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**To cite this article:** Katleen Fagard, Evelien Gielen, Mieke Deschodt, Els Devriendt & Johan Flamaing (2022) Risk factors for severe COVID-19 disease and death in patients aged 70 and over: a retrospective observational cohort study, *Acta Clinica Belgica*, 77:3, 487-494, DOI: [10.1080/17843286.2021.1890452](https://doi.org/10.1080/17843286.2021.1890452)

**To link to this article:** <https://doi.org/10.1080/17843286.2021.1890452>



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Published online: 21 Feb 2021.



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## Risk factors for severe COVID-19 disease and death in patients aged 70 and over: a retrospective observational cohort study

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### ABSTRACT

**Objectives:** The COVID-19 pandemic resulted in rapid reorganisations of hospital care. In our hospital, the geriatrics team introduced the Clinical Frailty Scale (CFS) on the non-ICU COVID-19 units during these reorganisations. A retrospective analysis was performed to investigate the CFS as a risk factor for severe COVID-19 disease and in-hospital death in older patients with COVID-19.

**Methods:** In patients aged  $\geq 70$  years, an online geriatric assessment questionnaire was launched, from which the CFS was scored by the geriatrics team. Additional clinical data were collected from the electronic medical records. Risk factors related to ageing, such as the CFS, age-adjusted Charlson Comorbidity Index, living situation and cognitive decline, were examined alongside frequently reported risk factors in the general population. Outcomes were in-hospital death (primary outcome) and oxygen need of  $\geq 6$  litres and early warning score  $\geq 7$ , as parameters for severe disease (secondary outcomes). Baseline characteristics were described with descriptive statistics. Associations were analysed with uni- and multivariable analyses.

**Results:** One hundred and five patients were included, median age 82 years. CFS scores were 1–4 in 43, 5–6 in 45, and 7–9 in 17 patients. In multivariable analysis, CFS and cognitive decline were the only risk factors that were independently associated with in-hospital mortality. Chronic obstructive pulmonary disease, presence of respiratory symptoms on admission and male gender showed and independent association with severe disease.

**Conclusion:** A retrospective analysis shows that CFS and cognitive decline have added value for predicting in-hospital mortality in older patients with COVID-19 disease.

### KEYWORDS

Aged; cohort studies; COVID-19; frailty; prognostic factors



## Introduction

In December 2019 several pneumonia cases of unknown origin emerged in China, Wuhan. On January 9, 2020 a novel virus was detected as the causative agent [1]. The virus was highly similar to the Coronavirus (CoV) that caused an outbreak of severe acute respiratory syndrome (SARS) in 2003. Thus, it was named SARS-CoV-2 by the World Health Organization (WHO), and the associated disease was named COVID-19 disease [2]. By the end of January 2020 the first European cases were reported and by March 11 COVID-19 was declared a global pandemic by the WHO [1].

It soon became clear that the pandemic would have an enormous impact on health care resources. As it was feared that there would be insufficient hospital capacity to deal with all COVID-19 patients during the ascending curve, guidelines with triage criteria for hospitalisation or admission to an intensive care unit (ICU) were issued to prioritise those most likely to survive [3–5]. The guidelines included flow-charts with characteristics such as disease presentation, age,

comorbidities and frailty, and based identification of frailty on the Clinical Frailty Scale (CFS). The CFS was developed and validated by Rockwood et al. in 2005 and showed an increasing risk of death and institutionalisation with increasing frailty [6]. The rationale for including the frailty concept is clear: avoid under-treatment based on age and also disproportionate care for frail older patients. Published studies in ICU patients have shown that CFS is better associated with mortality in severe disease than age [7].

