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RESEARCH PAPER

Association of frailty with mortality in older inpatients with Covid-19: a cohort study

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Abstract

Background: COVID-19 has disproportionately affected older people.
Objective: The objective of this paper to investigate whether frailty is associated with all-cause mortality in older hospital inpatients, with COVID-19.
Design: Cohort study.
Setting: Secondary care acute hospital.
Participants: Participants included are 677 consecutive inpatients aged 65 years and over.
Methods: Cox proportional hazards models were used to examine the association of frailty with mortality. Frailty was assessed at baseline, according to the Clinical Frailty Scale (CFS), where higher categories indicate worse frailty. Analyses were adjusted for age, sex, deprivation, ethnicity, previous admissions and acute illness severity.
Results: Six hundred and sixty-four patients were classified according to CFS. Two hundred and seventy-one died, during a mean follow-up of 34.3 days. Worse frailty at baseline was associated with increased mortality risk, even after full adjustment ($P = 0.004$). Patients with CFS 4 and CFS 5 had non-significant increased mortality risks, compared to those with CFS 1–3. Patients with CFS 6 had a 2.13-fold (95% CI 1.34–3.38) and those with CFS 7–9 had a 1.79-fold (95% CI 1.12–2.88) increased mortality risk, compared to those with CFS 1–3 ($P = 0.001$ and 0.016, respectively). Older age, male sex and acute illness severity were also associated with increased mortality risk.
Conclusions: Frailty is associated with all-cause mortality risk in older inpatients with COVID-19.

Keywords: longitudinal study, mortality, COVID-19, frailty, older adults

Key Points

- Frailty is associated with all-cause mortality risk in older inpatients with COVID-19.
- Older age, male sex and acute illness severity were also associated with increased mortality risk.
- Frailty scoring should not be used in isolation for determining ceilings of care.

Introduction

Older age, underlying co-morbidities (such as chronic lung disease, hypertension, diabetes, ischaemic heart disease and obesity), social deprivation and ethnicity have been associated with worse outcomes from COVID-19 [1,2,3,4,5,6,7,8].

Frailty is defined as the propensity to deteriorate in the face of a stressor. It reflects homeostatic reserve and physiological resilience or 'biological age'. It is increasingly used to stratify clinical populations to reflect differing prognosis and clinical needs, in particular the need for an approach based on comprehensive geriatric assessment.

A specific, specialist, pathway for the assessment and management of frail older patients has been established in our Emergency Department since 2016, including routinely electronically recording the Clinical Frailty Scale (CFS) score

for patients over 65 year old [9]. From March 2020, electronic records included COVID-19 status.

The aim of our observational study was to explore the association between frailty and mortality in a cohort of adults aged 65 years and older, who were admitted to hospital and diagnosed with COVID-19.

Methods

We examined all adult admissions with COVID-19 from 1 March 2020 to 30 April 2020. Ethical approval was not required as the analysis entailed use of anonymised routinely collected data; audit office governance approval was obtained (project number 20-208C).

We identified patients who were admitted and diagnosed with COVID-19 in the presence of clinical symptoms and by a positive real time reverse transcriptase-polymerase chain reaction (RT-PCR) nasopharyngeal swab test, by radiological diagnosis, or by clinical criteria as decided by the responsible clinician. Radiological evidence of COVID-19 was defined by a chest radiograph or computed tomography of the chest showing classical signs [10,11]. Clinical diagnosis was reached in patients with a new continuous cough or fever and/or new desaturation requiring supplemental oxygen and/or haematological and/or radiological findings suggestive of COVID-19. Clinical judgement was applied for those who presented with atypical features, particularly among older patients [12].

Demographic and clinical data were retrieved from computer systems including Medway Live, NerveCentre and Unity Digital Health Records.

Ethnicity

Ethnicity is routinely recorded based on the categories by the Census of UK (2011), which we recategorised as: white British or Irish; ethnic minorities (African descent, Asian descent, any other ethnic group and any mixed background, white—other); unknown or not stated.

