vulnerable, and frail patients were 7 (4–10), 8 (5–11), and 7 (5–10), respectively ( $p = 0.59$ ). The patients' median body temperatures were as follows: fit 37.5 (36.5–38.5) $^{\circ}\text{C}$ ; vulnerable 37.5 (36.4–38.6) $^{\circ}\text{C}$ ; and frail 37.0 (36.3–38.1) $^{\circ}\text{C}$  ( $p < 0.01$ ). C-reactive protein levels of fit, vulnerable, and frail patients were 13.6 (4.6–24.5), 12.1 (3.9–24.9), 10.5 (3.0–21.0) mg/dL, respectively ( $p < 0.01$ ). In-hospital mortality did not statistically differ according to frailty ( $p = 0.19$ ). Kaplan–Meier survival curves showed little difference in the mortality rate during the acute phase. However, more vulnerable and frail patients died after the acute phase than fit patients; this difference was not statistically significant ( $p = 0.25$ ). Compared with fit or vulnerable patients, fewer frail patients were discharged.

**Conclusion:** Frail and vulnerable patients with suspected infection, including sepsis, tend to have poor disease outcomes after the acute phase of infection.

## Background

Frailty is a clinical status and a multidimensional syndrome characterized by the loss of physiologic and cognitive reserves.<sup>1,2</sup> Although the assessment of frailty is challenging,<sup>3–5</sup> there are two major approaches to its measurement: the phenotypic frailty model and the frailty index of deficit accumulation.<sup>6</sup> The phenotypic frailty model focuses predominantly on physical symptoms, such as weight loss, exhaustion, weakness, slowness, and reduced physical activity. The frailty index of deficit accumulation focuses on comorbidities, illness, laboratory abnormalities, and functional impairments.

There is a growing interest in the impact of frailty on patients with critical illness due in part to the increased risk of morbidity and mortality in patients with critical illnesses in intensive care units (ICUs).<sup>7</sup>

However, most previous studies have described the clinical features of frailty in the elderly<sup>8-10</sup> or patients with heterogeneous diseases in ICUs.<sup>11-14</sup> The specific clinical characteristics of frail patients with suspected infection, including sepsis, which is one of the major causes of admission to ICUs, are unknown.<sup>15</sup>

Therefore, we aimed to investigate the association between frailty and patient characteristics, clinical features, and outcomes among adult patients with suspected infection in ICUs.

## Methods

### Design and participants

This is a secondary analysis of data from the Japanese Association for Acute Medicine (JAAM) Sepsis Prognostication in Intensive Care Unit and Emergency Room (SPICE) study, a multicenter study of patients with sepsis. The JAAM SPICE study was composed of a SPICE emergency room cohort and a SPICE ICU cohort. We used the SPICE ICU cohort. The SPICE ICU cohort included adult patients (aged  $\geq 16$  years) admitted to a participating ICU with a suspected infection. We excluded patients who had missing data on frailty.

### Data collection

Data were collected by the SPICU ICU investigators as part of the routine clinical workup. Patient information included demographic characteristics, admission source, comorbidities, frailty, sites of infection, sepsis-related severity scores including the Sequential Organ Failure Assessment (SOFA) score and the Acute Physiology and Chronic Health Evaluation II score, and laboratory data. In addition, we collected data regarding in-hospital mortality, place after discharge, ventilator-free days (VFDs), ICU-free days (IFDs), and length of hospital stay (LOS).

### Definitions

Suspected infection was defined as the administration of antibiotics and the sampling of any bacterial culture or imaging test undertaken for the purpose of investigating the source of infection. Sepsis and septic shock were defined on the basis of Sepsis-3 criteria.<sup>16</sup> Frailty was evaluated using the Clinical Frailty Scale (CFS) score.<sup>1</sup> The CFS score is a 9-point assessment tool used to quantify frailty. Clinicians determined patients' CFS scores by interviewing them or their surrogates and reviewing their medical records upon admission to the hospital. No training on the use of the CFS score was provided as the score was deemed to be easily understandable by clinicians. VFDs were defined as the number of days within the first 28 days after enrollment during which a patient was able to breathe without a ventilator. Patients who died during the study period were assigned a VFD score of 0. IFDs were calculated in a similar manner to the VFDs.