The clinical spectrum of COVID-19 disease ranges from asymptomatic to severe respiratory failure, multi-organ failure and death [8,9]. For well-founded clinical decisions, it is important to identify prognostic factors related to more severe disease and mortality. Several observational cohort studies examining risk factors for severe COVID-19 disease and death in the general population have been published. Apart from older age, the main risk factors described are male gender, obesity, and comorbidities such as hypertension, diabetes, cardiovascular disease, chronic pulmonary disease, cancer, chronic kidney disease [10–12]. Hereafter we call them ‘conventional’ risk

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factors. Publications studying risk factors such as frailty and comorbidity indices in COVID-19 patients were non-existing when we initiated the frailty screening on the non-ICU COVID-19 units. Because of this knowledge-gap we decided to study the CFS, the Charlson Comorbidity Index (CCI), age-adjusted CCI, living situation and cognitive decline as 'ageing-related' risk factors for severe COVID-19 disease and death in addition to the 'conventional' risk factors named above.

In this study, we investigate the association between 'ageing-related' and 'conventional' risk factors with in-hospital mortality, high oxygen need ( $\geq 6$  litres), and high early warning scores (EWS  $\geq 7$ ) in patients aged 70 and over admitted to a COVID-19 hospitalisation unit.

## Methods

### Study design, setting and sample

A single-centre retrospective observational cohort study was conducted in the University Hospitals (UH) Leuven in Belgium. Patients hospitalised with COVID-19 disease that had a Clinical Frailty Score performed between March 16 and May 16, 2020 were eligible for inclusion.

The diagnosis of COVID-19 disease was made based on a positive polymerase chain reaction (PCR) test or, in the absence of a positive PCR test, based on the clinical picture and a chest CT scan. Patients that screened negative on the PCR test with an alternative diagnosis, e.g. heart failure, bacterial pneumonia, after admission to the COVID-19 hospitalisation unit were excluded from the analysis. The medical ethics committee of the UH Leuven approved the study (S64222). The study is reported according to the STROBE guidelines.

### Data collection procedures

Co-workers of the low-care COVID-19 hospitalisation units (non ICU-units) were instructed to contact the families of newly admitted patients aged  $\geq 70$  years by telephone. The patients were either admitted to the low-care unit immediately from the emergency department, from another hospital unit or after a stay in the ICU. Their family was asked to complete an online geriatric assessment questionnaire and to report the situation before admission and illness. From the questionnaire, the CFS was scored by the geriatrics team. The CFS and the geriatric assessment were reported in the electronic medical record. Data for this study were collected retrospectively from the electronic medical records.

### Variables and measurements

The following *demographic data* were collected: age, gender, living situation.

The following *clinical data* were collected: Body Mass Index (BMI) [13], symptoms on admission (flu-like symptoms or fever, respiratory symptoms, gastrointestinal symptoms), treatment for COVID-19, a history of cardiovascular disease, chronic pulmonary disease, cancer, hypertension, the CCI (a comorbidity index that is calculated based on weighted scores assigned to the following conditions: myocardial infarction, chronic heart failure, peripheral vascular disease, cerebrovascular accident or transient ischemic attack, chronic cognitive deficit, chronic obstructive pulmonary disease (COPD), connective tissue disease, peptic ulcer disease, liver disease, diabetes, hemiplegia, chronic kidney disease, solid tumour, leukaemia, lymphoma, acquired immunodeficiency syndrome) [14], and the CFS [6]. In addition to the CCI the age-adjusted CCI was calculated [15]. A history of cognitive decline reported on the electronic geriatric assessment questionnaire was regarded as presence of cognitive decline and was classified as 'chronic cognitive deficit' in the CCI. Apart from a history of diabetes the glycated haemoglobin value was recorded.

The following *outcome variables* were collected: In-hospital death (primary outcome), and severe disease, defined in two ways: an oxygen need of 6 litres or more and an EWS of 7 or more during hospitalisation (secondary outcomes) [16].