Deprivation

From each patient's postcode, we estimated deprivation by the index of multiple deprivation (IMD) quintile. The IMD is a small area-level index, which takes into account income, employment, education, health, crime, barriers to housing and services and living environment, and forms the official measure of relative deprivation in the UK [13,14]. The higher the quintile, the less deprived.

National Early Warning Score 2

We retrieved the admission National Early Warning Score 2 (NEWS-2) for each patient. NEWS-2 is a trigger score for clinical deterioration and is a proxy for the severity of acute illness based on a patient's clinical observations. It includes respiratory rate, oxygen saturations, systolic blood pressure, pulse rate, level of consciousness or confusion and temperature. The higher the NEWS-2 score, the more severe the illness of the patient [15].

Frailty

The CFS score is widely used to stratify older adults into different levels of frailty [9]. CFS score should reflect the baseline frailty 2 weeks prior to admission to the hospital for acute illness. Frontline clinicians within our hospital have been trained to score CFS, using pictorial diagrams, since 2016. Most CFS scores were attributed by the admitting clinician, within the Emergency Department, and then gathered from Medway Live. The remaining were assigned retrospectively by a doctor experienced in using the scale, using a combination of medical, physiotherapy and occupational therapist notes. Insufficient information was collected to identify CFS scores in 13 patients (1.9%). We categorised all patients into these frailty categories, based on CFS scores: CFS 1–3 (including 'very fit', 'well' and 'managing well'), CFS 4 ('vulnerable'), CFS 5 ('mildly frail'), CFS 6 ('moderately frail'), CFS 7–9 (including 'severely frail', 'very severely frail' and 'terminally ill').

We retrieved all elective, emergency and day-case admissions in 2019 for each patient, and categorised these as none versus one or more.

Mortality

All-cause mortality was obtained from electronic hospital records. The follow-up period was the time between admission and death, discharge or 28 May 2020. For those patients who died in hospital, we retrieved the cause of death from the death certificate. We categorised the deaths that occurred in hospital as COVID-19 deaths versus non-COVID-19 deaths.

Statistical analysis

We used IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, NY, USA) for all the analyses. We reported baseline characteristics of patients as number of patients (percentage) for categorical variables and as mean [standard deviation (SD)] for continuous variables. We tested differences between men and women, and across frailty categories, among those aged 65 years and older. We tested differences in baseline characteristics using χ^2-test for categorical variables and Student t-test and analysis of variance for continuous variables, as appropriate. We assessed the bivariate correlation between NEWS-2 score and CFS categories by two-tailed Spearman's rho correlation coefficient.

We performed Cox regression to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between frailty and all-cause mortality, among patients aged 65 years and older.

Analyses were performed in three steps. Model 0 presents the crude, unadjusted association between CFS categories and all-cause mortality. In Model 1, analyses were adjusted

