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ORIGINAL ARTICLE
Heart Failure

Usefulness of Clinical Frailty Scale for Comprehensive Geriatric Assessment of Older Heart Failure Patients

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Background: Comprehensive geriatric assessment (CGA) is a multidisciplinary diagnostic process to identify the physical, psychological, and social functions of patients with frailty. The Clinical Frailty Scale (CFS) might aid in effectively identifying older patients with heart failure (HF) and frailty who would then reap maximum benefits from the CGA.

Methods and Results: A single-centre prospective cohort study that enrolled consecutive hospitalised patients (age ≥75 years) with HF was conducted. The Barthel index (BI), Mini Mental State Examination (MMSE), the Charlson comorbidity index (CCI), and the COntrolling NUTritional (CONUT) for CGA was used. Among 190 enrolled patients (mean age, 85.4 years; 47.9% male), all-cause mortality (primary endpoint) occurred in 45 patients and HF-related rehospitalization (secondary endpoint) in 59 patients within 1 year. The cumulative incidence of all-cause mortality was significantly higher in the high CFS group (low 6.3%, high 30.5%, P<0.001). However, the cumulative incidence of HF-related rehospitalization was not significantly different (low 26.3%, high 32.0%, P=0.304). The multivariable analysis revealed that the CFS group was independently associated with the risk of all-cause mortality. CFS showed a strong correlation with the BI and moderate correlation with the MMSE.

Conclusions: The CFS was associated with all-cause mortality within 1 year and was correlated with frailty domains of CGA.

Key Words: Clinical Frailty Scale; Comprehensive geriatric assessment; Frailty; Geriatrics; Heart failure

As the aging of society accelerates in most developed countries, the proportion of geriatric patients with heart failure (HF) and frailty is steadily increasing.[1–3] Frailty is defined as reduced physiological reserve and vulnerability to external stressors.[4,5] Evaluating and managing patients with HF and frailty has been recognised as a major problem for all healthcare providers engaged in cardiology.

Frailty comprises multiple risk domains, including physical, psychological, and social functions. Domain overlap becomes more pronounced as age increases, and a greater number of frailty domains are associated with a worse prognosis.[6] Comprehensive geriatric assessment (CGA) is a multidisciplinary diagnostic and treatment process that identifies the frailty domains of an older person to develop a coordinated plan to maximise overall health with aging. Although useful,[7–12] CGA is also time consuming and labour intensive;[13] therefore, its unqualified application for the assessment of this increasingly growing demographic (older patients with HF) is not pragmatic.

Frailty screening has thereby been recommended and various screening tools have been developed.[14,15] We hypothesise that using the Clinical Frailty Scale (CFS) as a means of screening might aid in effectively identifying frail geriatric patients with HF who would then obtain maximum benefits from CGA. The CFS is an overall judgment-based frailty tool that generates a frailty score ranging from 1 (very fit) to 9 (terminally ill).[16,17] It is acknowledged to be simple and time-saving.[18] Previous studies have shown that frailty evaluated using the CFS is related to prognosis in older patients with HF,[19,20] but its effect as a screening tool for CGA has not been widely verified.

Methods

Study Design and Population

This single-centre prospective cohort study enrolled 190 patients aged ≥75 years who were hospitalised with decompensated HF between January 2019 and December 2021. Only the first hospitalisation during the study period was recorded. HF decompensation was diagnosed using Framingham criteria. The exclusion criteria were as follows: (1) end-stage renal failure defined by estimated glomerular filtration rate (eGFR) <15 mL/min/1.73 m^2 or haemodialy-

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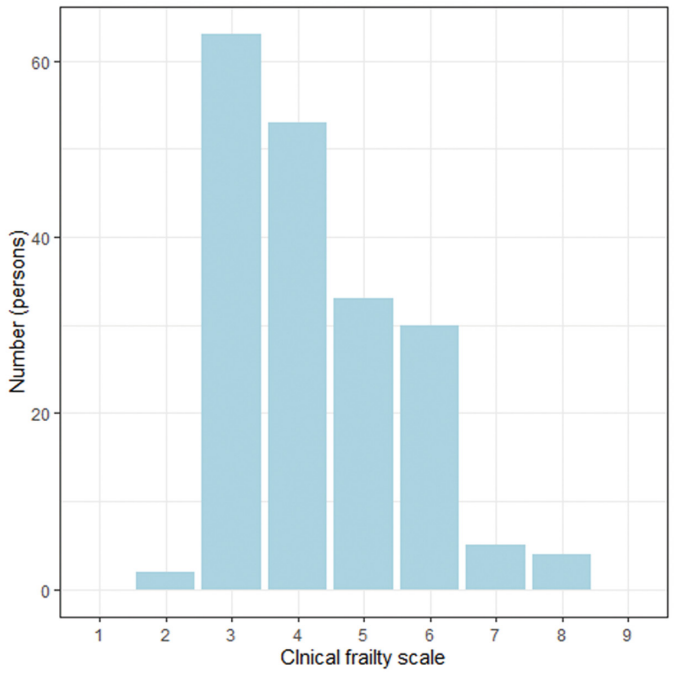