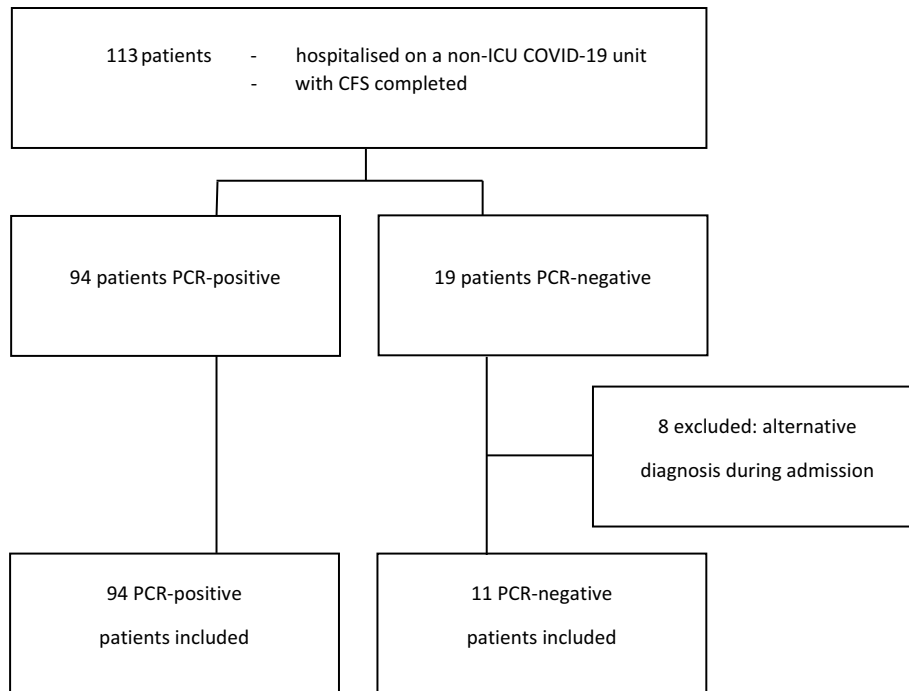
### Data analysis

Continuous variables were reported as medians with interquartile ranges (IQR). Categorical variables were reported as numbers and percentages. Univariable analyses were performed, comparing patient outcome groups on demographic and clinical variables. Dichotomous and nominal variables were analysed using Pearson Chi-squared tests, or Fisher's exact tests if  $\geq 1$  cell had an expected count of less than 5. Ordinal and continuous variables were analysed using Mann-Whitney U tests. Multivariable logistic regression models were used to determine independent predictors for the primary and secondary outcomes. Variables showing significant association with the outcome variable in univariable analysis were entered in a multivariable forward stepwise selection procedure. P-values, odds ratios (OR), and 95% confidence intervals (CI) are reported. All tests were 2-tailed, assuming a 5% significance level. All analyses were performed using SPSS version 20.0 (Statistical Package for the Social Sciences Inc., Chicago, Illinois).

## Results

### Description of the sample

Only patients that had a CFS performed on admission to the low-care COVID hospitalisation units



**Figure 1.** Flow-chart of in- and exclusions. Legend: CFS: Clinical Frailty Scale; PCR: Polymerase Chain Reaction; ICU: Intensive Care Unit;

( $n = 113$ ) were eligible for inclusion. **Figure 1** displays the in- and exclusion process. One hundred and five patients were included in the study. Patient and clinical characteristics are summarized in **Table 1**. The median age was 82 years (range 70–97). The male/female ratio was 1.1. Sixty-two patients lived at home, 10 in an assisted living facility, 33 in a nursing home. CFS scores were 1 or 2 in 13 patients (12.4%), 3 or 4 in 30 patients (28.6%), 5 or 6 in 45 patients (42.9%), and 7 or 8 in 17 patients (16.2%). None of the patients had a CFS of 9. Sixty-eight patients had flu-like symptoms or fever, 73 patients had respiratory symptoms and 17 patients complained of gastro-intestinal symptoms on admission. The most common treatment at the time of the study was a combination of hydroxychloroquine (77.1%) and antibiotics (83.8%). Eighteen-patients stayed in ICU during admission, of whom 12 were between 70 and 79 years old and 6 between 80 and 85. The median CFS for patients with ICU transfer was 3.5 (IQR 2–4.25, range 1–6), compared to 6.0 (IQR 4–6, range 1–8) for patients without ICU transfer. Fourteen (13.3%) patients died during hospitalisation, 40 patients (38.1%) needed 6 or more litres of oxygen during admission, and 72 patients (68.6%) had an EWS score  $\geq 7$  during hospitalisation. None of the study patients that were transferred from the low-care COVID unit (i.e. patients in which the CFS was performed) to the ICU died in the ICU. The total ICU mortality for patients aged  $\geq 70$  years during the study period, regardless of study participation, was 12% (4/33).