### Analysis

We compared baseline patient characteristics and outcomes between three frailty groups based on the CFS score, fit (score 1–3), vulnerable (score 4), and frail (score 5–9), and evaluated the findings in light of previous reports.<sup>8,17</sup> Continuous variables were summarized using the median and interquartile range (IQR) and compared using the Mann–Whitney *U* test. Categorical variables were summarized using numbers and percentages and compared using the chi-squared test or Fisher exact test, where appropriate. Kaplan–Meier survival curves for 90-day survival were produced and compared using a log-rank test. We conducted a Cox proportional hazards regression analysis to assess the impact of frailty on 90-day survival. Adjusted variables in the analysis included age, sex, the Charlson comorbidity index, and the SOFA score, which were selected on the basis of clinical relevance and previous reports.<sup>8,11</sup> We tested for interactions between frailty and age, frailty and the Charlson comorbidity index, and age and the Charlson comorbidity index. We also conducted a subgroup analysis of patients diagnosed with sepsis based on Sepsis-3 criteria. A *p*-value of <0.05 was considered to indicate statistical significance. All statistical analyses were performed with EZR (version 1.38; Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R (version 3.5.0; The R Foundation for Statistical Computing, Vienna, Austria).<sup>18</sup> EZR is a modified version of the R commander designed to apply statistical functions that are frequently used in biostatistics.

## Results

We enrolled 650/652 patients with suspected infection from the SPICE-ICU database, after excluding 2 patients who had missing data on frailty. The median age of the patients was 72 years (IQR 60 – 81), and 369 (56.8%) were men. The median CFS score was 3 (IQR 3–5). There were 337 (51.8%) fit patients, 109 (16.8%) vulnerable patients, and 204 (31.4%) frail patients (Table 1 and Fig. 1). The age of patients increased with increasing frailty: fit 67 years (IQR 54 – 78); vulnerable 73 years (IQR 64 – 81); and frail 77 years (IQR 69 – 84), *p* < 0.01. Comorbidities including congestive heart failure, cerebrovascular diseases, dementia, and chronic obstructive pulmonary disease (COPD) were more common in vulnerable and frail patients than in fit patients (*p* < 0.01). The SOFA scores of fit, vulnerable, and frail patients were 7 (4–10), 8 (5–11), and 7 (5–10), respectively (*p* = 0.59). The patients' median body temperatures were as follows: fit 37.5 (36.5–38.5)°C; vulnerable 37.5 (36.4–38.6)°C; and frail 37.0 (36.3–38.1)°C, *p* < 0.01. C-reactive protein levels in fit, vulnerable, and frail patients were 13.6 (4.6–24.5) mg/dL, 12.1 (3.9–24.9) mg/dL, 10.5 (3.0–21.0) mg/dL, respectively (*p* < 0.01).

Table 1  
 Characteristics of patients with suspected infection

		Fit (CFS 1–3)	Vulnerable (CFS 4)	Frail (CFS 5–9)	p-value
		n = 337 (51.8)	n = 109 (16.8)	n = 204 (31.4)	
Age at admission (years old)		67 (54–78)	73 (64–81)	77 (69–84)	< 0.01
Sex, male		199 (59.1)	68 (62.4)	102 (50.0)	0.05
BMI (kg/m <sup>2</sup> )		22.4 (20.0–25.0)	22.5 (19.6–24.9)	20.8 (17.8–23.6)	< 0.01
Coexisting conditions	Myocardial infarction	11 (3.3)	7 (6.4)	7 (3.4)	0.33
	Congestive heart failure	20 (5.9)	11 (10.1)	28 (13.7)	< 0.01
	Peripheral vascular disease	9 (2.7)	7 (6.4)	7 (3.4)	0.17
	Cerebrovascular disease	20 (5.9)	9 (8.3)	30 (14.7)	< 0.01
	Dementia	12 (3.6)	15 (13.8)	48 (23.5)	< 0.01
	COPD	12 (3.6)	13 (11.9)	30 (14.7)	< 0.01
	Connective tissue disease	14 (4.2)	13 (11.9)	19 (9.3)	< 0.01
	Peptic ulcer disease	13 (3.9)	1 (0.9)	10 (4.9)	0.19
	Diabetes mellitus without organ damage	47 (13.9)	22 (20.2)	42 (20.6)	0.09

Reported counts (proportions) for categorical and median (interquartile range) for continuous variables.

