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Clinical Frailty Score vs Hospital Frailty Risk Score for predicting mortality and other adverse outcome in hospitalised patients with COVID-19: Spanish case series

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Abstract

Objectives: Frailty can be used as a predictor of adverse outcomes in people with coronavirus disease 2019 (COVID-19). The aim of the study was to analyse the prognostic value of two different frailty scores in patients hospitalised for COVID-19.

Material and Methods: This retrospective cohort study included adult (≥18 years) inpatients with COVID-19 and took place from 3 March to 2 May 2020. Patients were categorised by Clinical Frailty Score (CFS) and Hospital Frailty Risk Score (HFRS). The primary outcome was in-hospital mortality, and secondary outcomes were tocilizumab treatment, length of hospital stay, admission in intensive care unit (ICU) and need for invasive mechanical ventilation. Results were analysed by multivariable logistic regression and expressed as odds ratios (ORs), adjusting for age, sex, kidney function and comorbidity.

Results: Of the 290 included patients, 54 were frail according to the CFS (≥5 points; prevalence 18.6%, 95% confidence interval [CI]: 14.4-23.7) vs 65 by HFRS (≥5 points; prevalence: 22.4%, 95% CI 17.8-27.7). Prevalence of frailty increased with age according to both measures: 50-64 years, CFS 1.9% vs HFRS 12.3%; 65-79 years, CFS 31.5% vs HFRS 40.0%; and ≥80 years, CFS 66.7% vs HFRS 40.0% ($P < .001$). CFS-defined frailty was independently associated with risk of death (OR 3.67, 95% CI 1.49-9.04) and less treatment with tocilizumab (OR 0.28, 95% CI 0.08-0.93). HFRS-defined frailty was independently associated with length of hospital stay over 10 days (OR 2.89, 95% CI 1.53-5.44), ICU admission (OR 4.18, 95% CI 1.84-9.52) and invasive mechanical ventilation (OR 5.93, 95% CI 2.33-15.10).

Conclusion: In the spring 2020 wave of the COVID-19 pandemic in Spain, CFS-defined frailty was an independent predictor for death, while frailty as measured by the HFRS was associated with length of hospital stay over 10 days, ICU admission and use of invasive mechanical ventilation.

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1 | INTRODUCTION

Frailty is defined as "a medical syndrome with multiple causes and contributors, characterized by diminished strength, endurance, and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death."[1] Fried et al[2] described a frailty phenotype based on five dimensions, including weight loss, exhaustion, physical activity, walking speed and grip strength. According to this phenotype, fulfilment of at least three criteria indicates frailty, while people with one or two are defined as prefrail and those who do not meet any criteria are considered robust. This measure also enables calculating a frailty index for each individual from 0 to 1 by dividing the total number of deficits present by the total number of deficits possible (higher values indicating more frailty).[3]

Frailty is a reliable measure for predicting clinical and healthcare-related outcomes in people with different conditions.[4-6] However, the notion of frailty as a predictor of adverse outcomes in older patients with coronavirus disease 2019 (COVID-19) remains unclear.[7,8] Existing studies have been heterogeneous in terms of the frailty measures used, clinical context, design, definition of adverse outcomes and results.[9-19] The Clinical Frailty Score (CFS)[20] is the most common instrument for measuring frailty in COVID-19, but alternative scales may also be used, including the Hospital Frailty Risk Score (HFRS).[21] More evidence is still needed about the relevance of frailty for mortality, admission to the intensive care unit (ICU), use of invasive mechanical ventilation (IMV) and other adverse outcomes in people infected with COVID-19.

The aim of this study was to analyse the prognostic value of two different frailty scores, the CFS[20] and the HFRS,[21] in inpatients with COVID-19 during the spring 2020 wave of the pandemic in Spain. We hypothesised that CFS- and HFRS-defined frailty would be strong predictors of adverse outcomes.

What's known

- Frailty is a reliable predictor of clinical and healthcare-related outcomes in people with different conditions.
- The Clinical Frailty Score (CFS) is the most common measure of frailty in COVID-19.

What's new

- We assessed frailty using the CFS and the Hospital Frailty Risk Score in inpatients with COVID-19.
- CFS-defined frailty was an independent predictor for death.

2 | MATERIAL AND METHODS

2.1 | Study design and population

This retrospective cohort study took place from 3 March to 2 May 2020 at the General University Hospital of Alicante (Spain). Eligible patients were adults (≥18 years) admitted to hospital and diagnosed with COVID-19 pneumonia using the reverse transcriptase polymerase chain reaction (RT-PCR) test for SARS-CoV-2.

