# Comparison of different prognostic scores in estimating short- and long-term mortality in COVID-19 patients above 60 years old in a university hospital in Belgium

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## 1. Title and abstract

**Comparison of different prognostic scores in estimating short- and long-term mortality in COVID-19 patients above 60 years old in a university hospital in Belgium.**

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**Key summary points**

Aim: Determining among 6 different scores which one most accurately predicted short-and long-term mortality in hospitalized COVID-19 patients above 60 years old.

Findings: Among 6 different prognostic scales, the 4C Mortality Score (4CMS) was the best to predict intrahospital mortality and mortality at 30 days and 6 months. To predict 12-month mortality, the Charlson Comorbidity Index (CCI) had the best performance.

Message: This study reflects the importance of considering comorbidities for short and long-term mortality after COVID-19.

**Abstract**

PURPOSE: Multiple scoring systems were used for risk stratification in COVID-19 patients. The objective was to determine among 6 scores which performed the best in predicting short-and long-term mortality in hospitalized COVID-19 patients ≥ 60 years.

METHODS: An observational, retrospective cohort study conducted between 21/10/2020 - 20/01/2021. 6 scores were calculated (Clinical Frailty Scale (CFS), Charlson Comorbidity Index (CCI), 4C Mortality Score (4CMS), NEWS score (NEWS), quick-SOFA score (qSOFA), and Quick COVID-19 Severity Index (qCSI)). We included unvaccinated hospitalized patients with COVID-19 ≥ 60 years old in Brugmann hospital, detected by PCR and/or suggestive CT thorax images. Old and nosocomial infections, and patients admitted immediately at the intensive care unit were excluded.

RESULTS: 199 patients were included, mean age was 76.2 years (60 - 99). 56 patients (28%) died within 1 year after the first day of hospitalization. The 4CMS predicted the best intrahospital, 30 days and 6 months mortality, with area under the ROC curve (AUROC) 0.695 (0.59-0.8), 0.76 (0.66-0.86) and 0.73 (0.64-0.82) respectively. The CCI came right after with respectively AUROC of 0.68 (0.58-0.77), 0.74 (0.66-0.82) and 0.72 (0.64-0.8). To predict mortality at 12 months after hospitalization, the CCI had the highest AUROC with 0.74 (0.66-0.81), before the 4CMS with 0.695 (0.61-0.78).

CONCLUSION: Among 6 scores, the 4CMS was the best to predict intrahospital, 30-day and 6-month mortality. To predict mortality at 12 months, CCI had the best performance before 4CMS. This reflects the importance of considering comorbidities for short- and long-term mortality after COVID 19.

**Keywords**

COVID-19, older adults, prognostic scores, mortality

**Statements and declarations**

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## 2. Introduction

In March 2020 a global pandemic caused by SARS-CoV-2 was declared by the World Health Organization (WHO) [1,2]. SARS-CoV-2 infection has many faces and clinical presentation can vary from an asymptomatic infection to a severe respiratory infection with need of admission at an intensive care unit (ICU) [3,4]. Whilst fighting the virus during the first waves, hospitals suffered a shortage of human and technical resources [5]. With this in mind, many hospitals were faced with an ethical question of how these resources could be most adequately allocated. In the Brugmann University hospital (Brussels, Belgium), several mortality scores (Clinical Frailty Scale (CFS), Charlson Comorbidity Index (CCI) and one COVID-19 specific score; the 4C Mortality Score (4CMS)) were performed. Based on these scores, scarce resources were allocated in the most efficient way, with respect for every patients values and goals.