Continuous variables were compared using the Mann–Whitney U test. Categorical variables were compared using the Fisher’s exact test or chi square test, where appropriately.

Missing data: BMI = 5; Metastatic tumor = 1; Mechanical ventilation = 2; Systolic blood pressure = 2; Heart rate = 1; Temperature = 1; Hematocrit = 1; PT–INR = 5; Lactate = 15; Glucose = 6; Total bilirubin = 1; C-reactive protein = 2; Positive blood cultures = 37

CFS: Clinical frailty scale, BMI: Body mass index, COPD: Chronic obstructive pulmonary disease, AIDS: Acquired immunodeficiency syndrome, CCI: Charlson comorbidity index, SOFA: Sequential organ failure assessment, APACHE: Acute physiology and chronic health evaluation, PT-INR: International normalized ratio of prothrombin time

		Fit (CFS 1–3)	Vulnerable (CFS 4)	Frail (CFS 5–9)	
	Diabetes mellitus with organ damage	28 (8.3)	19 (17.4)	14 (6.9)	< 0.01
	Chronic kidney disease	19 (5.6)	20 (18.3)	16 (7.8)	< 0.01
	Hemiplegia	3 (0.9)	3 (2.8)	25 (12.3)	< 0.01
	Malignancy (solid)	30 (8.9)	19 (17.4)	28 (13.7)	0.03
	Malignancy (blood)	6 (1.8)	0	1 (0.5)	0.18
	Metastatic tumor	6 (1.8)	4 (3.7)	5 (2.5)	0.46
	Mild liver disease	8 (2.4)	11 (10.1)	9 (4.4)	< 0.01
	Moderate to severe liver disease	13 (3.9)	1 (0.9)	9 (4.4)	0.26
	AIDS	0	0	0	
CCI		1 (0–2)	2 (1–4)	2 (1–3)	< 0.01
SOFA score		7 (4–10)	8 (5–11)	7 (5–10)	0.59
APACHE II score		18 (12–25)	22 (17–28)	21 (15–27)	< 0.01
Septic shock		60 (17.8)	23 (21.1)	28 (13.7)	0.22
Mechanical ventilation		132 (39.3)	46 (43.4)	74 (36.5)	0.49
Vital signs	Glasgow coma scale	13 (8–15)	11 (8–15)	12 (7–14)	< 0.01

Reported counts (proportions) for categorical and median (interquartile range) for continuous variables.

Continuous variables were compared using the Mann–Whitney U test. Categorical variables were compared using the Fisher’s exact test or chi square test, where appropriately.

Missing data: BMI = 5; Metastatic tumor = 1; Mechanical ventilation = 2; Systolic blood pressure = 2; Heart rate = 1; Temperature = 1; Hematocrit = 1; PT–INR = 5; Lactate = 15; Glucose = 6; Total bilirubin = 1; C-reactive protein = 2; Positive blood cultures = 37

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		<b>Fit (CFS 1–3)</b>	<b>Vulnerable (CFS 4)</b>	<b>Frail (CFS 5–9)</b>	
	Systolic blood pressure (mmHg)	107 (87–128)	105 (80–137)	109 (86–128)	0.97
	Heart rate (/min)	105 (88–125)	108 (90–120)	103 (86–118)	0.18
	Respiratory rate (/min)	24 (19–29)	22 (18–27)	23 (19–30)	0.42
	Body temperature (°C)	37.5 (36.5–38.5)	37.5 (36.4–38.6)	37.0 (36.3–38.1)	0.03
Laboratory data	White blood cells (/μL)	11000 (5780–15580)	10520 (6700–16000)	11780 (7450–17200)	0.32
	Hematocrit (%)	35.4 (29.3–40.8)	33.1 (26.8–39.1)	34.4 (29.4–39.9)	0.07
	Platelet (/μL)	16.3 (9.8–24.4)	18.0 (11.2–24.3)	18.1 (12.9–25.5)	0.16
	PT-INR	1.2 (1.1–1.4)	1.2 (1.1–1.4)	1.2 (1.1–1.4)	0.83
	Lactate (mmol/L)	2.6 (1.4–4.4)	2.7 (1.6–5.7)	2.5 (1.4–4.4)	0.27
	Glucose (mg/dL)	142 (112–205)	150 (109–210)	138 (103–194)	0.39
	Sodium (mEq/L)	138 (134–141)	138 (135–141)	138 (134–141)	0.94
	Potassium (mEq/L)	4.0 (3.6–4.5)	4.0 (3.4–4.7)	4.1 (3.6–4.6)	0.40
	Creatinine (mg/dL)	1.5 (0.8–2.6)	1.6 (0.9–2.9)	1.2 (0.7–2.1)	0.02

Reported counts (proportions) for categorical and median (interquartile range) for continuous variables.

