ORIGINAL RESEARCH
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Premorbid Clinical Frailty Score and 30-day mortality among older adults in the emergency department

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Abstract

Objectives: The association between frailty and short-term prognosis has not been established in critically ill older adults presenting to the emergency department. We sought to examine the association between premorbid frailty and 30-day mortality in this patient population.

Methods: This is a retrospective observational study on older adults aged over 75 who were triaged as Level 1 resuscitation with subsequent admissions to intermediate units or intensive care units (ICUs) in a single critical care center, from January to December 2019. We excluded patients with out-of-hospital cardiac arrest or those transferred from other hospitals. Frailty was evaluated by the Clinical Frailty Scale (CFS) from the patients' chart reviews. The primary outcome was 30-day mortality, and we examined the association between frailty scored on the CFS and 30-day mortality using a multivariable logistic regression model with CFS 1–4 as a reference.

Results: A total of 544 patients, median age: 82 years (interquartile rang 78 to 87), were included in the study. Of these, 29% were in shock and 33% were in respiratory failure. The overall 30-day mortality was 15.1%. The adjusted risk difference (95% confidence interval [CI]) in mortality for CFS 5, CFS 6, and CFS 7–9 was 6.3% (-3.4 to 15.9), 11.2% (0.4 to 22.0), and 17.7% (5.3 to 30.1), respectively; and the adjusted risk ratio (95% CI) was 1.45 (0.87 to 2.41), 1.85 (1.13 to 3.03), and 2.44 (1.50 to 3.96), respectively.

Conclusion: The risk of 30-day mortality increased as frailty advanced in critically ill older adults. Given this high risk of short-term outcomes, ED clinicians should consider goals of care conversations carefully to avoid unwanted medical care for these patients.

KEYWORDS
aged over 75, clinical frailty scale, critically-ill, frailty, older adults, 30-day mortality

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1 | INTRODUCTION

1.1 | Background

Older adults visit emergency departments for a wide variety of reasons, including the unmet care needs of advanced medical illnesses.[1–3] As a result, the management of these older adults requires a higher level of competencies among emergency medical staff. One of the most difficult of these is the ability to evaluate a patient's prognosis correctly and make clinical decisions that are compatible with the needs and wishes of this segment of the population.[3,4] The challenge stems from communication barriers resulting from the confluence of acute sickness, significant comorbid diseases, and audiovisual impairments.[5,6] In critically ill older adult patients, lifesaving measures may be prioritized without sufficient evaluation of the prognosis or patient's values, especially in those countries or regions, such as Japan, that do not have legal advance directives.[3] This may lead to medical care that patients may not have wanted if they had had the time to understand their prognosis and share the decision-making process.[3,7,8]

There is a need for clinical indicators that can estimate prognosis as accurately and quickly as possible and help clinicians communicate with older adults and their families for decision-making. There have been many studies that have investigated prognostic factors, most notably the use of screening instruments, such as the Identification of Seniors at Risk and Triage Risk Screening Tool or vital signs.[9–12] However, the results were not clinically meaningful, possibly because such prognostic indicators do not necessarily reflect the diverse clinical backgrounds of older adults.

1.2 | Importance

To overcome this problem, frailty has recently become the focus of attention.[13] Frailty refers to an individual's vulnerability for developing increased dependency and/or mortality when exposed to a physiological stressor.[14] This definition itself encompasses the special characteristics of older adult patients. However, diagnostic criteria, such as the Frailty Index, were cumbersome, and their clinical use was limited until the Clinical Frailty Scale (CFS) was proposed by the Canadian Study of Health and Aging. The CFS is a simple method of measuring frailty that has been shown to be comparable to the Frailty Index in predicting the prognosis of adverse health outcomes and does not require any particularly complicated measurement.[15] Several studies have confirmed its effectiveness as a prognostic indicator in the ED.[16,17] However, the results of these studies are of questionable relevance to critically ill older adults because they included mainly clinically stable older adults for whom rapid and challenging decision-making is not an issue in the ED. Therefore, it remains unclear as to whether frailty evaluated by the CFS can be a clinical indicator of prognosis in critically ill older adults and its confirmation would be important and useful for the emergency care of this patient population.

