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

Jose-Manuel Ramos-Rincon1,2 | Oscar Moreno-Perez2,3  |
Hector Pinargote-Celorio4 | Jose-Manuel Leon-Ramirez5  |
Sergio Reus2,4 | Cristian Herrera-García1  |
Jose Gil5 | Rosario Sanchez-Martinez1  |
the COVID-19 ALC Research Group

1Internal Medicine Department, Alicante General University Hospital—Alicante Institute of Sanitary and Biomedical Research (ISABIAL), Alicante, Spain  
2Clinical Medicine Department, Miguel Hernández University, Elche, Spain  
3Endocrinology and Nutrition Department, Alicante General University Hospital—Alicante Institute of Sanitary and Biomedical Research (ISABIAL), Alicante, Spain  
4Infectious Diseases Unit, Alicante General University Hospital—Alicante Institute of Sanitary and Biomedical Research (ISABIAL), Alicante, Spain  
5Pneumology Department, Alicante General University Hospital—Alicante Institute of Health and Biomedical Research (ISABIAL), Alicante, Spain  
6Rheumatology Department, Alicante General University Hospital Alicante Institute of Health and Biomedical Research (ISABIAL), Alicante, Spain  

Correspondence  
Jose-Manuel Ramos-Rincon, Internal Medicine Department, Alicante General University Hospital-ISABIAL, Alicante, Spain.  
Email: jose.ramosr@umh.es

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.
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.” Fried et al. 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).

Frailty is a reliable measure for predicting clinical and healthcare-related outcomes in people with different conditions. However, the notion of frailty as a predictor of adverse outcomes in older patients with coronavirus disease 2019 (COVID-19) remains unclear. Existing studies have been heterogeneous in terms of the frailty measures used, clinical context, design, definition of adverse outcomes and results. The Clinical Frailty Score (CFS) 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). 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 and the HFRS, 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.

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. 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. 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. 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.

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. 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). 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.\textsuperscript{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.\textsuperscript{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 $\chi^2$ 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 HFRS was moderate ($r_s = 0.51$, $P < .001$), between the CFS and CCI, high ($r_s = 0.79$, $P < .001$), between the HFRS 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).
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                       | Clinical Frailty Score | Hospital Frailty Risk Score |
|-------------------------------|------------------------|----------------------------|
|                               | Overall (n = 290)      | Low risk (<5) (n = 225)    |
|                               | No frailty (1-4)       | Intermediate risk (5-15) (n = 49) |
|                               | Mild-to-moderate frailty (5-6) (n = 33) | High risk (>15) (n = 16) |
|                               | Severe frailty (7-9) (n = 21) | P value*                  |
| In-hospital mortality         | 48 (16.6)              | 29 (12.9)                  | .007                      |
|                               | 19 (8.1)               | 15 (30.6)                  |                           |
|                               | 15 (45.5)              | 14 (66.7)                  | <.001                     |
|                               | 29 (33.7)              | P value*                  |                           |
| Treatment with tocilizumab    | 80 (27.6)              | 59 (26.2)                  | .002                      |
|                               | 76 (32.2)              | 17 (34.7)                  |                           |
|                               | 4 (12.1)               | 4 (25.0)                   | .495                      |
|                               | 4 (7.4)                | P value*                  |                           |
| Hospital stay >10 days        | 131 (45.2)             | 89 (39.6)                  | .002                      |
|                               | 109 (46.2)             | 31 (63.3)                  |                           |
|                               | 15 (45.5)              | 11 (68.8)                  |                           |
| Admission in intensive care unit | 47 (16.2)           | 42 (64.6)                  | .002                      |
|                               | 44 (18.6)              | 17 (26.2)                  |                           |
|                               | 2 (6.1)                | .019                      |                           |
|                               | 3 (5.5)                |                           |                           |
| Invasive mechanical ventilation | 37 (12.8)            | 30 (13.3)                  | .039                      |
|                               | 35 (14.8)              | 12 (24.5)                  |                           |
|                               | 2 (6.1)                | 5 (31.3)                   |                           |
|                               | 3 (5.5)                | .013                      |                           |

*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).