Figure 1. Clinical Frailty Scale distribution.

sis at admission; (2) a brain natriuretic peptide (BNP) level <100 pg/mL or N-terminal proBNP (NT-proBNP) level <300 pg/mL at admission; (3) HF caused by acute coronary syndrome; and (4) a lifetime expectancy of <6 months.

Baseline information, such as medical history, physical findings, medication, blood tests, and echocardiography data, were collected during the stable phase before discharge. The Get With the Guideline-Heart Failure (GWTG-HF) score and Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC) score without the New York Heart Association (NYHA) classification score (hereinafter, referred to as 'modified MAGGIC') were calculated from the baseline information as HF severity scores.[21–24] This was done as the NYHA classification score could not be measured due to the frailty and disability of the patients.

Written informed consent was obtained from all patients. The study protocol was approved by the Ethics Committee of Takatsuki General Hospital, and the study was conducted in accordance with the Declaration of Helsinki.

CGA and CFS Instruments

The CGA and CFS were measured during the stable phase before discharge by well-trained doctors, nurses, or therapists.

The following CGA instruments were chosen in the present study to evaluate frailty domains. Physical function was assessed using the Barthel index (BI), which scales mobility and performance in activities of daily life.[25,26] Cognition in psychological function was assessed with the Mini Mental State Examination (MMSE), which is arguably the best-known and most often used short screening tool for cognitive impairment.[27,28] Comorbidity was assessed with the Charlson comorbidity index (CCI), the gold-standard measurement used to assess the same in clinical research.[29,30] Nutritional state was assessed using the COntrolling NUTritional (CONUT) tool, which is widely used to identify undernourished patients in the hospitalized population.[31,32]

The CFS was introduced by Rockwood et al to summarise the overall frailty level of older adults.[16,17] It quickly evolved for clinical use and has been widely used as a judgment-based tool to screen for frailty, and broadly stratify degrees of frailty. A patient's condition was classified into one of the following categories: (1) very fit; (2) well; (3) managing well; (4) living with very mild frailty; (5) living with mild frailty; (6) living with moderate frailty; (7) living with severe frailty; (8) living with very severe frailty; and (9) terminally ill. We divided patients into two groups (CFS 1–3, and CFS 4–9) based on CFS ≥4, which is reportedly associated with lower survival or avoidance of institutional care in older populations.[17]

Outcomes

Patient prognoses within 1 year of discharge were prospectively collected until December 2022. The primary outcome was all-cause mortality, and the secondary outcome was HF-related rehospitalization. Prognostic data were obtained from outpatient medical records, or otherwise by telephone interviews.

Statistical Analysis

Continuous variables are expressed as means with standard deviations for normally distributed variables and as medians with interquartile ranges (IQR) for non-normally distributed variables. Categorical variables were expressed as numbers and percentages. The cumulative incidence functions for all-cause mortality in each group were estimated using the Kaplan-Meier method and compared between the CFS groups using the log-rank test. The cumulative incidence functions for HF-related rehospitalization in each group were estimated with the all-cause mortality as