The Bottom Line

When caring for critically ill older adult patients, emergency physicians may be called on to prognosticate on the likelihood a patient will survive the acute illness. This study evaluated the association of frailty, as measured by the Clinical Frailty Score, with 30-day mortality among 544 critically ill older emergency department patients. Increasing frailty was associated with higher mortality, with a mortality rate of 26% among severely frail or terminally ill older adults.

1.2.1 | Goals of this investigation

The purpose of this study is to investigate the association between premorbid frailty evaluated by the CFS and 30-day mortality among older adults who are deemed to require resuscitation in the ED.

2 | METHODS

2.1 | Study design and settings

We conducted a single-center retrospective study at Kobe City Medical Center General Hospital (KCGH), Kobe, Japan between January and December 2019. KCGH is located in the center of the city, which has a population of 1.5 million residents in an area of 557 km^2 including its urban and rural communities. The ED of KCGH is a certificated critical care center approved by Japan's Ministry of Health, Labour and Welfare and receives an average of 35,000 patient visits and 10,000 ambulance arrivals each year, managing more than half the number of severely ill patients in this area. KCGH's ethics committee approved the study protocol (ID 20229).

2.2 | Selection of participants

The target population was older adults, aged over 75 years, who were triaged as "Level 1 resuscitation" based on the Canadian Triage and Acuity Scale (CTAS) .[18,19] The CTAS is a validated 5-level ED triage algorithm developed in Canada and defines Level 1 resuscitation as conditions that are threatening to life or limb (or imminent risk of deterioration) requiring immediate aggressive interventions. In our ED, all patients are evaluated on admission using the CTAS. We first collected data on all patients who were categorized as being at Level 1 resuscitation in the ED and subsequently admitted to intermediate units or ICUs.[20] We excluded patients with out-of-hospital cardiac arrest (OHCA) and those who had been transferred from other hospitals.

2.3 | Data collection

We obtained the data from electronic medical records: age, sex, admission from nursing facilities, body mass index (BMI), the Charlson Comorbidity Index, the National Early Warning Score2 (NEWS2), vital signs on ED arrival, use of oxygen, disease category (cardiovascular disease, stroke, infectious disease, surgical disease, and other) on admission, tracheal intubation, use of vasopressors, and admission to the ICU.

Shock was defined as low systolic blood pressure (< 100 mmHg), shock index (> 1), or clinical signs of insufficient peripheral circulation, and respiratory failure was defined as tachypnea (respiratory rate > 25 per minute) and supplemental oxygen with some complaints of dyspnea or desaturation (pulse oximetry saturation ≤92%).[21–24]

2.4 | CFS

The CFS is a 9-point scale representing different grades of frailty, from 1 (very fit) to 8 (very severely frail) and 9 (terminally ill). It can be scored by 4 features: how the person moved, functioned, thought, and felt about their health over the previous 2 weeks, not on arrival at the ED (A free CFS app is available at https://www.acutefrailtynetwork.org.uk/Clinical-Frailty-Scale/Clinical-Frailty-Scale-App). A patient's frailty at the time of admission was assessed using the CFS. Three emergency physicians (JYH, YM, and HK) retrospectively rated the CFS of patients randomly assigned to each physician by reviewing electronic medical records, admission charts entered by attending nurses, rehabilitation records, and hospitalization documents where the family provided written information including the patient's level of daily activity before admission to the hospital. To evaluate the association between the CFS and 30-day mortality, we divided patients into 4 groups according to the CFS: CFS 1–4 (fit to vulnerable), CFS 5 (mildly frail), CFS 6 (moderately frail), and CFS 7–9 (severely frail to terminally ill). Further, we randomly selected 50 patients, assigned them to the 3 raters, and assessed interrater reliability by calculating weighted kappa statistics.[25]

2.5 | Outcome measures

The outcome of interest was mortality at 30 days after admission to the hospital. When there was no information in the electronic medical charts on outcomes at 30 days, we followed up by making contact with the patients, their family members, their attending health care workers, or family physicians on the phone.

