## COVID-19 Mortality Differences: Patient-related Data and Intensive Care Unit Load Are Prerequisites

*To the Editor*:

We read with great enthusiasm the study by Nishikimi and colleagues, evaluating the mortality differences in mechanically ventilated patients with coronavirus disease (COVID-19) hospitalized in traditional versus expanded intensive care units (ICUs) (1). In comparing the initially higher mortality rate found in the expanded ICUs (departments converted to ICUs during the pandemic) than in original ICUs, this difference disappeared when the analysis considered certain confounders. The authors performed unadjusted and adjusted Cox regression analyses to evaluate in-hospital 28-day mortality. The adjusted analysis included patient-related data and, most important, information on disease severity upon ICU admission and data on hospital and ICU patient load. Adjusted analyses smoothed the initially observed mortality differences (1).

The authors should be congratulated on their work. They conducted manual chart reviews, carefully collected demographic data and comorbidities, and assessed illness severity (1). We believe that studies reporting mortality, especially mortality variations across disparate settings, should always consider factors that may be possible confounders. Among these, disease severity is of no doubt. This is true not only when comparing expanded with original ICUs but also when reporting regional or even between-ICU mortality differences. Patient-related data are of great importance in mortality analysis. Bravata and colleagues examined variations in between-center mortality, considering past medical history, vital signs, and laboratory examination results (2). They found that despite ICU mortality variation across facilities (from 0 to 100%), the heterogeneity resulted only from differences in patient characteristics (i.e., comorbidities, clinical disease severity) (2).

Especially for critically ill patients, mortality analyses should always consider multiple aspects; otherwise, the reports may be misleading. Disease severity, multiorgan failure upon ICU admission, different criteria and strategies concerning the optimal intubation time in COVID-19 acute respiratory distress syndrome (partly depending on ICU bed availability), and ICU admission policies (admitting nonintubated patients as well) have a substantial impact on ICU mortality (3). We have shown that when patients experienced respiratory distress (hypoxemia, arterial oxygen tension/fraction of inspired oxygen $<$100 mm Hg; and tachypnea, respiratory rate $>$25 breaths/min) for more than 7 hours before intubation, they presented impaired respiratory system mechanics, greater multiorgan involvement (depicted through the severity scores on the Sequential Organ Failure Assessment and Acute Physiology and Chronic Health Evaluation II), and higher mortality than patients intubated earlier (3). Intrahospital mortality differences may even be present, arising from different treatment protocols (i.e., excessive immunosuppression). The wide use of excess immunosuppressive treatments in regions with an increased incidence of multidrug- and pan–drug-resistant microorganisms may further affect mortality, increasing the risk for secondary bacterial infections in COVID-19, as was lately shown in a multicenter study (4). A recent report pointed to significant regional variations in mortality on a national level, but without considering patient-centered data (5). These superficial analyses may lead to conflicts between healthcare workers in the same country or may even affect decisions on a national level.

A second major factor that should always be considered in mortality reports is the patient load. Recently, it was shown that the hazard ratio for all-cause mortality was increased to 1.67 when the ICU load was greater than 75–100%, reaching 2.35 when the load was 100% and more (6). Nishikimi and colleagues calculated the hospital occupancy at each time point and adjusted mortality for this covariant. Mortality differences disappeared after adjusting for these two major factors: disease severity and hospital occupancy. Thus, the newly expanded ICU presented mortality rates similar to the classical units even when the ICU load was impressive; maintenance of a nurse-to-patient ratio of 1:2 and being cared by certified specialists in critical care, factors not considered in many studies (5), may have contributed (1).

In conclusion, when dealing with mortality, reports should always consider patient-related outcomes such as disease severity and hospital strain; otherwise, the results should always be considered with skepticism. ■

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## Understanding the Impact of Intensive Care Unit Personnel on Intensive Care Unit Mortality during Times of High Demand

*To the Editor*:

Nishikimi and colleagues (1) recently compared the outcomes of mechanically ventilated patients in existing and expanded intensive care unit (ICU) areas during the first wave of the coronavirus disease (COVID-19) pandemic and found there to be no increased risk of 28-day mortality in expanded ICU areas (1). This finding contrasts with earlier reports in which the opening of new ICU beds was linearly associated with mortality (2) and with prepandemic studies in which critically ill patients treated outside of existing ICUs had decreased survival (3). The authors suggest their findings support the opening of new ICU areas as a solution to successfully manage critically ill patients during times of excess demand. Before such a recommendation can be justified, it is relevant to consider potential differences between extant and expanded ICU areas.

We recently reported the outcomes of mechanically ventilated patients with COVID-19 in expanded and existing ICUs at a large academic center (4). In contrast to Nishikimi and colleagues, we found that patients in expanded ICU beds had decreased survival despite receiving similar treatment. Both areas had access to the same technological resources and infrastructure.

Expanded ICU beds can be staffed with caregivers (i.e., nurses and doctors), all or only some of whom are trained in critical care. In some settings, internists and general nurses lead teams with oversight supervision from an intensivist. In these areas, specialist care becomes diluted. In our study, although a 1:2.5 general nurse-to-patient ratio was maintained, the ICU prepandemic nurse-to-patient and intensivist-to-patient ratios were diluted from 1:2 and 1:5 to 1:4 and 1:6, respectively, in existing ICUs. However, in expanded ICU areas, 1:13 nurse-to-patient and 1:10 intensivist-to-patient ratios were established. Similarly, Simchen and colleagues (5) reported increased mortality in critically ill patients treated outside the ICU with diluted nurse ratios but no intensivist oversight.

In contrast, Nishikimi and colleagues described expanded ICUs with a 1:2 nurse-to-patient ratio and direct supervision by critical care or cardiology physicians in both areas. We believe the higher mortality seen in expanded ICUs in our study, when compared with that of Nishikimi and colleagues, is most likely explained by differences in the availability of ICU-trained individuals to staff the expanded areas.

Several retrospective studies have proposed thresholds for ICU nurse-to-patient and intensivist-to-patient ratios above which mortality appears to increase: approximately 2.5 for ICU nurses and 7.5 for intensivists in high-acuity settings (6, 7). Although the specific number varies widely, depending on the region and type of ICU, workload seems to be the limiting factor. Objective workload measures (e.g., high Nursing Activities Score, work hours, staff turnover) are strongly associated with mortality, particularly in settings where patient acuity is high (8), as in the study by Nishikimi and colleagues and in our study. We believe the conclusion put forth by Nishikimi and colleagues will likely hold true only in settings where human resources are sufficient to maintain a ratio of patients to subspecialized personnel which nearly approximates that in existing ICUs. Given ongoing shortages of ICU nurses and intensivists (9), it seems unlikely that expanding ICUs in times of excess capacities, such as a pandemic, can otherwise provide care similar to that in existing ICUs. ■

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