### **Risk factors for severe disease and death**

Univariable analysis (**Table 1**) showed that age, CFS, CCI, age-adjusted CCI and cognitive decline are associated with in-hospital mortality. Living situation, male gender, obesity, cardiovascular disease, chronic pulmonary disease, diabetes, severe kidney disease, cancer and hypertension were not significantly associated. Male gender, presence of respiratory symptoms on admission, and COPD were associated with high EWS ( $\geq 7$ ); the first two were associated with high oxygen need ( $\geq 6$  litres) during admission. In multivariable logistic regression analysis a higher CFS score and the presence of cognitive decline showed an independent association with in-hospital mortality (**Table 2**). Multivariable analysis for the secondary outcomes is shown in **Table 3** (oxygen need  $\geq 6$  litres) and **Table 4** (EWS  $\geq 7$ ).

**Figure 2** shows the relation between the CFS, cognitive decline, and mortality. Mortality rates were higher in patients with CFS 5–6 (7/45, 15.6%) and CFS 7–9 (7/17, 41.2%) with no mortality in CFS 1–4 (0/43, 0%). In the deceased group cognitive decline was very prevalent: 92.9% (13/14) of deceased patients versus 29.7% (27/91) of patients that survived had reported cognitive decline before admission.

### **Discussion**

The aim of the current study was to investigate ‘ageing-related’ risk factors in older patients, in addition to ‘conventional’ risk factors for severe COVID-19 disease, regarding their association with severe disease or

Table 1. Patient and clinical characteristics and association with in-hospital mortality and severe disease (oxygen need  $\geq 6$  l, EWS  $\geq 7$ ).