---

It is clear that advanced age increases the risk of mortality, as evidenced by the findings of several studies. In the study conducted by Hägg et al.,\(^{15,18,19}\) the prevalence of frailty in patients aged 65 years or older was 30.6%, in the intermediate-risk group, and 25% in the high-risk group. However, the association between frailty and mortality was not observed in the low-risk group, suggesting that frailty may not be a significant predictor of mortality in younger age groups. Similarly, Steinhauer et al.\(^{33}\) observed that frailty was associated with mortality in hospitalised patients with COVID-19. Interestingly, recent studies have shown that frailty is independently associated with mortality, even in older people.\(^{15-19,22}\) However, the association between frailty and mortality is not universal, and further research is needed to elucidate the complex relationship between frailty and mortality in different populations.

---

Prevalence of frailty in COVID-19 patients depends on the scale used and the age of the sample population. Using the CFS, Pocock et al.\(^{25}\) reported a prevalence of frailty in patients aged 65 years or older of 25%, and Tehraniet al.\(^{26}\) reported a prevalence of frailty in patients aged 65 years or older of 50%. In our study, we found that 38% of patients had a CFS of 5 or more, while Miles et al.\(^{32}\) reported that 67.4% of the 12,234 patients admitted to a geriatric unit (median age 81 years) were in the high-risk group, and 33% were in the intermediate-risk group. These results are consistent with our findings, indicating that frailty is a significant predictor of mortality in COVID-19 patients, especially in older age groups. However, the age-related difference in frailty prevalence highlights the importance of considering age as a confounding factor in mortality analysis.

---

Despite the known association between frailty and mortality, the impact of frailty on other outcomes, such as hospital stay and admission to intensive care, remains unclear. In our study, we observed significant differences in hospital stay and admission to intensive care between frailty categories. However, further research is needed to explore the mechanisms underlying these associations and to develop effective interventions to mitigate the adverse outcomes associated with frailty in COVID-19 patients.
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.\textsuperscript{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

| Outcome                      | Crude OR (95% CIs) | P value | Model A | aOR (95% CI) | P value | Model B† | 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   | <.001   | 2.58    | 0.93-7.13   | .066    | 1.82     | 0.63-5.219  | .26     |
| Severe frailty (7-9)         | 22.84 (4.19-21.83) | <.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     | 0.09-5.99   | .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 CFS              |                    |         |         |             |         |          |             |         |
| No frailty (1-4) (ref)       | 1                  |         | 1       |             |         | 1        |             |         |
| Mild-to-moderate frailty (5-6)| 0.29  | .025    | 0.34    | 0.10-1.11   | .74     | 0.45     | 0.13-1.54   | .21     |
| Severe frailty (7-9)         | — — — — — —        |         | — —     | — —        |         | 0.44     | 0.14-1.32   | .44     |
| 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  | .94     | 0.72    | 0.31-1.81   | .53     | 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  | .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       |             |         | 1        |             |         |
| Mild-to-moderate frailty (5-6)| 0.37  | .19     | 0.51    | 0.10-2.60   | .42     | 0.84     | 0.15-4.17   | .85     |

(Continues)
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, 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.\(^{(15)}\)

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, 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; 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.

