LETTER

Letter to the Editor Regarding "Influence of Baseline Physical Activity as a Modifying Factor on COVID-19 Mortality: A Single-Center, Retrospective Study"

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Dear Editor,

We congratulate Salgado-Aranda et al. on their paper "Influence of Baseline Physical Activity as a Modifying Factor on COVID-19 Mortality: A Single-Center, Retrospective Study", which discusses the possible influence of baseline physical activity level on COVID-19 mortality [1]. We endorse regular physical activity for a healthy lifestyle, but some data and interpretation included in this paper can be misleading.

The authors conclude on the basis of a retrospective and observational study that sedentary behavior increases the mortality of hospitalized patients with COVID-19 (13.8%

and 1.8% for sedentary and active group, respectively). However, there are many problems that may hinder these conclusions. The data presented by the authors do not support these conclusions mentioned in the abstract and in the full text, and this characterizes "spin" or misleading reports [2]. Additionally, the authors also gave some recommendations for clinical practice based on an observational study [3]. It is important to highlight that recommendations from observational (and retrospective) studies can be unfortunately flawed for clinical practice.

Therefore, some points need to be emphasized. First, the physical activity level was measured using the Rapid Assessment of Physical Activity Scale (RAPA) questionnaire, where patients self-reported their previous physical activity data by telephone. However, as described by the authors, in the case of patients who died (45 subjects), the questionnaire was filled out by a family member. Obviously, this is not the best method and it is important to provide more details about these patients and RAPA data. In this case, family members probably did not know about the patient's level of physical activity. Self-reported physical activity level questionnaires have a memory bias, which may make it impossible to conclude the outcome of the study. It seems that if a family member answers the questions, bias may be even greater. Additionally, there was no mention about

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RAPA 2, which provides valuable information on the type of physical exercise performed. Why did the authors not include this information? There is no mention about criteria defining physical activity habits.

This is relevant information considering that the last physical exercise bout could affect the prognosis of a hospitalized patient. As well, we have some studies suggesting that lockdown can affect physical activity levels. Additionally, the way you measure physical activity can have different impacts, such as different follow-up, amount of physical activity measures, and measurement methods (by accelerometer or questionnaires) [4].

In the baseline data (Table 1), age and the prevalence of comorbidities between the sedentary (group 1) and active group (group 2) are different for some chronic diseases. This imbalance between groups makes the conclusion of the study inappropriate. In a sense, to the best of our knowledge, sicker patients can impact reverse causality problems. For example, did the patients die as a result of COVID-19 complications due to being sick at the baseline or owing to sedentary lifestyle? It is necessary to have a control for pre-existing diseases at baseline or exclude patients with chronic diseases (e.g., hypertension, diabetes mellitus, and dyslipidemia) at baseline [5].

The study was not clear about the primary outcome. The sample size calculation is missing and unfortunately the study has no statistical power. We recalculated the sample size for this study considering alpha of 0.05, beta of 95%, a 50% proportion of exposed and unexposed subjects, and a relative hazard of 20%. The total number of subjects needed to achieve the number of events is 1104 (552 for each group) with a total number of events needed of 462. Moreover, multivariate Cox regression analysis was not adjusted for several comorbidities such as male, hypertension, pulmonary disease, heart disease, cerebrovascular disease, and liver disease. With only four deaths in the active group and with a short follow-up it is hard to conclude that sedentary lifestyle has an HR of 5.91 (1.80–19.41). This huge confidence interval shows that the study has several methodological issues to be discussed.

Finally, we appreciate the opportunity to read this paper. However, we would like these points to be considered in order to improve transparency and scientific integrity.

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