Clinical course and mortality risk of severe COVID-19

Published Online
March 17, 2020
https://doi.org/10.1016/S0140-6736(20)30633-4
See Online/Articles
https://doi.org/10.1016/S0140-6736(20)30566-3

Several published reports of early clinical descriptions of coronavirus disease 2019 (COVID-19) have emerged from Hubei province in China, and many more will come. These early reports, typically simple descriptive case series of patients hospitalised with COVID-19 (mostly with pneumonia), provide valuable information on the more severe end of the disease spectrum. We tend to hear more about the most severe cases in the early stages of a new disease, as these are the ones first brought to the public's attention and are associated with deaths. However, it is important to bear in mind that the current best estimate is that about 81% of people with COVID-19 have mild disease[1] and never require hospitalisation. These cases have not yet featured much in published clinical descriptions.

In *The Lancet*, Fei Zhou and colleagues[2] provide further insight into the clinical course and mortality risk for adults with COVID-19 severe enough to require hospitalisation. They report findings from 191 patients with COVID-19 from Wuhan during the first month of the outbreak, and follow them through to discharge (n=137) or death (n=54). The follow-up until discharge or death is a point of difference from other case series to date. Their cohort had many characteristics in common with other reports[3–5]—a median age of 56·0 years (IQR 46·0–67·0), a high percentage (62%) of men, and nearly half (48%) of patients with comorbidities. In-hospital death was associated with, on admission, older age (odds ratio 1·10, 95% CI 1·03–1·17; p=0·0043), a higher Sequential Organ Failure Assessment score (5·65, 2·61–12·23; p<0·0001), and blood d-dimer greater than 1 µg/mL (18·42, 2·64–128·55; p=0·0033), findings known to be associated with severe pneumonia.[6,7] The study also presents early data on changes in clinical and laboratory findings over time, which could help clinicians to identify patients who progress to more severe disease. In-hospital mortality was high (28%), much higher than in other reports that had incomplete follow-up data,[3,5,8] and was very high among the 32 patients requiring invasive mechanical ventilation, of whom 31 (97%) died. This might reflect a higher proportion of patients admitted with severe disease in the early stages of the outbreak. In another report from Wuhan, mortality was 62% among critically ill patients with COVID-19 and 81% among those requiring mechanical ventilation.[9] While the world awaits further information from other locations, including from outside China, the current message is that mortality is high among the minority of people with COVID-19 who get severe disease.

The cohort design of this study provides excellent front-line information about mortality risk. It is essential for readers to understand that this truly is a retrospective cohort design, even if it might appear otherwise at first. Careful consideration of the design is essential to understanding the findings. The authors were able to collect a wealth of information from admission to discharge on many of the earliest known cases of coronavirus in the world. By identifying this large group of patients united by their disease and tracking them to these endpoints, the authors have provided us with insight into risk factors for in-hospital death. Even though their cohort does not include the censored observations of patients admitted during the study timeframe but not discharged by the end timepoint, these results can still be considerably useful for epidemiological description of the disease in terms of person-level risk. By excluding incomplete observations, it is possible that the reported mortality rate is biased to appear larger than it is, as data from those patients who were not discharged by the end timepoint were not included. However, as a true population at risk of mortality, these patients are representative of the earliest onset of COVID-19. Excluding patients

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who began treatment well into the epidemic brings homogeneity to the exposure level and treatment. These preliminary data provide an important framework to build on as the world moves forward in the fight against this pandemic. The timeliness and value of this information far outweigh the slight bias stemming from the exclusion of patients with incomplete data at the end of the study period.

The report by Zhou and colleagues also provides data on viral shedding.[2] Throat swabs were obtained every other day and were PCR positive for a median of 20·0 days (IQR 16·0–23·0) after onset of symptoms. In survivors, median duration of viral shedding was 20·0 days (17·0–24·0), ranging from 8 to 37 days, but the virus was detectable until death in non-survivors. These early findings are similar to those reported for the severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome coronaviruses,[10–12] and we await more detailed information on viral load kinetics and shedding of SARS coronavirus 2 in various disease states. Importantly, PCR positivity does not necessarily indicate viable virus, and additional data are needed to better understand the infectious period of COVID-19 and implications for treatment and infection control.

Although there is always the limitation of generalisability in epidemic investigations, this study adds to a rapidly growing knowledge base on the clinical course and mortality risk of COVID-19. We now have a better understanding of the severity of hospitalised COVID-19, but more data are needed on treatment options that improve survival.

We declare no competing interests.

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