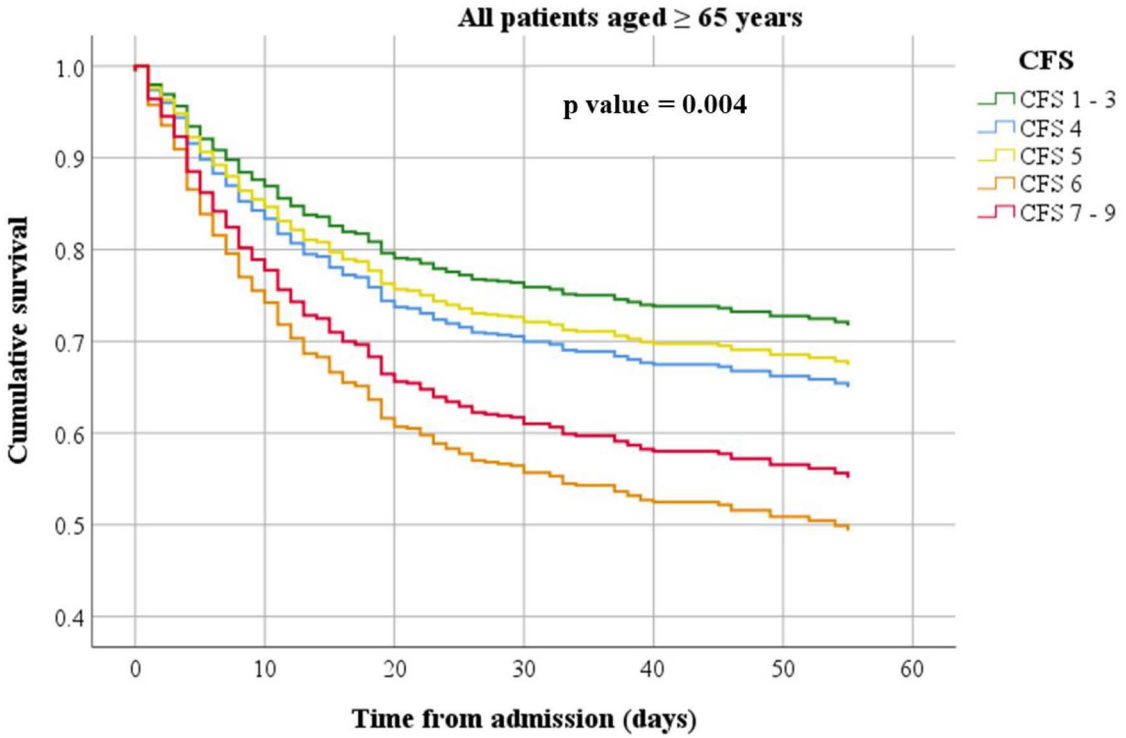

Figure 1. All-cause mortality by frailty in patients aged 65 years and older. This figure presents the survival curves for 664 patients aged 65 years and older with known CFS category. The *P* value is for the association between CFS category and all-cause mortality, after full adjustment for age, sex, ethnicity, IMD quintile, NEWS-2 score on admission and previous admissions in 2019 (Cox regression). Number of patients in each CFS category: CFS 1–3, $n = 97$; CFS 4, $n = 96$; CFS 5, $n = 101$; CFS 6, $n = 203$; CFS 7–9, $n = 166$. Number of patients who died during follow-up in each CFS category: CFS 1–3, $n = 26$; CFS 4, $n = 30$; CFS 5, $n = 31$; CFS 6, $n = 102$; CFS 7–9, $n = 81$. One patient with CFS 4, who died during follow-up, was excluded from the analysis for missing NEWS 2 score on admission.

for age and sex. In Model 2, they were fully adjusted for age, sex, ethnicity, IMD quintile, previous hospital admissions in 2019 and NEWS-2 score.

We performed sensitivity analyses by including only those patients with a positive RT-PCR test, and those with a COVID-19 cause of death. Univariate and multivariate Cox regression analyses were also used to assess the association between demographic (age, sex, ethnicity, IMD quintile) and clinical (previous hospital admissions in 2019, NEWS-2 score) variables and all-cause mortality.

Results

From 1 March 2020 to 30 April 2020, 982 patients aged 18 years and older were admitted and diagnosed with COVID-19. Among these, 305 patients were aged 18–64 years and 677 patients were aged 65 years and older (Supplementary Table S1). Patients aged 65 years and over were included in our study (Supplementary Figure S1, flow chart of study design). Table 1 shows the baseline characteristics of our study population, by gender. Among all patients aged 65 years and over, mean age was 81.1 years (SD 8.1), 311 (45.9%) were women, mean NEWS-2 score was 3.7 (SD 2.9) and 506 (74.7%) had a positive RT-PCR test. Ninety-seven (14.3%) were fit or well on the CFS, and 369 (54.5%) were moderately or severely frail. No difference in the proportion of those with positive RT-PCR test, radiological and clinical diagnosis of COVID-19 was observed between men and women (Table 1). Supplementary Figure S2 shows the distribution of NEWS-2 score.

Table 2 shows the characteristics of patients aged 65 years and older, across frailty categories. Mean age and mean NEWS-2 score were highest among those patients with CFS 7–9, compared to the other frailty categories ($P < 0.001$ and 0.035, respectively). There was a significantly higher number of patients with one or more hospital attendances in 2019 for higher CFS groups 6 and 7–9, compared with those in the lower groups ($P < 0.001$). The proportion of women did not differ across frailty categories.