Table 1. Basal Characteristics According to CFS Groups

Variable	Overall (n=190)	High CFS (n=125)	Low CFS (n=65)
Age (years)	85.4 (5.8)	87.2 (5.4)	82.0 (5.1)
Sex (male)	91 (47.9)	50 (40.0)	41 (63.1)
Body mass index (kg/m^2)	20.4 (3.5)	20.0 (3.5)	21.2 (3.2)
SBP (mmHg)	114.7 (18.1)	113.5 (19.3)	117.0 (15.5)
Heart rate (beats/min)	72.6 (14.8)	73.3 (14.9)	71.3 (14.5)
Creatinine (mg/dL)	1.3 (0.5)	1.3 (0.5)	1.3 (0.5)
Sodium (mEq/L)	139.0 (4.0)	138.8 (4.0)	139.3 (3.9)
Hemoglobin (g/dL)	11.7 (2.1)	11.3 (1.9)	12.4 (2.3)
NT-proBNP (pg/mL) at admission (n=168)	5,202 [2,888, 11,500]	5,550 [3,040, 11,800]	4,111 [2,257, 9,652]
BNP (pg/mL) at admission (n=144)	684 [441, 1,135]	646 [409, 1,048]	770 [489, 1,316]
EF (%)	48.8 (15.5)	49.8 (15.5)	46.8 (15.3)
HFpEF	94 (49.5)	64 (51.2)	30 (46.2)
HFmrEF	39 (20.5)	26 (20.8)	13 (20.0)
HFrEF	57 (30.0)	35 (28.0)	22 (33.8)
Etiology			
Ischemic	35 (18.4)	20 (16.0)	15 (23.1)
Valvular	36 (18.9)	23 (18.4)	13 (20.0)
Arrhythmic	63 (33.2)	44 (35.2)	19 (29.2)
Hypertensive	11 (5.8)	8 (6.4)	3 (4.6)
Cardiomyopathy	13 (6.8)	4 (3.2)	9 (13.8)
Medication			
ACEI/ARB/ARNI	114 (60.0)	70 (56.0)	44 (67.7)
β-blocker	124 (65.3)	78 (62.4)	46 (70.8)
SGLT2i	6 (3.2)	2 (1.6)	4 (6.2)
Inotrope	13 (6.8)	11 (8.8)	2 (3.1)
Loop diuretic	157 (82.6)	106 (84.8)	51 (78.5)
MRA	90 (47.4)	58 (46.4)	32 (49.2)
Tolvaptan	39 (20.5)	30 (24.0)	9 (13.8)
Comorbidity			
Hypertension	125 (65.8)	80 (64.0)	45 (69.2)
Diabetes mellitus	59 (31.1)	42 (33.6)	17 (26.2)
Atrial fibrillation	113 (59.5)	72 (57.6)	41 (63.1)
Stroke	29 (15.3)	21 (16.8)	8 (12.3)
COPD	19 (10.0)	14 (11.2)	5 (7.7)
Prior HF history	92 (48.4)	69 (55.2)	23 (35.4)
Dementia	56 (29.4)	49 (39.2)	7 (10.8)
Cancer	20 (10.5)	12 (9.6)	8 (12.3)

Values are presented as mean (standard deviation), n (%), or median [interquartile range]. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; BNP, brain natriuretic peptide; CFS, Clinical Frailty Scale; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; HFpEF, heart failure with preserved EF; HFmrEF, heart failure with mid-range EF; HFrEF, heart failure with reduced EF; NT-proBNP, N-terminal proBNP; MRA, mineralocorticoid receptor antagonist; SBP, systolic blood pressure; SGLT2i, sodium glucose co-transporter 2 inhibitor.

a competing risk and compared between the CFS groups using the Grey's test. Univariable and multivariable analyses were performed using the Cox proportional hazard model. In the univariable analysis, we assessed the model using age, sex, body mass index (BMI), systolic blood pressure, heart rate, creatinine, left ventricular ejection fraction, prior HF history, angiotensin-converting enzyme inhibitors (ACE-I)/angiotensin receptor blocker (ARB)/angiotensin receptor neprilysin inhibitor (ARNI), and β-blockers. These variables were pre-specified in accordance with previous studies. We performed multivariable analysis using covariates with P values <0.10 in univariable analysis. For multivariable analysis, the variable selection was performed using a backward stepwise method, with Akaike's information criterion as the evaluation measure. The time-dependent receiver operator characteristic (ROC) curve for the 1-year survival rate was used to calculate the area under the ROC (AUROC) curve for CFS, GWTG-HF, and modified MAGGIC score. Spearman's correlation test was used to determine the CGA scores. Statistical significance was set at a two-tailed P value of <0.05. Statistical analyses were performed using R (version 4.2.1; R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline Characteristics and CGA Scores

During the study period, 190 hospitalised patients aged

Table 2. CFS, CGA Score and Correlation With CFS

CFS and CGA instruments	Median [IQR]	Correlation coefficient with CFS	P value
CFS	4.0 [2.0, 5.0]	–	–
BI	82.5 [60.0, 100]	−0.80	<0.001
MMSE (n=130)	23.0 [20.0, 28.0]	−0.41	<0.001
CCI	2.0 [1.0, 3.0]	0.30	<0.001
CONUT	4.0 [3.0, 6.0]	0.30	<0.001

BI, Barthel index; CCI, Charlson comorbidity index; CFS, Clinical Frailty Scale; CGA, comprehensive geriatric assessment; CONUT, COntrolling NUTritional; IQR, interquartile range; MMSE, Mini Mental State Examination.