ACKNOWLEDGEMENTS

We acknowledge the members of the COVID-19 ALC Research Group: Esperanza Merino, Joan Gil, Vicente Boix, Ximo Portilla, Oscar Moreno-Pérez, Mariano Andrés, Jose-Manuel Leon-Ramirez, Santos Asensio, Cleofé Fernandez, Alfredo Candela, Mª del Mar García, Rosario Sánchez, Diego Torrus, Sergio Reus, Pilar González, Silvia Otero, Jose M Ramos, Beatriz Valero, Alex Scholz, Antonio Amo, Héctor Pinargote, Paloma Ruiz, Raquel García-Sevila, Ignacio Gayá, Violeta Esteban, Isabel Ribes, Julia Portilla, Cristina Herreras, Alejando Cintas, Alicia Ferradas, Ana Marti, Blanca Figueres, Marcelo Giménez, María-Ángeles Martínez, María-Mar García-Mullor, María Angeles Martínez, Irene Calabuig, Marisa Peral, Ernesto Tovar, M Carmen López, Paloma Vela, Pilar Bernabéu, Ana Yuste, José Ponce, Bertomeu Massuti, Vicente Climent, Vicente Arrarte, Fernando Torres, Laura Valverde, Laura Delegido, Cristina Cambra, Miriam Sandín, Teresa Lozano, Amaya García-Fernández, Alejandro Do Campo, Eduardo Vergara, Nicolás López, Elena Elvira, Fátima López, Fernando Dahl, Blanca Serrano, Sarai Moliner, Carmína Díaz, Dolores Cañaño, Beatriz López, Antonio Picó, Joaquín Serrano, Sol Serrano, María Marín-Barnuevo, María Diaz, Cristina Gilbert, Estela Martínez, Elena Vivó, Noelia Balibre, Miguel Perdigueru, Carolina Mangas, Lucía Medina, Oscar Murcia, María Rodríguez, Rodrigo Jover, Javier López, Marina Morillas, Mercedes Khartabil, Cristina Gil, Carlos Salazar, Eva Vera, Helena López, Vanesa Rodríguez, Sandra Baile, Norma Guerra, Mar Blanes, Jaime Guijarro, José Carlos Pascual, Iris Gonzalez, Pedro Sanso, José Manuel Ramos, Jaime Javaloy, Clara Llopis, Olga Coronado, Esther García, Gonzalo Rodríguez, Paola Melgar, Mariano Franco, Félix Lluis, Carmen Zaragoza, Cándido Alcaraz, Ana Carrón, Celia Vilodre, Emilio Ruiz de la Cuesta, Cristina Alenda, Francisca Peiró, María Planelles,
### Table 4: Results of multivariable logistic regression analyses, according to Hospital Frailty Risk Score

| Outcome | Crude OR (95% CI) | P value | Model A<sup>a</sup> |          | Model B<sup>b</sup> |          |
|---------|-------------------|---------|---------------------|---------|---------------------|---------|
|         |                   |         | 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 (0.14-2.38) | .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 |         |                  |         |                  |         |
| 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 | 0.58 (0.14-2.23) | .46 |
| 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 |         |                  |         |                  |         |
| 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 (0.91-9.32) | .071 | 3.05 (0.92-9.78) | .061 |
| Intermediate-high risk (<5) | 2.79 (1.57-4.98) | .002 | 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 |         |                  |         |                  |         |
| 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 (1.33-21.38) | .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 |         |                  |         |                  |         |
| 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.

<sup>a</sup> Adjusted for age, gender and estimated glomerular filtration rate (eGFR).

<sup>b</sup> Adjusted for age, gender, eGFR and Charlson comorbidity index.

Bold indicates statistically significant differences.

Laura Greco, Sandra Silvia, Antonio Francia, Iván Verdú, Juan Sales, Ana Palacios, Hortensia Ballester, Antonio García-Valentín, Marta Márquez, Eva Canelo, Andrea Juan, Elena Vives, Andrea Revert, Gonzalo Fuente, Ester Nofuentes, Carolina Mangas, Eva Vera, Alicia Ferradas, Helena López, Cristian Herrera, Beatriz López, Marina Morillas, Vanesa Rodríguez, Mercedes Khartabil, Mario Giménez, Ernesto Tovar, Estela Martínez, Lucía Medina, Sandra Baile, Carlos Salazar, Norma Guerra, Sarai Moliner, Mari-Carmen López-González and Blanca Figueres.