2.2 | Frailty assessment

Frailty was assessed using two instruments: the CFS and HFRS. The CFS bases the frailty assessment on the patient's condition 2 weeks prior to hospital admission.[20] Patients are scored on an ordinal hierarchical scale from 1 to 9, with a score of 1 indicating the person is very fit; 2 well; 3 managing well; 4 vulnerable; 5 mildly frail; 6 moderately frail; 7 severely frail; 8 very severely frail; and 9 terminally ill.[15,20] Frailty level was retrospectively decided for all patients by one junior physician, and all borderline cases were adjudicated by a specialist physician in line with previous studies.[18,19] Data collected for taking the decision included reported physical activity levels, number of falls in the last year, visual and hearing deficits, history of cognitive impairment, fatigue, weight loss in the last year and functional status according to the Barthel Index.[22]

We did not anticipate that there would be adequate number of events for each score, so we grouped them as 1-4 (no frailty), 5-6 (mild-to-moderate frailty: initial signs of frailty but with some degree of independence) and 7-9 (severe frailty) for the purposes of the analyses (Table S1). We also analysed CFS as a continuous and dichotomous variable (no frailty [1-4] vs frailty [5-9]).

The HFRS was previously developed and validated in a British cohort of older people.[21] To calculate this score, we reviewed clinical records from the Admission Service of our hospital for diagnostic codes from the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM), looking for 10 conditions recorded during any hospitalisation within the last 2 years. Each code registered was assigned a certain number of points (see Table S2 for itemised scoring criteria).

Based on the calculated score, patients were classified into three frailty risk groups based on previously validated cut points for the HFRS: low (<5 points), intermediate (5-15 points) and high risk (>15 points).[21] Patients with scores of 5 or above were defined as frail in a dichotomous analysis (frailty vs no frailty), and we also used the HFRS as a continuous variable.

2.3 | Data collection and variables definitions

The sample size was not calculated. All inpatients diagnosed with COVID-19 by PCR from 3 March to 2 May 2020 were included. Patients with missing clinical variables were not included in the analysis of these variables. More in-depth information about the data collection and definition of variables has been provided in papers by

the COVID-19 ALC research group.[23,24] For patients diagnosed with COVID-19 during their hospital stay (nosocomial infection), the date of diagnosis was used in lieu of the date of admission. Preadmission comorbidities were collected from the patient's electronic medical record. Laboratory data were collected at admission, and renal function was evaluated by estimated glomerular filtration rate (eGFR) according to the CKD-EPI equation. The burden of comorbidities was assessed using the age-adjusted Charlson comorbidity Index (CCI), a method of estimating mortality risk from comorbid disease at 10 years.[25]

2.4 | Outcome variables

The primary outcome was in-hospital mortality from any cause. Secondary outcomes were treatment with intravenous tocilizumab (TCZ) (reserved for severe cases at admission or those with progressive clinical, analytical and radiological deterioration), length of hospital stay (continuous variable), length of hospital stay ≥10 days (dichotomous), ICU admission and need for IMV.

2.5 | Statistical analysis

Categorical variables are expressed as frequencies (percentages) and continuous variables as medians (interquartile range) or mean (standard deviation, SD). Differences in CFS- and HFRS-defined frailty were examined using the χ^2 test for categorical variables and the Mann–Whitney *U*-test for continuous variables. Agreement between the two measures was assessed by Kappa score with 95% confidence intervals (CIs), while the Spearman's rho test was used to test correlation between the age, CFS, HFRS and CCI. Time-to-event analyses were reported with a Kaplan–Meier survival plot.

We then analysed the outcomes using two logistic regression models: model A (adjusted for age, sex and eGFR) and model B (adjusted for age, sex, eGFR and CCI), calculating results for CFS and HFRS as continuous variables (score) and both dichotomous variables and categorical variables, as described above. Associations were expressed as adjusted odds ratios (OR) and 95% CIs. Two-tailed *P* values of less than .05 were considered significant. All analyses were performed using SPSS v25.

3 | RESULTS

3.1 | Frailty assessment

From 3 March to 2 May 2020, 290 adults with PCR-confirmed COVID-19 were admitted to Alicante General University Hospital. Mean CFS was 3.5 (SD 1.6), and 54 (18.6%, 95% CI 14.4-23.7) patients were defined as frail (CFS ≥5 points): 33 (11.4%) presented mild-to-moderate frailty (5-6 points) and 21 (7.2%), severe frailty (7-9 points). Regarding the HFRS assessment, patients' mean score was 3.6 (SD 5.1), and 65 (22.4%) were defined as frail (HFRS >5 points): 49 (16.9%) with intermediate risk (5-15 points) and 16 (5.5%) with high risk (>15 points).

The HFRS showed moderate concordance with the CFS (kappa = 0.38, 95% CI 0.24-0.52). Using the Spearman rank test, correlation between the CFS and HFSR was moderate ($r_s = 0.51$, $P < .001$), between the CFS and CCI, high ($r_s = 0.79$; $P < .001$), between the HFSR and CCI, moderate ($r_s = 0.50$, $P < .001$), between age and CFS, high ($r_s = 0.748$) and between age and HFRS, moderate ($r_s = 0.485$).