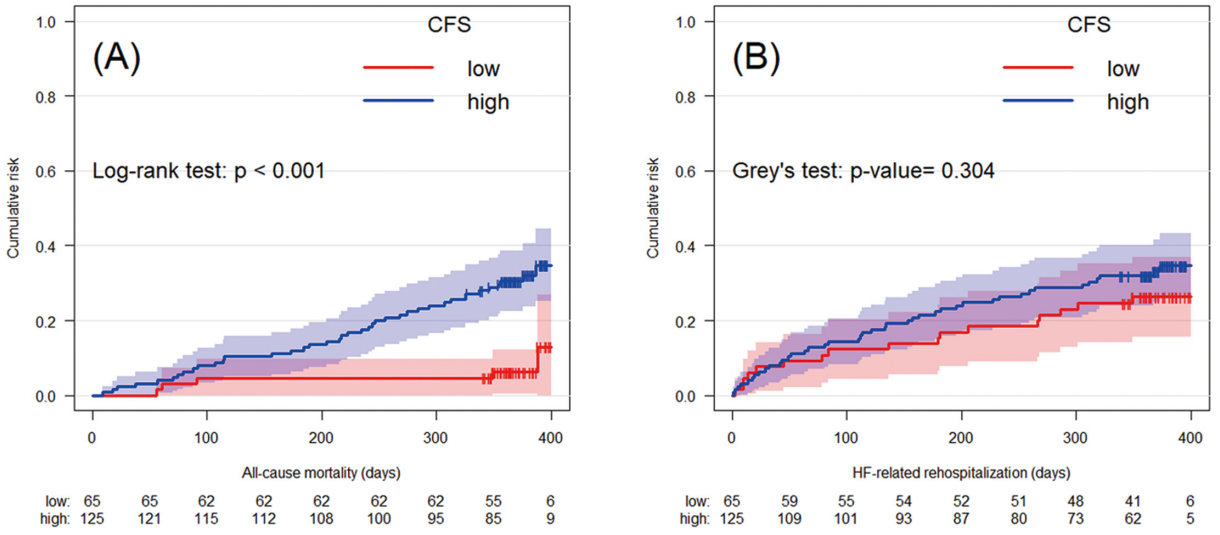

Figure 2. Kaplan-Meier curve of (**A**) all-cause mortality, and (**B**) heart failure (HF)-related rehospitalization, categorizing the Clinical Frailty Scale (CFS) into low (1–3) and high (4–9).

≥75 years were prospectively enrolled into the study. Overall, the mean age was 85.4 years, and 47.9% were male. Of the 190 patients, 65 (34%) had low CFS (1–3) and 125 (66%) had high CFS (4–9; **Figure 1**). Patients with a high CFS were older, had lower BMI and lower haemoglobin levels, and there were more females than patients with low CFS. The baseline characteristics stratified by CFS groups are summarised in **Table 1**. The median CGA scores were: BI, 82.5 [IQR 60.0, 100]; MMSE, 23.1 [IQR 20.0, 28.0]; CCI, 2.0 [IQR 1.0, 3.0]; and CONUT, 4.0 [IQR 3.0, 6.0] (**Table 2**).

Outcomes

Prognostic data were available for all 190 (100%) enrolled patients and the median follow-up period was 366 [IQR 247, 384] days. All-cause mortality and HF-related rehospitalization occurred in 45 and 59 patients, respectively, in the overall cohort. On comparing the low and high CFS groups, the cumulative incidence of all-cause mortality was significantly higher in the high CFS group (low 6.3%, high 30.5%, P<0.001). However, the cumulative incidence of HF-related rehospitalization was not significantly different between the two groups (low 26.3%, high 32.0%, P=0.304; **Figure 2**). In the multivariable analysis, the CFS group was independently associated with the risk of all-cause mortality (**Table 3**). ROC curves indicated that CFS could more accurately predict all-cause mortality than GWTG-HF and modified MAGGIC scores. The AUROC of the CFS, GWTG-HF, and modified MAGGIC scores were 0.74, 0.63, and 0.69, respectively (**Figure 3**). CFS showed a strong correlation with BI, a moderate correlation with MMSE, and a weak correlation with CCI and CONUT scores (**Table 2**). The MMSE data of 60 patients were missing as they could not respond due to dementia or communication-related disabilities.

