Frailty in patients with acute decompensated heart failure in a super-aged regional Japanese cohort

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Abstract

Aims The aim of this study was to investigate clinical characteristics of frail patients based on a comprehensive frailty assessment in patients hospitalized for acute decompensated heart failure (HF) (ADHF) in super-aged regional Japanese cohort.

Methods and results We established the Kochi Registry of Subjects with Acute Decompensated Heart Failure (Kochi YOSACOI) study, which was a prospective multicentre community-based cohort study in six participating hospitals in Kochi Prefecture, Japan. We enrolled 1061 patients (median age, 81 years; 50.0% men) hospitalized for ADHF between June 2017 and December 2019 in this registry. Patients were classified into the three groups by the severity of frailty using the Kihon Checklist: we identified frailty in 510 patients (53.7%), prefrailty in 293 patients (30.9%), and non-frailty in 146 patients (15.4%). Compared with prefrail and non-frail patients, frail patients were older (84 years interquartile range [IQR, 77–88] vs. 79 years [IQR, 69–86] and 72 years [IQR 65–81], P < 0.001) and more often had prior HF hospitalization (29.6% vs. 21.8% and 16.4%, P < 0.05), chronic kidney disease (81.6% vs. 71.7% and 61.0%, P < 0.01), anaemia (75.3% vs. 61.4% and 50.0%, P < 0.001), cerebrovascular accident (19.0% vs. 9.9% and 4.1%, P < 0.01). The proportion of patients with three or more comorbidities was larger in the frailty group than in the other groups (78.0% vs. 67.2% and 63.0%, P < 0.01). The frequency of functional decline in all domains increased with frailty status. Approximately 70% of frail patients were identified as functional decline in physical function and socialization domains. Fifty to sixty per cent of frail patients had functional decline in instrumental activities of daily living, cognitive function, and depression domains. The percentage of worsening walking ability during hospitalization was increasing with the frailty status (frailty, 27.5%; prefrailty, 21.8%; non-frailty, 8.9%). In multivariate logistic regression analysis, frailty was associated with age [odds ratio (OR) 1.031, 95% confidence interval (CI) 1.011–1.052, P = 0.003], prior HF hospitalization (OR 1.789, 95% CI 1.165–2.764, P = 0.008), brain natriuretic peptide level at discharge (OR 1.001, 95% CI 1.000–1.001, P = 0.020) and prior cerebrovascular accident (OR 2.549, 95% CI 1.484–4.501, P < 0.001).

Conclusions More than half of patients with ADHF were frail and had functional decline across multiple domains, not only physical function domain. The Kihon Checklist provided useful and valuable information for easily identifying frail patients and comprehensive management of HF.

Keywords Frailty; Acute decompensated heart failure; Elderly; Functional decline; Kihon Checklist

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Introduction

Heart failure (HF) is one of the leading causes of hospitalization and death, and the number of patients with HF has been increasing worldwide.1,2 The prevalence of HF increases with ageing, and 6–10% of people older than 65 years of age have the disorder.3 Several studies have suggested that outcomes are particularly poor in elderly patients with HF.4–6 The population of Japan is ageing more rapidly than that of any other country. The proportion of people in Japan aged 65 years or
older was 27.7% in 2017. Frailty is a clinical status with increased vulnerability to stressors resulting from decreased reserves of multiple physiological systems. It was shown that frailty is associated with adverse health outcomes such as disability and mortality in a community-dwelling older population. However, there have been few studies on clinical features of frailty status of HF patients in a prospective community-based unselected cohort in Japan. Therefore, in 2017, we established a prospective, multicentre, community-based cohort study, named the Kochi Registry of Subjects with Acute Decompensated Heart Failure (Kochi YOSACOI study) in which patients hospitalized for acute decompensated HF (ADHF) in a super-ageing area of Japan were enrolled. This registry consists of six hospitals that are responsible for the acute treatment of cardiovascular diseases in Kochi Prefecture. Although the physical domain of frailty was assessed by Fried et al. in previous studies focusing on cardiovascular disease, frailty is recognized as a multidimensional vulnerability consisting of not only physical but also psychological and social domains, and multifaceted assessment of frailty is recommended to improve management of elderly patients with HF and health outcomes. The Kihon Checklist (KCL) was developed by the Japanese Ministry of Health, Labor and Welfare for identifying community-dwelling older adults to have a high risk of requiring care/support in the long-term care insurance (LTCI) system, and has been widely used in Japan. The KCL has been proven to be valid and reliable for assessing multifaceted aspects of frailty, such as functional declines, instrumental activities of daily living (IADL) limitation, physical impairment, depressive mood, and others. The purpose of the present study was to investigate the clinical characteristics and prevalence of frailty based on functional declines of daily living assessed by a comprehensive simple questionnaire, KCL, in patients with ADHF.

Methods

Patient population

In the Kochi YOSACOI study, 1061 consecutive patients with ADHF in Kochi Prefecture, Japan were recruited during the period from May 2017 to December 2019. The six hospitals participating in this registry are in charge of treatment for acute HF in Kochi Prefecture. Standard treatment for acute HF based on guidelines is practiced at all these hospitals. Cardiac surgery can be performed at three hospitals. One of them is a university hospital. Kochi Prefecture is located in the southwest part of Japan and is one of the most ageing areas of Japan. The population of Kochi Prefecture is approximately 706,000 and the proportion of people aged 65 years or older reached 34.7% in 2018. The inclusion criteria for the registry were age of 20 years or older and admission for ADHF to one of the six hospitals. We diagnosed ADHF by confirming the presence of at least two major criteria or one major criterion based on the Framingham criteria including symptoms, physical examination, chest X-ray, and echocardiographic findings. Exclusion criteria were as follows: (i) unavailable data (n = 4) and (ii) patients who have not been assessed by the KCL or have been incompletely assessed (n = 108). Informed consent was given by all patients or their proxies in accordance with the guidelines of the Ethics Committee on Medical Research of Kochi Medical School. The present study was conducted in compliance with the Declaration of Helsinki, and the study protocol was approved by the Ethics Committee on Medical Research of Kochi Medical School (approval no. 28-68) and the ethics committees of all participating hospitals.

