

What is the True Mortality in the Critically Ill Patients with COVID-19?

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The coronavirus disease 2019 (COVID-19) pandemic is stressing our healthcare system in an unprecedented manner with physicians having to consider allocation of ventilators, medications, and other essential resources. In these times, appropriate assessment of morbidity and mortality of the SARS-CoV-2 infection is crucial. Reporting the overall case fatality rate (CFR) for COVID-19 is challenging given that the epidemic is still rapidly evolving (therefore, in a disease with a long incubation period, the number of cases at the current time will be larger than a few weeks prior) and the lack of widespread testing leads to underdiagnosis. Both these factors lead to an overestimation of the overall CFR.

During a novel pandemic, the need for data warrants accelerated publications, often without prolonged patient follow-up. This, especially in the intensive care unit (ICU), with the prolonged length of critical illness in patients with COVID-19, makes following up every patient until death or discharge challenging. In addition, these mortality rates can change depending upon the subjects studied and the treatment they receive. Therefore, when mortality rates are reviewed, they need to be put in context to the time and place of assessment. In contrast to the overall CFR, in the ICU, we can have a problem of mortality underestimation. While we have the ability to detect almost every case in the ICU (depending upon test sensitivity), it is challenging to report accurate mortality rates based on interim data from studies that include patients who are currently sick and may eventually die of the disease.

In a retrospective case series of 1,591 critically ill patients infected with SARS-CoV-2 by Grasselli et al.,¹ from Italy, the overall

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mortality was 26% (405/1581). Given that the median length of ICU stay for patients discharged from the ICU was 8 days (5–12), and that 58% of the patients, despite a minimum follow-up of 7 days, were still in the ICU at the end of their follow-up period (March 25, 2020), there is a concern that the overall mortality is much higher than 26%, as many of these patients will eventually die. Other studies, though much smaller, have reported mortality rates from 17 to 62% in patients admitted to the ICU. However, in these studies too, 12–38% of the study population continued to be in the ICU at the end of their respective follow-up periods (Table 1).^{1–8}

Table 1: Studies assessing mortality in critically ill patients with SARS-CoV-2

Study	Date published	Location	n	Mortality	Discharged from ICU	In the ICU at end of follow-up
Goyal et al. NEJM, 2020 ⁸	April 17, 2020	New York, USA	130*	15% (19)*	23	68% (88)
Wang et al. ARJCCM, 2020 ²	April 8, 2020	Wuhan, China	344	39% (133)	54% (185)**	7% (26)**
Grasselli et al. JAMA, 2020 ¹	April 6, 2020	Lombardy, Italy	1581	26% (405)	16% (256)	58% (920)
Bhatraju et al., NEJM, 2020 ⁵	March 30, 2020	Seattle, USA	24	50% (12)	38% (9)	12% (3)
Arentz et al., JAMA, 2020 ⁶	March 19, 2020	Washington state, USA	21	52% (11)	10% (2)	38% (8)
Zhou et al., Lancet, 2020 ⁷	March 11, 2020	Wuhan, China	50	78% (39)	22% (11)	
Yang et al., Lancet Respiratory Medicine, 2020 ³	February 24, 2020	Wuhan, China	52	62% (32)	15% (8)***	23% (12)***
Wang et al., JAMA, 2020 ⁴	February 7, 2020	Wuhan, China	36	17% (6)	53% (19)	30% (11)

*A total of 130 out of 393 patients admitted to the hospital required mechanical ventilation and admission to the ICU. Unclear if other patients required the ICU level of care. The data presented are only for patients in the ICU requiring invasive mechanical ventilation. Discharges are for the discharge from the hospital, and thus it is unclear if some of these patients were discharged from the ICU but still admitted to the hospital

**Of the 211 survivors, 185 were “discharged”; it is unclear whether they were discharged from the ICU to a non-ICU bed, or from the hospital. It is also unclear whether the remaining 26 survivors were still in the ICU or admitted in a non-ICU ward

***Eight patients were discharged from the hospital. Three patients were still on invasive mechanical ventilation, one was on noninvasive ventilation, two were using high-flow nasal cannula, and six were using nasal cannula

We may not realize the true mortality of SARS-CoV-2 until this pandemic is over. But to allow physicians around the globe to better understand both the morbidity and mortality in patients with COVID-19, it is essential that the future studies report their follow-up data on all patients. Also, the published studies with interim data reported should provide a follow-up for us to assess the true CFR. In a study by Zhou et al.⁴ ($n = 50$), where all patients were followed for their complete length of stay, the mortality rate was noted to be significantly higher, at 78%. Another example of longer follow-up yielding more accurate mortality data on a large subset of their population is the study by Wang et al.² ($n = 344$), wherein the authors report outcomes at 28 days. In this study, the mortality was 42% (133/318) in the 92.5% of patients who had a definitive outcome (discharge or death).

It is thus essential that all future studies either comment on the mortality of only those patients who have had adequate follow-up (i.e., until discharge or death) or provide follow-up data for patients still admitted to the hospital. Until then, it is imperative that the mortality data from interim studies should be interpreted with caution.

DISCLOSURE STATEMENT

This paper, including any part of it, has not been published elsewhere and is not under consideration for publication elsewhere. All authors read and approved the final draft and give permission to the journal to use any material from the paper if it should choose to publish it.

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