	In-hospital mortality <sup>1</sup>				EWS $\geq 7$					
	All patients N = 105		NO N = 91		YES N = 14		NO N = 65		YES N = 40	
Age, median (IQR)	82 (76–87)	82 (75–87)	87 (81.5–90)	<b>0.016</b>	82 (75–88)	82 (77–87)	82 (75–86)	82 (77–89)	0.934	0.347
Living situation				0.153					0.365	0.520
-at home, alone	11 (10.5)	11 (12.1)	0 (0)		6 (9.2)	5 (12.5)	3 (9.1)	8 (11.1)		
-at home, with others	51 (48.6)	46 (50.5)	5 (35.7)		28 (43.1)	23 (57.5)	13 (39.4)	38 (52.8)		
-nursing home	33 (31.4)	25 (27.5)	8 (57.1)		24 (36.9)	9 (22.8)	13 (39.4)	20 (27.8)		
-assisted living facility	10 (9.5)	9 (9.9)	1 (7.1)		7 (10.8)	3 (7.5)	4 (12.1)	6 (8.3)		
Male gender	55 (52.4)	45 (49.5)	10 (71.4)	0.125	26 (40.0)	29 (72.5)	10 (30.3)	45 (62.5)	<b>0.001</b>	<b>0.002</b>
BMI <sup>2</sup> , median (IQR)	24.9 (22.9–27.7) <sup>2</sup>	24.8 (22.7–27.0) <sup>2</sup>	26.5 (23.2–28.5)	0.223	24.8 (22.3–27.7)	25.1 (23.1–27.7) <sup>2</sup>	24.9 (21.9–28.1)	24.9 (23.1–27.7) <sup>2</sup>	0.456	0.740
Obese (BMI $\geq 30$ ) <sup>2</sup>	13 (12.5)	12 (13.3)	1 (7.1)	1.000	9 (13.8)	4 (10.3)	5 (15.2)	8 (11.3)	0.762	0.751
CFS, median (IQR)	5 (3–6)	5 (3–6)	6.5 (6–7)	<b>0.000</b>	5 (4–6)	4.5 (3–6)	5 (4–6)	5 (3–6)	0.305	0.947
CFS groups				<b>0.000</b>					0.131	0.661
-1, 2	13 (12.4)	13 (14.3)	0 (0)		5 (7.7)	8 (20.0)	2 (6.1)	11 (15.3)		
-3, 4	30 (28.6)	30 (33.0)	0 (0)		18 (27.7)	12 (30.0)	10 (30.3)	20 (27.8)		
-5, 6	45 (42.9)	38 (41.8)	7 (50.0)		31 (47.7)	14 (35.0)	17 (51.5)	28 (38.9)		
-7, 8, 9	17 (16.2)	10 (11.0)	7 (50.0)		11 (16.9)	6 (15.0)	4 (12.1)	13 (18.1)		
CCI, median (IQR)	2 (1–4)	2 (1–4)	3 (2–5.25)	<b>0.043</b>	2 (1–4)	2 (1–3.75)	2 (1–4)	2 (1–4)	0.725	0.661
ACCI, median (IQR)	6 (4–8)	6 (4–7)	7 (5.75–9.25)	<b>0.040</b>	6 (4–8)	6 (4.25–7.0)	6 (4–7.5)	6 (4–8)	0.873	0.870
Cardiovascular disease	48 (45.7)	41 (45.1)	7 (50.0)	0.730	30 (46.2)	18 (45.0)	15 (45.5)	33 (45.8)	0.908	0.971
Cognitive decline	40 (38.1)	27 (29.7)	13 (92.9)	<b>0.000</b>	24 (36.9)	16 (40.0)	9 (27.3)	31 (43.1)	0.753	0.122
COPD	10 (9.5)	8 (8.8)	2 (14.3)	0.620	4 (6.2)	6 (15.0)	0 (0)	10 (13.9)	0.175	<b>0.029</b>
Chronic pulmonary disease	18 (17.1)	15 (16.5)	3 (21.4)	0.704	9 (13.8)	9 (22.5)	3 (9.1)	15 (20.8)	0.253	0.138
Respiratory symptoms <sup>3</sup>	73 (69.5)	63 (69.2)	10 (71.4)	1.000	37 (56.9)	36 (90.0)	16 (48.5)	57 (79.2)	<b>0.000</b>	<b>0.002</b>
Diabetes	43 (41.0)	35 (38.5)	8 (57.1)	0.186	23 (35.4)	20 (50.0)	13 (39.4)	30 (41.7)	0.139	0.826
HbA1C $\geq 6.5\%$	35 (33.3)	29 (31.9)	6 (42.9)	0.543	18 (27.7)	17 (42.5)	7 (21.2)	28 (38.9)	0.118	0.074
Severe kidney disease <sup>4</sup>	5 (4.8)	3 (3.3)	2 (14.3)	0.131	5 (7.7)	0 (0)	3 (9.1)	2 (2.8)	0.154	0.177
Cancer <sup>5</sup>	17 (16.2)	15 (16.5)	2 (14.3)	1.000	11 (16.9)	6 (15.0)	6 (18.2)	11 (15.3)	0.795	0.708
Hypertension	78 (74.3)	69 (75.8)	9 (64.3)	0.345	49 (75.4)	29 (72.5)	27 (81.8)	51 (70.8)	0.743	0.232

LEGEND: ACCI: Age-adjusted Charlson Comorbidity Index; BMI: Body Mass Index; CCI: Charlson Comorbidity Index; CFS: Clinical Frailty Scale; COPD: Chronic Obstructive Pulmonary Disease; EWS: Early Warning Score; HbA1C: glycosylated haemoglobin; IQR: interquartile range; l: litres; n: number; O<sub>2</sub>: oxygen; <sup>1</sup> during the total hospital stay (COVID + non-COVID if discharged from COVID-unit to acute care non-COVID unit); <sup>2</sup>one patient with missing data; <sup>3</sup>on admission; <sup>4</sup>baseline creatinine  $\geq 3$  mg/dl or dialysis; <sup>5</sup>cancer: solid tumour under treatment in the last five years or leukaemia or lymphoma.