Assessment of frailty by the Kihon Checklist

The KCL is a 25-item self-administered questionnaire, as a screening tool for predicting older adults who are vulnerable to frailty and have a high risk of becoming dependent (Table 1). The KCL is a comprehensive assessment tool that assesses physical, functional, psychological, and social aspects of independent older adults in multiple domains. The questionnaire consists of 25 yes/no questions that are categorized into seven domains: IADL, physical function, nutritional status, oral function, socialization, cognitive function, and depressive mood. In the present study, we defined a total KCL score of ≥8 points as frailty, 4–7 points as prefrailty, and 0–3 points as non-frailty according to the previous report. The seven functional categories of the KCL also have cut-off points for assessing frailty that were defined in a previous report. The criteria for functional declines of the seven categories were defined by the following cut-off points: IADL domain ≥3 points, physical function domain ≥3 points, malnutrition domain = 2 points, oral function domain ≥2 points, socialization domain ≥1 point, cognitive function domain ≥1 point, and depression domain ≥2 points.

Patient data collection

Data were collected by investigators at the participating hospitals during the registration period. We obtained information on clinical characteristics including patient demographics, aetiology of HF, medical history, social status (i.e. living environment, persons who live and eat with the patient, and LTCI), frailty status (living functions before hospitalization assessed by the KCL), activities of daily living before admission and at discharge, HF symptoms (New York Heart Association class) and vital signs at admission and on discharge, discharge prescription, laboratory data, and echocardiography data. Walking ability just before admission.
Frailty in acute heart failure in a super-aged region

Table 1  Kihon Checklist

| No. | Questions                                                                 | 0. YES | 1. NO |
|-----|---------------------------------------------------------------------------|--------|-------|
| 1   | Do you go out by bus or train by yourself?                                |        |       |
| 2   | Do you go shopping to buy daily necessities by yourself?                  |        |       |
| 3   | Do you manage your own deposits and savings at the bank?                  |        |       |
| 4   | Do you sometimes visit your friends?                                      |        |       |
| 5   | Do you turn to your family or friends for advice?                         |        |       |
| 6   | Do you normally climb stairs without using handrail or wall for support?  |        |       |
| 7   | Do you normally stand up from a chair without any aids?                   |        |       |
| 8   | Do you normally walk continuously for 15 minutes?                         |        |       |
| 9   | Have you experienced a fall in the past year?                             |        |       |
| 10  | Do you have a fear of falling while walking?                              |        |       |
| 11  | Have you lost 2 kg or more in the past 6 months?                          |        |       |
| 12  | Height: cm, weight: kg, BMI: kg/m². If BMI is less than 18.5, this item is scored. |        |       |
| 13  | Do you have any difficulties eating tough foods compared to 6 months ago? |        |       |
| 14  | Have you choked on your tea or soup recently?                             |        |       |
| 15  | Do you often experience having a dry mouth?                               |        |       |
| 16  | Do you go out at least once a week?                                       |        |       |
| 17  | Do you go out less frequently compared to last year?                      |        |       |
| 18  | Do your family or your friends point out your memory loss?                |        |       |
| 19  | Do you make a call by looking up phone numbers?                           |        |       |
| 20  | Do you find yourself not knowing today’s date?                            |        |       |
| 21  | In the last 2 weeks have you felt a lack of fulfillment in your daily life? |        |       |
| 22  | In the last 2 weeks have you felt a lack of joy when doing the things you used to enjoy? |        |       |
| 23  | In the last 2 weeks have you felt difficulty in doing what you could do easily before? |        |       |
| 24  | In the last 2 weeks have you felt helpless?                               |        |       |
| 25  | In the last 2 weeks have you felt tired without a reason?                 |        |       |

Working Group on Frailty in Japanese Geriatrics Society. BMI, body mass index.

(categorized as independent outdoor walking, independent indoor walking, indoor walking with assistance, and abasia)\(^{15}\) was evaluated on admission, and its ability was re-evaluated at discharge. Worsening walking ability during hospitalization was defined as downgrades in the four walking ability categories during the period from admission to discharge. Cognitive function was evaluated by Hasegawa Dementia Scale-Revised. Hypertension was defined as peripheral blood pressure \(>140/90\) mmHg or taking medication for hypertension. Diabetes mellitus was diagnosed using haemoglobin A1c (National Glycohemoglobin Standardization Program) \(\geq 6.5\)% and casual blood glucose level \(\geq 200\) mg/dL as the standard and/or assumed if the patient was taking medicine for diabetes. Dyslipidaemia was diagnosed if total cholesterol was \(\geq 220\) mg/dL, if low-density lipoprotein cholesterol was \(>140\) mg/dL, if high-density lipoprotein cholesterol was \(>40\) mg/dL, if triglycerides were \(>150\) mg/dL, or if the patient was taking medicine for dyslipidaemia. Chronic kidney disease (CKD) was diagnosed as an estimated glomerular filtration rate (eGFR) \(< 60\) mL/min/1.73 m\(^2\). Anaemia was diagnosed as haemoglobin \(<13\) g/dL in men and \(<12\) g/dL in women. We used echocardiographic data at the time when HF status was stabilized during hospitalization.

Statistical analysis

Normally distributed data are expressed as means ± standard deviation, non-parametric data are expressed as medians [interquartile range (IQR)], and categorical data are expressed as numbers and percentages. Differences in continuous variables among the three groups were assessed using one-way analysis of variance. Pearson’s \(\chi^2\) test was used for comparisons between categorical variables, and Fisher’s exact test was used when the expected frequency was lower than 5. The Bonferroni post-hoc test was used to determine differences between the frailty group, prefrailty group, and non-frailty group. Multivariate logistic regression analysis was performed to estimate the odds ratios (ORs) for determinant factors of frailty. Variables with \(P < 0.1\) in univariate analysis were incorporated into the multivariate model. The propensity score matching was performed using a logistic regression model that adjusted age and sex to determine differences between the frailty group, prefrailty group, and non-frailty group. Statistical significance was defined by two-sided \(P \leq 0.05\). All statistical analyses were performed using SPSS version 21 (IBM Corporation, Armonk, NY, USA) and Microsoft R Open version 4.0.2 (Microsoft, Redmond, WA, USA).

