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The relevance of nutritional and metabolic derangements in COVID-19 patients

Dear Editor,

We are glad of the high interest received regarding our original data on the level of muscularity, comorbidities and outcomes among critically ill COVID-19 patients [1–3]. In particular, of note was that the prevalence of comorbidities in our cohort was approximately 2-times more common in those patients who died [1] and that the non-survivors were older than survivors, suggesting the importance also of aging in the development of sarcopenia [1,2]. In this light, we agree with the observation [2] that the presence of comorbidities (including obesity) - associated with aging - might have promoted the development of sarcopenia and in turn mortality in our cohort of patients.

Regarding the most accurate diagnosis of sarcopenia, we believe that the assessment of muscle strength/performance is particularly important, however, not feasible in COVID-19 ICU patients, especially if ventilated. Therefore, the method we used was previously performed in the same clinical setting unveiling high reliability [4].

Moreover, the data by *Qaisar* et al. [3] are of interest, indicating that individuals with sarcopenia at baseline or after the COVID-19 infection showed worse disease severity scores than those without sarcopenia, extending our findings [1].

Also, we agree with the authors [3] that the measurement of novel circulating biomarkers may offer the possibility to diagnose sarcopenia in those conditions, including ICU, where muscle strength cannot be easily assessed. For these reasons, *Qaisar* et al. explored the association between c-terminal argin fragment 22 (CAF22) plasma levels (a product of neuromuscular junction degeneration) and sarcopenia in COVID-19 patients showing that, among the non-sarcopenic individuals, at baseline the group which developed sarcopenia presented with higher CAF22 levels than the remaining participants [3]. This is in line with a previous study which evaluated the CAF22 levels in patients with a recent acute stroke performing rehabilitation [5]; in this study, CAF22 levels were associated with muscle performance, in particular patients who showed physical recovery presented a significant association with higher CAF22 concentrations and with markers of muscle integrity at the body composition analysis [5].

Interestingly, also in non-ICU settings, patients with COVID-19 may experience severe nutritional derangements, mainly represented by unvoluntary body weight loss, which was associated with worse clinical outcomes, including a prolonged disease duration, increased systemic inflammation, and decreased renal function [6].

Finally, recent preliminary data have shown a high percentage of malnutrition also among patients who survived at COVID-19 [7], highlighting the clinical relevance of poor nutritional status not only at baseline, conditioning patients outcomes during ICU stay, but also developed during hospital stay, suggesting the urgent need for clear nutritional therapeutic interventions in this setting.

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