Demographics, comorbidities, laboratory findings and outcomes according to frailty (CFS or HFRS) are shown in Table 1 (all covariates are presented in Table S3). Prevalence of frailty increased with age according to both measures: 50-64 years, CFS 1.9% vs HFRS 12.3%; 65-79 years, CFS 31.5% vs HFRS 40.0%; and ≥80 years, CFS 66.7% vs HFRS 40.0% ($P < .001$).

3.2 | Mortality and frailty

Table 2 presents the study outcomes according to CFS and HFRS categories. The primary outcome, in-hospital mortality, was observed in 48 (16.6%, 95% CI 12.7-21.3) patients. These rates increased with frailty according to the CFS categories: no frailty 8.1%, mild-to-moderate frailty 45.5% and severe frailty 66.7% ($P < .001$, Table 2). In-hospital mortality also differed according to the HFRS categories: low risk 12.9%, intermediate risk 30.6% and high risk 25.0% ($P = .007$). Both the CFS and the HFRS categories were significantly associated with survival (Figure 1).

3.3 | Other adverse outcomes

Long hospital stays (≥10 days) were observed in 131 (45.2%) patients, treatment with TCZ in 80 (27.6%), ICU admission in 47 (16.2%) and IMV in 37 (12.8%). By CFS categories, long hospital stay was similar in people with no frailty and moderate-to-severe frailty. However, fewer moderately to severely frail patients were treated with TCZ ($P < .001$), admitted to the ICU ($P = .019$) or needed IMV ($P = .027$, Table 2). According to the three-category HFRS analysis, long hospital stay was associated with frailty risk ($P = .002$), as was ICU admission ($P = .039$) and use of IMV ($P = .018$), while treatment with TCZ was similar between groups (Table 2).

In the multivariable analysis, after adjusting for age, sex and renal function (model A), the CFS was significantly associated with higher odds of mortality, both as a continuous and categorical measure. However, after also adjusting for CCI (model B), only severe frailty was significantly associated with mortality. In both models, CFS-defined frailty (continuous and categorical) was significantly associated with lower odds of treatment with TCZ, but not with long hospital stay, ICU admission or requirement for IMV (Table 3).

According to both models A and B, the HFRS (continuous and categorical) was not associated with mortality or TCZ treatment. However, it was significantly associated with higher odds of long hospital stay, ICU admission and IMV (Table 4).

TABLE 1 Baseline characteristics of the study cohort according to Clinical Frailty Score and Hospital Frailty Risk Score

	Clinical Frailty Score			Hospital Frailty Risk Score		
Variables	Non-frail (1-4) (N = 236) n (%)*	Frail (5-9) (N = 54)	*P* value	Low risk (<5) (N = 225)	Intermediate-high risk (≥5) (N = 65)	*P* value
Age in y, median (IQR)	61 (48-72)	87 (76-90)	**<.001**	61 (49-74)	78 (71-88)	**<.001**
Age group (y)			**<.001**			**<.001**
<50	62.(26.3)	0 (0.0)		57 (25.3)	5 (7.7)	
50-64	77 (32.6)	1 (1.9)		70 (31.1)	8 (12.3)	
65-79	73 (30.9)	17 (31.5)		64 (28.4)	26 (40.0)	
>80	24 (10.2)	36 (66.7)		34 (15.1)	26 (40.0)	
Men	144 (61.0)	27 (50.0)	.14	135 (60.0)	36 (55.5)	.51
Nosocomial infection	8 (3.4)	9 (16.7)	**<.001**	10 (4.4)	7 (10.8)	.056
Long-term care resident	5 (2.1)	17 (31.5)	**<.001**	10 (4.4)	12 (18.5)	**<.001**
Comorbidities						
Hypertension	103 (43.6)	42 (77.8)	**<.001**	101 (44.9)	44 (67.7)	**.001**
Diabetes	44 (18.6)	20 (37.0)	**.003**	41 (18.2)	23 (35.4)	**.003**
Cardiovascular disease	21 (8.9)	18 (33.3)	**<.001**	20 (8.9)	19 (29.2)	**<.001**
Chronic respiratory disease	41 (17.4)	18 (33.3)	**.009**	45 820.0)	14 (21.5)	.79
Charlson comorbidity index, median (IQR)	2 (1-4)	7.5 (6-9)	**<.001**	2 (1-5)	5 (4-7)	**<.001**
Clinical presentation						
Clinical duration, median (IQR)	7 (4-9)	3 (1-7)	**.001**	7 (4-9)	5 (1-7)	**.003**
Fever (N = 288)	185 (76.7)	22 (41.5)	**<.001**	167 (74.9)	40 (61.5)	**.035**
Dry cough (N = 287)	158 67.5)	19 (35.9)	**.001**	145 (65.0)	32 (50.0)	**.029**
Wet cough (N = 288)	43 (18.3)	8 (15.1)	.58	40 (17.9)	11 (16.9)	.85
Dyspnea (N = 288)	125 (53.4)	33 (61.1)	.31	122 (54.5)	36 (56.3)	.80
Asthenia (N = 275)	100 (44.6)	12 (23.5)	**.006**	91 (42.59)	21 (34.4)	.26
Diarrhoea (N = 283)	64 (27.8)	8 (15.4)	**.005**	58 (26.3)	14 (22.6)	.56
Confusion	15 (6.4)	21 (38.9)	**.001**	19 (8.4)	17 (26.2)	**<.001**
Myalgias-arthralgias (N = 279)	76 (33.3)	1 (2.0)	**<.001**	68 (31.2)	9 (14.8)	**.011**
Anosmia dysgeusia (N = 274)	30 (13.5)	3 (3.9)	.056	30 (14.0)	2 (3.3)	**.023**
Length of stay						
Days of admission, median (IQR)	9 (6-15)	7 (3-14)	**.023**	8 (5-12)	12 (7-26)	**<.001**
Days in intensive care unit, median (IQR)	11 (6.5-22)	15 (4–35)	.093	9 (4-13)	26 (16-43)	**<.001**
Days until death, median (IQR)	15 (9-28)	9 (5.0-15.2)	**.008**	12.5 (6.5-18.5)	11.0 (6.0-22)	.89