Discussion

The present study focused on older patients with HF with a mean age of 85.4 years, consistent with the increasing older population with HF in Japan.[33] A high CFS score was suggested to be significantly associated with a high rate of all-cause mortality in patients with HF within 1 year. Multivariable analysis revealed that the CFS was independently associated with a high risk of all-cause mortality within 1 year. It also had a significant correlation with frailty domains evaluated using CGA.

The high CFS group had a significantly higher cumulative incidence of all-cause mortality within 1 year than the low CFS group. Univariable analysis indicated that CFS

Table 3. Univariable and Multivariable Cox Proportional Hazard Models for All-Cause Mortality

Variable	Univariable analysis			Multivariable analysis			Stepwise method		
	HR	95% CI	P value	HR	95% CI	P value	HR	95% CI	P value
CFS (high)	4.70	1.86–11.9	0.001	3.14	1.15–8.64	0.026	3.39	1.32–8.72	0.011
Age	1.09	1.04–1.15	0.001	1.01	0.95–1.07	0.790	–	–	–
Sex (male)	0.70	0.39–1.28	0.247	–	–	–	–	–	–
Body mass index	0.82	0.74–0.91	<0.001	0.86	0.77–0.96	0.006	0.86	0.77–0.95	0.005
SBP	0.99	0.97–1.00	0.100	–	–	–	–	–	–
Heart rate	1.01	0.99–1.04	0.195	–	–	–	–	–	–
Creatinine	0.97	0.53–1.79	0.920	–	–	–	–	–	–
EF	1.00	0.98–1.02	0.930	–	–	–	–	–	–
Prior HF history	1.84	1.01–3.35	0.046	1.16	0.61–2.19	0.660	–	–	–
ACEI/ARB/ARNI	0.41	0.23–0.75	0.004	0.51	0.28–0.95	0.034	0.50	0.27–0.91	0.022
β-blocker	0.40	0.22–0.72	0.002	0.46	0.24–0.86	0.016	0.43	0.24–0.78	0.005

CI, confidence interval; HF, heart failure; HR, hazard ratio. Other abbreviations as in Table 1.

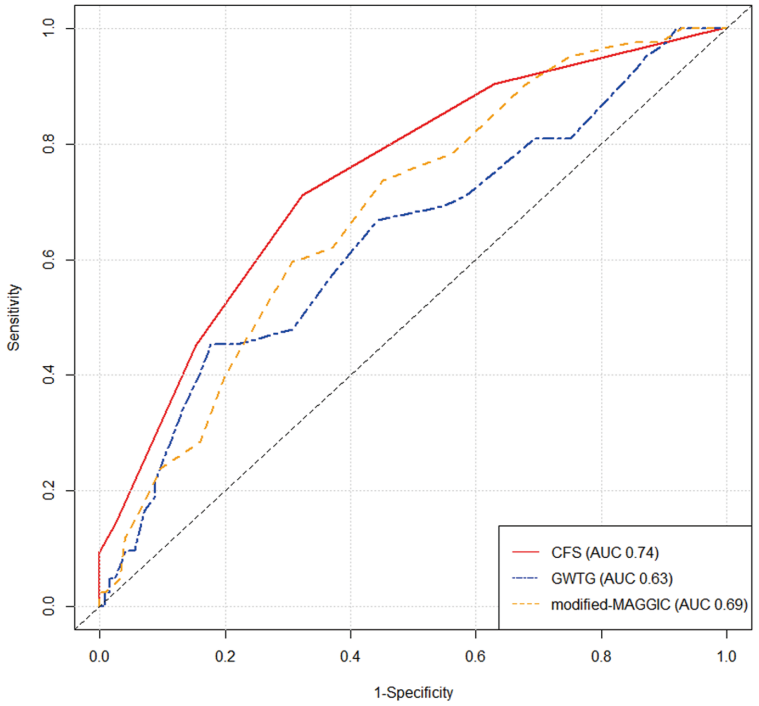

Figure 3. Time-dependent receiver operator curve of the Clinical Frailty Scale (CFS), Get With The Guideline-Heart Failure (GWTG-HF) score, and modified Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC) score for all-cause mortality within 1 year.

