Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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LETTER TO THE EDITOR

Coronary Calcium Score in COVID-19 Hospitalized Patients

We read with interest the article of Dillinger et al. (1). Although their rationale makes sense, several issues should be discussed.

The authors stated that coronary artery calcium (CAC) score assessed on low-dose computed tomography predicts the need for ventilation and death in a cohort of 209 hospitalized coronavirus disease-2019 (COVID-19) patients. We analyzed the same endpoint in a similar population of 280 patients with COVID-19. We excluded patients with previous history of cardiovascular disease.

Although CAC score indeed predicted the same combined endpoint, adjusting for age made its additional predictive value nonsignificant (**Figure 1**). Because the correlation between CAC and age is extremely strong, this is not astonishing. Additionally, during the peak of pandemic, access to intensive care unit (ICU) was limited for older patients because of the saturation of ICU beds. In our cohort, mortality was the main driver of events and was artificially higher in the older population (with higher CAC score) not having access to the ICU. Mortality was very low compared with previous series (2) and with our results (4.3% vs. 16.0%), although the authors reported only the mortality in the ICU. In our cohort, among the 72 patients who were transferred to the ICU, 19 (26.4%) patients died.

The proportion of an elevated CAC score in patients younger than 62 years of age was also surprisingly high compared with results from our cohort (32% vs. 6.2%) and with data reported by the MESA (Multi-Ethnic Study of Atherosclerosis) registry for the same age and ethnicity (3). This might be explained by the technical limitations of the method used for CAC score assessment: absence of triggering, lower temporal resolution, and a larger field of view, which alters the voxel size, leading to an overestimated CAC score (4).

The differences between various patient series suggest that the evidence linking cardiovascular disease with COVID-19 remains incomplete, and further research with more robust analyses are warranted.

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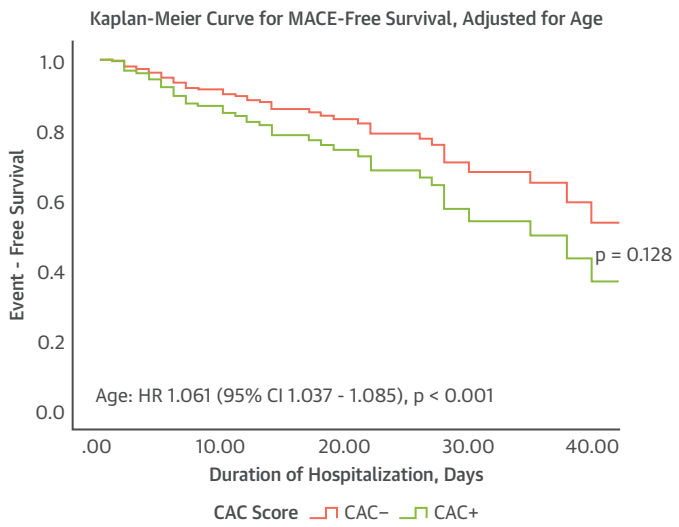
FIGURE 1 Kaplan-Meier Curve for the Combined Endpoint



Coronary artery calcium (CAC) score had a nonsignificant additional predictive value for the combined endpoint when adjusted for age. MACE = major adverse cardiac event (mechanical noninvasive/invasive ventilation, extracorporeal membrane oxygenation or death).

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REPLY TO LETTER:

We read with interest the letter from Dr. Cosyns and colleagues reporting that coronary artery calcium (CAC) was associated with the need for ventilation or

death. This may be contrasted to our study (1), in which the main parameter studied was not an Agatston score, but rather was the presence or absence of coronary artery calcification on a noncontrast chest computed tomography scan. We report a significant association between the presence of CAC and the primary outcome, defined as mechanical noninvasive or invasive ventilation, extracorporeal membrane oxygenation, or death, for both older and younger patients. By comparison, Dr. Cosyns and colleagues noted that the prognostic value of CAC score measured in their cohort was age dependent. Reasons for this difference may underlie varied patient population, outcome of interest, or statistical consideration (adjusted odds ratio was used by Dr. Cosyns and colleagues, while we evaluated age in 2 subgroups). Additionally Dr. Cosyns and colleagues reported that mortality was the main driver of events, with a mortality rate of 16.0%. In our study, the main driver of the primary endpoint associating CAC was noninvasive ventilation ($p < 0.0001$), while mortality ($p = 0.49$) was not significantly different. Our study included all patients presenting to the emergency unit of the hospital and diagnosed with COVID-19 and did not include only the most severely ill patients requiring intensive care. We put forth that this is the primary reason for the difference in mortality between our study and the Dr. Cosyns and colleagues' cohort (4.5% vs. 16.0%). Interestingly, a recent meta-analysis also revealed a similar mortality rate of 5% as compared with our study (2). Of note, during the first wave of COVID-19 infections in France, most patients diagnosed with COVID-19 were hospitalized due to a lack of prognostic indicators for even milder forms of infection.

The other interesting point noted by Cosyns and colleagues is the fact that mean CAC score value of patients <62 years of age was higher than the CAC score values usually described in general population, especially in the MESA (Multi-Ethnic Study of Atherosclerosis) study (3). We agree with our colleagues that technical aspects can explain this difference. The measurements of CAC score in our study was performed on chest computed tomography for the purpose of assessing COVID-19-induced lung damage. Thus, the acquisition was performed at 2.0-mm thickness, without electrocardiography gating, with a lower temporal resolution, with a wider field of view, and with a different tube voltage (100 kV). This analysis may lead to an overestimation of CAC (4).

In conclusion, the evaluation of prognostic factors associated with the severity of COVID-19 infection appears complex and is influenced by the heterogeneity of populations described in the varied studies and endpoints. We put forth that the presence of CAC provides an easy measure and may prove useful across future explorations in COVID-19 registries. We agree with Dr. Cosyns and colleagues that further large multicenter studies are needed to completely answer this question.

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