As it has been studied before, we know that frailty and comorbidities were associated with an important increase in mortality risk, also in COVID-19 patients [6]. The use of the Canadian scale known as CFS was recommended by the Belgian Geriatric and Gerontologic Society during the pandemic, whereas this score was already used in our geriatrics department [7]. Although less specific for the elderly patients, the CCI was included in the evaluation for its ease of use, good reliability and reproducibility considering the impact of comorbidities on the risk of mortality. It calculates the 10-year mortality risk in different pathologies [8] and has proved its place in predicting mortality in COVID-19 patients [9]. After validation of the 4CMS, it was immediately used by the team. This score considered comorbidities as well as physiological parameters and laboratory values at admission. Literature confirms its good predictive value for intrahospital mortality in critically ill COVID-19 patients [10]. Since then, many more specific mortality risk assessment scales have been developed for the COVID-19 infection. With our data, some of them could be evaluated retrospectively such as the National Early Warning Score (NEWS), the quick-SOFA score (qSOFA) and the quick COVID-19 Severity Index (qCSI). These 3 scores take into account the vital parameters of the patient at the emergency room. The NEWS is an early warning score used in different kinds of pathology to identify patients at risk of developing critical illness. It uses basic clinical observations including heart rate, respiratory rate, blood pressure, oxygen saturation, and level of consciousness [11]. It was also proved to be a sensitive predictor of 7-day admission at the ICU or death in SARS-CoV-2 infections [12,13]. The qSOFA score had proven prognostic accuracy in predicting mortality in patients with suspected sepsis [14]. And finally, the qCSI was a score developed specifically to evaluate COVID-19 patients to estimate which patient will progress to respiratory failure within 24 hours [15].

Among these different scores used during the pandemic period, our objective is to evaluate which of these 6 scores (CFS, CCI, 4CMS, NEWS, qSOFA or qCSI) performed the best estimation of mortality.

## 3. Methods

### 3.1 Study design, setting, participants and objective

This is a single-center, observational, retrospective study, conducted in patients ≥ 60 years old hospitalized in the Brugmann University Hospital between October 21st, 2020, and January 20th, 2021, with SARS-CoV-2 infection. This study was approved by the ethical committee of Brugmann University Hospital (reference CE 2020/228).

Patients included were all unvaccinated hospitalized patients with COVID-19 infection aged 60 and over, detected by positive PCR (nasal or pharyngeal swabs or lower respiratory tract aspirates) or suggestive CT thorax images, described as such by the radiologist. Patients excluded from the study are nosocomial cases, patients admitted immediately at the ICU, and old COVID-19 infections (PCR COVID-19 positive > 14 days before hospitalization or positive IgG antibodies against COVID-19 infection).

The primary objective was to evaluate which of these 6 scores (CFS, CCI, 4CMS, NEWS, qSOFA or qCSI) performed the best estimation of intrahospital, 30-day, 6-month and 1 year-mortality after the start of the hospitalization with a COVID-19 infection for patients aged ≥ 60 years old, as we know age is an important risk factor in COVID-19 infections [16,17]. We also described the demographic and clinical characteristics of the study cohort.

### 3.2 Variables

Data collection were extracted from the electronic medical folder files: demographic (age, sex and living situation), clinical (respiratory rate, peripheral oxygen saturation, supplemental oxygen, temperature, systolic blood pressure, heart rate, Alert, Vocal, Pain, Unresponsive score (AVPU) and Glasgow Coma Scale (GCS)), and laboratory data (urea, creatinine, C-Reactive Protein (CRP) and albuminemia), as well as chest computer tomography protocols. Frailty was classified by the CFS [7]. Comorbidities were defined by the CCI (myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular accident or transient ischemic attack, dementia, chronic pulmonary disease (including astma), connective tissue disease, peptic ulcer disease, liver disease, diabetes mellitus, renal disease, hemiplegia, solid tumor, leukemia, lymphoma, AIDS). Cognitive status was – when available- evaluated by Mini Mental State Examination (MMSE) (n=35). Activity of daily living was evaluated by the Katz scale (n=90) [18].

Three scores were calculated directly at the admission (CFS, CCI and 4CMS) and three were calculated retrospectively (NEWS, qSOFA and qCSI) for every patient included in the study. The 4CMS, the NEWS, qCSI score and qSOFA, were calculated based on parameters and lab results taken at the urgency ward.

The length of stay was considered as the period of time between admission and discharge, and for the intrahospital non survivors, the date of death.

To establish the intrahospital, 30-day, 6-month and 1 year-mortality after the start of hospital admission, the vital status was searched in the medical files (Xcare, Abrumet, National population register).

### 3.3 Statistical methods

All statistical analyses were done with SPSS version 28. Continuous variables were reported as mean. Parametric tests were done for variables with gaussian distribution (QQ plot). Otherwise non-parametric tests were used. Categorical variables were reported as absolute number (percentage) and are compared by chi-square test (with Fisher's test if

appropriate). Sensitivity, specificity, positive (PPV) and negative predictive value (NPV), and the area under the receiver operating characteristic (AUROC) curve of each score for predicting all-cause intra hospital mortality, mortality at 30 days, at 6 months and mortality at 1 year were calculated. Youden's index was calculated to find the optimal cutoff points for the different scores. A value of $P \leq 0.05$ was noted as statistically significant. We excluded scores with incomplete data.