**Table 2.** Risk factors for mortality: multivariable logistic regression analysis.

	Univariable analysis		Multivariable model	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age	1.113 (1.017–1.219)	0.020	-	
CFS	3.243 (1.597–6.585)	0.001	2.325 (1.094–4.941)	0.028
CCI	1.275 (0.990–1.642)	0.060	-	
ACCI	1.277 (1.005–1.624)	0.046	-	
Cognitive decline	30.815 (3.838–247.419)	0.001	11.497 (1.317–100.345)	0.027

Legend: ACCI: Age-adjusted Charlson Comorbidity Index; CCI: Charlson Comorbidity Index; CFS: Clinical Frailty Scale; CI: Confidence Interval; OR: Odds Ratio.

**Table 3.** Risk factors for O2 need ≥6 litres: multivariable logistic regression analysis.

	Univariable analysis		Multivariable model	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Male gender	3.955 (1.685–9.282)	0.002	3.221 (1.315–7.889)	0.010
Respiratory symptoms	6.811 (2.170–21.375)	0.001	5.622 (1.741–18.149)	0.004

Legend: CI: Confidence Interval; O2: oxygen; OR: Odds Ratio.

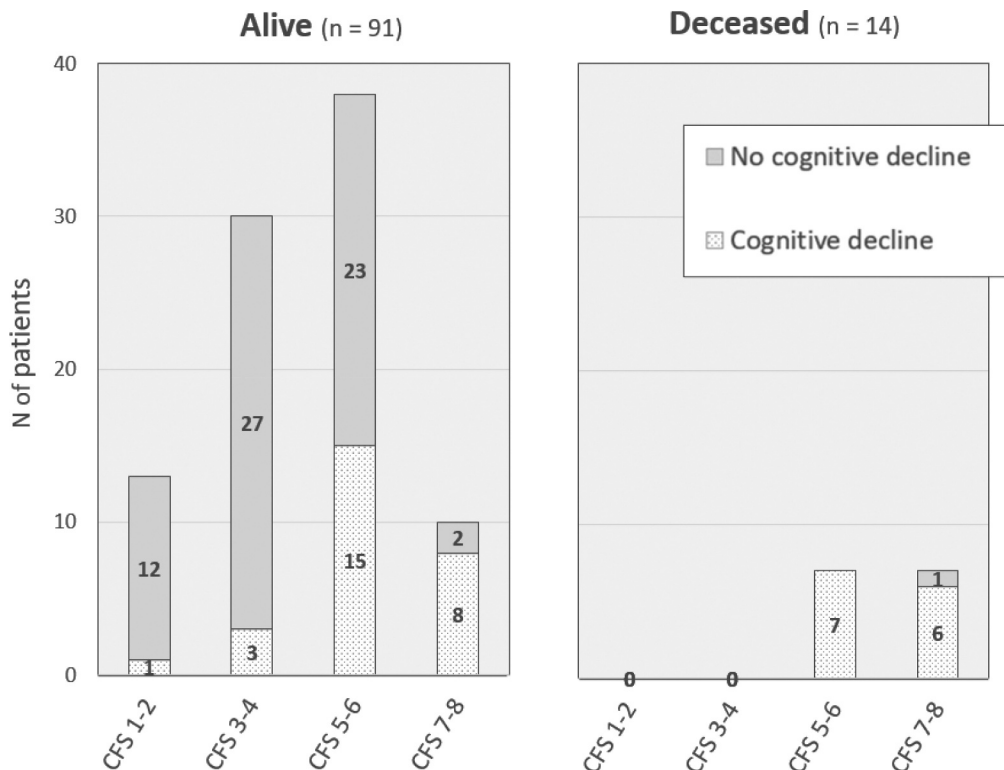
**Table 4.** Risk factors for EWS ≥7: multivariable logistic regression analysis.

