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

Background: The COVID-19 pandemic resulted in a rapid reorganization of hospital care. In our hospital, the Clinical Frailty Scale (CFS) was introduced as a result of these reorganizations. A retrospective analysis was performed to investigate whether typical geriatric risk factors, such as frailty, comorbidity, living situation and cognitive decline, have added value compared to conventional risk factors in predicting severe COVID-19 disease and in-hospital death.

Methods: In patients aged 70 years and over, 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. 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. Univariable analysis showed age, CFS, Charlson Comorbidity Index (CCI), age-adjusted CCI and cognitive decline associated with in-hospital mortality. Male gender, obesity, cardiovascular disease, chronic pulmonary disease, diabetes, cancer and hypertension were not significantly associated. In multivariable analysis, CFS and cognitive decline were independent predictors for in-hospital mortality. Chronic obstructive pulmonary disease, presence of respiratory symptoms on admission and male gender were associated with severe disease (univariable analysis).

Conclusion: Through action of the geriatrics team at the time of rapid changes in the hospital, the frailty concept was introduced in the COVID-19 hospitalization units. A retrospective analysis shows that geriatric risk factors exceed conventional risk factors for predicting in-hospital mortality.

1. Background

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].

Soon it became clear that the pandemic was having a huge impact on health care resources. Concern arose that there would be insufficient hospital capacity available to accommodate all COVID-19 patients during the ascending curve. Rapid guidelines with triage criteria for admission to hospital or admission to an intensive care unit (ICU), based on disease presentation, age, comorbidities and frailty, were issued to prioritize those most likely to survive [3-5]. As these guidelines based identification of ‘frailty’ on the Clinical Frailty Scale (CFS), the geriatrics department of the University Hospitals Leuven, Belgium, introduced an online geriatric assessment questionnaire to be able to reach relatives of patients admitted with COVID-19 disease in times of restricted visits and patients in isolation rooms. Relatives were contacted by telephone and asked to complete the questionnaire, from which the CFS was scored by the geriatrics team. The geriatrics team reported the geriatric assessment and the CFS in the

electronic medical records to facilitate risk estimation and clinical decision making in the older patient population admitted to hospital with COVID-19 disease.

The clinical spectrum of COVID-19 disease ranges from asymptomatic to severe respiratory failure, multi-organ failure and death [6, 7]. For well-founded clinical decisions, it is important to identify prognostic factors related to more severe disease and mortality. Several observational cohort studies that examine risk factors for severe disease and death 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 [8-10]. Hereafter we call them 'conventional risk factors'. Because publications including 'geriatric' risk factors were scarce when we initiated this study, we decided to study the CFS, the Charlson Comorbidity Index (CCI), age-adjusted CCI, living situation and cognitive decline as risk factors for severe COVID-19 disease and death in addition the 'conventional' risk factors named above.

In this article, we investigate the association between 'conventional' and 'geriatric' risk factors with in-hospital mortality (primary outcome) and severe disease (secondary outcome) in patients aged 70 and over admitted to a COVID-19 hospitalization unit. Additionally, we examine whether 'geriatric' risk factors have an added value compared to 'conventional' risk factors in predicting in-hospital mortality in older patients.

2. Methods

2.1 **Study design, setting and sample**

A single-centre retrospective observational cohort study was conducted in the University Hospitals Leuven in Belgium. Patients hospitalized 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 hospitalization unit were excluded from the analysis. The medical ethics committee of the University Hospitals Leuven approved the study (S64222).

2.2 **Data collection procedures**

Co-workers of the low-care COVID-19 hospitalization units (non ICU-units) were instructed to contact the families of newly admitted patients aged ≥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 evaluation 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.

2.3 **Variables and measurements**

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

The following *clinical data* were collected: Body Mass Index (BMI) [11], symptoms on admission (flu-like symptoms or fever, respiratory symptoms, gastro-intestinal 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) [12], and the CFS [13]. In addition to the CCI the age-adjusted CCI was calculated [14]. 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), highest oxygen need during admission and highest early warning score (EWS) during admission as markers for disease severity (secondary outcomes) [15]. Severe disease was defined in two ways, analysed separately: an oxygen need during admission of 6 litres or more and an EWS during admission of 7 or more.

2.4 **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 ≥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 both outcomes. Variables showing significant association with the outcome variable in univariable analysis were considered in a forward model selection procedure. To determine the added value of geriatric risk factors to conventional risk factors, an additional model selection was performed for geriatric risk factors, forcing conventional risk factors that were selected in univariable analysis into the model. 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).