The bivariate correlation between NEWS-2 score and CFS categories on admission was non-significant, with a two-tailed Spearman's rho coefficient of 0.071 ($P = 0.067$, $n = 663$ patients, Supplementary Figure S3).

During a mean follow-up of 34.3 days, 271 (40.8%) patients aged 65 years and older, with a known frailty score, died. For 234 of these 271 patients, death certificates were

Table 1. Characteristics of patients aged 65 years and older at baseline, by gender

	All ($n = 677$)	Men ($n = 366$)	Women ($n = 311$)	P value
Age (years), mean (SD)	81.1 (8.1)	80.5 (8.0)	81.7 (8.2)	0.050
Ethnicity, *n* (%)				
Of African descent	20 (3.0)	12 (3.3)	8 (2.6)	0.020
Of Asian descent	10 (1.5)	8 (2.2)	2 (0.6)	
Any other ethnic group	8 (1.2)	6 (1.6)	2 (0.6)	
Any other mixed background	0 (0)	0 (0)	0 (0)	
White British or Irish	535 (79.0)	271 (74.0)	264 (84.9)	
White—other	10 (1.5)	6 (1.6)	4 (1.3)	
Unknown or not stated	94 (13.9)	63 (17.2)	31 (10.0)	
IMD quintile, *n* (%)				
First	177 (26.1)	95 (26.0)	82 (26.4)	0.606
Second	115 (17.0)	69 (18.9)	46 (14.8)	
Third	99 (14.6)	49 (13.4)	50 (16.1)	
Fourth	118 (17.4)	65 (17.8)	53 (17.0)	
Fifth	168 (24.8)	88 (24.0)	80 (25.7)	
Admissions in 2019, *n* (%)				
None	333 (49.2)	183 (60.0)	150 (48.2)	0.646
1 or more	344 (50.8)	183 (50.0)	161 (51.8)	
NEWS-2 score (points), mean (SD)	3.7 (2.9)	3.7 (3.0)	3.6 (2.8)	0.568
Positive RT-PCR test, *n* (%)	506 (74.7)	284 (77.6)	222 (71.4)	0.064
Radiological diagnosis, *n* (%)	76 (11.2)	42 (11.5)	34 (10.9)	0.824
Clinical diagnosis, *n* (%)	237 (35.0)	118 (32.2)	119 (38.3)	0.102
CFS, *n* (%)				
CFS 1–3	97 (14.3)	64 (17.5)	33 (10.6)	0.096
CFS 4	97 (14.3)	56 (15.3)	41 (13.2)	
CFS 5	101 (14.9)	56 (15.3)	45 (14.5)	
CFS 6	203 (30.0)	103 (28.1)	100 (32.2)	
CFS 7–9	166 (24.5)	80 (21.9)	86 (27.7)	
Unknown	13 (1.9)	7 (1.9)	6 (1.9)	

P values are calculated by using chi-square test for categorical variables and student t-test for age and NEWS-2 score. n, number.

Table 2. Characteristics of patients aged 65 years and older at baseline, by frailty

