

Correspondence on "Electrocardiographic findings and prognostic values in patients hospitalised with COVID-19" by "Pinto-Filho"

We read with great interest the manuscript of Martins Pinto-Filho *et al.*¹ It is a multicentre study about the prognostic values of electrocardiographic findings, where such a gap was provided by the US Preventive Services Task Force that the current evidence was insufficient to relate such findings to predict and thus prevent CVD events.²

Clinical findings must have proper statistical analysis to ensure reliability.³ It is especially important for clinical prediction, where the experimental design, validation framework and source of biases must be precisely taken into account.⁴⁻⁶ Various standards, including TRIPOD,⁷ have been proposed in the literature and have become part of the author guidelines of journals such as *BMJ Heart*. The multiple logistic regression model (MLR) was used by Pinto-Filho *et al.*¹ as a multivariable prediction model. The following issues are critical to implementation, among which some items are based on TRIPOD Checklist: Prediction Model Development and Validation (TCPM):

1. It is not clear why the authors did not check missing randomness⁸⁻¹⁰ before running the MICE, as it assumed such randomness (eg, MCAR) (TCPM.9). It is especially important when different centres participate in the study to make sure that systematic missing is not present. Variables such as smoking had a missing rate of 25.1%, making it important to check the assumption. However, the missing rate is not the only factor for multiple imputation decisions.¹¹
2. Although the multicentre study provided a good chance to perform external validation, it was not used. The model could be designed in some centres and tested in others to ensure its generalisation capability. Moreover, no internal validation was provided for the MLR. No goodness-of-fit measures (including pseudo-R² statistics and the Hosmer-Lemeshow test, which is critical for clinical prediction systems) were provided. Briefly, regression diagnostics is entirely missing in this work, thus preventing it from being rigorously reliable in clinical

prediction due to possible biased coefficients, inefficient estimates or invalid statistical inferences.¹²⁻¹³ Some implementation details are also missing, such as the intercept in the MLR (TCPM 10b,15a).

3. In the MLR method, the risk factors' contribution to disease depends on the follow-up period.¹⁴ Moreover, as 30% of the ECGs were performed not at the admission, the ECG findings are time-dependent covariates, and a suitable prediction method with adjusted time must be used. Alternatively, time-to-event adjusted survival models provide a reasonable solution. The relative time of the ECG recording compared with the patient's admission must also be reported (TCPM.7a).
4. It is unclear whether a similar treatment strategy was used in the entire centres, as the study included LMIC, HIC, LIC and UMIC groups. It could be an important confounder of the study and must be discussed in the paper (TCPM.5c). How did the imbalanced sample size of the centres participating in the study affect the paper's conclusion? Moreover, the low prevalence of some of the electrocardiographic abnormalities (eg, AF (1.7%), BBB (4.9%) and prolonged QT (3.2%)) introduces uncertainty in the analysis and conclusion, given that no sample size calculation method was used in the study (TCPM.8).
5. The MLR method could discriminate between patients with/without events. It is unclear why the paper did not provide related outputs and parameters, such as ROC and Harrell's C-index. Moreover, as a clinical prediction model, the calibration plot and its parameters (eg, calibration in large and slope) must be provided, especially for external validation.¹⁵ Proper discrimination and calibration avoid overfitting to ensure the clinical application of the models worldwide.

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