3. Results

3.1 Description of the sample

One hundred and five patients were included in the study. **Figure 1** displays the in- and exclusion process. 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 hospitalization, 40 patients (38.1%) needed 6 or more liters of oxygen during admission, and 72 patients (68.6%) had an EWS score ≥7 during hospitalization.

Table 1: Patient and clinical characteristics and association with in-hospital mortality and severe disease (oxygen need ≥6 l, EWS ≥7)

	All patients	In-hospital mortality[1]			O2 ≥6 l			EWS ≥7		
		NO	YES	P-value	NO	YES	P-value	NO	YES	P-value
	N=105	N=91	N=14		N=65	N=40		N=33	N=72	
Age, median (IQR)	82 (76-87)	82 (75-87)	87 (81.5-90)	**0.016**	82 (75-88)	82 (77-87)	0.934	82 (75-86)	82 (77-89)	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 (22.5)		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)	**0.001**	10 (30.3)	45 (62.5)	**0.002**
BMI[2], median (IQR)	24.9 (22.9-27.7)[2]	24.8 (22.7-27.0)[2]	26.5 (23.2-28.5)	0.223	24.8 (22.3-27.7)	25.1 (23.1-27.7)[2]	0.456	24.9 (21.9-28.1)	24.9 (23.1-27.7)[2]	0.740
Obese (BMI ≥30)[2]	13 (12.5)	12 (13.3)	1 (7.1)	1.000	9 (13.8)	4 (10.3)	0.762	5 (15.2)	8 (11.3)	0.751
CFS, median (IQR)	5 (3-6)	5 (3-6)	6.5 (6-7)	**0.000**	5 (4-6)	4.5 (3-6)	0.305	5 (4-6)	5 (3-6)	0.947
CFS groups				**0.000**			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)	**0.043**	2 (1-4)	2 (1-3.75)	0.725	2 (1-4)	2 (1-4)	0.661
ACCI, median (IQR)	6 (4-8)	6 (4-7)	7 (5.75-9.25)	**0.040**	6 (4-8)	6 (4.25-7.0)	0.873	6 (4-7.5)	6 (4-8)	0.870
Cardiovascular disease	48 (45.7)	41 (45.1)	7 (50.0)	0.730	30 (46.2)	18 (45.0)	0.908	15 (45.5)	33 (45.8)	0.971
Cognitive	40	27	13	**0.000**	24	16	0.753	9	31	0.122

decline	(38.1)	(29.7)	(92.9)		(36.9)	(40.0)		(27.3)	(43.1)	
COPD	10 (9.5)	8 (8.8)	2 (14.3)	0.620	4 (6.2)	6 (15.0)	0.175	0 (0)	10 (13.9)	**0.029**
Chronic pulmonary disease	18 (17.1)	15 (16.5)	3 (21.4)	0.704	9 (13.8)	9 (22.5)	0.253	3 (9.1)	15 (20.8)	0.138
Respiratory symptoms[3]	73 (69.5)	63 (69.2)	10 (71.4)	1.000	37 (56.9)	36 (90.0)	**0.000**	16 (48.5)	57 (79.2)	**0.002**
Diabetes	43 (41.0)	35 (38.5)	8 (57.1)	0.186	23 (35.4)	20 (50.0)	0.139	13 (39.4)	30 (41.7)	0.826
HbA1C ≥6.5%	35 (33.3)	29 (31.9)	6 (42.9)	0.543	18 (27.7)	17 (42.5)	0.118	7 (21.2)	28 (38.9)	0.074
Severe kidney disease[4]	5 (4.8)	3 (3.3)	2 (14.3)	0.131	5 (7.7)	0 (0)	0.154	3 (9.1)	2 (2.8)	0.177
Cancer[5]	17 (16.2)	15 (16.5)	2 (14.3)	1.000	11 (16.9)	6 (15.0)	0.795	6 (18.2)	11 (15.3)	0.708
Hypertension	78 (74.3)	69 (75.8)	9 (64.3)	0.345	49 (75.4)	29 (72.5)	0.743	27 (81.8)	51 (70.8)	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; O2: oxygen; [1]during the total hospital stay (COVID + non-COVID if discharged from COVID-unit to acute care non-COVID unit); [2]one patient with missing data; [3]on admission; [4]baseline creatinine ≥ 3 mg/dl or dialysis; [5]cancer: solid tumour under treatment in the last five years or leukaemia or lymphoma.

3.2 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 (≥7); the first two were associated with high oxygen need (≥6 litres) during admission.