	CFS 1–3 ($n = 97$)	CFS 4 ($n = 97$)	CFS 5 ($n = 101$)	CFS 6 ($n = 203$)	CFS 7–9 ($n = 166$)	Unknown ($n = 13$)	P value
Age (years), mean (SD)	75.6 (7.7)	77.8 (7.0)	80.6 (7.5)	84.0 (7.3)	83.2 (7.8)	76.8 (9.2)	< 0.001
Women, *n* (%)	33 (34.0)	41 (42.3)	45 (44.6)	100 (49.3)	86 (51.8)	6 (46.2)	0.096
Ethnicity, *n* (%)							
Of African descent	2 (2.1)	4 (4.1)	1 (1.0)	6 (3.0)	7 (4.2)	0 (0)	0.007
Of Asian descent	3 (3.1)	2 (2.1)	2 (2.0)	1 (0.5)	1 (0.6)	1 (7.7)	
Any Other Ethnic group	2 (2.1)	1 (1.0)	3 (3.0)	2 (1.0)	0 (0)	0 (0)	
White British or Irish	65 (67.0)	73 (75.3)	83 (82.2)	163 (80.3)	144 (86.7)	7 (53.8)	
White—other	4 (4.1)	1 (1.0)	0 (0)	5 (2.5)	0 (0)	0 (0)	
Unknown or not stated	21 (21.6)	16 (16.5)	12 (11.9)	26 (12.8)	14 (8.4)	5 (38.5)	
IMD quintile, *n* (%)							
First	19 (19.6)	21 (21.6)	24 (23.8)	55 (27.1)	57 (34.3)	1 (7.7)	0.099
Second	15 (15.5)	16 (16.5)	18 (17.8)	34 (16.7)	31 (18.7)	1 (7.7)	
Third	16 (16.5)	21 (21.6)	15 (14.9)	33 (16.3)	13 (7.8)	1 (7.7)	
Fourth	22 (22.7)	15 (15.5)	18 (17.8)	38 (18.7)	21 (12.7)	5 (30.8)	
Fifth	25 (25.8)	24 (24.7)	26 (25.7)	43 (21.2)	44 (26.5)	6 (46.2)	
Admissions in 2019, *n* (%)							
None	68 (70.1)	51 (52.6)	55 (54.5)	77 (37.9)	72 (43.4)	10 (76.9)	< 0.001
1 or more	29 (29.9)	46 (47.4)	46 (45.5)	126 (62.1)	94 (56.6)	3 (23.1)	
NEWS-2 score, mean (SD)	3.7 (2.9)	3.3 (2.4)	3.3 (2.4)	3.5 (2.9)	4.3 (3.3)	3.3 (3.0)	0.035
Positive RT-PCR test, n (%)	77 (79.4)	72 (74.2)	66 (65.3)	155 (76.4)	129 (77.7)	7 (53.8)	0.078
Radiological diagnosis, n (%)	22 (22.7)	14 (14.4)	8 (7.9)	19 (9.4)	10 (6.0)	3 (23.1)	0.001
Clinical diagnosis, n (%)	22 (22.7)	30 (30.9)	42 (41.6)	78 (38.4)	61 (36.7)	4 (30.8)	0.063

P values are calculated by using chi-square test for categorical variables and ANOVA for age and NEWS-2 score.

Table 3. Characteristics of patients aged 65 years and older with known CFS category, by survival status ($n = 664$ patients)

	All ($n = 664$)	All survivors ($n = 393$)	All deceased ($n = 271$)	COVID-19 deceased ($n = 216$)	HR [95% CI]	*P* value
CFS, *n* (%)						
CFS 1–3	97 (14.6)	71 (18.1)	26 (9.6)	23 (10.6)	1 (reference)	< 0.001
CFS 4	97 (14.6)	66 (16.8)	31 (11.4)	24 (11.1)	1.23 [0.73–2.07]	
CFS 5	101 (15.2)	70 (17.8)	31 (11.4)	24 (11.1)	1.18 [0.70–1.99]	
CFS 6	203 (30.6)	101 (25.7)	102 (37.6)	77 (35.6)	2.20 [1.43–3.39]	
CFS 7–9	166 (25.0)	85 (21.6)	81 (29.9)	68 (31.5)	2.20 [1.41–3.43]	
Age (years), mean (SD)	81.2 (8.1)	80.2 (8.0)	82.6 (8.0)	82.3 (8.1)	1.03 [1.01–1.05]	< 0.001
Sex, n (%)						
Female	305 (45.9)	208 (52.9)	97 (35.8)	79 (36.6)	1 (reference)	< 0.001
Male	359 (54.1)	185 (47.1)	174 (64.2)	137 (63.4)	1.66 [1.29–2.13]	
Ethnicity, n (%)						
White British or Irish	528 (79.5)	309 (78.6)	219 (80.8)	170 (78.7)	1 (reference)	0.839
Ethnic minority	47 (7.1)	28 (7.1)	19 (7.0)	17 (7.9)	0.99 [0.62–1.58]	
Unknown or not stated	89 (13.4)	56 (14.2)	33 (12.2)	29 (13.4)	0.90 [0.62–1.29]	
IMD quintile, *n* (%)						
First	176 (26.5)	102 (26.0)	74 (27.3)	60 (27.8)	1 (reference)	0.434
Second	114 (17.2)	70 (17.8)	44 (16.2)	34 (15.7)	0.90 [0.62–1.30]	
Third	98 (14.8)	64 (16.3)	34 (12.5)	24 (11.1)	0.74 [0.49–1.11]	
Fourth	114 (17.2)	68 (17.3)	46 (17.0)	39 (18.1)	0.95 [0.66–1.38]	
Fifth	162 (24.4)	89 (22.6)	73 (26.9)	59 (27.3)	1.09 [0.79–1.50]	
Admissions in 2019, *n* (%)						
None	323 (48.6)	191 (48.6)	132 (48.7)	103 (47.7)	1 (reference)	0.868
1 or more	341 (51.4)	202 (51.4)	139 (51.3)	113 (52.3)	1.02 [0.80–1.30]	
NEWS-2 score, mean (SD)	3.7 (2.9)	3.1 (2.5)	4.5 (3.2)	5.0 (3.3)	1.18 [1.13–1.22]	< 0.001