Abbreviation: IQR, interquartile range.

*Data shown as n (%) unless otherwise specified. In bold, statistically significant differences.

4 | DISCUSSION

This study compares two scales for measuring frailty in inpatients with COVID-19 and assesses their association with mortality and other severe adverse events. According to both scales, about one in every five adults admitted to our hospital with COVID-19 was frail. CFS-defined frailty was associated with in-hospital mortality, after adjusting for age, sex and eGFR, but not after adjusting for comorbidities (CCI), except in the "severe frailty" category. HFRS-defined frailty was not associated with in-hospital mortality.

TABLE 2 Outcomes according to frailty assessment scores

Outcome	Overall (n = 290)	Clinical Frailty Score			P value*	Hospital Frailty Risk Score			P value*
		No frailty (1-4) (n = 236)	Mild-to-moderate frailty (5-6) (n = 33)	Severe frailty (7-9) (n = 21)		Low risk (<5) (n = 225)	Intermediate risk (5-15) (n = 49)	High risk (>15) (n = 16)	
In-hospital mortality	48 (16.6)	19 (8.1)	15 (45.5)	14 (66.7)	**<.001**	29 (12.9)	15 (30.6)	4 (25.0)	**.007**
			Frail (5-9) (n = 54)				*Intermediate-high risk (≥5)*		
			29 (53.7)		***<.001***		*19 (29.2)*		***.002***
Treatment with tocilizumab	80 (27.6)	76 (32.2)	4 (12.1)	0 (0.0)	**.001**	59 (26.2)	17 (34.7)	4 (25.0)	.495
			4 (7.4)		***<.001***		*21 (32.3)*		*.334*
Hospital stay >10 days	131 (45.2)	109 (46.2)	15 (45.5)	7 (33.3)	.53	89 (39.6)	31 (63.3)	11 (68.8)	**.002**
			22 (40.7)		*.47*		*42 (64.6)*		***<.001***
Admission in intensive care unit	47 (16.2)	44 (18.6)	2 (6.1)	1 (4.8)	.062	30 (13.3)	12 (24.5)	5 (31.3)	**.039**
			3 (5.5)		***.019***		*17 (26.2)*		***.013***
Invasive mechanical ventilation	37 (12.8)	35 (14.8)	2 (6.1)	0 (0.0)	.070	22 (9.8)	11 (22.4)	4 (25.0)	**.018**
			3 (5.5)		***.027***		*15 (23.1)*		***.005***

*P values in bold are statistically significant. Comparisons of frailty categories by three categories (no frailty vs mild-to-moderate frailty vs severe frailty; low risk vs intermediate risk vs high risk) and by two categories (in italics: no frailty vs frailty; low risk vs intermediate-high risk).

Prevalence of frailty in COVID-19 patients depends on the scale used and the age of the sample population. Using the CFS, Poco et al[19] reported a prevalence of frailty in patients aged over 50 years of 25%, and Tehrani et al[18] in patients aged 65 years or older, of 50%. In patients admitted to a geriatric unit (median age 81 years), Hägg et al[12] found that 38% had a CFS of 6 or more, while Miles et al,[26] studying hospitalised patients aged over 70 years, reported a CFS of 5 or more in 53.5%. These results are consistent with ours; 18.6% were frail overall, but prevalence rose sharply with age, from 31.5% in the 65- to 79-year age group to 66.7% in those over 80 years.

