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## Letter to the Editor: Premorbid Frailty is a Better Prognostic Indicator Than Age in Oldest-Old Hospitalized With COVID-19



### To the Editor:

Older people have a higher susceptibility for coronavirus disease 2019 (COVID-19) and a higher risk of developing severe COVID-19 symptoms and mortality.<sup>1</sup> Current studies examining the relation between outcome and frailty in COVID-19 show contrasting results<sup>2–7</sup>; however, these studies did not include illness severity as an effect. We conducted a multicenter cohort study in patients aged 80 years and older who were admitted with COVID-19 to 10 different acute hospitals in March and April 2020 in order to better understand the relation between frailty and in-hospital mortality combined with respiratory failure.

In this cohort of 711 persons aged 80 and older hospitalized with COVID-19, one-third came from a nursing home. Median premorbid Clinical Frailty Score (CFS)<sup>8</sup> was 7 (severely frail) on a scale that ranged from 1 (least frail) to 9 (greatest frailty). Comorbidities were frequent: more than 80% had cardiovascular disease and about 40% dementia, metabolic, and/or chronic kidney disease. Overall, observed all-cause in-hospital mortality was 34.6% (246/711) and did not differ between home-dwelling (150/447, 33.6%) vs patients admitted from a nursing home (96/264, 36.4%) ( $P = .757$ ). Forty-seven percent of the cohort developed respiratory failure. In Table 1, the observed all-cause in-hospital mortality in relation to frailty, respiratory failure, and intensive care unit (ICU) treatment are shown.

By means of a generalized estimating equation model, we compared the odds of mortality between older patients with different premorbid CFS and with and without respiratory failure during hospitalization. We found a significant interaction between CFS and respiratory failure ( $P = .027$ ). For every increase in CFS, the odds ratio (OR) for mortality was 2.185 [95% confidence interval (CI) 1.469, 3.249] in the oldest old not developing respiratory failure vs 1.333 (95% CI 1.054, 1.687) in respiratory failure. Other variables significantly associated were variables reflecting the severity of respiratory failure (peripheral oxygen saturation ( $P < .001$ , OR 0.918, 95% CI 0.883, 0.954), amount of supplemental oxygen delivery ( $P < .001$ , OR 1.227, 95% CI 1.154, 1.304) and complications acute renal failure ( $P = .035$ , OR 1.715, 95% CI 1.038, 2.836) and septic shock ( $P < .001$ , OR 15.713, 95% CI 4.12, 59.927). Baseline patient characteristics age category (80–84, 85–89, 90+), gender, residence (nursing home vs home-dwelling), number of comorbidities, and ICU treatment ( $P = .33$ , OR 1.981, 95% CI 0.501,

**Table 1**  
In-Hospital Mortality Related to Premorbid Clinical Frailty Scale Score, Respiratory Failure, and ICU Treatment in 710 Hospitalized Patients Aged 80 Years or Older