The HRs [95% CI] refer to the association between each variable and all-cause mortality and were calculated by univariate Cox regression.

available; 216 patients were certified as dying from COVID-19. We could not retrieve the death certificate for 37 patients who died following discharge.

Supplementary Table S2 shows the distribution of diagnostic criteria for COVID-19, by survival status.

Table 3 shows the univariate, unadjusted association between frailty, demographic and clinical variables and all-cause mortality, among 664 patients aged 65 years and older with known frailty category. Older age, male sex and higher NEWS-2 score were associated with increased risk of all-cause mortality (all $P < 0.001$). In contrast, ethnicity, IMD quintile and previous admissions in 2019 were not associated with mortality.

Figure 1 illustrates the association between frailty and all-cause mortality, after full adjustment for covariates. During follow-up, the proportion of those who died was lowest among those with CFS 1–3 (26.8%) and highest among those with CFS 6 (50.2%) and CFS 7–9 (48.8%).

Table 4 shows the HRs and CIs for the association between frailty and all-cause mortality. In the whole cohort of 664 patients, higher frailty scores were associated with the increased risk of mortality ($P = 0.004$, after full adjustment). After adjustment for covariates, patients with CFS 4 and CFS 5 had non-significant 1.30-fold (95% CI 0.76–2.21) and 1.19-fold (95% CI 0.70–2.03) increased mortality risk, respectively, compared to those with CFS 1–3 ($P = 0.338$ and 0.530, respectively). In contrast, those with CFS 6 had a 2.13-fold (95% CI 1.34–3.38) and those with CFS 7–9 had a 1.79-fold (95% CI 1.12–2.88) increased mortality risk, respectively, compared to those with CFS 1–3 ($P = 0.001$ and 0.016, respectively).

After full adjustment, older age, male sex and higher admission NEWS-2 score were associated with increased risk of mortality ($P = 0.002$, $P < 0.001$ and $P < 0.001$, respectively), while ethnicity, IMD quintiles and previous hospital admissions in 2019 were not (Table 4).

A minority of patients aged 65 years and older was admitted to an intensive treatment unit (ITU) ($n = 37$, 5.6%). Among these, mean age was 71.8 years (SD 5.4), 16 (43.2%) were women and mean admission NEWS-2 score was 5.2 (SD 3.5); 21 (56.8%) had CFS 1–3, 13 (35.1%) had CFS 4 and 3 (8.1%) had CFS 6 (Supplementary Table S5). Of these patients, 15 (40.5%) died during follow-up; in all cases, death was due to COVID-19. In comparison, those that were not admitted to ITU were frailer, older, and more had a hospital admission in 2019.

In sensitivity analyses, the association between frailty and mortality was similar when cases were confined to RT-PCR positive cases (Supplementary Figure S4 and Supplementary Table S2) and those in whom death was attributed to COVID-19 (Supplementary Table S3 and Supplementary Table S4).