In a national cohort of hospitalised patients aged 65 years or older with COVID-19, Kundi et al[14] reported that 67.4% of the 12 234 patients assessed with the HFRS qualified as frail (HFRS > 5), and 15.4% were categorised in the highest level of frailty (HFRS > 15). In our study, prevalence of frailty was lower (22.4%), probably because we included adults of all ages, not just those in older age groups.

It is clear that advanced age increases the risk of mortality and other adverse events in people with COVID-19,[12,17,27,28] just as it increases the risk of frailty. A substantial body of research also shows that frailty is independently associated with mortality, regardless of age.[17-19,29] Likewise, other studies in COVID-19 patients have also found that a CFS of 5 or higher increases the risk of mortality, especially in older people.[15,18,19,30,31] In fact, in the large scale, multicentre COVID-19 in Older People study in Europe, Hewitt et al[15] found that CFS level was a better predictor of outcomes than age or comorbidities. In our study, a CFS of 5 or higher was an independent prognostic factor for death, after adjusting for age, gender and kidney function.

However, the association between frailty and in-hospital mortality has not been universally observed. Miles et al[26] included 217 older people with COVID-19 and 160 older non-COVID-19 controls, while Owen et al[32] included older people with frailty, both with (n = 285) and without (n = 786) COVID-19; both studies reported that frailty was not a good predictor of prognosis in COVID-19. Similarly, Steinmeyer et al's[33] study, in three acute geriatric wards, screened 94 patients with COVID-19 for frailty using the Frail Non-Disabled survey, finding that frailty and geriatric characteristics were not correlated with mortality.

Using the HFRS, Kundi et al[14] observed in-hospital mortality rates of 12.0%, 18.2% and 31.0% in COVID-19 patients with low, intermediate and high hospital frailty risk, respectively. The authors concluded that HFRS provides clinicians and health systems with a standardised tool for effectively detecting and grading frailty in patients with COVID-19. However, our results were discordant and showed an unclear gradient of mortality risk: 12.9% in the low-risk group, 30.6% in the intermediate-risk group and 25% in the high-risk group. An HFRS of 5 or higher was not an independent prognostic factor for death, so these differences may be caused by the inclusion of patients with a wider age range or because of the small sample size (for example, we had only 16 patients in the high-risk category). However, like us, Hägg et al[12] also failed to find an independent association between the HFRS (as a continuous variable) and mortality.