Results

Clinical characteristics at registration

Of the 1061 patients enrolled in our HF registry, we excluded patients with incomplete evaluation by the KCL \((n = 108)\) and

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patients for whom information about clinical status was unavailable (n = 4). Finally, 949 patients were included in the present study. The median age of the patients at registration was 81 years (IQR, 72–87 years), and 530 patients (51.4%) were men. Patients were classified into the three groups by the KCL: we identified frailty in 510 patients (53.7%), prefrailty in 293 patients (30.9%), and non-frailty in 146 patients (15.4%). The distribution of each frailty status according to age is shown in Figure 1. More than half of the patients aged 70 years or older had frailty. Furthermore, the proportion of patients with frailty gradually increased with ageing. On the other hand, even in the patients under the age of 65 years old, frail and prefrail patients accounted for 28.7% and 35.6%, respectively. The clinical characteristics of the patients according to frailty status are presented in Table 2. The age of patients in the frailty group was significantly higher among the three groups. The proportion of women in the frailty group was significantly larger than that in the prefrailty group and was larger than that in the non-frailty group. The most common aetiology of HF in all three groups was ischaemic heart disease. The proportion of patients in the frailty group who had a history of HF hospitalization was larger than the proportions of such patients in the prefrailty and non-frailty groups. The median left ventricular ejection fractions determined by echocardiography were similar in the three groups. Serum albumin, eGFR, and haemoglobin levels in the frailty group were lower than those in the prefrailty and non-frailty groups, and plasma B-type natriuretic peptide (BNP) level in the frailty group was higher than that in the non-frailty group. Compared with prefrail and non-frail patients after adjusting for age and sex, frail patients had a higher prior HF hospitalization (Table 3). The proportion of patients with LVEF ≥50% was smaller in the frailty group. Frail patients had lower albumin, haemoglobin, and eGFR levels and had higher BNP level at discharge. In multivariate logistic regression analysis, frailty was associated with age (OR 1.031, 95% confidence interval (CI) 1.011–1.052, P = 0.003), prior HF hospitalization (OR 1.789, 95% CI 1.165–2.764, P = 0.008), BNP level at discharge (OR 1.001, 95% CI 1.000–1.001, P = 0.020) and prior cerebral vascular accident (CVA) (OR 2.549, 95% CI 1.484–4.501, P < 0.001) (Table 4).

**Association between comorbidities and frailty**

Hypertension, diabetes mellitus, dyslipidaemia, coronary artery disease, chronic obstructive pulmonary disease, bronchial asthma, and malignant disease were equally present among the three groups (Table 2). The proportions

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**Figure 1. Distribution of each frailty status according to age.**

![Figure 1](image-url)
Frailty in acute heart failure in a super-aged region

Clinical characteristics of patients according to frailty status

|                          | All patients (n = 949) | Frailty (n = 510) | Prefrailty (n = 293) | Non-frailty (n = 146) | P value |
|--------------------------|------------------------|------------------|---------------------|----------------------|---------|
| Age (years)              | 81 [72–87]             | 84 [77–88]**      | 79 [69–86]**        | 72 [65–81]           | <0.001  |
| ≥80 years                | 530 (55.8)             | 343 (67.3)***     | 143 (48.8)***       | 44 (30.1)            | <0.001  |
| Women                    | 461 (48.6)             | 273 (53.5)*       | 125 (42.7)          | 63 (43.2)            | 0.004   |
| BMI (kg/m²)              | 21.0 [18.7–23.3]       | 20.4 [17.9–22.6]** | 21.4 [19.5–23.9]‡   | 22.3 [20.0–24.4]     | <0.001  |
| NYHA Class III/IV on admission | 718 (75.7)            | 397 (77.8)        | 219 (74.7)          | 102 (69.9)           | 0.094   |
| NYHA Class III/IV at discharge | 24 (2.5)              | 20 (3.9)†         | 4 (1.4)             | 0 (0.0)              | 0.009   |
| Discharge to home        | 810 (85.4)             | 399 (78.2)**      | 271 (92.5)          | 140 (95.9)           | <0.001  |
| Length of hospital stay (days) | 18 [13–29]            | 20 [14–33]**      | 17 [12–27]          | 15 [12–21]          | <0.001  |
| Aetiology of HF          |                        |                  |                     |                      |         |
| IHD                      | 223 (23.5)             | 118 (23.1)        | 67 (22.9)           | 38 (26.0)            | 0.733   |
| Valvular                 | 163 (17.2)             | 102 (20.0)        | 39 (13.3)           | 22 (15.1)            | 0.041   |
| Cardiomyopathy           | 168 (17.7)             | 91 (17.8)         | 51 (17.4)           | 26 (17.8)            | 0.987   |
| Hypertensive             | 103 (10.9)             | 49 (9.6)          | 35 (11.9)           | 19 (13.0)            | 0.390   |
| Echocardiographic parameters |                      |                  |                     |                      |         |
| LVEF (%)                 | 49 [35–62]             | 49 [35–63]        | 49 [35–62]          | 46 [32–60]           | 0.265   |
| ≥50%                     | 448 [47.2]             | 244 [47.8]        | 142 [48.5]          | 62 [42.5]            | 0.485   |
| Frailty assessment       | 8 [5–12]               | 11 [9–14]**       | 5 [4–7]**           | 2 [1–3]              | <0.001  |
| No. of domains with functional decline | 2 [1–4]             | 4 [3–5]**       | 1 [1–2]**           | 0 [0–0]              | <0.001  |
| HDS-R score              | 26 [21–29]             | 24 [18–28]**      | 27 [23–29]**        | 29 [27–30]           | <0.001  |
| Medical history          | 4 [2–5]                | 4 [3–5]**        | 3 [2–5]             | 3 [2–5]              | <0.001  |
| No. of comorbidities     | 687 (72.4)             | 398 (78.0)**      | 197 (67.2)          | 92 (63.0)            | <0.001  |
| Prior hospitalization due to HF | 239 (25.2)         | 151 (29.6)**     | 64 (21.8)           | 24 (16.4)            | 0.001   |
| Hypertension             | 608 (64.1)             | 325 (63.7)        | 188 (64.2)          | 95 (65.1)            | 0.956   |
| Diabetic mellitus        | 248 (26.1)             | 130 (25.5)        | 75 (25.6)           | 43 (29.5)            | 0.611   |
| Dyslipidaemia            | 361 (38.0)             | 195 (38.2)        | 104 (35.5)          | 62 (42.5)            | 0.363   |
| Prior myocardial infarction | 134 (14.1)          | 79 (15.5)        | 34 (11.6)           | 21 (14.4)            | 0.312   |
| CAD                      | 279 (29.4)             | 153 (30.0)        | 85 (29.0)           | 41 (28.1)            | 0.890   |
| COPD                     | 69 (7.3)               | 39 (7.6)          | 23 (7.8)            | 7 (4.8)              | 0.454   |
| Bronchial asthma         | 44 (4.6)               | 27 (5.3)          | 13 (4.4)            | 4 (2.7)              | 0.425   |
| CVA                      | 132 (13.9)             | 97 (19.0)**       | 29 (9.9)            | 6 (4.1)              | <0.001  |
| Atrial fibrillation      | 404 (42.6)             | 231 (45.3)**      | 127 (34.3)          | 46 (31.5)            | 0.012   |
| Peripheral vascular disease | 86 (9.1)            | 52 (10.2)        | 25 (8.5)            | 9 (6.2)              | 0.304   |
| Malignancy               | 94 (9.9)               | 60 (11.8)         | 23 (7.8)            | 11 (7.5)             | 0.177   |
| Dementia                 | 138 (14.5)             | 107 (21.0)**      | 26 (8.9)            | 5 (3.4)              | <0.001  |
| Anaemia                  | 637 (67.1)             | 384 (75.3)**      | 180 (61.4)          | 73 (50.0)            | <0.001  |
| CKD                      | 715 (75.3)             | 416 (81.6)**      | 210 (71.7)          | 89 (61.0)            | <0.001  |
| Treatment in the acute phase |                  |                  |                     |                      |         |
| Respiratory management   |                        |                  |                     |                      |         |
| Oxygen inhalation        | 577 (60.8)             | 324 (63.5)        | 170 (58.0)          | 83 (56.8)            | 0.235   |
| NPPV                     | 125 (13.2)             | 64 (12.5)         | 37 (12.6)           | 24 (16.4)            | 0.380   |