Discussion

In our cohort of older adults aged 65 years and older, admitted to a secondary care hospital with COVID-19, worsening frailty on admission was associated with an increased risk of

Table 4. Association between frailty, demographic and clinical variables and all-cause mortality in patients aged 65 years and older

	HR [95% CI]*	P value*	HR [95% CI]**	P value**	HR [95% CI]***	P value***
CFS						
CFS 1–3	1 (ref)	< 0.001	1 (ref)	0.001	1 (ref)	0.004
CFS 4	1.23 [0.73–2.07]		1.23 [0.73–2.08]		1.30 [0.76–2.21]	
CFS 5	1.18 [0.70–1.99]		1.14 [0.68–1.94]		1.19 [0.70–2.03]	
CFS 6	2.20 [1.43–3.39]		2.06 [1.31–3.23]		2.13 [1.34–3.38]	
CFS 7–9	2.20 [1.41–3.43]		2.06 [1.31–3.26]		1.79 [1.12–2.88]	
Age (years), mean (SD)	na	na	1.02 [1.004–1.04]	0.016	1.03 [1.01–1.05]	0.002
Sex, *n* (%)						
Female	na	na	1 (reference)	< 0.001	1 (reference)	< 0.001
Male			1.79 [1.40–2.30]		1.81 [1.41–2.33]	
Ethnicity, *n* (%)						
White British or Irish	na	na	na	na	1 (reference)	0.565
Ethnic minority					1.02 [0.63–1.64]	
Unknown or not stated					0.82 [0.56–1.20]	
IMD quintile, *n* (%)						
First	na	na	na	na	1 (reference)	0.596
Second					0.95 [0.65–1.39]	
Third					0.98 [0.64–1.48]	
Fourth					1.18 [0.81–1.72]	
Fifth					1.22 [0.87–1.70]	
Admissions in 2019, *n* (%)						
None	na	na	na	na	1 (reference)	0.353
1 or more					0.89 [0.69–1.14]	
NEWS-2 score, mean (SD)	na	na	na	na	1.19 [1.14–1.23]	< 0.001

*Model 0: crude (CFS category only). **Model 1: adjusted for CFS category, age and sex. ***Model 2: adjusted for CFS category, age, sex, NEWS-2 score, IMD quintile, hospital spells and ethnicity The HRs [95% CI] refer to the association between frailty, demographic and clinical variables and all-cause mortality and were calculated by Cox regression. The Cox regression analyses were carried out: in Model 0, in 664 patients; in Model 1 in 664 patients; in Model 2, in 663 patients (one patient was excluded for missing NEWS-2 score).

all-cause mortality. This association was independent of age, sex, ethnicity, deprivation, previous admission to hospital and clinical severity on admission. We confirmed that age and male sex were associated with an increased risk of mortality.

Context

Increasing age has previously been associated with COVID-19 mortality. Our study shows an association between frailty and mortality in older adults with COVID-19. It is in line with prior literature, showing an association between frailty and non-COVID mortality in older adults in the community as well as among older adults admitted to hospital [16,17,18,19]. It is also in line with a previous report showing that frailty may negatively affect recovery from another viral illness, influenza, and its associated acute respiratory illness in older adults [20].

In our study, the association between frailty and clinical severity on admission, as measured by NEWS-2 score, was non-significant and the effect size very small (Spearman's rho 0.071) [21]. This is contrary to previous studies, showing positive although weak associations between frailty and clinical severity on admission to acute hospital settings in the UK (Spearman's rho 0.17 and 0.23, respectively) [16,22]. These studies have suggested that CFS scoring in the acute hospital may inadvertently incorporate acuity into the scoring, rather than measuring baseline frailty in the 2 weeks prior to admission. Given that no association between frailty and clinical severity on admission was found in our cohort of patients with COVID, we think that this is unlikely to have occurred in our study. Previous reports suggested that frail patients may present later to the hospital, with high acute illness severity, after failed attempts to manage them in the community [16,23]. However, there may be a prompt referral to the hospital of frail patients with suspected COVID infection, for fear of contagion in the community. Furthermore, we speculate that the clinical acuity of patients with COVID may be unrelated to frailty, contrary to that of other infectious illnesses, as immune reaction responses may differ.