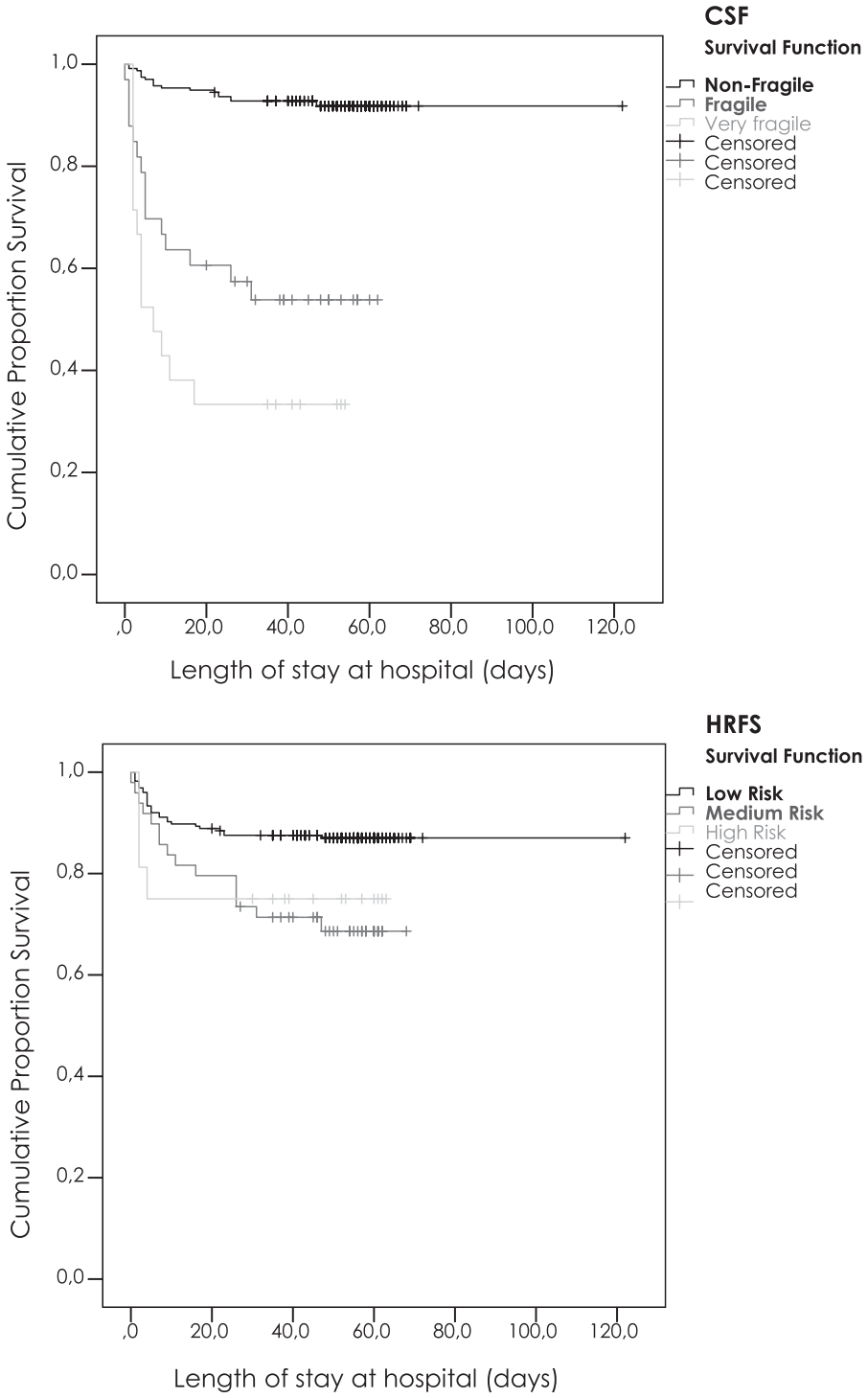

FIGURE 1 Kaplan–Meier survival plot for study outcomes. Small vertical tick marks indicate individual patients whose survival times have been right censored

The use of life-sustaining therapies (ICU admission, IMV and treatment with TCZ) was more limited in patients with CFS-defined frailty, but after adjusting for age, sex, kidney function and comorbidity, this difference was significant only for TCZ treatment. The limited use of TCZ treatment in the first COVID-19 wave in people with CFS-defined frailty could be caused by supply shortages, with physicians restricting its use to patients with no frailty or dependence. This may explain the relationship between greater frailty and less use of TCZ. In relation with ICU admission and IMV, Tehrani et al[18] assessed the number of patients for whom IMV therapy was withheld among survivors and non-survivors within the different CFS categories, finding that these decisions were based on futility rather than exhausted hospital capacity.

In our study, HFRS-defined frailty was associated with long hospital stay, ICU admission and use of IMV after adjusting for age, gender, kidney function and comorbidity. In contrast, CFS-defined frailty was not associated with long hospital stay, ICU admission or the use of IMV. These differences may be because the CFS measures clinical frailty based on the patient's abilities prior to admission, while HFRS-defined frailty is based on the diseases coded into

TABLE 3 Results of multivariable logistic regression analyses, according to Clinical Frailty Score