As the geriatric risk factors were only associated with death and not with the severity of the disease, multivariable logistic regression was only performed for the primary outcome (in-hospital mortality) (**Table 2**). In a five-factor model with age, CFS, CCI, age-adjusted CCI and cognitive decline, a higher CFS score and the presence of cognitive decline were independent predictors of mortality. As age was the only 'conventional' risk factors that was significant, the regression analysis was repeated with age forced into the model in order to determine the relative importance of geriatric versus conventional risk factors. Again only CFS (OR 0.275, 95% CI 1.047-4.940) and cognitive decline (OR 0.089, 95% CI 0.010-0.783) reached significance.

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% of deceased patients versus 28.7% of patients that survived had reported cognitive decline before admission.

Table 2: Risk factors for mortality: multivariable logistic regression analyses

	Single Factor Model		Five Factor Model		Age forced into Five Factor Model	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Age	1.113 (1.017-1.219)	0.200	-		1.057 (0.950-1.177)	0.306
CFS	3.243 (1.597-6.585)	**0.001**	2.325 (1.094-4.941)	**0.028**	2.275 (1.047-4.940)	**0.038**
CCI	1.275 (0.990-1.642)	0.600	-		-	
ACCI	1.277 (1.005-1.624)	**0.046**	-		-	
Cognitive decline	0.032 (0.004-0.261)	**0.001**	0.087 (0.010-0.759)	**0.027**	0.089 (0.010-0.783)	**0.029**
Legend: ACCI: Age-adjusted Charlson Comorbidity Index; CCI: Charlson Comorbidity Index ; CFS: Clinical Frailty Scale; CI: Confidence Interval; OR: Odds Ratio						

4. Discussion

The aim of the current study was to investigate geriatric risk factors in older patients, in addition to conventional risk factors for severe COVID-19 disease, regarding their association with severe disease or 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 respiratory symptoms on admission, and COPD were associated with high EWS (≥ 7); the first two were associated with high oxygen need (≥6 litres) during admission.

Previous studies have shown that older patients and patients with specific comorbidities are at risk for severe COVID-19 disease and death [8, 10]. However, the impact of aging and diseases on physical reserves, resulting in frailty, could be even more important [16, 17]. Our study found that frailty and cognitive decline are more important risk factors for in-hospital mortality in patients with COVID-19 disease than age and comorbidity. Several other studies identified a higher CFS score as a risk factor for mortality [18-24]. De Smet et al. studied COVID-19 patients on a geriatric hospitalization unit and found that CFS was independently associated with in-hospital[1] 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 0.7443 (95% CI 0.6213-0.8673), with a

positive and negative predictive value of 57% and 80% respectively [22]. The largest study, a multicentre European study that included 1564 patients, analyzed 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 [23]. 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 [23]. 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) [22]. This might be due to the difference in operationalization 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 [25]. 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. We did not find an association between higher scores on the comorbidity scales CCI and age-adjusted CCI and higher odds of mortality, neither did we find an association between specific comorbidities and mortality, as many other studies did [8, 10].

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 [26]. 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 ≥30/minute, blood oxygen saturation ≤93%, PaO2/FiO2 ratio <300, and/or lung infiltrates >50% of the lung field within 24 to 48 hours [27]. The definition of severe COVID-19 disease in the present study was different from the WHO definition. At the time of the study there were problems with the supply of large quantities of oxygen in nursing homes and in the community. Therefore, we considered an oxygen need of 6 or more as a trigger for hospitalization and thus as ‘severe disease’. In addition, an EWS score of 7 or more during hospitalization was regarded as ‘severe disease’, because 7 is the threshold for prompt emergency medical assessment and may require transfer of the patient to a critical care service [15].

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 hospitalization 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 [28].

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 generalizability 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 hospitalization 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 [29]. 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 [30]. The strength of this study is the fact that few studies describe geriatric risk factors and frailty and that the findings of this study can help physicians in decision making for older patients.

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

5. Conclusions

The speed of the first COVID-19 wave overwhelmed health-care workers and in the midst of the crisis it was a challenge to organize 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 'geriatric' risk factors, e.g. frailty and cognitive decline, than to 'conventional' risk factors, such as gender, obesity and specific comorbidities.

List Of Abbreviations

CCI: Charlson Comorbidity Index

CI: confidence interval

CFS: Clinical Frailty Scale

COPD: chronic obstructive pulmonary disease

CoV: Coronavirus

EWS: early warning score

ICU: intensive care unit

IQR: interquartile range

OR: odds ratio

PCR: polymerase chain reaction

SARS: severe acute respiratory syndrome

SPSS: Statistical Package for the Social Sciences.