| Premorbid Clinical Frailty Scale | Total Cohort:<br>Total Mortality<br>Overall,<br>n/n (%) | No Respiratory Failure<br>(n=373)                     |                                    |   | Respiratory Failure*<br>(n=337)                    |                                     |   |
|----------------------------------|---|---|------------------------------------|---|--|-------------------------------------|---|
|                                  |   | Total Mortality<br>No Respiratory Failure,<br>n/n (%) | ICU Admission,<br>n/n (%)<br>(n=7) | No ICU Admission,<br>n/n (%)<br>(n=366) | Total Mortality<br>Respiratory Failure,<br>n/n (%) | ICU Admission,<br>n/n (%)<br>(n=45) | No ICU Admission,<br>n/n (%)<br>(n=292) |
| 1: very fit                      | 0/8<br>(0)  | 0/4<br>(0)  | 0/1<br>(0)                         | 0/3<br>(0)                              | 0/4<br>(0)   | 0/4<br>(0)                          | —                                       |
| 2: fit                           | 9/28<br>(32.1)  | 0/13<br>(0)   | —                                  | 0/13<br>(0)                             | 9/15<br>(60.0)                                     | 6/9<br>(66.7)                       | 3/6<br>(50.0)                           |
| 3: managing well                 | 18/64<br>(28.0)   | 0/34<br>(0)   | 0/1<br>(0)                         | 0/33<br>(0)                             | 18/30<br>(60.0)                                    | 6/8<br>(75.0)                       | 12/22<br>(54.5)                         |
| 4: vulnerable                    | 32/86<br>(37.2)   | 2/36<br>(5.6)   | 0/1<br>(0)                         | 2/35<br>(5.7)                           | 30/50<br>(60.0)                                    | 9/12<br>(75.0)                      | 21/38<br>(55.3)                         |
| 5: mildly frail                  | 35/119<br>(29.4)  | 5/64<br>(7.8)   | 2/2<br>(100)                       | 3/62<br>(4.8)                           | 30/55<br>(54.5)                                    | 3/6<br>(50.0)                       | 27/49<br>(55.1)                         |
| 6: moderately frail              | 62/191<br>(32.5)  | 16/112<br>(14.3)                                      | 1/1<br>(100)                       | 15/111<br>(13.5)                        | 46/79<br>(58.2)                                    | 4/5<br>(80.0)                       | 42/74<br>(56.8)                         |
| 7: severely frail                | 74/195<br>(37.9)  | 14/99<br>(14.1)                                       | 0/1<br>(0)                         | 14/98<br>(14.1)                         | 60/96<br>(62.5)                                    | 1/1<br>(100)                        | 59/95<br>(62.1)                         |
| 8: very severely frail           | 13/16<br>(81.3)   | 6/8<br>(75.0)   | —                                  | 6/8<br>(75.0)                           | 7/8<br>(87.5)                                      | —                                   | 7/8<br>(87.5)                           |
| 9: terminally ill                | 2/3<br>(66.7)   | 2/3<br>(66.7)   | —                                  | 2/3<br>(66.7)                           | —  | —                                   | —                                       |
| P value                          | .005  | <.001   |                                    |   | .18  |                                     |   |

1 missing on Clinical Frailty Score, P values: GEE model with random effect for hospital, unadjusted for other demographic and clinical characteristics.

\*Criteria for respiratory failure were as follows: Pao<sub>2</sub> ≤60 mmHg and/or low Spo<sub>2</sub> (≤90% with supplemental oxygen or ≤88% without supplemental oxygen) and/or in need of more than 5 L/min oxygen supplementation.

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7.834) were not significantly associated with in-hospital mortality.

Importantly, neither age category nor residence but premorbid frailty was associated with in-hospital mortality. The association between frailty and in-hospital mortality was more pronounced in the oldest old without respiratory failure. Hospitalized patients with CFS 8-9 had high odds of dying, even when there was no respiratory failure. This may support that hospital referral of people with CFS 8-9 might only be appropriate if supportive or palliative care is insufficient in the (nursing) home or if requested by the individual.

For older people living with CFS 1-7, hospital referral can be medically appropriate when supportive measures are insufficient in the (nursing) home; however clinicians should timely (preferably before hospital admission) think about whether or not to escalate care when respiratory failure develops. Octogenarians in this cohort who developed respiratory failure had an in-hospital mortality of about 60%. The results of this study point in the direction that the severity of the acute (pulmonary) reaction is predominant in determining the short-term outcome in the older person with COVID-19. We also found that ICU treatment was not associated with improved outcome either in the frail or in the fit oldest old in this study.

In short, premorbid frailty is associated with in-hospital mortality in particular in moderate COVID-19 disease. No benefit from ICU treatment could be shown in frail older persons developing respiratory failure due to COVID-19. These study results help inform advance care planning in the nursing home.<sup>9,10</sup>

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