Continuous variables were compared using the Mann–Whitney U test. Categorical variables were compared using the Fisher’s exact test or chi square test, where appropriately.

Missing data: BMI = 5; Metastatic tumor = 1; Mechanical ventilation = 2; Systolic blood pressure = 2; Heart rate = 1; Temperature = 1; Hematocrit = 1; PT–INR = 5; Lactate = 15; Glucose = 6; Total bilirubin = 1; C-reactive protein = 2; Positive blood cultures = 37

CFS: Clinical frailty scale, BMI: Body mass index, COPD: Chronic obstructive pulmonary disease, AIDS: Acquired immunodeficiency syndrome, CCI: Charlson comorbidity index, SOFA: Sequential organ failure assessment, APACHE: Acute physiology and chronic health evaluation, PT-INR: International normalized ratio of prothrombin time

		Fit (CFS 1–3)	Vulnerable (CFS 4)	Frail (CFS 5–9)	
	Total bilirubin (mg/dL)	0.8 (0.5–1.5)	0.8 (0.5–1.5)	0.7 (0.5–1.1)	0.02
	C-reactive protein (mg/dL)	13.6 (4.6–24.5)	12.1 (3.9–24.9)	10.5 (3.0–21.0)	0.04
	Positive blood cultures	141 (44.2)	49 (47.6)	85 (44.5)	0.84
Site of infection at final diagnosis	Lung	103 (30.6)	39 (35.8)	81 (39.7)	< 0.01
	Abdomen	74 (22.0)	21 (19.3)	35 (17.2)	
	Urinary tract	49 (14.5)	13 (11.9)	44 (21.6)	
	Soft Tissue	43 (12.8)	18 (16.5)	20 (9.8)	
	Others	35 (10.4)	9 (8.3)	7 (3.4)	
Reported counts (proportions) for categorical and median (interquartile range) for continuous variables.					
Continuous variables were compared using the Mann–Whitney U test. Categorical variables were compared using the Fisher’s exact test or chi square test, where appropriately.					
Missing data: BMI = 5; Metastatic tumor = 1; Mechanical ventilation = 2; Systolic blood pressure = 2; Heart rate = 1; Temperature = 1; Hematocrit = 1; PT–INR = 5; Lactate = 15; Glucose = 6; Total bilirubin = 1; C-reactive protein = 2; Positive blood cultures = 37					
CFS: Clinical frailty scale, BMI: Body mass index, COPD: Chronic obstructive pulmonary disease, AIDS: Acquired immunodeficiency syndrome, CCI: Charlson comorbidity index, SOFA: Sequential organ failure assessment, APACHE: Acute physiology and chronic health evaluation, PT-INR: International normalized ratio of prothrombin time					

Table 2 shows the outcomes among fit, vulnerable, and frail patients. There was no statistically significant difference in in-hospital mortality between the three frailty groups: fit 55/335 (16.4%); vulnerable 23/107 (21.5%); and frail 45/203 (22.2%),  $p = 0.19$ . There were no significant differences in IFDs, VFDs, or LOS between the three frailty groups. Frailty was associated with disposition after discharge (discharge to home: fit 125/280 [44.6%]; vulnerable 36/84 [42.9%]; and frail 40/158 [25.3%],  $p < 0.01$ ).