WHO: World Health Organization

Declarations

Ethics approval and consent to participate

The study was approved by the medical ethics committee of the University Hospitals Leuven. Informed consent was obtained from the participants.

Availability of data and materials

Study data are available from the corresponding author upon request.

Competing interests

There are no competing interests to declare.

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Authors' contributions

Katleen Fagard: Conceptualization; Methodology; Investigation; Formal analysis; Visualization; Writing - Original draft preparation

Evelien Gielen: Conceptualization; Methodology; Writing - Reviewing & editing

Mieke Deschodt: Methodology; Writing - Reviewing & editing

Els Devriendt: Conceptualization; Methodology; Writing - Reviewing & editing

Johan Flamaing: Conceptualization; Methodology; Writing - Reviewing & editing; Supervision

Reporting

The study was reported according to the STROBE guidelines (www.strobe-statement.org).

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Figures

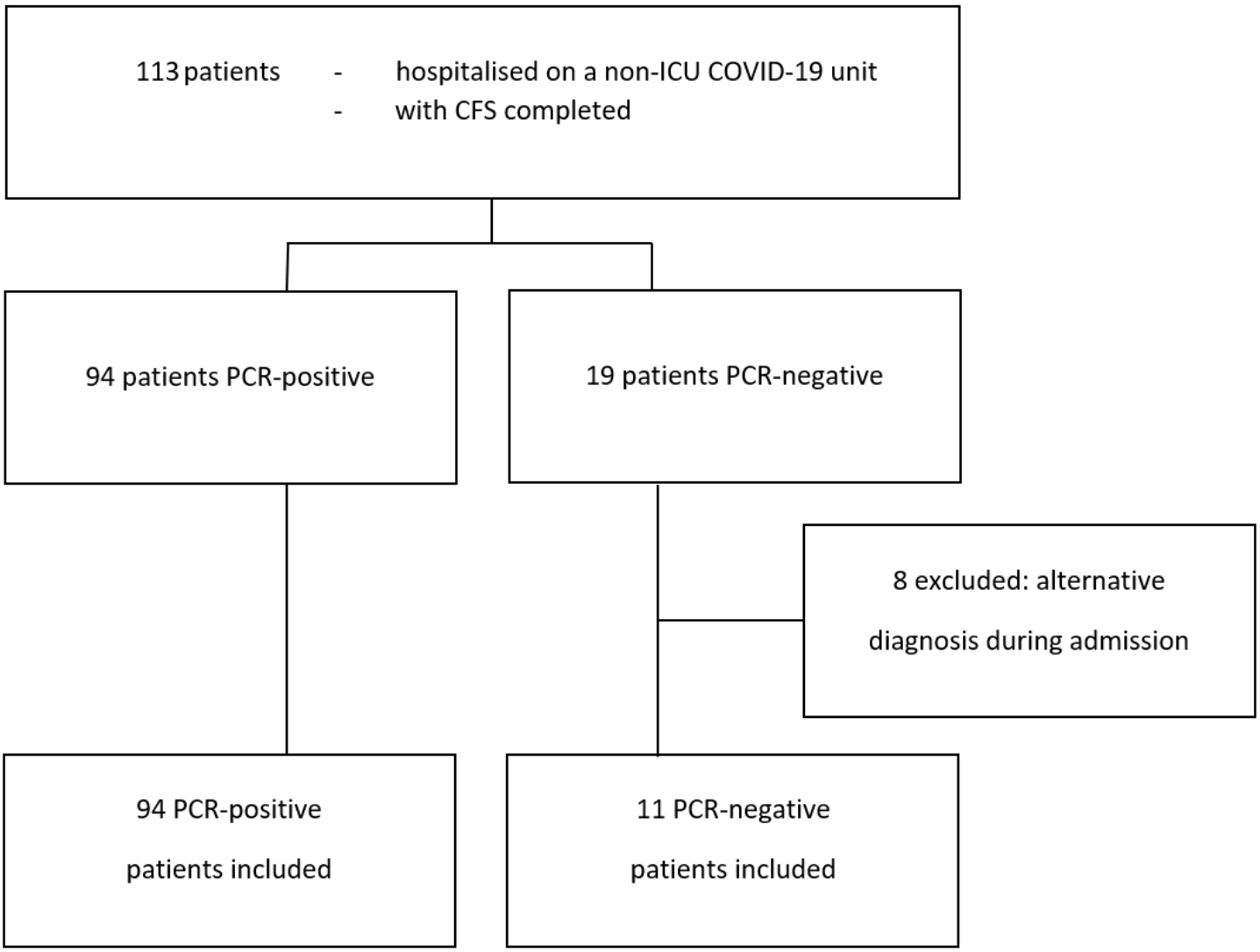

Figure 1

Flow-chart of in- and exclusions. CFS: Clinical Frailty Scale; PCR: Polymerase Chain Reaction

