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de la Asunción, Gemma Grau, Oriol Llugués, Aina Mateu, Franklyn Ferney Meza, Ginebra Libori-Roch, Siena Molina, David Clemente, Ana Martínez-Urrea, Tere Moreno-López, Lluís Simón-Pascua, and Laura M. Gisbert.

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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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Changing and Unchanging Trends for an Old Disease



To the Editor:

We were interested in the research letter published in *CHEST* (May 2020) by Nayak et al,¹ which presented the epidemiology and trends in the management of thoracic empyema in Ontario during the last two decades. The broad overview provided by this article was informative because of the study's large patient cohort and long study period. We acknowledge that this was a database-derived analysis and that in-depth research was difficult. However, we have three issues, the solutions to which will strongly reinforce the value of this study as one of the largest population-based cohort studies with a focus on thoracic empyema.

First, the major aim of this study was to provide insight into best practices. Therefore, data stratification of the patients' characteristics according to the treatment group (nonoperative treatment, video-assisted thoracic surgery decortication, and open decortication groups) will reveal how the disease management differed (or did not differ) according to the patients' backgrounds. Data of baseline characteristics, such as age, sex, and the Charlson Comorbidity Index score in each treatment group would indicate which patients were likely to undergo surgical treatment and which patients tended to undergo nonsurgical treatment in a real-world setting.

Second, an analysis of outcomes, such as the length of hospitalization, treatment cost, and mortality rates according to the treatment group would also be invaluable data, because patients who promptly undergo surgery are usually considered to have higher treatment success and reduced hospital stay.² Even though the surgical treatment group in this study included a mix of patients who underwent surgery early and those who were referred to surgery after failure of long-term conservative therapy, we would still be interested in how the results may differ in this large study cohort.

Finally, a brief presentation of the standard fibrinolytic agents used in Canada would be relevant. We have followed the results of studies on new or combined use of fibrinolytics, especially those of tissue plasminogen activator and DNase.³ However, these agents are not covered by insurance worldwide and may not be affordable or accessible for all. It would be informative to present the standard choices of fibrinolytic agents in Canada during this study period and at what point new treatment agents were introduced into usual clinical practice. Overall, we believe that this straightforward and large-scale study will become a reference point regarding the treatment of empyema for the following decades.

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