## 4. Results

Among the 409 patients hospitalized with a COVID-19 infection at Brugmann University Hospital between October 21st, 2020, and January 20th, 2021, 139 were younger than 60 years old and were excluded from the study. Were also excluded: 62 patients with a nosocomial COVID-19 infection and 9 patients with an old COVID-19 infection (Figure 1). Finally, a total number of 199 patients were included in the study. Mean age was 76.2 years old (minimum 60 – maximum 99). 105 patients were male (52.8%) and 28.3 % of the patients were institutionalized before hospitalization. We observed an intrahospital mortality rate of 18% (N=36) a 30-day mortality rate of 17% (N=33), a 6-month mortality rate of 24% (N=48) and a 1-year mortality rate of 28% (N=56).

Table 1 shows the demographic and clinical characteristics of the enrolled patients divided in different groups (all population, survivors and deceased at different time points). We highlight a significant difference between the survivors and the group who died after 1 year by age ($p<0.001$), renal disease ($p<0.001$), and urea level at admission ($p=0.01$). The different vital parameters at admission did not highlight a significant difference in any group (not included in Table 1).

*For intrahospital mortality*

Figure 2.a shows that in using the area under the Receiver Operating Characteristic (AUROC) curve to predict the intrahospital mortality, the 4CMS has the highest AUROC curve 0.695 (0.59-0.8), followed by CCI 0.68 (0.58-0.77), NEWS 0.65 (0.55-0.75), qSOFA 0.65 (0.54-0.75), CFS 0.64 (0.54–0.75) and qCSI 0.599 (0.49-0.71). But the best sensitivity was attributed to CCI with a value of 0.72 and a negative predictive value of 91.1% where the 4CMS had a better specificity with a value of 0.78 and the best positive predictive value of 36% (Table 2)

*For the 30-day mortality*

Figure 2.b shows the highest AUROC curve for the 4CMS 0.76 (0.66-0.86), followed by CCI 0.74 (0.66-0.82), CFS 0.71 (0.61-0.81), NEWS 0.66 (0.57-0.756) qSOFA 0.65 (0.54–0.76) and qCSI 0.599 (0.49-0.71). 4CMS had the best sensitivity with a value of 0.82 and a negative predictive value of 94%, closely followed by CFS and CCI with a negative predictive value of respectively 93% et 92.7%. The qCSI had the highest specificity with a value of 0.64 and a positive predictive value of 24.6% (Table 2).

*For the 6-month mortality*

Figure 2.c shows that 4CMS has the highest AUROC curve 0.73 (0.64-0.82), followed by CCI 0.72 (0.64-0.80), CFS 0.68 (0.59-0.77), qSOFA 0.64 (0.54-0.73), NEWS 0.62 (0.53–0.71) and qCSI 0.6 (0.49-0.71). CFS had the best

sensitivity with a value of 0.76 and a negative predictive value of 89.4%, followed by CCI with a sensitivity of 0.75 and a negative predictive value of 89.3%. The CCI had the highest specificity with a value of 0.66 and a positive predictive value of 41.1% (Table 2).

*For the one-year mortality*

Figure 2.d shows that the CCI has the highest AUROC curve 0.74 (0.66-0.81), followed by the 4CMS 0.695 (0.61-0.78), CFS 0.67 (0.58-0.76), NEWS 0.58 (0.495-0.67), qSOFA 0.58 (0.49–0.67) and qCSI 0.56 (0.47-0.64). CCI had the best sensitivity with a value of 0.73 and a negative predictive value of 86.6%. This is closely followed by the CFS with a value of 0.72 and a negative predictive value of 85.2%. The 4CMS had the highest specificity with a value of 0.81 and a positive predictive value of 51.7% (Table 2).

## 5. Discussion

Between the survivor and the deceased group of the enrolled patients; age, renal disease and urea level at admission were significantly different. Age is often reviewed as an important risk factor for a higher mortality in COVID-19 [16,17], and even though we only looked at a population older than 60 years old, we still withheld a significant difference in age between the survivors and the deceased. It is also well known that renal function and COVID-19 infection was associated with a higher mortality [19,20]. These 3 criteria were not included in CFS, NEWS, qCSI or qSOFA. CCI uses age and moderate to severe chronic kidney disease (CKD) and 4CMS uses age, urea level and renal function with the glomerular filtration ≤30ml/min as cut-off point, which could explain a better association with mortality in all different time points.

