Learning more about what can make COVID-19 deadly: Insights from the Atlanta Metropolitan Area

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As the first wave of the novel coronarvirus, SARS-CoV-2, washes over the United States, identification of key characteristics that place people at risk for severe SARS-CoV-2 infection becomes paramount in preparing for the next tide. In “Predictors at admission of mechanical ventilation and death in an observational cohort of adults hospitalized with COVID-19” by Jackson and the other members of the Centers for Disease Control and Prevention Team (CDC), the investigators endeavor to highlight the key characteristics that lead to the unfortunate sequelae of severe SARS-CoV-2 infection, namely intermittent mechanical ventilation (IMV) and death in a predominantly metropolitan non-hispanic black population.

The authors provide an elegant, innovative, and thorough analysis of potential risk factors for death and IMV amongst a unique hospitalized Covid-19 population. While many papers have outlined the key risk factors for severe SARS-CoV-2 infection [1, 2, 3], there is an emerging concern regarding the disproportionate effect COVID-19 has on vulnerable populations [4]. This particular study is primarily composed of non-hispanic black patients receiving medical care at a mix of academic and community locations isolated to a metropolitan area in a regional hotspot within the United States (Atlanta, Georgia).

Jackson et al found that individuals aged 65–74 years and ≥75 years were the strongest single independent predictor of death when compared with comorbidity matched younger patients (<45 years). Other important factors influencing mortality emerged after close examination of the data, specifically the presence of an elevated BUN or AST on admission. Moreover, those patients that reside in sub-acute nursing facilities were more likely to die, but did not show any demonstrable increase in risk of IMV.

Notably and contrary to many existing studies, Jackson et al, found a striking lack of correlation between risk factors elucidated by other larger cohort studies. Peculiarly, the lack of influence that chronic lung disease, immunocompromise, tobacco use, and obesity in either IMV initiation or mortality was surprising. The influence of pre-hospital anti-hypertensive regimens stands as another difference between contemporary studies and the data presented by the authors. In their analysis, the prehospital use of angiotensin II receptor blockers (ARBs) lead to an increased risk of both IMV and mortality. While this is biologically feasible given the role of the ACE2 receptor to viral entry, other studies have refuted this finding [5].

Interestingly, the prehospital use of dihydropyridine calcium channel blocker (dCCB) shared a similar two-fold increased risk for IMV and death as ARBs. In another study, with a smaller as well as a demographically different cohort of patients, dCCBs proved to reduce both IMV and mortality [6]. While the protective relationship dCCB may be mechanistically attributable to relaxation of pulmonary vasoconstriction, the potential harmful effects found by Jackson et al. in this study lacks any hitherto understood biologic plausibility. The juxtaposition of responses between the dCCB studies both warrants further validation, and in depth investigation should a causal relationship be made.

Remaining true to the science, the authors are forthright with the shortcomings of their study. Pointedly, they recognize the primarily metropolitan sample, with a relatively small number of enrollees, and a short enrollment period spanning approximately three months. In order to mitigate the aforementioned handicaps, the authors used robust random Forest models to allow for improved control of confounders. However, the authors recognize that despite employing statistical rigor, the large number variables explored, and their failure to incorporate adjustments for multiple testing lends a bias toward the null. Furthermore, Jackson et al recognize that the decision to commit a patient to IMV is heterogeneous, highly influenced by individual clinical practice, and in itself a plausible source of bias.

As with all observational studies, the results should not serve to direct care, but rather fuel innovation, and further research. Jackson et al.'s article stands as a challenge for other researchers to pick up the gauntlet they have thrown down. This article highlights the urgency of investigating vulnerable populations, the importance of casting aside preformed bias, and the value of embracing the scientific method as our principle weapon in the war against COVID-19.

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