



Fibrosis-4 (FIB-4) index and mortality in COVID-19 patients admitted to the emergency department: a new interesting predictive index for patients with COVID-19 disease?

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Received: 28 June 2022 / Accepted: 1 July 2022 / Published online: 12 August 2022
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Dear Editor,

We read with great interest the article by Bucci et al., which investigated the Fibrosis-4 (FIB-4) Index and mortality in COVID-19 patients admitted to the emergency department [1].

We want to congratulate to authors about this originally. However, we consider that there are some key aspects that need to take into account for proper clinical extrapolation.

First, during COVID-19 pandemic, prediction factors are needed to help front-line providers to identify who might be at higher risk of mortality for respiratory failure needing intensive care admission and ventilator support. Several complex models have been developed to predict these outcomes using clinical data and markers of increased systemic inflammation associated with infection [2]. Recent studies show that the FIB-4 Index, initially developed to predict advanced fibrosis in those with liver disease, may be affected by other systemic diseases, such as COVID-19 through non-hepatic mechanisms, including systemic inflammation and/or bone marrow suppression [3]. Before this study, Sterling et al. demonstrated that FIB-4 is associated with the need for mechanical ventilation and 30-day mortality in patients admitted with COVID-19 [3]. Li et al. demonstrated that FIB-4 is associated with mortality in COVID-19, independent of underlying conditions including liver diseases [4]. In these aspects, we consider that following these published

studies the single factor composing FIB-4 score was not predictive of mortality or need for ICU admission, so it is very important to understand how the composite index work so well.

Second, age is a very important factor, because it is in the numerator of the FIB-4 formula and the authors reported a statistically significant difference ($p < 0.001$) in the age in the group of patients with a FIB-4 > 3.25 for the group with a FIB-4 < 3.25 with a mean age of 76 (70–81) and 57 (51–64), respectively [1].

The missing link is to understand how lung commission in terms of inflamed lung tissue, COVID-related ARDS and extension of lung involvement can be correlated with this index. Also, time to respiratory failure development is another important missing key factor that is interesting to know.

Finally, FIB-4 is an index developed to predict liver fibrosis so it is very interesting to study if this index can predict long-COVID and in particular lung fibrosis development [5].

Further clinical trials need to confirm these observations about the power of FIB-4 as an index and mortality.

Acknowledgements None.

Declarations

Conflict of interest Paolo Ruggeri and Antonio Esquinas have no conflicts of interest relating to this manuscript. They disclose financial or non-financial interests that are directly or indirectly related to this manuscript.

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