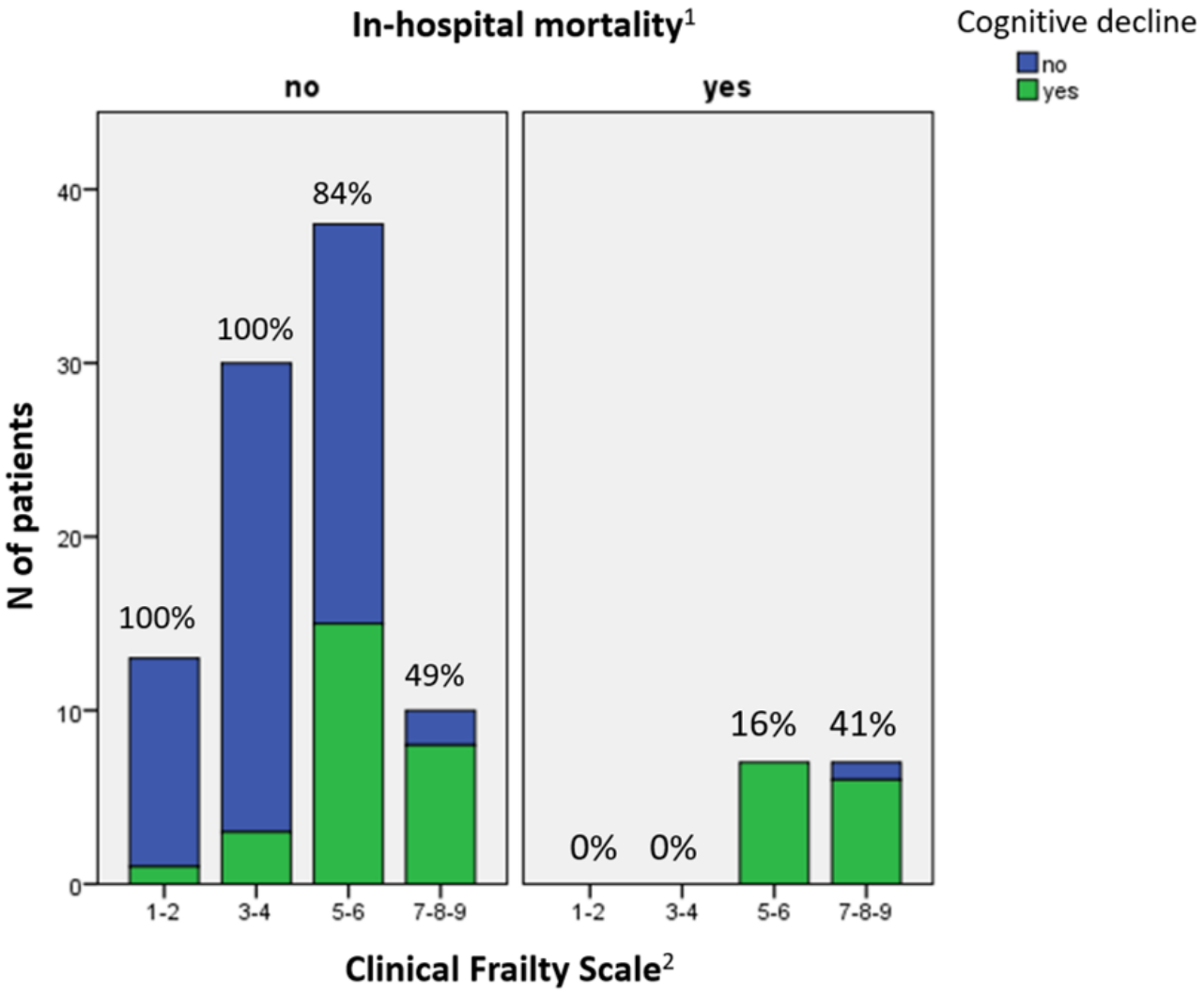

Figure 2

Relation between the CFS score, cognitive decline, and in-hospital mortality. CFS: Clinical Frailty Scale; N: number; 1above each column the percentage of patients who survived / died in that frailty group; 2none of the patients had a CFS score = 9