			Model A*		Model B†	
Outcome	**Crude OR (95% CIs)**	***P* value**	**aOR (95% CI)**	***P* value**	**aOR (95% CI)**	***P* value**
In-hospital mortality						
Continuous CFS	2.11 (1.70-2.62)	**<.001**	1.52 (1.17-1.97)	**.002**	1.30 (0.98-1.73)	.067
Categorical CFS						
No frailty (1-4) (*ref*)	1		1		1	
Mild-to-moderate frailty (5-6)	9.51 (4.19-21.83)	**<.001**	2.58 (0.93-7.13)	.066	1.82 (0.63-5.219	.26
Severe frailty (7-9)	22.84 (8.22-63.42)	**<.001**	6.66 (1.99-22.13)	**.002**	3.63 (1.03-12.73)	**.044**
Frailty (5-9)	13.24 (6.50-26.98)	**<.001**	3.67 (1.49-9.04)	**.005**	2.32 (0.0.90-5.99)	.080
Treatment with tocilizumab						
Continuous CFS	0.67 (0.54-0.83)	**<.001**	0.63 (0.46-0.86)	**.004**	0.71 (0.51-0.99)	**.049**
Categorical						
No frailty (1-4) (*ref*)	1		1		1	
Mild-to-moderate frailty (5-6)	0.29 (0.09-0.85)	**.025**	0.34 (0.10-1.11)	.074	0.45 (0.13-1.54)	.21
Severe frailty (7-9)	—	—	—	—	—	—
Frailty (5-9)	0.17 (0.06-0.48)	**.001**	0.19 (0.06-0.61)	**.005**	0.28 (0.08-0.93)	**.038**
Length of hospital stay >10 days						
Continuous CFS	1.00 (0.87-1.16)	.93	0.92 (0.75-1.19)	.43	0.96 (0.76-1.12)	.74
Categorical CFS						
No frailty (1-4) (*ref*)	1		1		1	
Mild-to-moderate frailty (5-6)	0.97 (0.46-2.01)	.94	0.72 (0.31-1.62)	.45	0.75 (0.31-1.81)	.53
Severe frailty (7-9)	0.58 (0.23-1.48)	.26	0.41 (0.14-1.16)	.095	0.44 (0.14-1.32)	.44
Frailty (5-9)	0.80 (0.44-1.46)	.47	0.58 (0.28-1.21)	.15	0.62 (0.28-1.36)	.24
Admission in intensive care unit						
Continuous CFS	0.77 (0.60-0.98)	**.039**	0.85 (0.65-1.18)	.35	0.95 (0.66-1.36)	.81
Categorical CFS						
No frailty (1-4) (*ref*)	1		1		1	
Mild-to-moderate frailty (5-6)	0.28 (0.65-1.22)	.09	0.40 (0.08-1.98)	.27	0.50 (0.09-2.57)	.41
Severe frailty (7-9)	0.21 (0.03-1.66)	.14	0.36 (0.04-2.53)	.27	0.46 (0.05-3.82)	.45
Frailty (5-9)	0.25 (0.07-0.86)	**.028**	0.36 (0.09-1.39)	.14	0.41 (0.11-1.94)	.31
Invasive mechanical ventilation						
Continuous CFS	0.69 (0.51-0.94)	**.019**	0.68 (0.44-1.04)	.079	0.82 (0.51-1.31)	.41
Categorical CFS						
No frailty (1-4) (*ref*)	1		1			
Mild-to-moderate frailty (5-6)	0.37 (0.08-1.61)	.19	0.51 (0.10-2.60)	.42	0.84 (0.15-4.17)	.85

(Continues)

TABLE 3 (Continued)

Outcome	Crude OR (95% CIs)	*P* value	Model A* aOR (95% CI)	*P* value	Model B† aOR (95% CI)	*P* value
Severe frailty (7-9)	—	—	—	—	—	—
Frailty (5-9)	0.22 (0.05-0.94)	**.042**	0.29 (0.06-1.45)	.13	0.55 (0.10-3.12)	.51

Abbreviations: aOR, adjusted odds ratio (OR); CFS, Clinical Frailty Score; CI, confidence interval.

* Adjusted for age, gender and estimated glomerular filtration rate (eGFR).

† Adjusted for age, gender, eGFR and Charlson comorbidity index.

Bold indicates statistically significant differences.

the hospital database. The patients who were admitted to the ICU and received IMV had a higher number of diagnostic codes on discharge, some of which are included in the HFRS. The coding was higher in patients with longer stays, who were admitted to the ICU or required IMV. Thus, the relationship of these two measures of frailty with outcomes was fundamentally different.

Finally, we compared the two different frailty measurements as predictors of adverse outcomes. Although agreement between the HFRS and CFS was only moderate, it was higher than in the study by Gilbert et al,[21] describing the development and validation of the HFRS in older people. We also observed good correlation between the two measures in COVID-19 patients, better than that found in other research ($r_s = 0.345$).[12]

Our results should be interpreted in light of the study's limitations. First of all, the CFS was evaluated retrospectively, so its calculation relied on information obtained from electronic health records,[18] which may have resulted in an underestimation of prevalence. However, several published studies have also used retrospective methods for assessing the CFS.[18,19] Secondly, it is unclear whether the HFRS is a true measure of frailty or rather a complex comorbidity index[14]; like Kundi et al,[6] we opted for the former application. Another limitation, derived from the retrospective nature of the study, is the potential misclassification of administrative coding for some comorbidities and complications compared with prospective collection using standard clinical trial definitions.[14] Moreover, patients admitted to the ICU may have more codes registered because of complexity, causing an overestimation bias for frailty in patients admitted to the ICU. A fourth limitation is that the HFRS and CFS have not been validated in younger adults. That said, the CFS at least has been used in younger populations, as reported by Hewitt et al[15] Finally, this is a single-centre study, so caution is warranted when extrapolating our results to other healthcare settings.

5 | CONCLUSIONS

In this study of COVID-19 patients admitted to a university hospital in Spain, we found that CFS-defined frailty was a prognostic factor for death, after adjusting for age, gender and kidney function. Moreover, frailty was associated with limited use of TCZ treatment during the spring 2020 wave of the pandemic. On the other hand, and unlike the HFRS, the CFS was not associated with length of hospital stay, ICU admission or use of IMV. On the basis of our results and those published in the literature,[12,15,16,18,19,30] CFS should be part of a decision-making process with COVID-19, especially in older patients.

Further, multicentre and prospective studies are necessary to determine the real relevance of frailty for the prognosis and other outcomes in people with COVID-19.

