Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

References

1. Cottee AM, Seccombe LM, Thamrin C, King GG, Peters MJ, Farah CS. Bronchodilator response assessed by the forced oscillation technique identifies poor asthma control with greater sensitivity than spirometry. *Chest*. 2020;157(6):1435-1441.
2. Lipworth B, Chan R, Kuo CR. Criteria for airway oscillometry reversibility in asthma. *Chest*. 2020;158(3):1282-1283.
3. Cottee AM, Seccombe LM, Thamrin C, King GG, Peters MJ, Farah CS. Response to letter to the editor: criteria for airway oscillometry reversibility in asthma. *Chest*. 2020;158(3):1283-1284.
4. Kaminsky DA. What is a significant bronchodilator response? *Ann Am Thorac Soc*. 2019;16(12):1495-1497.
5. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung volumes and forced ventilatory flows. *Eur Respir J*. 1993;6(suppl 16):5-40.
6. Thamrin C, Gangell CL, Kusel MM, et al. Expression of bronchodilator response using forced oscillation technique measurements: absolute versus relative. *Eur Respir J*. 2010;36(1):212.
7. Oostveen E, Dom S, Desager K, Hagendorens M, De Backer W, Weyler J. Expression of bronchodilator response using forced oscillation technique measurements: absolute versus relative. *Eur Respir J*. 2010;36(1). 213-213.

Risk Factors for Mortality in Hospitalized Coronavirus Disease 2019 Patients

To the Editor:

We read with interest the article published in *CHEST* (July 2020) by Chen and coworkers,[1] about mortality risk factors in hospitalized coronavirus disease 2019 (COVID-19) patients. In our opinion, the article deserves some attention. First, the same cohort with similar objectives has simultaneously appeared in another journal (*JAMA Internal Medicine*).[2] The most relevant difference between the two studies was the variable analyzed, mortality vs a composite variable (death, ICU admission, or mechanical ventilation). Both articles develop a multicomponent score, with a different statistical approach (logistic regression vs multivariate Cox regression). This may explain the different variables selected. In the companion study, 10 predictive variables were included, of which only four were maintained in the current analysis, and two new variables were included. We believe that because the two articles were published simultaneously, the inclusion of different variables to predict evolution in the same cohort merits discussion to avoid reader confusion.

Second, and more relevantly, the current model cannot be applied without an external validation in other populations. External validation is essential in all multicomponent prognostic scores, but in this case it is mandatory, because population and evolution differ greatly from what is reported in other areas of the world, and even other Chinese hospitals on the same dates. This suggests that in most cases the hospital admission criteria in this cohort seem to be related more to epidemiological reasons than clinical disease severity.[3] The mortality reported was clearly lower than that observed in European and American cohorts in which it reaches percentages of 10% to 25%. Of note, the mortality reported in the same cohort in Hubei was 7.3%, and outside Hubei it is 0.3%, whereas in three other cohorts of 828 patients hospitalized in Wuhan, mortality on February 7, 2020 was 18.6%, 19.2%, and 16%, respectively.[4,5] For comparative purposes, in our hospital (a 500-bed tertiary hospital in Spain), 723 patients were hospitalized for COVID-19 between February 5 and May 30, 2020. Of these, 29% developed a critical illness, and 17.4% died during admission.

Obviously, with these data, it seems that hospitalization criteria in this cohort may have contributed to containing the spread of the virus, but this strategy was not feasible in other areas where the health system was close to collapsing. More importantly, in our opinion, these differences preclude direct application of the proposed model without a previous external validation in different populations.

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References

1. Chen R, Liang W, Jiang M, et al. Risk factors of fatal outcome in hospitalized subjects with coronavirus disease 2019 from a nationwide analysis in China. *Chest*. 2020;158(1):97-105.
2. Liang W, Liang H, Ou L, et al. Development and validation of a clinical risk score to predict the occurrence of critical illness in hospitalized patients with COVID-19. *JAMA Intern Med*. 2020;180(8):1-9.
3. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. *JAMA*. 2020;323(13):1239-1242.
4. Liang WH, Guan WJ, Li CC, et al. Clinical characteristics and outcomes of hospitalised patients with COVID-19 treated in Hubei (epicentre) and outside Hubei (non-epicentre): a nationwide analysis of China. *Eur Respir J*. 2020;55(5):2000547.
5. Zhang S, Guo M, Duan L, et al. Development and validation of a risk factor-based system to predict short-term survival in adult hospitalized patients with COVID-19: a multicenter, retrospective, cohort study. *Crit Care*. 2020;24(1):438.

Response

To the Editor:

We thank Dr Dietl and colleagues for their interest in our work and their thoughtful opinions on the predictive model for mortality in patients with coronavirus disease 2019 (COVID-19).

Yes, as Dr Dietl and colleagues mentioned, the different main outcomes (fatal outcome vs a composite outcome, including death, ICU admission, or mechanical ventilation), statistical methods (stepwise selection vs LASSO, Cox regression vs Logistic regression), and coding method of variables (continuous variables vs categorical variables), would contribute to the discrepancy of the final risk model's variables in two papers.[1,2] In the early stage of the pandemic, little was known about the prognosis of hospitalized patients with COVID-19, so it was urgent to explore the risk factors for mortality. The nationwide database was set up by January 31; we then immediately started to construct a predictive model for the fatal outcome, aiming to provide more information for management and prevention as soon as possible.

We agreed with the point by Dr Dietl that performing the external validation is important. Because of the urgent situation in the early peak of the pandemic, it was difficult to recruit other cohorts for external validation at that time. We had mentioned this as a limitation of our study in the discussion part.[1] Alternatively, internal validation could be performed for the development of a prediction model. Some studies had used bootstrap resampling to assess the developed nomogram without the external validation.[3,4] We also performed bootstrapping in the paper, and the C-index for prediction was 0.91, which indicated a reliable capacity for predicting. The calibration curves also implied good consistency between the prediction and the observation.

At the early phase of this pandemic, it was reported that a high proportion of critical illness subjects would be deteriorated into fatality. It was also necessary to assess which are at high risk of developing critical illness, which might be useful to aid in delivering proper treatment and optimizing use of resources. Since mid February, the spread of the COVID-19 in China started to decrease with the effective prevention and isolation strategy. Our institute then was able to obtain data from four additional cohorts. These continuous cohorts made it possible to perform the external validation in the companion study finished in late March, which aimed to construct a predictive risk score to estimate the risk of developing critical illness.

Model-based prediction regarding COVID-19 could help physicians identify patients with poor prognosis at an early stage. If possible, performing the complete validation would be better because of the different population with predisposing factors such as race or spectrum of comorbidities. Meanwhile, some other external factors might be relevant to the disease progression. Collapse of medical resources, especially the overload of ICU capacity, might account for a higher case fatality rate in critically ill patients with COVID-19.[5] In the future, with the development of advanced algorithms such as deep learning and artificial intelligence, prognostic prediction models will be more comprehensive and able to take into account different application scenarios.

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