Of note, in our study, older adults who were classified as vulnerable or mildly frail did not have an increased mortality risk, compared to the fittest. Our numbers were insufficient to make very precise estimates of mortality for each individual CFS grade, although a broad dichotomy (CFS 1–5 versus 6–9) was suggested, and increase in mortality risk was noted only for those adults with moderate or severe frailty, compared to the fittest. It could be that our study was underpowered to detect differences in mortality risk between these groups. As an alternative explanation, vulnerable and mildly frail older adults may have a mortality risk similar to that of the fittest, in the context of the COVID-19 pandemic.

Furthermore, our findings remained consistent when using different diagnostic criteria for COVID-19. First, we showed the association between frailty and mortality, in the whole cohort of patients, where diagnosis of COVID-19 could be reached by positive RT-PCR, radiological criteria or clinical criteria. We initially included the whole cohort of patients not to miss any cases of COVID-19, as the sensitivity of RT-PCR could be as low as 60–70% [24]. Later, when excluding patients with only radiological or clinical criteria but a negative RT-PCR, who could have been misclassified as COVID-19, our findings remained unchanged.

We selected all-cause mortality as our main outcome. Clinical determination of the cause of death is frequently inaccurate in older adults [25]. All-cause mortality is the most robust outcome but may include non-COVID deaths. Moreover, COVID-19 may have contributed to a clinical decline—possibly through hospitalisation—also in those patients who were not certified as deceased for COVID-19. Furthermore, when we performed the analyses on the association between frailty and only COVID-19 certified mortality, we found similar findings.

Strengths and limitations

The strengths of our study are the longitudinal design, the large sample size and the use of an internationally validated scale to define frailty. Although there is no universal definition of frailty, many scales have been proposed to measure it [26]. CFS is described by brief descriptions and pictograms, largely describing functional activity (disability) states. It thus only approximates to the theoretical construct of frailty; however, it has the advantages of being brief, practical, and widely used in clinical practice. It should be based on premorbid function 2 weeks prior to admission, for this to have validity and uniformity in the assessment. However, CFS scoring could be subjective and the degree of frailty may have been misinterpreted as a consequence of presenting illness acuity.

Our study was based in a single centre. We did not include frail older adults, on a palliative trajectory prior to COVID-19, who may have received palliative care in the community without being admitted to hospital. The findings of our study may thus not be generalisable to these older adults. Every effort was made to follow-up the patients for mortality, but we may not have ascertained all those who died after leaving the hospital, or whether their death was attributed to COVID-19. As our main focus was on all-cause mortality, this is likely to be a minor limitation. We had to estimate CFS from clinical records where these had not been recorded electronically, and data were incomplete for 13 patients.

Implications for practice

Our data may inform discussion on prognosis in the clinical setting, and this information may be useful for discussions with families, and may also indicate a group in whom 'twin-tract' active and palliative management may be appropriate and should be considered.

Our findings could also be useful in case-mix adjustment for governance purposes.

There has been much debate about defining ceilings of care for older patients with COVID-19 disease. Some guidance suggests that patients with a CFS score of 5 or more would be unlikely to benefit from ITU care [27,28]. As our patient group was managed predominantly on standard medical wards, rather than critical care, we do not feel able to give recommendations on ITU allocation. However, we highlight that about half of our patients with moderate to severe frailty survived the hospital admission due to COVID-19.

This adds to the argument that frailty alone should not be used in determining active medical treatment [29].

Conclusion

Frailty is associated with all-cause mortality in older adults diagnosed with COVID-19, who are admitted to hospital, independent of age, sex, acute illness severity, deprivation status, hospital admissions in the previous year and ethnicity. Increasing age, male sex and acute illness severity are also associated with increased mortality risk. Although frailty score should not be wholly utilised for determining ceilings of care, we feel that it can be useful, in conjunction with other prognostic markers, for discussions with patients and/or their next of kin regarding clinical management decisions.

Supplementary Data: Supplementary data are available in *Age and Ageing* online.

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