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Replication of a mortality prediction model in Dutch patients with COVID-19

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ARISING FROM Yan et al. *Nature Machine Intelligence* https://doi.org/10.1038/s42256-020-0180-7 (2020)

There is a clear need for a simple mortality prediction model to help guide clinical decision making for patients with COVID-19. Yan et al. demonstrated the strong predictive capacity of a decision rule consisting of three readily available laboratory measures for COVID-19 mortality: lactate dehydrogenase (LDH), high-sensitivity C-reactive protein (hs-CRP) and percent lymphocytes[1].

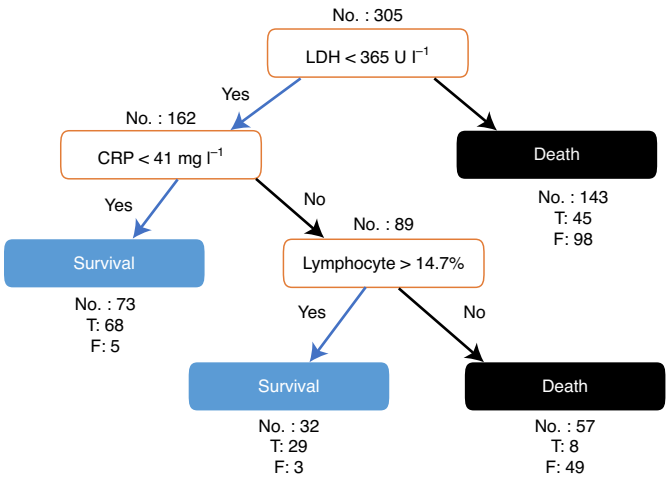
We performed an independent replication of their model using data from our large general hospital (St Antonius Hospital, Nieuwegein, the Netherlands). We included 305 patients over 18 years of age who presented to the emergency room with a clinical suspicion of COVID-19 between 19 March and 4 May 2020, with a positive SARS-CoV-2 polymerase chain reaction (PCR) result and for whom data for the three biomarkers were available at presentation. Mortality data were collected on 14 May 2020 at an average follow-up duration of 41 days.

The average age of the patients was 62.7 years and 188 (62%) were male. Of these patients, 61 died (at 1–33 days after admission, with a median of 7 days). We found that the model has 92% survival prediction accuracy but only 27% mortality prediction accuracy. This compares to a 100% survival prediction and 81% mortality prediction found by Yan et al.

In our population, 42 out of 303 patients were admitted to the intensive care unit (ICU). Of these patients, 36 (86%) had an unfavourable outcome from the decision rule, but only 15 (36%) of them died (all with LDH > 365 U l^{-1}).

We conclude that, in Dutch patients, a favourable outcome of the decision rule was indeed a good predictor of non-admission to the ICU and of survival. Although an unfavourable outcome of the decision rule could have been interpreted as a warning sign, the majority of our patients thus classified still survived. We hypothesize that this discrepancy between our data and those of Yan et al. may be due to genetic differences in the expression of the presented biomarkers. For example, LDH expression has been reported to display substantial genetic heterogeneity between Asians and Caucasians[2]. Alternatively, differences in treatment protocol or in baseline characteristics of the patients may have influenced the outcome.

In conclusion, our analysis supports the high survival prediction accuracy of the decision rule proposed by Yan et al., but fails to confirm its high mortality prediction accuracy. The identification of patients with COVID-19 with a low risk of mortality can be useful to inform the level of surveillance within or outside the hospital.



The decision rule using three key features and their thresholds in absolute value. Num, the number of patients in a class; T, the number of correctly classified; F, the number of misclassified patients.

Reporting Summary

Further information on research design is available in the Nature Research Reporting Summary linked to this Article.

Data availability

The data that support the findings of this study are available in the Supplementary Information.

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2. Lv, J. et al. Prognostic value of lactate dehydrogenase expression in different cancers: a meta-analysis. *Am. J. Med. Sci.* **358**, 412–421 (2019).

Author contributions

M.J.R.Q. conceived of the presented idea. M.J.R.Q., T.C.v.H., P.C.G.-v.d.V. and J.W. extracted and analysed the data. All authors discussed the results and contributed to the final manuscript.

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Competing interests
The authors declare no competing interests.

Additional information
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Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	EPIC Caboodle. MicrosoftSQL server 2016 Management Studio v 13.0.16106.4
Data analysis	Excel

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Sample size	305 patients
Data exclusions	No data is excluded
Replication	No replication
Randomization	no randomization
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Outcomes	Primary outcome death, secondary outcome survival