2.6 | Statistical analysis

We provide descriptive statistics as medians with interquartile ranges (IQRs) or averages with SDs for continuous variables and as counts and proportions for categorical variables.

We conducted the primary analysis using the complete data set and compared outcomes between the 4 groups: CFS 1–4 (fit to vulnerable), CFS 5 (mildly frail), CFS 6 (moderately frail), and CFS 7–9 (severely frail to terminally ill). Adjusted risk differences and risk ratios were calculated using a logistic model with adjustment for the following variables: age (in 5-year increments), sex, NEWS2 (low, medium, high), BMI (< 18.5, 18.5 to 25, ≥25), and the Charlson Comorbidity Index (0, 1 to 2, 3 to 4, ≥5). We selected these variables based on biological plausibility and preexisting knowledge.[26–28]

Further, we conducted a sensitivity analysis for missing covariates with multivariate imputation by chained equations. To impute the missing data, we used all measured variables, including outcomes, and generated 20 imputed data sets based on the assumption that the data were missing randomly.

In the subgroup analysis, we planned to perform a priori subgroup analyses, as we recognized potential and clinically important heterogeneity in a population that required resuscitation in the ED. In these analyses, patients were divided into 2 groups: CFS 1–4 and CFS 5–9. We then evaluated the association between the CFS and 30-day mortality in each predetermined subgroup: tracheal intubation (yes or no), use of vasopressor (yes or no), shock (yes or no), respiratory failure (yes or no), and disease categories. These definitions of shock and respiratory failure are broader and determined by clinical presentation, and so they overlapped the subgroups categorized by interventions such as administration of vasopressors and tracheal intubation.

We used STATA version 15.1 (StataCorp, College Station, TX, USA) for the statistical analyses. All P values were 2 tailed, with a significance level of P < 0.05.

3 | RESULTS

3.1 | Study population

Of a total of 33,058 ED visits, 7550 patients (22.8%) were aged over 75 years, of whom 3453 cases (45.7%) were brought to our ED by ambulance. Among these older adult cases, 644 cases (8.5%) were resuscitated in the ED and subsequently admitted to intermediate units or ICUs. After excluding OHCA cases (15 patients) and patients transferred from other hospitals (42 patients), we included the 544 patients with complete data sets for our primary analysis (Figure 1). Information on patients with missing data is described in Table S3.

3.2 | Patient characteristics

Table 1 shows the baseline characteristics of older adult patients who were triaged as Level 1 resuscitation in the ED.

