

Prehospital Spinal Muscle Mass Is Unlikely to Be a Predictor of COVID-19 Mortality

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To the Editor

We read with interest the article by Schinas et al on a retrospective study of the cross-sectional area (CSA) of the spinal muscles at the T10 level as an outcome predictor in 84 patients with coronavirus disease 2019 (COVID-19) pneumonia admitted between April 2020 and February 2021 to two academic teaching hospitals in Greece [1]. Outcome was assessed according to survival status and computed tomography severity score (CT-SS) [1]. CSA correlated with CT-SS and with white blood cell counts, C-reactive protein, fibrinogen, and D-dimers [1]. Furthermore, CSA predicted CT-SS variation and predicted mortality with a sensitivity of 66.7% and a specificity of 88.9% [1]. The study is impressive, but some points require discussion.

The first point is that the study had a retrospective design [1]. Retrospective designs have the disadvantage that data can be missing, the accuracy of the data cannot be easily checked, desired missing or new data can no longer be generated, and indications for certain examinations are often not comprehensible. We should know how much data of the cohort was missing and to what extent this affected the results. How many patients were excluded due to missing data? Other disadvantages of the design are that it was only national, bicentric and uncontrolled.

The second point is that the test-retest reliability and inter-observer variabilities of the CSA measurements were not calculated. To assess whether CSA measurements are truly suitable as outcome measures, it would have been useful to repeat the measurements after 24 or 48 h and assess them by the second radiology team.

The third point is the discrepancy between the statement that only patients who had undergone chest CT at admission were included and the statement that CT images obtained within 48 h of admission were included in the analysis. We should know whether in fact only CT scans performed on hospital day 1 or whether CT scans performed on hospital day 2 or hospital day 3 were also included. If CT scans performed on hospital day 2 or 3 were also included, anti-severe acute respiratory syndrome

coronavirus 2 (SARS-CoV-2) medications started on hospital 1 could have had an influence on CSA.

The fourth point is that several differential causes of sarcopenia of the spinal muscles have not been sufficiently ruled out. In addition to primary or secondary myopathies, degenerative disease, poorly controlled endocrine disorders, nutritional deficiencies, or treatments that could affect muscle mass (steroids, chemotherapy), sarcopenia may be due to an immunological disease, motor neuron disease, or malignancy. Since the CSA of the spinal muscles highly depends on the prehospital physical condition of the included patient, we should know how many exercised regularly, how many were retired, or how many were admitted from a nursing home. Since SARS-CoV-2 infection can be complicated by a variety of central and peripheral nervous diseases [2], such as Guillain-Barre syndrome (GBS) [3], neuropathy [4], or myositis [5], it is essential to exclude these before using CSA measurements of the spinal muscles as a tool to predict outcome and survival of COVID-19 pneumonia. We should know how new-onset myositis, GBS and vasculitis with neuropathy were excluded in all 84 enrolled patients. Have all patients undergone screening tests for neuromuscular disease?

A fifth point is that those who died were significantly older than those who survived, suggesting that advanced age could be a predictor of mortality. Was age identified as an outcome predictor on multivariate analysis?

In summary, before recommending the measurement of spinal muscle CSA at the T10 levels to predict the outcome of SARS-CoV-2-infected patients in the intensive care unit, an international, prospective and controlled study in a large cohort needs to be conducted.

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None to declare.

Conflict of Interest

The authors declare that the research was conducted in the ab-

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sence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author Contributions

JF was responsible for the design and conception, wrote the first draft, and gave final approval.

Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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Reply From Dr. Georgios Schinas et al

We appreciate the comments and observations provided by the correspondent regarding our study on the prognostic value of the cross-sectional area (CSA) of the spinal muscles at the T10 level in COVID-19 patients [1]. Below, we address each of the points raised:

1) Retrospective design and data completeness

We acknowledge the limitations inherent in a retrospective study design and have thoroughly discussed them in the limitations section of our article. According to the methods of our study, patients with incomplete medical records and missing

data on key variables were excluded. In total, 53 patients were excluded due to missing radiologic measurements and/or disease outcome. In the analysis, seven patients with missing laboratory values were included (three from the mortality group and four from the survival group). Additionally, two patients were missing total length of stay data (one from each group). While some laboratory values were missing randomly across patients, no variable had more than 20% missing data, which is a commonly accepted threshold for incorporating missing data in statistical analyses. As discussed in the limitations section, our study was bicentric and uncontrolled, which could have led to differences in computed attenuation values between CT machines and patient positioning. We recognize the need for prospective studies to validate our findings.

2) Test-retest reliability and inter-observer variability

We agree that assessing the test-retest reliability and inter-observer variability is crucial for validating CSA measurements. Although our study did not include repeated measurements within 48 h, two independent radiologists from each center, blinded to the outcomes and relative clinical information, conducted the analyses, and consensus was reached on the final measurements. Future studies should incorporate test-retest protocols and inter-observer variability assessments to their study design.

3) Inclusion criteria for CT scans

The inclusion criterion was chest CT scans performed upon admission. While most CT scans were performed within the first 24 h, and consequently, the patients were admitted to the COVID-19 ward, the decision to include CT scans performed within 48 h of hospital admission was made due to the logistical constraints of the pandemic. Some patients who could not undergo imaging within the first 24 h, had their CT scans conducted on the second day of hospitalization before any anti-SARS-CoV-2-specific medications had been initiated. This consistency reduces the likelihood of treatment effects influencing the CSA measurements.

4) Differential diagnosis and exclusion criteria

We excluded patients with known myopathies, degenerative diseases, poorly controlled endocrine disorders, nutritional deficiencies, and recent treatments affecting muscle mass. While we did not perform specific screening for all potential neuromuscular diseases, there was no clinical indication of such conditions in the medical records of the included patients. The conditions referenced in the letter, such as GBS, myositis, and neuropathy, typically develop following infection, not during the acute stage of the disease [2-5]. This is well-documented in the literature, where case reports and series clearly indicate that these conditions have a post-infectious or para-infectious pattern, suggesting an immune-mediated response triggered by the virus [2]. It is understood that such conditions cannot develop

overnight, and thus, they were not present in the acute phase of the disease in our study cohort. We acknowledge that prehospital physical condition and other factors could influence CSA and suggest that future studies should include more comprehensive screening to rule out these confounding factors.

5) Age as a predictor of mortality

Our multivariate analysis did include age as a covariate, and it was identified as a significant predictor of mortality. However, even after adjusting for age, T10-CSA remained an independent predictor of survival. This highlights the potential utility of T10-CSA in conjunction with other established predictors, such as age, to improve prognostication in COVID-19 patients. The impact of age on mortality and its relationship with sarcopenia were discussed in the limitations section of our study.

Conclusion and future directions

We agree that before the widespread recommendation of T10-CSA measurements, larger, prospective, and controlled studies are needed. Our study serves as an initial step in identifying a potentially valuable prognostic marker, but validation in diverse and larger cohorts is necessary. We welcome collaborations and further research to explore and confirm the clinical utility of T10-CSA in predicting outcomes in COVID-19 and other critical illnesses.

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