	Univariable analysis		Multivariable model	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Male gender	3.833 (1.586–9.265)	0.003	2.840 (1.115–7.234)	0.029
COPD	N/A	N/A	N/A	N/A
Respiratory symptoms	4.037 (1.660–9.818)	0.002	3.381 (1.311–8.716)	0.012

Legend: COPD: Chronic Obstructive Pulmonary Disease; CI: Confidence Interval; EWS: Early Warning Score; N/A: not applicable, all patients with COPD had an EWS ≥7 which precludes calculating an OR; OR: Odds Ratio

death. We found age, CFS, CCI, age-adjusted CCI and cognitive decline associated with in-hospital mortality. A higher CFS score and the presence of cognitive decline were independent predictors for in-hospital

mortality. Living situation, male gender, obesity, cardiovascular disease, chronic pulmonary disease, diabetes, severe kidney disease, cancer and hypertension were not significantly associated. Male gender, presence of



**Figure 2.** Relation between the CFS score, cognitive decline, and in-hospital mortality. Legend: CFS: Clinical Frailty Scale (note: none of the patients had a CFS score = 9); N: number.



respiratory symptoms on admission, and COPD were independently associated with high EWS ( $\geq 7$ ); the first two were independently associated with high oxygen need ( $\geq 6$  litres) during hospitalisation.

Previous studies in COVID-19 patients have identified older age and specific comorbidities as risk factors for severe disease and death [10,12]. Our study did not find an association with specific comorbidities in older patients, and comorbidity indices and age did not remain as independent predictors for in-hospital mortality in multivariable analysis. Presumably, the impact of ageing and diseases on physical reserves, resulting in frailty, is more important than age and disease alone in the older patient population [17,18]. In our study, frailty and cognitive decline were more important risk factors for in-hospital mortality than age and comorbidity. Meanwhile, several other studies identified a higher CFS score as a risk factor for mortality [19]. De Smet et al. studied COVID-19 patients on a geriatric hospitalisation unit and found that CFS was independently associated with in-hospital<sup>1</sup> mortality among other risk factors such as age, gender, place of residence, dementia, polypharmacy, radiographic and laboratory findings. With each increase on the frailty scale, the odds ratio for mortality increased with 1.705 (95% CI 1.173–2.750). In a bivariate model with age and CFS combined, only the CFS remained significantly associated with mortality. The area under the ROC curve for the CFS in this model was 0.744 (95% CI 0.621–0.867), with a positive and negative predictive value of 57% and 80% respectively [20]. The largest study, a multicentre European study that included 1564 patients, analysed the effect of frailty on survival in patients with COVID-19 in patients of all ages and concluded that increasing frailty was associated with higher mortality [21]. Compared with CFS 1–2, the adjusted hazard ratios for 7-day mortality were 1.22 (95% CI 0.63–2.38) for CFS 3–4, 1.62 (0.81–3.26) for CFS 5–6, and 3.12 (1.56–6.24) for CFS 7–9 [21]. Cognitive decline was most prevalent in the CFS 4–6 group in our study, an indication that patients with cognitive decline and higher frailty scores might not have been transferred to the hospital. It is likely that patients with dementia and severe COVID-19 disease received palliative care in their home environment. In contrast to our study, De Smet et al. did not find a significant association between a diagnosis of dementia and in-hospital mortality ( $p = 0.77$ ) [20]. This might be due to the difference in operationalisation of dementia. While De Smet et al. only included dementia diagnoses reported in the medical history, we considered all patients of whom the relatives reported cognitive decline in the online assessment questionnaire as patients with cognitive decline. Covino et al. studied patients aged 80 years and over admitted to hospital

with COVID-19 disease and concluded that severe dementia was an independent risk factor for 30-day mortality [22]. Cognitive decline is likely to be associated with poorer outcomes because of underlying frailty, less compliance with safety measures and treatments, and risk of delirium. Another explanation is that patients with dementia more often have had advance care planning with higher therapeutic restriction codes and that patients with cognitive decline are less often transferred to ICU.