**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.

REFERENCES
1. Morley JE, Vellas B, Abellan van Kan G, et al. Frailty consensus: a call to action. J Am Med Dir Assoc. 2013;14(6):392-397. https://doi.org/10.1016/j.jamda.2013.03.022
2. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56(3):M146-M156. https://doi.org/10.1093/gerona/56.3.m146
3. Rockwood K, Mitnitski A. Frailty in relation to the accumulation of deficits. J Gerontol A Biol Sci Med Sci. 2007;62(7):722-727. https://doi.org/10.1093/gerona/62.7.722
4. Kundi H, Wadhra RK, Strom JB, et al. Association of frailty with 30-day outcomes for acute myocardial infarction, heart failure, and pneumonia among elderly adults. JAMA Cardiol. 2019;4(11):1084-1091. https://doi.org/10.1001/jamacardio.2019.3511
5. Hewitt J, Carter B, McCarthy K, et al. Frailty predicts mortality in all emergency surgical admissions regardless of age. An observational study. Age Ageing. 2019;48(3):388-394. https://doi.org/10.1093/ageing/afy217
6. Kundi H, Popma JJ, Reynolds MR, et al. Frailty and related outcomes in patients undergoing transcatheter valve therapies in a nationwide cohort. Eur Heart J. 2019;40(27):2231-2239. https://doi.org/10.1093/eurheartj/ehz187
7. Moog S, Carter B, Myint PK, Hewitt J, McCarthy K, Pearce L. Decision-making in COVID-19 and frailty. Geriatr. 2020;5(2):30. https://doi.org/10.3390/GERIATRICSS020030
8. Boreskiv KF, Boreskiv PE, Melady D. Age is just a number – and so is frailty: strategies to inform resource allocation during the COVID-19 pandemic. Can J Emerg Med. 2020;22(4):411-413. https://doi.org/10.1017/cem.2020.358
9. Bellelli G, Rebora P, Valsecchi MG, et al. Frailty index predicts poor outcome in COVID-19 patients. Intensive Care Med. 2020;46(8):1634-1636. https://doi.org/10.1007/s00134-020-06087-2
10. Malteese G, Corsonello A, Di Rosa M, et al. Frailty and COVID-19: a systematic scoping review. J Clin Med. 2020;9(7):2106. https://doi.org/10.3390/jcm9072106
11. Petermann-Rocha F, Hanlon P, Gray SR, et al. Comparison of two different frailty measurements and risk of hospitalisation or death from COVID-19: findings from UK Biobank. BMC Med. 2020;18(1):355. https://doi.org/10.1186/s12916-020-01822-4
12. Hägg S, Jyllhävä J, Wang Y, et al. Age, frailty, and comorbidity as prognostic factors for short-term outcomes in patients with coronavirus disease 2019 in geriatric care. J Am Med Dir Assoc. 2020;21(11):1555-1559.e2. https://doi.org/10.1016/j.jamda.2020.08.014
13. Shi SM, Bakaev I, Chen H, Travison TG, Berry SD. Risk factors, presentation, and course of coronavirus disease 2019 in a large, academic long-term care facility. J Am Med Dir Assoc. 2020;21(10):1378-1383.e1. https://doi.org/10.1016/j.jamda.2020.08.027
14. Kundi H, Cetin EHO, Canpolat U, et al. The role of frailty on adverse outcomes among older patients with COVID-19. J Infect. 2020;81(6):944-951. https://doi.org/10.1016/j.jinf.2020.09.029
15. Hewitt J, Carter B, Vilches-Moraga A, et al. The effect of frailty on survival in patients with COVID-19 (COPE): a multicentre, European, observational cohort study. Lancet Public Health. 2020;5(8):e444-e451. https://doi.org/10.1016/S2468-2667(20)30146-8
16. Conway J, Gould A, Westley R, et al. Clinical characteristics and progression of COVID-19 confirmed cases admitted to a single British clinical centre—a brief case series report. Int J Clin Pract. 2021;75(3):e13807. https://doi.org/10.1111/ijcpr.13807