The overall median age was 82 years (IQR, 78 to 87), with age tending to be higher in the more advanced CFS category. Approximately half of the patients were female, and CFS 7–9 had a higher proportion of female patients compared to other CFS categories. Only 34 cases (6.3%) were admitted to the ED from nursing facilities, with almost 60%
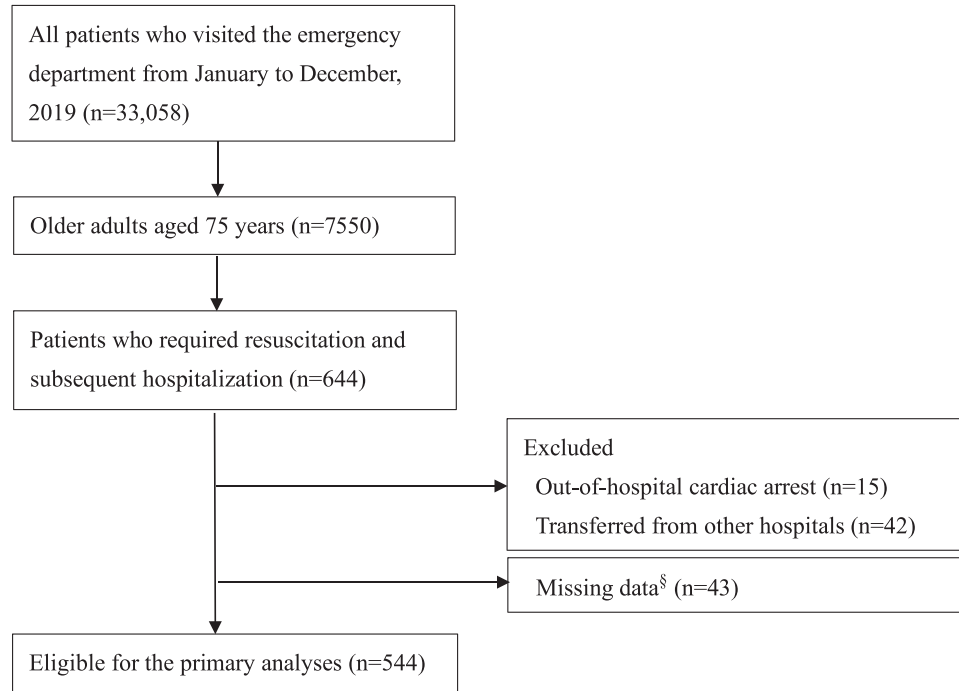
FIGURE 1 Flow chart of the study. For the primary analysis, we precluded patients with missing data for the logistic model as follows: age, sex, National Early Warning Score score, Charlson Comorbidity Index score, Clinical Frailty Score, and 30-day mortality

TABLE 1 Baseline characteristics of older adult patients who were triaged as Level 1 resuscitation in the emergency department

	Total (n = 544)	CFS 1–4 (n = 226)	CFS 5 (n = 127)	CFS 6 (n = 100)	CFS 7–9 (n = 91)
Age, median (IQR)	82 (78 to 87)	80 (77 to 84)	83 (78 to 88)	85 (81 to 90)	86 (81 to 91)
Female, n (%)	257 (47)	88 (39)	61 (48)	47 (47)	61 (67)
Admission from nursing facilities, n (%)	34 (6.3)	0 (0)	5 (3.9)	9 (9.0)	20 (22)
BMI, median (IQR)	21.3 (18.8 to 23.8)	22.1 (19.8 to 24.1)	21.3 (19.1 to 24.8)	20.5 (17.6 to 23.3)	19.9 (17.6 to 22.6)
NEWS2 score, median (IQR)	7 (4 to 9)	6 (4 to 9)	6 (5 to 9)	7 (5 to 10)	8 (6 to 10)
Charlson Comorbidity Index, median (IQR)	2 (1 to 4)	1 (0 to 3)	2 (1 to 4)	2 (1 to 5)	3 (1 to 6)
Shock[a]	156 (29)	51 (23)	33 (26)	27 (27)	45 (49)
Respiratory failure[b]	179 (33)	58 (26)	48 (38)	43 (43)	30 (33)
Disease category					
Cardiovascular disease	116 (21)	54 (24)	28 (22)	25 (25)	9 (9.9)
Stroke	133 (24)	69 (31)	27 (21)	22 (22)	15 (16)
Infectious disease	88 (16)	19 (8.4)	25 (20)	19 (19)	25 (27)
Surgical disease	74 (14)	38 (17)	13 (10)	11 (11)	12 (13)
Tracheal intubation, n (%)	86 (16)	40 (18)	18 (14)	15 (15)	13 (14)
Use of vasopressors, n (%)	138 (25)	54 (24)	31 (24)	25 (25)	28 (31)
Admission to ICU, n (%)	205 (38)	91 (40)	46 (36)	39 (39)	29 (32)

Abbreviations: CFS, Clinical Frailty Scale; ED, emergency department; IQR, interquartile range; BMI, body mass index; NEWS2, National Early Warning Score 2.

[a]Defined as low systolic blood pressure (< 100 mmHg), shock index (> 1), or clinical signs of insufficient peripheral circulation.

