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SHORT SCIENTIFIC REPORT

Baseline functional status impairment as a factor predictive of a poor benefit of ICU admission in patients aged over 80 years with severe acute respiratory syndrome coronavirus 2 infection

The frailty-ICU-elderly-COVID (FRICE-CoV) study

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Editor,

Both age and frailty have been associated with high mortality among intensive care unit (ICU) patients.[1] The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic and the associated risk of ICU bed shortage have raised many ethical issues, especially regarding ICU admission of older and/or frail patients.[2] A recent study highlighted the poor prognosis of patients aged over 80 years presenting SARS-CoV-2 infection with a functional impairment corresponding to any impairment in the Instrumental Activities of Daily Living (IADL) score on admission to an ICU.[3] In a recent review, Guidet *et al.*[4] reiterated the importance of functional assessment of very old patients before the ICU admission. For other authors, age *per se* may be used as a selection criterion in times of scarcity of ICU facilities.[2] In the specific context of SARS-CoV-2 infection, as both functional reserve and immune system capacity were deemed to be insufficient to overcome the consequences of a foreseeably prolonged ICU stay,[5,6] old patients were sometimes alternatively maintained in a conventional unit with oxygen, physiotherapy and palliative care provided if necessary. This approach was mandatory in our university hospital during the first wave of the pandemic as its capacities were overwhelmed. During that period, ICU admission was systematically denied to patients aged at least 80 years whatever their functional status. We evaluated the outcomes of older patients with SARS-CoV-2 infection according to their in-hospital location (ICU or conventional unit), and their functional status.

In this pragmatic quasi-experimental study, we analysed in parallel the 43 patients over 80 years admitted to an ICU (ICU group) between March 2020 and May 2020 in the Senior-COVID-rea study[3] to 58 patients included in the FRICE-CoV retrospective study that included patients aged at least 80 years admitted in another university hospital and presenting ICU admission criteria during the same period (conventional unit group). The criteria for inclusion in FRICE-CoV study were precisely defined as clinical symptoms of acute respiratory failure (respiratory rate >30 cycles min^{-1}, SpO_2 <92% despite ≥9 l min^{-1} of oxygen), and/or impaired consciousness (Glasgow scale score <15) and/or haemodynamic instability (systolic arterial pressure <90 mmHg, mottled skin). COVID-19 infection was confirmed by a positive swab with PCR and a radiological diagnosis based on a lung computed tomography scan.

Senior-COVID-Rea study protocol was previously published.[7] The FRICE-CoV study protocol was approved on 17 March 2021 by the local ethics committee ('Terre d'Ethique', Centre Hospitalier Universitaire de Saint-Etienne, France, Chairperson P. Vassal, reference: IRBN432021/CHUSTE). This committee ruled that formal written consent was not required as the study was observational.

In both cohorts, the functional status and comorbidities one month before hospital admission were assessed including the Activities of Daily Living (ADL) score, the IADL score, the Clinical Frailty Scale (CFS) and the Cumulative Illness Rating Scale for Geriatrics (CIRS-G) score. The primary outcome was 30-day mortality after the date of acute respiratory failure onset in 'conventional unit' patients and after ICU admission in the Senior-COVID-Rea 'ICU' patients. Multivariable logistic regression models were used to estimate the independent risk factors for 30-day mortality. These multivariate models integrating frailty scores were built to adjust on gender and age. Only the odds ratio of the corresponding frailty score was provided for a given three-variable multivariate model. The threshold for statistical significance was set at P less than 0.05.

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Table 1 Population characteristics

	ICU group ($N = 43$)	Conventional unit group ($N = 58$)	P
Age	83 (82–86)	85 (82–89)	0.15
Gender (M/F)	35/8	35/23	0.03
ADL score, median (range)	6 (5.5–6)	5 (4–6)	0.0084
IADL score, median (range)	7 (4–8)	5 (2–7)	0.0084
IADL score = 8, no. (%)	20 (46.5)	7 (12)	0.0002
CIRS-G score, median (range)	7 (4–11)	5 (3–8)	0.029
CFS score, median (range)	3 (2–5)	4 (3–5)	0.0035
CFS score $\geq$ 5, no. (%)	11 (26)	21 (36)	0.28
D30 mortality rate, no. (%)	25 (58)	28 (48)	0.28

ADL, Activities of Daily Living scale; CFS, Clinical Frailty Scale; CIRS-G, Cumulative Illness Rating Scale for Geriatrics; IADL, Instrumental Activities of Daily Living scale; ICU, intensive care unit.

In total, 43 'ICU' patients aged at least 80 years included in the Senior-COVID-Rea study and 58 'conventional unit' patients aged at least 80 years included in the FRICE-cov2 study were pooled in this analysis. In the ICU group, the median (range) hospital length of stay was 10.5 (4–26) days, 37% were mechanically ventilated (either invasively or non-invasively), and 37% received high-flow oxygen therapy on admission. The median (range) values of the Sequential Organ Failure Assessment (SOFA) score and Simplified Acute Physiology Score (SAPS II) were 5 (3–8) and 43 (36–51), respectively. In the conventional unit group, the median (range) hospital length of stay was 14 (6–19) days ($P = 0.72$ versus ICU group).