Table 2  
Outcomes of patients with suspected infection

		Fit (CFS 1–3)	Vulnerable (CFS 4)	Frail (CFS 5–9)	p-value
		n = 337 (51.8)	n = 109 (16.8)	n = 204 (31.4)	
In-hospital mortality		55/335 (16.4)	23/107 (21.5)	45/203 (22.2)	0.19
Dispositions	Home	125/280 (44.6)	36/84 (42.9)	40/158 (25.3)	< 0.01
	Transfer	155/280 (55.4)	48/84 (57.1)	118/158 (74.7)	
ICU-free days		16 (0–22)	17 (0–22)	15 (0–22)	0.85
Ventilator-free days		21 (0–28)	21 (8–28)	20 (0–28)	0.71
Length of hospital stay		22 (10–49)	23 (14–41)	23 (11–40)	0.86
Reported counts (proportions) for categorical and median (interquartile range) for continuous variables. Continuous variables were compared using the Mann–Whitney U test. Categorical variables were compared using the Fisher’s exact test or chi square test, where appropriately.					
Missing data: In–hospital mortality = 5; ICU–free days = 41; Ventilator–free days = 41; Length of hospital stay = 5					
CFS: Clinical frailty scale, ICU: Intensive care unit					

Figure 2 shows the Kaplan–Meier survival curves stratified by the three groups. There was little difference in in-hospital mortality between the groups during the acute disease phase. However, more vulnerable and frail patients died after the acute disease phase than did fit patients, although this difference was not statistically significant ( $p = 0.25$ ). Cox proportional hazards regression analysis did not demonstrate an association between in-hospital mortality and frailty (vulnerable vs. fit: adjusted hazard ratio 1.16 [95% confidential interval, 0.70–1.92],  $p = 0.57$ , frail vs. fit: adjusted hazard ratio 1.13 [95% confidential interval 0.75–1.72],  $p = 0.56$ ), and there were no interactions between frailty and age, frailty and the Charlson comorbidity index, and age and the Charlson comorbidity index (Table 3).

Table 3  
Univariable and multivariable analysis for mortality associated with frailty in patients with suspected infection

Univariable analysis		HR	95% CI		p-value
Frailty	Vulnerable vs fit	1.33	0.82	2.16	0.25
	Frail vs fit	1.36	0.92	2.01	0.13
Multivariable analysis		HR	95% CI		p-value
Age		1.01	1.00	1.03	0.04
Sex, male		1.10	0.76	1.61	0.61
Charlson comorbidity index		1.04	0.95	1.15	0.39
SOFA score		1.18	1.14	1.24	< 0.01
Frailty	Vulnerable vs fit	1.16	0.70	1.92	0.57
	Frail vs fit	1.13	0.75	1.72	0.56
HR: Hazard ratio, CI: Confidence Interval, SOFA: Sequential organ failure assessment					

Among patients with suspected infection, 599 (92.2%) patients were diagnosed with sepsis. The subgroup analysis of patients with sepsis gave similar results to the primary analysis (Supplementary Tables 1 and 2). Similarly, there was no association between in-hospital mortality and frailty in patients with sepsis (vulnerable vs. fit: adjusted hazard ratio 1.22 [95% confidential interval, 0.73–2.04],  $p = 0.45$ , frail vs. fit: adjusted hazard ratio 1.26 [95% confidential interval 0.82–1.93],  $p = 0.29$  [Supplementary Table 3]).

## Discussion

We investigated the association between frailty and clinical characteristics and outcomes among patients with suspected infection in ICUs. Approximately one third of patients in this study population were classified as frail according to their CFS scores. Vulnerable and frail patients appeared to have poor outcomes after the acute disease phase compared with fit patients, although there were no differences between the groups in terms of short-term in-hospital mortality.

Some of the results of our study differed from those of previous studies. The proportion of elderly patients in our study was higher than that in previous studies; the median age of patients in our study was 72 years; in other studies, the median age was 62<sup>11</sup> and 64 years<sup>12</sup>. However, the percentage of frail patients in our study was equivalent or lower than that in previous studies (31.4% vs. 29.5%<sup>11</sup> and 43.0%<sup>12</sup>). The higher proportion of elderly patients in our study may be explained by the fact that Japan has one of the world's oldest populations.<sup>19</sup> Another explanation may be that our cohort included a large proportion of patients with sepsis.<sup>20</sup> Regarding the prevalence of frailty, there may have been less frail

patients in this study because our study institutions were tertiary emergency care centers and only patients admitted to ICUs were included. Alternatively, it may have been due to the difference between the trajectory of sepsis and the trajectory of chronic diseases such as heart failure<sup>21</sup> and respiratory failure.<sup>22</sup>

We confirmed that frail and vulnerable patients had more comorbidities compared with fit patients. Comorbidities included congestive heart failure, cerebrovascular diseases, and COPD as well as those described in previous studies.<sup>23,24</sup> Our results were very similar to previous reports that included heterogeneous diseases, although we selected patients with suspected infection only. There exists a controversy regarding the relationship between individual comorbidities and frailty.<sup>25</sup> The combination of individual comorbidities and frailty may not be related to the primary disease, although it is natural that more comorbidities lead to greater frailty.