A systematic review by Jain et al. that reports seven studies, including 1813 COVID-19 patients of all ages, identified dyspnoea ( $p < 0.001$ ), cough ( $p = 0.04$ ), COPD, cardiovascular disease and hypertension (all  $p < 0.001$ ) as predictors for severe disease. They notice that severe COVID-19 disease was not consistently defined across the included studies [23]. It is worth mentioning that the WHO-China joint mission on Coronavirus disease published a report on February 28, 2020 in which severe disease was defined as having dyspnoea, respiratory frequency  $\geq 30$ /minute, blood oxygen saturation  $\leq 93\%$ , PaO<sub>2</sub>/FiO<sub>2</sub> ratio  $< 300$ , and/or lung infiltrates  $> 50\%$  of the lung field within 24 to 48 hours [24]. The definition of severe COVID-19 disease in this study was different from the WHO definition. We considered an oxygen need of 6 or more as a trigger for hospitalisation, and thus as 'severe disease', because at the time of the study there were problems with the supply of large quantities of oxygen in nursing homes and in the community. In addition, an EWS score of 7 or more during hospitalisation was regarded as an alternative definition for 'severe disease', because 7 is the threshold for prompt emergency medical assessment and may require transfer of the patient to a critical care service [16].

Finally, it is challenging to translate the continuous scores of the CFS into a cut-off score that predicts unfavourable disease outcome and that should be used as a threshold in clinical decisions regarding hospital admission or admission to ICU. This study showed that higher frailty scores predispose to worse outcomes. In our study there were no patients that died in the CFS 1–4 group. The mortality rose from 15.6% in the CFS 5–6 group to 41.2% in the CFS 7–9 group. This underlines the chosen cut-off scores of 5 to 7 in the algorithms mentioned above [3–5], although caution is warranted. Decision algorithms should not be interpreted as a mandatory decision guides, but should serve as guidance for well-considered clinical decisions. When considering whether or not to upgrade the level of care, one should also take into account the patients' previous hospitalisation history, the patients' personal preferences and comfort-level. Available resources in long-term care facilities or home care should also be considered: availability of skilled personnel in adequate

numbers, available drugs, PCR swabs, oxygen supply, protective equipment for health care workers, and possibility of isolation to prevent further spread of the disease [25].

There are several limitations to this study. First, it is a single centre study with a small study sample. This limits the power of the analysis and the generalisability of the results. Unfortunately, we only received completed online geriatric assessment questionnaires in about half of all potential candidates. Implementation of the online questionnaire during a period of crisis was challenging: contacting the family to complete the questionnaire was not always considered a priority by the responsible team. Another factor that could have played a role is that older relatives of patients may not have had access to the internet. Second, the study included patients on admission to low-care COVID-19 units. Patients who died during a primary ICU stay were not included in the study. Moreover, there may have been referral bias due to published decision algorithms with triage criteria for hospital or ICU admission. In addition, therapeutic restriction codes in patients with dementia, severe comorbidity or frailty, may have influenced therapeutic decisions and mortality rates. Third, all patients were admitted to a COVID-19 hospitalisation unit but only 90% of included patients had a positive PCR test. Some PCR-negative patients, whose diagnosis was based solely on the clinical picture and a chest CT scan, were also included. However, we excluded PCR-negative patients with alternative diagnoses during admission. An argument for including PCR-negative patients without alternative diagnoses is the fact that the sensitivity of the PCR test is only 60 to 70%, so a negative test does not rule out a COVID-19 infection [26]. Fourth, clinical symptoms other than respiratory symptoms on admission, as well as laboratory findings and radiographic characteristics were not analysed in this study. Neither was the applied therapy included in the analysis. At the time of the study, the standard therapy for COVID-19 disease in our hospital (based on national guidelines) consisted of initiating hydroxychloroquine and ceftriaxone [27]. The strength of this study is the fact it considers ageing-related risk factors such as frailty and that the findings of this study can help physicians in decision making for older patients.

## Conclusion

The speed of the first COVID-19 wave overwhelmed health-care workers and in the midst of the crisis it was a challenge to organise well-designed clinical studies in the geriatric population. The present study, although carried out in a small sample, suggests that the risk of death from COVID-19 disease is more related to 'ageing-related' risk factors, e.g. frailty and cognitive

decline, than to 'conventional' risk factors, such as gender, obesity and specific comorbidities.

## Note

1. The authors considered 6-week mortality, but all deceased patients died in-hospital.

## Acknowledgments

The authors would like to thank Annouschka Laenen for providing statistical advice and the medical student trainees who helped collect the data.

## Disclosure statement

The authors report no declarations of interest.

## Funding

This work was not supported by a funding agency.

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