(high vs. low), age, BMI, prior HF history, ACEI/ARB/ARNI, and β-blocker use were related to all-cause mortality. Prespecified variables were selected from previous studies.[21–24] Multivariable analysis showed that CFS (high vs. low) was independently related to all-cause mortality within 1 year. This association has been demonstrated in previous studies on HF-related frailty, and the present study confirmed this result.[19,20] However, CFS failed to show a significant difference in HF-related rehospitalization. The reason for this is uncertain, but we speculate that HF-related rehospitalization might depend, to some extent, on the living environment of the patient after discharge. Frailty might then be modified by surrounding environmental support, which enhances and prevents the probability of HF-related rehospitalization.

The time-dependent ROC curve of the CFS at 1 year was also found to have surpassed those of HF prognosis predictors such as the GWTG-HF score and modified MAGGIC score. The AUROC of CFS, GWTG, and modified MAGGIC were 0.74, 0.63, and 0.69, respectively. Both GWTG-HF and MAGGIC scores have been previously validated for the prognosis of chronic HF.[21,24] The present study indicates that the simple CFS score was able to predict all-cause mortality within 1 year more precisely than these two well validated HF score systems.

The original MAGGIC score incorporated the NYHA classification into the mortality prediction. NYHA is a well known, simple, and powerful index for assessing exercise tolerance and predicting mortality.[34,35] However, in the present study, we could not measure NYHA classification

because the majority of older patients initially lacked exercise tolerance. We need to recognize that for older and frail patients (some of whom are bedridden or wheelchair users) it is difficult to evaluate the NYHA classification.

The CFS was strongly correlated with BI (R=0.80) and moderately correlated with the MMSE score (R=0.41). CCI (R=0.30) and CONUT (R=0.30) showed weak correlations. It also showed a positive relationship between functional limitations and cognitive status. Its advantages include saving time for assessment,[18,36,37] consistency between examiners, and ease of execution. Meanwhile, the CGA has an holistic approach, but is time-consuming and labour intensive,[13] which we assume is the reason why it is not applied in many older patients. Therefore, we recommend evaluating every hospitalised older patient with HF using the CFS first. A more detailed evaluation with each CGA instrument can then be implemented for each frailty domain in patients with a high CFS only. This more appropriate use of the CGA can offer significant benefits for patients, families, and healthcare providers. For example, informed decisions regarding interventions, such as physical rehabilitation, medication, and invasive treatment, can be made by considering the frailty stage. It also facilitates patient-centred decision-making and advance care planning.[38] The CGA instruments include various components.[15] The CGA instruments (BI, MMSE, CCI, and CONUT) used in the present study are representative CGA instruments for each frailty domain. They were chosen from the pool of CGA instruments because they have been well validated and evaluated in previous studies for patients with HF.

Although a part of the present study was conducted during the coronavirus disease 2019 (COVID-19) pandemic, there were no direct deaths or exacerbations of HF due to COVID-19. However, it is likely that medical services such as family visits, daycare services, and rehabilitation were restricted due to COVID-19 safety measures, and this might have had some impact on the data.

Study Limitations

There are several limitations to acknowledge concerning the present study. First, our results were collected in a single Japanese centre and included only 190 patients, and therefore cannot be generalised to other facilities. However, the study population could be said to represent that of a general community hospital in Japan. Therefore, developed countries with aged societies can refer to this result to some extent. Second, the CFS, BI, and MMSE scores are subjective. Although well trained medical personnel have judged and scored them, reproducibility was not evaluated. Third, within the CGA score, the MMSE section had many missing data as it required communication and cooperation from patients. Another cognitive assessment instrument such as the ABC dementia scale, which is a caregiver interview-based questionnaire, should have been considered for those patients.[39] Fourth, not all frailty domains were evaluated. Social frailty was eliminated because there is not yet a specifically validated instrument for social frailty. Fifth, we could not specify the cause of death. This is because many patients died in nursing care facilities or at home, and we obtained the information through telephone interviews with their families. Last, in the present study, the CFS has only a weak correlation with comorbidity and nutritional status. The CGA is expected to provide a 'comprehensive' assessment for geriatric patients. Therefore, further study of their correlation is necessary to ensure CFS is a more appropriate screening tool for CGA.

Conclusions

CFS was associated with all-cause mortality within 1 year and was correlated with frailty domains evaluated using CGA instruments. We propose using CFS as a frailty screening tool before conducting CGA in older patients with HF.

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Disclosures

The authors declare no conflicts of interest associated with this manuscript.

IRB Information

Aijinkai Healthcare Corporation Takatsuki General Hospital Ethical Review Board, 2019-70.

Data Availability

All of the individual participant data, after deidentification, study protocol, statistical analysis plan, informed consent form, clinical study report, and analytic code, are accessible immediately after publication to anyone who wants access.

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