Our findings with regard to body temperature and C-reactive protein levels suggest that frailty may be associated with a poor acute inflammatory response. Some studies have reported that frailty was associated with chronic changes in the immune response, including the imbalance of decline in immune function and increased inflammation.<sup>26,27</sup> Other studies have reported that aging was related to changes in the acute immune response,<sup>28,29</sup> due to dysfunction of immune cells or decreased cytokines working as a part of innate and adaptive immunity.<sup>28</sup> Both frailty and aging may be involved in weakening the acute inflammatory response. Further studies are needed to clarify the relationship between frailty, aging, and poor inflammatory responses.

Regarding mortality, we found that more vulnerable and frail patients died after the acute disease phase, although this difference was not statistically significant. This tendency was consistent with previous reports.<sup>1,11</sup> In the acute disease phase, disease severity may have had a greater impact on mortality than frailty. In the late disease phase, we did not observe the patients' status after discharge, and frail patients who transferred to other institutions in the early disease phase may have subsequently died. Further studies are needed to assess the association between frailty and long-term mortality in patients admitted to ICUs with suspected infection.

Moreover, our study showed that mortality rates in vulnerable and frail patients were similar, whereas previous studies in ICUs demonstrated that the severity of frailty was associated with mortality.<sup>8,14</sup> We may have provided a greater level of clinical care for very frail patients because the Japanese national health insurance system is universal. This may have contributed to the reduction of mortality among frail patients. Alternatively, the relationship between the severity of frailty and mortality may not have been linear among patients with sepsis. Mortality from septic shock is very high.<sup>15</sup> Vulnerable and frail patients may have already been at risk of death. Further studies are needed to assess the association between the severity of frailty and mortality in patients with sepsis.

## Limitations

This study had some limitations. First, fewer patients had CFS scores of 5 in our study compared with those in previous studies.<sup>8,11,14</sup> There is a possibility that some CSF scores were misclassified. The CFS score is not widely used to assess frailty in Japan. Education in the use of the CFS score may have been necessary although the CSF has been found to be a reliable tool even if the assessor is different.<sup>30</sup> Second, we did not follow up the patients' outcomes after hospital discharge. We used the last observation carried forward. Third, we did not have information about treatments that may have been related to the patients' outcomes in this database. However, most patients should have received appropriate treatments according to guidelines such as the Surviving Sepsis Campaign Guideline, which is used in national certified ICUs.<sup>31</sup>

## Conclusion

Among patients admitted to ICUs with suspected infection including sepsis, frail and vulnerable patients had poor outcomes after the acute disease phase; however, there were no statistically significant differences in outcomes between the three frailty groups.

## List Of Abbreviations

CFS Clinical Frailty Scale

COPD Chronic obstructive pulmonary disease

ICUs Intensive care units

IFDs ICU-free days

IQR Interquartile range

JAAM Japanese Association for Acute Medicine

LOS Length of hospital stay

SOFA Sequential Organ Failure Assessment

SPICE Sepsis Prognostication in Intensive Care Unit and Emergency

VFD Ventilator-free days

## Declarations

### Ethical Approval and consent to participate

The study protocol was reviewed and approved by the Research Ethics Committee of all participating institutions at the Japanese Association for Acute Medicine (JAAM) SPICE study group. Given the

retrospective and anonymized nature of this study in the routine care, the Ethics Committees waived the need for informed consent from the study participants. The Institutional Review Board of Hokkaido University, a leading institution in SPICE, approved this study (approval no. 016-0386).

### **Consent for publication**

Not applicable

### **Availability of data and materials**

The datasets analyzed during the current study is available with the corresponding author on reasonable request.

### **Competing interests**

All authors declare that they have no competing interests.