We did not find a significant difference in sex between the deceased group and the survivor group. Although has been described in literature that the male proportion is significantly higher in the deceased group [21]. When we looked at our results, we did see a trend towards a higher male proportion in the deceased group. We also saw that more male patients were hospitalized than female patients. This may be because more male patients had a severe COVID-19 infection [22]. Or maybe during this wave female patients were less commonly sent to the hospital, as has been shown in literature [23]. We also did not find a significant difference in proportion of institutionalized patients or patients dependent at home in the deceased group vs the survivor group. Although in literature it has been found that the case-fatality rate is 5 times higher in people who are institutionalized [24]. When looking into the details; we found that only 80 of the 199 patients included had a CFS > 3. We know that during these first waves people who were frail and institutionalized, were advised not to be hospitalized which led to avoidance or delay of urgent care [23]. This may be why we did not withhold a significant difference between the institutionalized patients and the non-institutionalized patients, although more research is needed.

We did not find a significant difference in physiological parameters at admission between the survivors and the groups of patients who died at different time points. This could possibly be attributed to the exclusion of acute patients who were immediately admitted at the ICU or patients with a nosocomial infection with severe altered vital parameters. We

did include patients who were too weak to be transferred to the ICU and patients hospitalized with palliative care, with severely impaired physiological parameters at admission.

Diabetes, dementia and obesity were not associated with a higher mortality in our study, despite the fact it was often described as an important risk factor in other studies [25,26,27]. It could be linked to the retrospective nature of the data received in acute and often isolated conditions. Also, to diagnose dementia you need physical examination, images of the brain and a neuropsychological examination and sometimes a lumbar puncture [28]. This might have been misdiagnosed for some participants or underdiagnosed for others.

To predict intrahospital mortality, mortality at 30 days and mortality at 6 months after hospitalization, we saw that 4CMS has the highest AUROC curve (Table 2 and Figure 1a, b and c). But for the 1-year mortality, CCI had the highest AUROC curve (Table 2 and Figure 1d). These results were also reflected in the way in which these scores are normally used: 4CMS is used to estimate intrahospital mortality [10], and CCI is used to estimate mortality after 10 years [8]. CCI had also already shown a good predictivity in mortality at 1 year in elderly patients experiencing a first acute heart failure hospitalization [29], as well as at 1 year after having had a hip fracture [30]. This suggests that we can use the CCI to estimate mortality 1 year after hospitalization, although more research is needed.
Following these results, it may be interesting to use the 4CMS until 6 months after hospitalization, and maybe also evaluate its use it in other diseases than COVID-19. To date, we did not find any articles that investigated its use in estimating more long-term mortality in other pathologies.

In our study, the CFS was not noted as the best way to estimate mortality, although it was widely considered a very important score in estimating intrahospital and 30-day mortality [31], as well as an important indicator of worse outcome in COVID-19 infections [32,33]. It did come on the third place in estimating 30-day mortality, 6 month-mortality and 1-year mortality, which is certainly not bad, if you consider the ease of use of this score.
NEWS, qSOFA and qCSI were scores that take into account the physiological parameters at hospitalization. Our study showed that they were not the best predictors of mortality in our population, neither on short-term nor on long-term. NEWS is known to identify patients at risk of developing critical illness [11], it is not a mortality score. Also, qCSI is a COVID-19 specific score to estimate which patient will progress to respiratory failure within 24 hours [15]. It only includes a limited number of parameters. Although these scores have proven their value in detecting acute deterioration in COVID-19 patients [34], we could not confirm a better estimation of mortality in our population. qSOFA is a mortality score in patients with suspected sepsis but has already been proven a poor indicator in estimating mortality in COVID-19 patients [35,36], possibly because of the limited number of parameters included and not taking into account oxygen saturation [37].

The 4CMS and CCI are both scores that take the comorbidities into consideration. The 4CMS is based on the CCI but also includes obesity. It focuses on the number of comorbidities. Once two comorbidities were included, you get the maximum score [10]. The CCI takes into account more specific consideration of the impact on the gravity of each comorbidity on the total score [8]. We saw a lower AUROC curve of the scores where only the vital parameters were taken into consideration. Comorbidities therefore had an important impact on mortality in our specific population. The

CCI and the CFS had a good sensitivity in all groups and 4CMS for 30-day and 6-month mortality. All these scores had the highest negative predictive value, which means they can best exclude the risk of further deterioration, although not any score was perfect.