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Table 2 (continued)

|                                | All patients (n = 949) | Frailty (n = 510) | Prefrailty (n = 293) | Non-frailty (n = 146) | P value |
|--------------------------------|------------------------|-------------------|----------------------|-----------------------|---------|
| Intubation                      |                         |                   |                      |                       |         |
| Intravenous                     |                         |                   |                      |                       |         |
| Inotropes                       | 96 (10.1)               | 47 (9.2)          | 33 (11.3)            | 16 (11.0)             | 0.609   |
| Diuretics                       | 742 (78.2)              | 417 (81.8)        | 218 (74.4)           | 107 (73.3)            | 0.015   |
| Carperitide                     | 385 (40.6)              | 196 (38.4)        | 122 (41.6)           | 67 (45.9)             | 0.244   |
| Nitrites                        | 159 (16.8)              | 83 (16.3)         | 52 (17.7)            | 24 (16.4)             | 0.860   |
| PDEIII inhibitors               | 18 (1.9)                | 7 (1.4)           | 6 (2.0)              | 5 (3.4)               | 0.270   |
| Nicardipine                     | 72 (7.6)                | 41 (8.0)          | 20 (6.8)             | 11 (7.5)              | 0.822   |
| Oral administration             |                         |                   |                      |                       |         |
| Tolvaptan                       | 237 (25.0)              | 139 (27.3)        | 73 (24.9)            | 25 (17.1)             | 0.045   |
| Medication at hospital discharge|                         |                   |                      |                       |         |
| RAS inhibitors                  | 430 (45.3)              | 214 (42.0)        | 139 (47.4)           | 77 (52.7)             | 0.041   |
| ACE inhibitor                   | 193 (20.3)              | 95 (18.6)         | 66 (22.5)            | 32 (21.9)             | 0.366   |
| Angiotensin receptor blockers   | 239 (25.2)              | 119 (23.3)        | 73 (24.9)            | 47 (32.2)             | 0.093   |
| β-blockers                      | 538 (56.7)              | 273 (53.5)        | 177 (60.4)           | 88 (60.3)             | 0.106   |
| MRAs                            | 318 (33.5)              | 170 (33.3)        | 96 (32.8)            | 52 (35.6)             | 0.831   |
| Diuretics                       | 773 (81.5)              | 433 (84.9)        | 229 (78.2)           | 111 (76.0)            | 0.011   |
| Tolvaptan                       | 237 (25.0)              | 142 (27.8)        | 71 (24.2)            | 24 (16.4)             | 0.018   |

Data were shown as the median [interquartile range] or n (%).
Bonferroni post-hoc test between frailty, prefrailty, and non-frailty.

\*P < 0.05; frailty vs. prefrailty.
\**P < 0.01; frailty vs. prefrailty.
\***P < 0.001; frailty vs. prefrailty.
\*P < 0.05; frailty vs. non-frailty.
\**P < 0.01; frailty vs. non-frailty.
\***P < 0.001; frailty vs. non-frailty.
\*P < 0.05; prefrailty vs. non-frailty.
\**P < 0.01; prefrailty vs. non-frailty.
\***P < 0.001; prefrailty vs. non-frailty.

ACE, angiotensin-converting enzyme; BMI, body mass index; BNP, B-type natriuretic peptide; CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVA, cerebral vascular accident; eGFR, estimated glomerular filtration rate; HDS-R, Hasegawa Dementia Rating Scale-Revised; HF, heart failure; IHD, ischaemic heart disease; KCL, Kihon Checklist; LVEF, left ventricular ejection fraction; MRAs, mineralocorticoid receptor blockers; No., number; NPPV, non-invasive positive pressure ventilation; NYHA, New York Heart Association; PDE, phosphodiesterase; RAS, renin–angiotensin system.
of patients who had a prior CVA, anaemia, and CKD were larger in the frailty group than in the other two groups. The number of comorbidities that the patients had was larger in the frailty group than in the other two groups. Moreover, the proportion of patients with three or more comorbidities was larger in the frailty group than in the other two groups. After adjusting for age and sex, prior CVA, dementia, and anaemia were significantly larger in frail patients (Table 3). The prevalence of atrial fibrillation and CKD were not significantly different in the frail and in the prefrail/non-frail patients.