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TABLE 4 Results of multivariable logistic regression analyses, according to Hospital Frailty Risk Score

			Model A[a]		Model B[b]	
Outcome	**Crude OR (95% CI)**	***P* value**	**aOR (95% CI)**	***P* value**	**aOR (95% CI)**	***P* value**
In-hospital mortality						
Continuous HFRS	1.08 (1.03-1.14)	**.002**	0.98 (0.92-1.05)	.70	0.98 (0.92-1.05)	.63
Categorical HFRS						
Low risk (<5) (*ref*)	1					
Intermediate risk (5-15)	2.98 (1.44-6.13)	**.003**	1.26 (0.52-3.01)	.60	1.29 (0.50-3.15)	.62
High risk (>15)	2.53 (0.68-7.45)	.18	0.58 (0.14-2.46)	.47	0.58 (0.14-2.238)	.46
Intermediate-high risk (≥5)	2.79 (1.44-5.41)	**.002**	1.05 (0.47-2.36)	.88	1.02 (0.44-2.38)	.95
Treatment with tocilizumab						
Continuous HFRS	1.15 (0.73-1.80)	.53	1.34 (0.81-2.23)	.25	1.50 (0.88-2.53)	.13
Categorical HFRS						
Low risk (<5) (*ref*)	1		1		1	
Intermediate risk (5-15)	1.49 (0.77-2.89)	.23	2.17 (1.06-4.49)	**.036**	0.45 (0.13-1.54)	.20
High risk (>15)	0.93 (0.29-3.02)	.91	0.93 (0.23-3.66)	.91	—	—
Intermediate-high risk (≥5)	1.34 (0.73-2.44)	.34	1.83 (0.93-3.60)	.079	2.08 (1.03-4.19)	**.040**
Length of hospital stay >10 days						
Continuous HFRS	1.11 (1.05-1.18)	**<.001**	1.12 (1.05-1.20)	**.001**	1.12 (1.05-1.21)	**.001**
Categorical HFRS						
Low risk (<5) (*ref*)	1		1		1	
Intermediate risk (5-15)	2.63 (1.38-4.98)	**.003**	2.79 (1.41-5.52)	**.003**	2.84 (1.43-5.65)	**.003**
High risk (>15)	3.36 (1.13-10.0)	**.029**	2.91 (0.091-9.32)	.071	3.05 (0.92-9.78)	.061
Intermediate-high risk (≥5)	2.79 (1.57-4.98)		2.89 (1.53-5.28)	**.001**	2.89 (1.53-5.44)	**.001**
Admission in intensive care unit						
Continuous HFRS	1.08 (1.02-1.14)	**.003**	1.14 (1.06-1.22)	**<.001**	1.15 (1.07-1.24)	**<.001**
Categorical HFRS						
Low risk (<5) (*ref*)	1		1		1	
Intermediate risk (5-15)	2.18 (0.99-4.49)	.053	3.66 (1.54-8.67)	**.003**	3.97 (1.63-9.42)	**.002**
High risk (>15)	2.98 (0.98-9.09)	.059	4.43 (1.15-17.08)	**.030**	5.35 (1.339-21.38)	**.018**
Intermediate-high risk (≥5)	2.30 (1.17-4.51)	**.015**	3.82 (1.17-8.52)	**.001**	4.18 (1.84-9.52)	**.001**
Invasive mechanical ventilation						
Continuous HFRS	1.08 (1.02-1.14)	**.004**	1.13 (1.06-1.22)	**<.001**	1.16 (1.08-1.25)	**<.001**
Categorical HFRS						
Low risk (<5) (*ref*)	1		1		1	
Intermediate risk (5-15)	2.67 81.19-5.95)	**.016**	4.77 (1.88-12.11)	**.001**	5.86 (2.20-15.62)	**<.001**
High risk (>15)	3.07 (0.91-10.35)	**.070**	4.08 (0.93-18.299)	**.066**	6.24 (1.27-30.90)	**.024**
Intermediate-high risk (≥5)	2.78 (1.34-5.71)	**.006**	4.62 (1.92-11.09)	**.001**	5.93 (2.33-15.10)	**<.001**

Abbreviations: aOR, adjusted odds ratio (OR); CI, confidence interval; HFRS, Hospital Frailty Risk Score.

[a] Adjusted for age, gender and estimated glomerular filtration rate (eGFR).

[b] Adjusted for age, gender, eGFR and Charlson comorbidity index.

Bold indicates statistically significant differences.

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DISCLOSURES

The authors declare no conflict of interest.

ETHICAL ASPECTS

The institutional review board approved the study; as it was retrospective, the requirement to obtain informed consent from participants was waived (EXP. 200145). The research was conducted according to the principles of the Declaration of Helsinki.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the Supporting Information section.

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