We observed an intrahospital mortality rate of 18% (N=36) a 30-day mortality rate of 17% (N=33), a 6-month mortality rate of 24% (N=48) and a 1-year mortality rate of 28% (N=56). In comparison, we saw a case-fatality ratio of 29% in Belgium in patients older than 85 years old, with proven COVID-19 infection and death within 3 weeks after confirmation of infection.

The limitations in this study were related to the retrospective characteristic of the study, the limited patients included and the exclusion criteria. Detection by CT elevated the risk of false positives [38]. Some positive PCR tests may be older COVID-19 infections that were non-detected in the 14 days before hospitalization. As this is a single-center observational study, information bias was possible if certain elements in different files were missing. We did not use the absolute value of the different physiological parameters, which may result in less powerful statistical analysis. To prevent selection bias we determined the CFS and the parameters at admission. To have better results we need more and larger studies.

## 6. Conclusion

In comparing the 6 different mortality risk scores, we found that 4CMS was the best predictor for intrahospital mortality, mortality at 30 days and 6 months after hospitalization. The CCI was the best predictor for the 12-month mortality. This reflected the importance of considering comorbidities for short- but particularly long-term mortality.
The 4CMS should be studied to evaluate mortality at 6 months in patients over 60 years old and in other pathologies than COVID-19.

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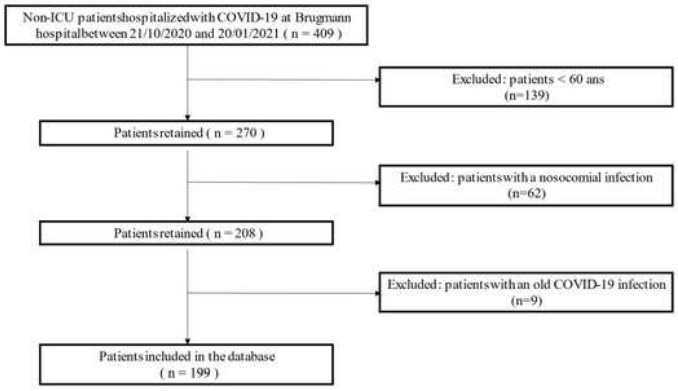
# Figures

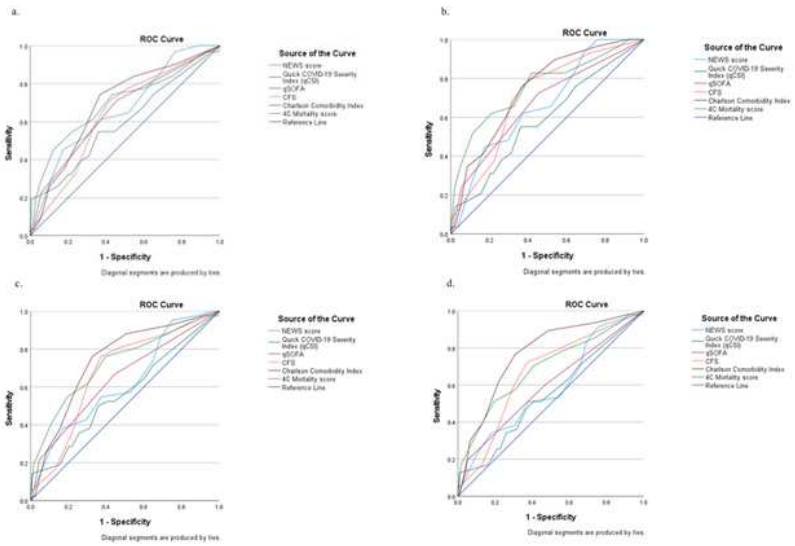
**Figure 1.** Flow chart of the study.




## Figure 1

See image above for figure legend

**Figure 2.a,b,c,d** Graphical representation of the receiver operating characteristic (ROC) curve of the evaluated score for respectively intrahospital mortality, mortality at 30 days, mortality at 60 days, mortality at 1 year after hospitalization.




## Figure 2

See image above for figure legend

# Supplementary Files

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- Table1.pdf
- Table2.pdf