[b]Defined as tachypnea (respiratory rate > 25 per minute) and supplemental oxygen with some complaints of dyspnea or desaturation (pulse oximetry saturation ≤92%).

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TABLE 2 Outcomes of older adult patients who were triaged as Level 1 resuscitation in the emergency department

	CFS 1–4 (n = 226)	CFS 5 (n = 127)	CFS 6 (n = 100)	CFS 7–9 (n = 91)
30-day mortality, n (%)	19 (8.4)	18 (14.2)	21 (21.0)	24 (26.4)
Unadjusted analysis				
Risk difference (95% CI), %	Reference	8.0 (−2.1 to 18.0)	15.9 (4.5 to 27.3)	21.8 (9.6 to 34.1)
Risk ratio (95% CI)	Reference	1.58 (0.96 to 2.61)	2.25 (1.42 to 3.56)	2.81 (1.81 to 4.35)
Adjusted analysis[a]				
Risk difference (95% CI), %	Reference	6.3 (−3.4 to 15.9)	11.2 (0.4 to 22.0)	17.7 (5.3 to 30.1)
Risk ratio (95% CI)	Reference	1.45 (0.87 to 2.41)	1.85 (1.13 to 3.03)	2.44 (1.50 to 3.96)

Abbreviations: BMI, body mass index; CFS, Clinical Frailty Scale; CI, confidence interval; ED, emergency department; NEWS2, National Early Warning Score 2.

[a]We calculated adjusted risk differences and risk ratios using a logistic model with adjustment for the following variables: age (in 5-year increments), sex, NEWS2 (low, medium, high), BMI (< 18.5, 18.5 to 25, ≥25), and the Charlson Comorbidity Index (0, 1 to 2, 3 to 4, ≥5).

of them being categorized as CFS 7–9 (see the Table S1 for interrater reliability).

The NEWS2 score was high, with an overall median score of 7 (high risk); the score was slightly higher in more advanced CFS categories. The overall median Charlson Comorbidity Index score was 2 (1 to 4), and there was no difference in distribution among CFS categories.

For shock, respiratory failure and each diagnostic category, there were no obvious differences in distribution across the CFS categories.

With regard to resuscitation procedures in the ED, tracheal intubation was performed in 86 cases (16%), whereas vasopressors were administered in 138 cases (25%). In addition, 205 cases (38%) were admitted to the ICU after resuscitation in the ED.

3.3 | Main results

The outcomes at 30 days were available for all eligible patients from chart reviews and direct contacts. The overall 30-day mortality was 15.1% (82/544). The mortality was higher in the more advanced CFS category, and more than 1 out of 4 died within 30 days of admission in the CFS 7–9 category (Table 2).

When CFS 1–4 was used as a reference, the adjusted risk difference in mortality for CFS 5, CFS 6, and CFS 7–9 was 6.3% (95% confidence interval [CI]: -3.4 to 15.9), 11.2% (95% CI: 0.4 to 22.0) and 17.7% (95% CI: 5.3 to 30.1), respectively; and the adjusted risk ratio (ARR) was 1.45 (95% CI: 0.87 to 2.41), 1.85 (95% CI: 1.13 to 3.03), and 2.44 (95%CI: 1.50 to 3.96), respectively. In Table S2, we described results relating to the multivariable logistic regression analysis.

The sensitivity analysis revealed similar results between the analysis with imputed data sets and the analysis with the complete data set (See Tables S3 and S4).

3.4 | Subgroup analyses

In the subgroup analysis, frailty referred to CFS 5–9 compared to a reference of CFS 1–4, and we described the subgroup analyses of the associations between frailty and 30-day mortality in Table 3.