Considering the functional parameters one month before hospital admission, patients included in the ICU group had significant better ADL and IADL scores and a significant lower CFS score than patients included in the conventional unit group (Table 1). Gender was also significantly different between groups (Table 1). Thirty days mortality rates were, respectively, 58% in the ICU group and 48% in the conventional unit group ($P = 0.28$). Survival during the study period was not significantly different between both groups (Fig. 1, log-rank test = 0.17). In multivariable analysis, no IADL impairment was the only independent factor linked to survival (Table 2), corresponding to 27 patients in total, 20 in the ICU group and 7 patients in the conventional unit group (47 *versus* 12%, $P = 0.0002$). For these patients, admission to an ICU was associated with a trend towards improved survival, odds ratio (OR) 0.57, 95% confidence interval (CI), 0.1–3.38, $P = 0.54$. Conversely, patients with any IADL impairment had a six-fold increased risk of dying in the case of ICU admission, OR 6.0, 95% CI, 1.55–23.16, $P = 0.009$.

Fig. 1 Overall survival of patients aged at least 80 years admitted in ICU (Senior-COVID-Rea study) or maintained in a conventional medical unit (FRICE-Cov2 study).

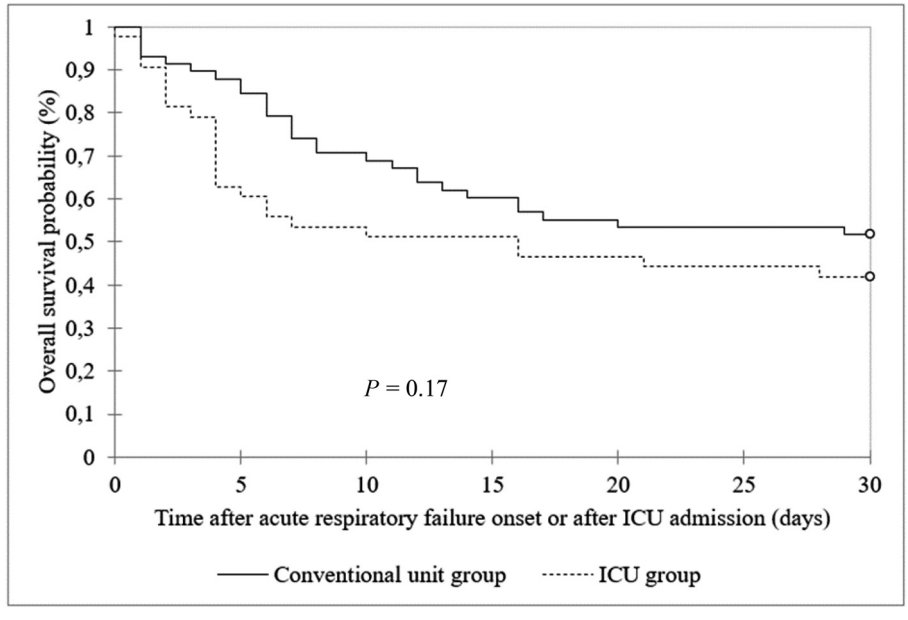

Table 2 Adjusted risk factors for 30-day mortality in the pooled analysis of patients aged at least 80 years admitted in ICU (Senior-COVID-Rea study) or maintained in a conventional medical unit (FRICE-Cov2 study)

	Adjusted OR[a]	95% confidence interval	*P*
ADL score	1.16	(0.84–1.6)	0.37
IADL score	0.91	(0.77–1.06)	0.23
IADL score = 8	0.27	(0.1–0.74)	0.01
CFS score	1.05	(0.79–1.39)	0.73
CFS score ≥5	1.05	(0.43–2.6)	0.91
CIRS-G score	1.1	(0.99–1.23)	0.06
ICU admission	1.55	(0.67–3.58)	0.30

ADL, Activities of Daily Living scale; CFS, Clinical Frailty Scale; CIRS-G, Cumulative Illness Rating Scale for Geriatrics; IADL, Instrumental Activities of Daily Living scale; ICU, intensive care unit. [a]Multivariate model adjusted on age and gender.

This study has some limitations, because of the quasi-experimental – and not strictly comparative – design. Patients from both groups were included in different hospitals, but during the same time period and in the same region of France, partially erasing differences in the characteristics of patients and care strategies. Moreover, the conjunction of SARS-CoV-2 pandemic and the induced shortage of beds gave the unique opportunity to evaluate *a priori* the benefit of an ICU admission in very old patients. Such attitude would be unethical in other circumstances. Patients were hospitalised during the first wave of the COVID-19 pandemic; even if care management has improved significantly since then, the same inclusion period limits the risk of differences attributable to treatments, the impact of vaccination or different variants of the virus. In addition, our study was underpowered to reach significance considering the effect of ICU admission, in the subgroup of patients with no IADL impairment. Finally, in light of the Very Old Intensive Care Patients (VIP) group studies,[1] our study also confirms the importance of functional independence prior to ICU admission for the very old patients.[4]

To conclude, and in this specific context of COVID-19 infection, patients aged at least 80 years with IADL impairment probably did not benefit from ICU admission. Larger studies are warranted to confirm such results, with the limits of a constantly evolving COVID-19 pandemic. Whether our results can be extended to older patients not presenting acute respiratory distress syndrome related to SARS-CoV-2 is beyond the scope of this study.

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