17. Chinnadurai R, Ogedengbe O, Agarwal P, et al. Older age and frailty are the chief predictors of mortality in COVID-19 patients admitted to an acute medical unit in a secondary care setting- a cohort study. BMC Geriatr. 2020;20(1):409. https://doi.org/10.1186/s12877-020-01803-5
18. Tehrani S, Killander A, Åstrand P, Jakobsson J, Gille-Johnson P. Risk factors for death in adult COVID-19 patients: frailty predicts fatal outcome in older patients. Int J Infect Dis. 2021;102:415-421. https://doi.org/10.1016/j.ijid.2020.10.071
19. Poco PCE, Alberti MJR, Dias MB, et al. Divergent: age, frailty, and atypical presentations of COVID-19 in hospitalized patients. J Gerontol A Biol Sci Med Sci. 2021;75(3):e46-e51. https://doi.org/10.1093/gerona/glaa280
20. Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. Canadian Medical Association Journal. 2005;173(5):489-495. https://doi.org/10.1503/cmaj.050051
21. Gilbert T, Neuburger J, Krandidler J, et al. Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. Lancet. 2018;391(10132):1775-1782. https://doi.org/10.1016/S0140-6736(18)30668-8
22. Rgy J, Engberg H, Mariadas P, et al. Barthel index at hospital admission is associated with mortality in geriatric patients: a Danish nationwide population-based cohort study. Clin Epidemiol. 2018;10:1789-1800. https://doi.org/10.2147/CLEP.S176035
23. Moreno-Pérez O, Andres M, Leon-Ramirez JM, et al. Experience with tocilizumab in severe COVID-19 pneumonia after 80 days of follow-up: a retrospective cohort study. J Autoimmun. 2020;114:102523. https://doi.org/10.1016/j.jaut.2020.102523
24. Moreno-P O, Leon-Ramirez FM, Fuertes-Kenney L, et al. Hypokalemia as a sensitive biomarker of disease severity and the requirement for invasive mechanical ventilation requirement in COVID-19 pneumonia: a case series of 306 Mediterranean patients. Int J Infect Dis. 2020;100:449-454. https://doi.org/10.1016/j.ijid.2020.09.033
25. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373-383. https://doi.org/10.1016/0021-9681(87)90171-8
26. Miles A, Webb TE, Mcloughlin BC, et al. Outcomes from COVID-19 across the range of frailty: excess mortality in fitter older people. Eur Geriatr Med. 2020;11(5):851-855. https://doi.org/10.1007/s41999-020-00354-7
27. Docherty AB, Harrison EM, Green CA, et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical
31. Moledina SM, Maini AA, Gargan A, et al. Clinical characteristics and predictors of mortality in patients with COVID-19 infection outside intensive care. Int J Gen Med. 2020;13:1157-1165. https://doi.org/10.2147/IGM.S271432

32. Owen RK, Conroy SP, Taub N, et al. Comparing associations between frailty and mortality in hospitalised older adults with or without COVID-19 infection: a retrospective observational study using electronic health records. Age Ageing. 2020;50(2):307-316. https://doi.org/10.1093/ageing/afaa167

33. Steinmeyer Z, Vienne-Noyes S, Piau A, et al. Acute care of older patients with COVID-19: clinical characteristics and outcomes. Geriatr. 2020;5(4):1-11. https://doi.org/10.3390/geriatrics5040065

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

How to cite this article: Ramos-Rincon J-M, Moreno-Perez O, Pinargote-Celorio H, et al; the COVID-19 ALC Research Group. Clinical Frailty Score vs Hospital Frailty Risk Score for predicting mortality and other adverse outcome in hospitalised patients with COVID-19: Spanish case series. Int J Clin Pract. 2021;75:e14599. https://doi.org/10.1111/ijcp.14599