| Table 3 Comparison of clinical characteristics of patients after adjusting for age and sex |
|---------------------------------|---------------------------------|----------------|
| Frail patients (n = 305) | Non-frail + prefrail patients (n = 305) | P value |
| Age (years) | 82 [75–87] | 82 [75–87] | 1.000 |
| ≥80 years | 182 (59.7) | 182 (59.7) | 1.000 |
| Women | 145 (47.5) | 145 (47.5) | 1.000 |
| BMI (kg/m²) | 20.4 [18–22.4] | 21.3 [19.4–23.4] | 0.001 |
| NYHA Class III/IV on admission | 242 (79.3) | 220 (72.1) | 0.088 |
| NYHA Class III/IV at discharge | 14 (4.6) | 2 (0.7) | 0.004 |
| Discharge to home | 242 (79.3) | 280 (91.8) | <0.001 |
| Length of hospital stay (days) | 20 [14–32] | 16 [12–25] | <0.001 |
| Aetiology of HF | | | |
| IHD | 77 (25.2) | 77 (25.2) | 1.000 |
| Valvular | 59 (19.3) | 46 (15.1) | 0.198 |
| Cardiomyopathy | 57 (18.7) | 39 (12.8) | 0.058 |
| Hypertensive | 31 (10.2) | 38 (12.5) | 0.443 |
| Laboratory data at discharge | | | |
| Albumin (g/dL) | 3.4 [3.1–3.7] | 3.5 [3.2–3.8] | 0.003 |
| BNP (pg/mL) | 312.0 [174.1–543.8] | 248.0 [137.0–485.9] | 0.006 |
| eGFR (ml/min./1.73 m²) | 40.8 [27.3–54.9] | 46.1 [34.9–60.8] | 0.002 |
| Haemoglobin (g/dL) | 11.0 [9.8–12.5] | 11.7 [10.2–13.0] | 0.003 |
| Sodium (mEq/L) | 139 [137–141] | 139 [137–141] | 0.623 |
| Echocardiographic findings | | | |
| LVEF (%) | 48.0 [33.8–62.0] | 54.0 [39.0–63.0] | 0.017 |
| ≥50% | 140 (45.9) | 173 (56.7) | 0.006 |
| Frailty assessment | | | |
| KCL score | 11 [9–14] | 5 [3–6] | <0.001 |
| No. of declined functional domains | 4 [3–5] | 1 [0–2] | <0.001 |
| HDS-R score | 24 [19–28] | 27 [24–29] | <0.001 |
| Medical history | | | |
| No. of comorbidities | 4 [3–5] | 4 [2–5] | 0.002 |
| ≥3 | 238 (78.0) | 216 (70.8) | 0.051 |
| Prior HF hospitalization | 98 (32.1) | 66 (21.6) | 0.003 |
| Hypertension | 192 (63.0) | 207 (67.9) | 0.233 |
| Diabetes mellitus | 85 (27.9) | 76 (24.9) | 0.462 |
| Dyslipidaemia | 115 (37.7) | 124 (40.7) | 0.507 |
| Prior myocardial infarction | 57 (18.7) | 43 (14.1) | 0.155 |
| CAD | 94 (30.8) | 97 (31.8) | 0.861 |
| COPD | 28 (9.2) | 26 (8.5) | 0.887 |
| Bronchial asthma | 15 (4.9) | 12 (3.9) | 0.695 |
| CVA | 59 (19.3) | 26 (8.5) | <0.001 |
| Atrial fibrillation | 141 (46.2) | 128 (42.0) | 0.328 |
| Peripheral vascular disease | 34 (11.1) | 28 (9.2) | 0.503 |
| Malignancy | 40 (13.1) | 28 (9.2) | 0.157 |
| Dementia | 63 (20.7) | 28 (9.2) | <0.001 |
| Anaemia | 227 (74.4) | 200 (65.6) | 0.017 |
| CKD | 246 (80.7) | 225 (73.8) | 0.052 |

Data were shown as the median [interquartile range] or n (%).
BMI, body mass index; BNP, B-type natriuretic peptide; CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVA, cerebral vascular accident; eGFR, estimated glomerular filtration rate; HDS-R, Hasegawa Dementia Rating Scale-Revised; HF, heart failure; IHD, ischaemic heart disease; KCL, Kihon Checklist; LVEF, left ventricular ejection fraction; No., number; NYHA, New York Heart Association.

Functional decline in daily functional domains

The total KCL score (median) in the frailty group was significantly higher than those in the prefrailty and non-frailty groups (11 [9–14], 5 [4–7], and 2 [1–3], respectively, P < 0.001). The number of domains with functional decline was significantly larger in the frailty group than in the prefrailty and non-frailty groups (Table 2). Of the 510 patients with frailty, 29.8% were diagnosed with frailty based on functional decline in several domains other than the physical function domain. The frequency of functional decline in daily functional domains
decline in all domains increased with frailty status (Figure 2). Seventy per cent of the frail patients were identified as having functional decline in the physical function domain and socialization domain, and 50–60% of the frail patients had functional decline in IADL, cognitive function, and depression domains. In comparison with the Kyoto–Kameoka study, which assessed frailty status with the KCL for community-dwelling older people, the rates of functional decline in all domains were higher in the present study.