The subgroup analysis revealed that none was shown to be statistically significant, perhaps because of the small sample size. We demonstrated ARR was 1.93 (95% CI: 0.90 to 4.14), 2.28 (95% CI: 0.99 to 5.23), and 2.23 (95% CI: 0.95 to 5.25) in the subgroups of tracheal intubation, shock, and respiratory failure, respectively. Among the subgroup analyses of disease classification, the influence of frailty appeared to be higher especially in cardiovascular disease (ARR, 5.41 [95% CI: 0.58 to 50.6]) and surgical disease (ARR, 3.44 [95% CI: 0.87 to 13.6]). On the other hand, it was attenuated in stroke (ARR, 1.57 [95% CI: 0.46 to 5.34]) or infectious diseases (ARR, 1.03 [95% CI: 0.48 to 2.20]).

3.5 | Limitations

Our study has several limitations. First, retrospectively-scored CFS may not be accurate and may be influenced by the evaluators. However, previous prospective studies showed accuracy of CFS scored from chart reviews and fair interrater reliability.[29,30] As we confirmed reasonable interrater reliability (Table S1), we do not believe the CFS scores used in this study limited the accuracy of our results. However, to be applied in clinical practice, it should be ensured by a prospective study that the accuracy of the CFS remains unchanged. Second, we should consider the influence of patients who were not included in the primary analysis because of missing data (Table S3). These patients appeared to be sicker than those without missing covariates, and we could not speculate the influence sufficiently from the available data set. However, considering that the sensitivity analysis demonstrated similar results between the complete data set and imputed data set, we think that the influence of missing data is unlikely to have affected our major conclusions. Third, we had only a small sample size in the subgroup analyses. The subgroup analysis suggested probable heterogeneity among the target population, but there were no statistically significant associations between the predefined groups, perhaps because of the limited sample size. It would be desirable to have a further investigation that targets 1 of these subgroups. Fourth, it remains unclear whether CFS is more accurate than physician gestalt. To the best of our knowledge, there are no reports of physician gestalt being effective in predicting prognosis but further studies,

TABLE 3 Subgroup analyses of associations between frailty and 30-day mortality in patients who required resuscitation in the emergency department

	Number of patients with outcome/Total patients (%)		
Subgroup	Patients with frailty[a]	Patient without frailty	Adjusted risk ratio (95% CI)
Total	63/318 (19.8)	19/226 (8.4)	1.84 (1.10 to 3.08)
Tracheal intubation			
Yes	19/46 (41.3)	7/40 (17.5)	1.93 (0.90 to 4.14)
No	44/272 (16.2)	12/186 (6.5)	1.79 (0.95 to 3.35)
Use of vasopressor			
Yes	26/84 (31.0)	7/54 (13.0)	1.88 (0.87 to 4.04)
No	37/234 (15.8)	12/172 (7.0)	1.78 (0.93 to 3.40)
Shock			
Yes	33/105 (31.4)	6/51 (11.8)	2.28 (0.99 to 5.23)
No	30/213 (14.1)	13/175 (7.4)	1.54 (0.81 to 2.93)
Respiratory failure			
Yes	28/121 (23.1)	6/58 (10.3)	2.23 (0.95 to 5.25)
No	35/197 (17.8)	13/168 (7.7)	1.79 (0.95 to 3.38)
Disease categories			
Cardiovascular disease	7/62 (11.3)	1/54 (1.9)	5.41 (0.58 to 50.6)
Stroke	10/64 (15.6)	4/69 (5.8)	1.57 (0.46 to 5.34)
Infectious disease	24/69 (34.8)	6/19 (31.6)	1.03 (0.48 to 2.20)
Surgical disease	5/36 (13.9)	3/38 (7.9)	3.44 (0.87 to 13.6)
Other	21/116 (18.1)	8/73 (11.0)	1.87 (0.86 to 4.04)

Note: Adjusted risk ratios were calculated using a logistic model with adjustment for the following variables: age (in 5-year increments), sex, NEWS2 (low, medium, high), BMI (< 18.5, 18.5 to 25, ≥25), and the Charlson Comorbidity Index (0, 1 to 2, 3 to 4, ≥5).
Abbreviations: BMI, body mass index; CI, confidence interval; NEWS2, National Early Warning Score 2.
[a]Frailty was defined as Clinical Frailty Scale 5–9 for the subgroup analyses.

including a comparison of CFS and physician gestalt, is needed before clinical application of CFS in prognostication. Finally, our results have limited generalizability because this is a retrospective study in a single emergency medical center in Japan. Differences in race, country, or the setting of various hospital EDs might influence the associations between the CFS and the patient's prognosis in critically ill patients. However, as the results of our study could be explained both clinically and by biological mechanisms, we consider our major conclusions are plausible. Further studies are therefore required to evaluate the usefulness of the CFS in different settings.