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### **Author contributions**

AK conceived of and designed this study, interpreted the data, drafted the manuscript, and revised the manuscript for important intellectual content. TA contributed to the acquisition of data, conceived of and designed this study, interpreted the data, and revised the manuscript for important intellectual content. KY contributed to the acquisition of data, conducted data cleaning, interpreted the data, and revised the manuscript for important intellectual content. SK, HO, DS, and SF contributed to the acquisition of data, jointly conceived of and designed this study, interpreted the data, and revised the manuscript for important intellectual content. All of the authors contributed to the acquisition of data, reviewed, discussed, and approved the final manuscript.

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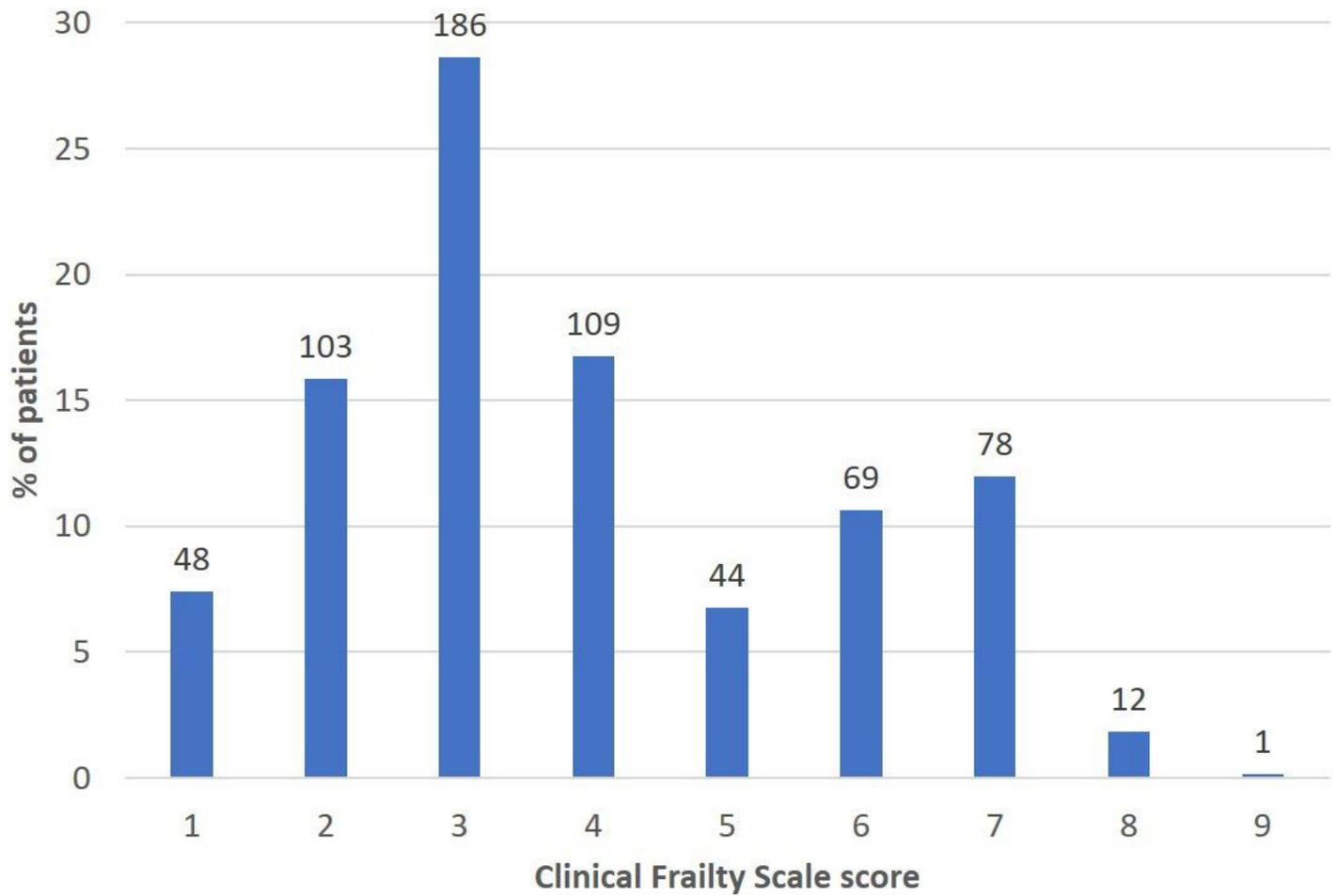
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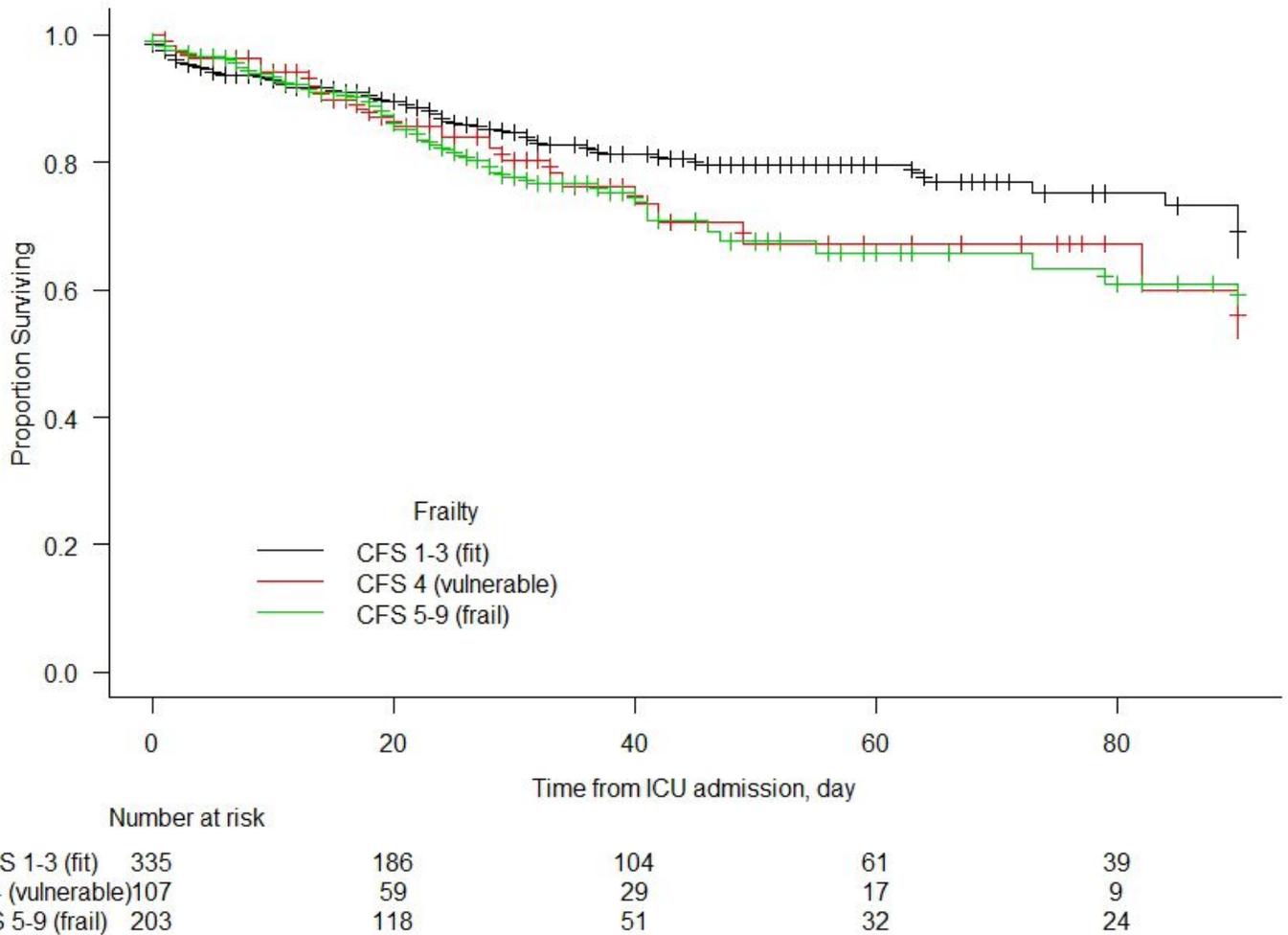
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## Figures



**Figure 1**

Distribution of Clinical Frailty Scale scores and prevalence of frailty among the enrolled patients. The number at the top of each graph shows the number of patients in each category.



**Figure 2**

Kaplan–Meier survival curves stratified by the three frailty groups. CFS: Clinical Frailty Scale. ICU: Intensive care unit

## Supplementary Files

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