Table 4  Clinical factors associated with frailty in all patients

|                | Univariate       | Multivariate    |
|----------------|------------------|-----------------|
|                | Odds ratio 95% CI | P value         | Odds ratio 95% CI | P value         |
| Age            | 1.057 1.044–1.071 | <0.001          | 1.031 1.011–1.052 | 0.003          |
| Female         | 1.537 1.190–1.990 | 0.001           | 1.152 0.776–1.711 | 0.482          |
| BMI            | 0.919 0.887–0.952 | <0.001          | 0.979 0.932–1.024 | 0.356          |
| Prior HF hospitalization | 1.746 1.283–2.389 | <0.001          | 1.789 1.165–2.764 | 0.008          |
| NYHA Class III/IV at discharge | 4.439 1.661–15.369 | 0.007           | 3.018 0.966–11.403 | 0.072          |
| IHD            | 0.958 0.709–1.294 | 0.777           |                 |                |
| LVEF           | 1.004 0.996–1.012 | 0.325           |                 |                |
| Albumin        | 0.402 0.287–0.556 | <0.001          | 0.720 0.444–1.60 | 0.179          |
| BNP at discharge | 1.001 1.000–1.001 | <0.001          | 1.001 1.000–1.001 | 0.020          |
| Haemoglobin    | 0.804 0.753–0.857 | <0.001          | 0.914 0.816–1.023 | 0.120          |
| eGFR           | 0.986 0.981–0.992 | <0.001          | 0.990 0.980–1.001 | 0.053          |
| Living alone   | 1.585 1.148–2.198 | 0.005           | 1.415 0.912–2.206 | 0.122          |
| HT             | 0.968 0.742–1.263 | 0.813           |                 |                |
| DM             | 0.931 0.696–1.245 | 0.627           |                 |                |
| CVA            | 2.711 1.816–4.133 | <0.001          | 2.549 1.484–4.501 | <0.001         |
| Af             | 1.273 0.983–1.650 | 0.068           | 0.704 0.471–1.046 | 0.084          |
| COPD           | 1.129 0.691–1.863 | 0.631           |                 |                |

95% CI, 95% confidence interval; Af, atrial fibrillation; BMI, body mass index; BNP, brain natriuretic peptide; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HF, heart failure; HT, hypertension; IHD, ischaemic heart disease; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

Figure 2  Percentage of patients with functional decline in each functional domains of the Kihon Checklist. Comparison of the frequency of functional decline between all patients in YOSACOI study and those in Kyoto–Kameoka study: *P < 0.001. Comparison of the frequency of functional decline according to frailty status in YOSACOI study: †P < 0.001. IADL, instrumental activities of daily living.
Treatment in the acute phase and medication at discharge

In the acute phase, the frequency of use of respiratory management and the frequency of use of intravenous drugs such as inotropes and vasodilators were not significantly different among the three groups (Table 2). The frequency of use of intravenous diuretics and tolvaptan was significantly higher in the frailty group. Regarding medication at discharge, renin–angiotensin system inhibitors (RAS inhibitors; angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers) were less frequently prescribed in frail patients. β-blockers and mineralocorticoid receptor antagonists were prescribed without significant differences among the three groups. Tolvaptan was more frequently prescribed in frail patients than in non-frail patients.

Social background

The proportion of patients in the frailty group who lived at home was smaller than the proportions of patients living at home in the prefrailty and non-frailty groups (Table 5). Ten per cent of the frailty patients lived in a facility for the elderly. The proportion of patients living alone was larger in the frailty group than in the non-frailty group (23.9% vs. 14.4%, \( P < 0.05 \)). Ninety-three per cent of the prefrail patients and 84% of the non-frail patients did not have certification for the need of LTCI. On the other hand, approximately half of the frail patients were certified as requiring support or care under the LTCI system.

Clinical presentation at discharge

At discharge, the prevalence of New York Heart Association Class III or IV in the frailty group was higher than that in the other two groups. The median length of hospital stay for all patients was 18 days (IQR, 13–29 days). The duration for frail patients was longer than that for prefrail patients and non-frail patients. The proportion of frail patients who were discharged to home was smaller than the proportions of prefrail patients and non-frail patients (Table 2). Compared with prefrail and non-frail patients after adjusting for age and

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**Table 5  Social background of patients according to frailty status**

| Living place                  | All patients (n = 949) | Frailty (n = 510) | Prefrailty (n = 293) | Non-frailty (n = 146) | P value |
|------------------------------|------------------------|-------------------|----------------------|-----------------------|---------|
| Living place                 |                        |                   |                      |                       |         |
| Home                         | 783 (82.5)             | 402 (78.8)***†††  | 255 (87.0)           | 126 (86.3)            | 0.001   |
| Facilities for the elderly people | 54 (5.7)              | 48 (9.4)***†††    | 6 (2.0)              | 0 (0.0)               | 0.001   |
| Hospitals                    | 25 (2.6)               | 19 (3.7)          | 3 (1.0)              | 3 (2.1)               | 0.075   |
| Living situation             |                        |                   |                      |                       |         |
| Alone                        | 203 (21.4)             | 122 (23.9)†       | 60 (20.5)            | 21 (14.4)             | 0.006   |
| With a partner only          | 252 (26.6)             | 117 (22.9)        | 84 (28.7)            | 51 (34.9)             | 0.059   |
| With children or other family members | 333 (35.1) | 167 (32.7) | 110 (37.5) | 56 (38.4) | 0.802   |
| Medical management           |                        |                   |                      |                       |         |
| Self-administration of medicine | 667 (70.3)        | 309 (60.6)***†††  | 238 (81.2)           | 120 (82.2)            | <0.001  |
| Supporter for daily living   | 669 (70.5)             | 370 (72.5)        | 201 (68.6)           | 98 (67.1)             | 0.618   |
| Long-term care insurance     |                        |                   |                      |                       |         |
| Not certified                | 622 (65.5)             | 242 (47.5)***†††  | 245 (83.6)†          | 135 (92.5)            | <0.001  |
| Certification of needed support | 114 (12.0)           | 88 (17.3)***†††   | 22 (7.5)             | 4 (2.7)               | <0.001  |
| Support required 1 (e.g. standing on 1foot) | 53 (5.6)           | 40 (7.8)***†      | 11 (3.8)             | 2 (1.4)               | 0.003   |
| Support required 2 (e.g. walking; possibly improved) | 61 (6.4)           | 48 (9.5)***†      | 11 (3.8)             | 2 (1.4)               | <0.001  |
| Certification of needed long-term care | 196 (20.7)      | 167 (32.7)***†††  | 22 (7.5)             | 7 (4.8)               | <0.001  |
| Care Level 1 (e.g. walking maintained) | 87 (9.2)           | 71 (13.9)***†††   | 11 (3.8)             | 5 (3.4)               | <0.001  |
| Care Level 2 (e.g. moving, wear/pull off trousers) | 56 (5.9)           | 47 (9.2)***††     | 8 (2.7)              | 1 (0.7)               | <0.001  |
| Care Level 3 (e.g. washing face and oral care) | 28 (3.0)           | 26 (5.1)***        | 1 (0.3)              | 1 (0.7)               | <0.001  |
| Care Level 4 (e.g. dietary intake and communication) | 20 (2.1)           | 18 (3.5)          | 2 (0.7)              | 0 (0.0)               | 0.004   |
| Care Level 5 (e.g. swallowing and memorization) | 5 (0.5)           | 5 (1.0)           | 0 (0.0)              | 0 (0.0)               | 0.114   |
| Unknown                      | 17 (1.8)               | 13 (2.5)          | 4 (1.4)              | 0 (0.0)               | 0.099   |

Data were shown as n (%). Bonferroni post-hoc test between frailty, prefrailty, and non-frailty.