4 | DISCUSSION

This retrospective observational study from a single emergency medical center in Japan found a correlation between the CFS and 30-day mortality in ED patients aged 75 years and older who were triaged as Level 1 resuscitation with subsequent hospitalization to intermediate units or ICUs. As frailty advanced based on the CFS, there was a progressive increase in the risk of 30-day mortality. In frail older adults with CFS 7 or above, it increased by 18.1%, with an ARR of 2.44 compared to non-frail older adults with CFS 1–4.

In the shared decision-making model of critically ill older adults, it is essential to take prognosis into consideration when discussing a treatment plan, but there has not yet been an established method for accurately estimating prognosis in the ED.[3–5] A recent systematic review quantified the prognostic accuracy of individual risk factors and ED-validated screening instruments found that the only predictor of patient outcomes was absence of functional dependence.[9] In addition, prospective observational studies in older adult patients with ICU admission or trauma demonstrated that premorbid functional decline was associated with higher in-hospital mortality.[31,32] As the CFS encompasses functional abilities and dependence within its scoring—mildly frail individuals require assistance with higher-order instrumental activities of daily living (ADLs) whereas those who are moderately and severely frail have increasing dependence on others for basic ADLs—it stands to reason that the CFS could predict those at risk of poor outcomes.[33] Two recent observational studies in EDs in Europe showed that risk of mortality increased progressively as frailty advanced on the CFS score.[16,17] However, to date, it has remained unclear whether the CFS can also be a predictor of short-term prognosis in critically ill older adult patients because these previous studies focused on general older adult patients and used a relatively long-term outcome of 2 years. We believe our study adds to the literature,

demonstrating that frailty scored by the CFS was associated with short-term prognosis in critically ill older adult ED patients.

The present study revealed that the CFS can be an effective tool in providing prognostic information in the shared decision-making with critically ill older adults and/or their families. It has been confirmed that early palliative care intervention including goals of care conversations resulted in less invasive therapies, which points to the importance of discussing goals that align with the wishes of patients and their families.[34,35] Therefore, in critically ill older adults, especially in frail older adults, considering their prognosis and starting a goals of care discussion is no less important than starting resuscitation for ED clinicians. In older adult ED patients, ED physicians are increasingly required to harmonize the 2 approaches, namely, lifesaving and palliative care, including goals of care discussions.[1,3,5] For which older adults ED physicians should follow such a harmonized approach remains in question, and frailty defined by the CFS could be one answer based on our results.

In summary, frailty scored by the CFS is associated with short-term prognosis and 30-day mortality increased as frailty advanced in line with the CFS in critically ill older adult ED patients. The CFS, which is easily scored by a simple medical history, can potentially be used as a prognostic indicator in the shared decision-making model of these patients. Further research is required for widespread clinical application of the CFS for prognostication.

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CONFLICT OF INTEREST

None of the authors has any relevant conflict of interest to disclose. This manuscript has not yet been published and is not under consideration for publication elsewhere.

AUTHOR CONTRIBUTIONS

All authors have read and given their approval for submission of this manuscript. Ji Young Huh and Yoshinori Matsuoka contributed to the study concept and design. Ji Young Huh, Yoshinori Matsuoka, Hiroki Kinoshita, Tatsuyoshi Ikenoue, Yosuke Yamamoto and Koichi Ariyoshi contributed to the acquisition, analysis, and interpretation of the data. Yoshinori Matsuoka was responsible for the statistical analyses. Ji Young Huh and Yoshinori Matsuoka prepared the manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.