\* \( P < 0.05 \); frailty vs. prefrailty.

\*\* \( P < 0.01 \); frailty vs. prefrailty.

\*\*\* \( P < 0.001 \); frailty vs. prefrailty.

\P < 0.05 \; frailty vs. non-frailty.

\P < 0.01 \; frailty vs. non-frailty.

\P < 0.001 \; frailty vs. non-frailty.

\P < 0.05 \; prefrailty vs. non-frailty.

\P < 0.01 \; prefrailty vs. non-frailty.

\P < 0.001 \; prefrailty vs. non-frailty.

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sex, frail patients had a longer length of hospital stay, a lower rate of discharge to home, and a more severe symptom of HF (Table 3). Walking ability before admission was assessed on admission in 920 patients, and the ability at discharge was re-evaluated in 899 patients. Table 6 shows walking abilities before admission, at discharge, and changes in walking ability from before admission to discharge. Before admission, the percentage of patients who could independently walk outdoors was significantly lower in the frailty group than in the prefrailty and non-frailty groups (66.1%, 91.5%, and 95.2%, respectively, \( P < 0.001 \)). At discharge, the percentage of patients who could independently walk outdoors decreased to 42.2% in the frailty group. The percentage of frail patients who could independently walk outdoors or indoors at discharge was lower than that before admission (76.0% at discharge vs. 84.9% before admission). Almost 30% of the frail patients had deterioration of walking ability during hospitalization. The percentage of patients with deterioration of walking ability during hospitalization increased with the frailty status (frailty, 27.5%; prefrailty, 21.9%; non-frailty, 8.9%, \( P < 0.001 \)). Although some patients in the frailty group had improvement in walking ability during hospitalization, the percentage of patients who had preserved walking ability during hospitalization was significantly lower in the frailty group than in the other two groups (frailty, 62.5%; prefrailty, 71.7%; non-frailty, 87.7%, \( P < 0.001 \)).

### Discussion

This study is the first study in which comprehensive assessment of frailty was carried out for HF patients using the KCL, which is widely used in Japan for the purpose of screening-like evaluation of daily functions. Management of HF requires a seamless system of care, including the community and hospital, and a multidisciplinary approach. Information obtained by the KCL can be shared seamlessly between medical staff and nursing care staff and is useful for management of elderly HF patients. In addition, this study was conducted in a rural area in which the ageing rate was approximately 35%\(^6\) and the median age of the patients in this study was 81 years. Patients aged 80 years or older accounted for 55.8% of the patients. The patients enrolled in this study were older than those in HF registries previously reported.\(^5,^18,^20\) The majority of HF patients in this cohort in a Japanese rural area was vulnerable to frailty. More than half of the frail patients had functional declines in IADL, physical function, socialization, cognitive function, and depression domains. Frail patients were admitted to the hospital for a longer period than were prefrail and non-frail patients. Additionally, deterioration of walking ability occurred more frequently in frail patients during hospitalization. In multivariate analysis, the determinants for frailty were age, prior HF hospitalization, prior CVA, and BNP level at discharge.

### Table 6  Walking ability according to frailty status

|                          | All patients (n = 949) | Frailty (n = 510) | Prefrailty (n = 293) | Non-frailty (n = 146) | \( P \) value |
|--------------------------|------------------------|------------------|---------------------|-----------------------|--------------|
| **Before admission**     |                        |                  |                     |                       |              |
| Independent outdoor walking | 744 (78.4)           | 337 (66.1)\(***\) | 268 (91.5)           | 139 (95.2)           | \(<0.001\)   |
| Independent indoor walking | 110 (11.6)           | 96 (18.8)\(***\) | 11 (3.8)            | 3 (2.1)              | \(<0.001\)   |
| Indoor walking with assistance | 27 (2.9)          | 24 (4.7)\(***\) | 3 (1.0)             | 0 (0.0)              | \(<0.001\)   |
| Abasia                   | 39 (4.1)             | 37 (7.3)\(**\)  | 2 (0.7)             | 0 (0.0)              | \(<0.001\)   |
| Unknown                  | 29 (3.1)             | 16 (3.1)         | 9 (3.1)             | 4 (2.7)              |              |
| **At discharge**         |                        |                  |                     |                       |              |
| Independent outdoor walking | 547 (57.6)          | 217 (42.5)\(***\) | 125 (85.6)          | \( P < 0.001 \)        |
| Independent indoor walking | 252 (26.6)          | 171 (33.5)\(***\) | 16 (11.0)           | \( P < 0.001 \)        |
| Indoor walking with assistance | 65 (6.9)           | 60 (11.8)\(**\)  | 5 (1.7)             | \( P < 0.001 \)        |
| Abasia                   | 35 (3.7)             | 31 (6.1)\(**\)  | 4 (1.4)             | \( P < 0.001 \)        |
| Unknown                  | 50 (5.3)             | 31 (6.1)         | 14 (4.8)            | 5 (3.4)              |              |
| **Changes in walking ability during hospitalization** | | | | | |
| Improved                 | 24 (2.5)             | 20 (3.9)\(***\) | 4 (1.4)             | 0 (0.0)              | \(<0.001\)   |
| Stable                   | 657 (69.2)           | 319 (62.5)\(***\) | 210 (71.7)\(***\) | 128 (87.9)           | \(<0.001\)   |
| Worsening                | 217 (22.9)           | 140 (27.5)\(**\) | 64 (21.8)\(**\)    | 13 (8.9)             | \(<0.001\)   |
| Unknown                  | 51 (5.4)             | 31 (6.1)         | 15 (5.1)            | 5 (3.4)              |              |
| Not independent walking at discharge | 103 (10.9)       | 94 (18.4)\(***\) | 9 (3.1)             | 0 (0.0)              | \(<0.001\)   |

Data were shown as \( n \) (%). Bonferroni post-hoc test between frailty, prefrailty, and non-frailty.

- \( P < 0.05 \); frailty vs. prefrailty.
- \( P < 0.01 \); frailty vs. prefrailty.
- \( P < 0.001 \); frailty vs. prefrailty.
- \( P < 0.05 \); frailty vs. non-frailty.
- \( P < 0.01 \); frailty vs. non-frailty.
- \( P < 0.001 \); frailty vs. non-frailty.
- \( P < 0.05 \); prefrailty vs. non-frailty.
- \( P < 0.01 \); prefrailty vs. non-frailty.
- \( P < 0.001 \); prefrailty vs. non-frailty.
Therefore, it was suggested that the severity of HF was involved in the development of frailty status. Frailty is considered to be a vulnerable condition that includes not only the physical domain but also multidimensional domains such as psychological and social domains. The Cardiovascular Health Study criteria focusing on physical domain, reported by Fried et al., were widely used in HF patients. The Comprehensive Geriatric Assessment has been used for assessment of multifaceted aspects in addition to assessment of physical aspects. A previous study showed that the prevalence of frailty in HF patients was 44.5%. Additionally, the prevalence of frailty was higher in studies in which multifaceted aspects were assessed than in those in which only the physical domain was assessed (47.4% vs. 42.9%).

In the present study, we used the KCL, which is a multidimensional assessment tool focusing on functional domains of daily living. As a result, 53.7% of the HF patients were identified as having frailty in the present study. This high frequency of frailty might be due to the older population than those in previous studies. The frequency of functional decline in each of the seven functional domains of the KCL significantly increased with increase in the degree of frailty. More than half of the frail patients with HF had functional decline in five domains including IADL, physical function, socialization, cognitive function, and depression domains. In addition, the number of domains with functional decline increased with the increase in frailty status. Approximately 30% of frail patients were diagnosed as having frailty based on functional decline in multiple domains other than the physical function domain. It has been suggested that multifaceted assessments as well as assessment of physical function are important for assessing frailty status in elderly HF patients. Compared with community-dwelling older people in the Kyoto–Kameoka study, the frequency of functional declines in IADL, physical function, malnutrition, and cognitive function domain was significantly higher in HF patients in the present study. The reason for these finding might be due to the difference of age between the two studies (81 years in the present study and 74 years in the Kyoto–Kameoka study). In addition, HF itself might lead to declines in multiple daily functional domains such as IADL, physical function, malnutrition, socialization, cognitive function, and depression. Several studies showed that frailty assessed by Fried criteria was associated with increased risks of mortality, hospitalization, and functional disability independent of the severity of HF. Additionally, elderly patients with HF often had deterioration of self-management such as medication adherence and self-monitoring due to physical and cognitive decline. Deterioration of self-management was the main cause of rehospitalization due to exacerbated HF, and decreased activities of daily living functioning were risk factors for mortality and hospitalization. Early intervention with social support for decreased activities of daily living function and poor self-management is expected to improve clinical outcomes. Therefore, it is possible to identify the domain with functional decline based on KCL assessment, and it is expected that early intervention will improve the disease management of HF at home and quality of life, which finally might lead to reduced mortality and reduction in readmission for worsening HF. In elderly patients with HF, the use of KCL for assessing multiple aspects such as physical, social, and psychological/cognitive aspects provided important information for multiple-disciplinary intervention for appropriate home service and care.

Investigation of the association between frailty status and changes in walking ability during hospitalization showed that most patients in the non-frailty group maintained independence of walking ability, whereas patients in the frailty group had decreased walking ability during hospitalization compared with those in the non-frailty group. It was reported that frail patients with HF had reduction in exercise tolerance as evaluated by cardiopulmonary exercise testing. These findings suggest that frail patients with HF have poor exercise tolerance and an increased risk of physical impairment during hospitalization. In previous studies, it was shown that HF patients with lower limb function assessed by a short physical performance battery before discharge had high risks of post-discharge ADL decline, readmission, and mortality. Cardiac rehabilitation improved exercise tolerance and quality of life and reduced readmission and cardiovascular death, which might be particularly beneficial for frail and prefrail patients with HF. Deterioration of walking ability during hospitalization was shown to be an independent risk factor for rehospitalization for worsening HF and mortality. In elderly HF patients, especially frail patients, it is necessary to maintain and improve walking ability during hospitalization by cardiac rehabilitation.

### Study limitations

There are several limitations to be acknowledged. First, the number of patients was not large as an HF cohort study. However, the population in the present study was considered to reflect the actual situation in an ageing region. Second, the KCL is self-administered and may not be accurate in patients with severe status of HF and cognitive impairment. Evaluation by the KCL in the present study reflected living functional status before hospitalization and may not reflect changes in physical and cognitive functions during hospitalization. The KCL is a simple questionnaire that can be repeated, and it is necessary to perform re-evaluation after discharge and use the information for intervention in clinical practice. Third, our registry has non-consecutive enrolment of patients. It might not be able to fully reflect the actual situation of HF patients in our area. However, because the hospitals participating in this registry are in charge of treatment for acute HF in Kochi Prefecture, it can be presumed that this registry
reflects the actual situation. Finally, this study is an observational study, and we are not able to investigate the effect of intervention on frailty. What kind of intervention contributes to improve frailty status and clinical outcomes for frail patients is an important issue in the future.

Future research

It is expected that home management of HF will be improved by evaluating living functions, introducing social support for functional decline in daily functional domains, and improving the living environment by coordinating with a caregiver. We need to investigate whether frailty status assessed by the KCL is associated with clinical outcomes in HF patients. Furthermore, it is necessary to examine whether interventions in the domain of impaired daily function will lead to improved quality of disease management and prognosis for HF patients.

Conclusions

More than half of patients with ADHF in a super-aged region in Japan were frail and had functional declines across multiple domains. The KCL provided useful and valuable information for easily identifying frail patients and for comprehensive management of HF. Moreover, information obtained by the KCL enables individualized interventions for each patient’s problems.

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Conflict of interest

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