Even in the early years of the 21st century, lessons can be learned in regard to adverse events of mass vaccination. The association of myopericarditis after smallpox (variola major) vaccination in preparation for a possible smallpox event from December 2002 to March 2003 noted an incidence of myopericarditis of 1 per 12,819 primary vaccines within 30 days.[4] This was associated with an odds ratio of 3.6 (95% confidence interval 3.33 to 4.11) compared with that for unvaccinated individuals.

With the current and future pandemics caused by emerging respiratory pathogens, it would be wise to evaluate interventions with possible consequences.[5] Attempting to modify hypothetical risks can lead to further risks, which may lead to collateral toxicity that was originally unforeseen at the initial intervention. Evidence-based medicine (whenever possible) with an appreciation of medical history should guide our risk-benefit decisional evaluations in the near future.

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COVID-19 and Shock: A Cautionary Tale for Elderly Patients From a Pooled Analysis

To the Editor:

The shocking scale of coronavirus disease 2019 (COVID-19) infections is worrisome, with more than 1 million confirmed cases and greater than 50,000 reported deaths across the globe by the end of March 2020. The unprecedented challenges brought by the COVID-19 pandemic have overwhelmed the health care system, strained health care workers, and raised a dire need to collect, analyze, and interpret real-time data to expedite understanding the etiopathogenesis, risk factors, and prognosis of COVID-19 and ways to curtail overall mortality rate.

Although the awareness of the natural progression of COVID-19 is increasing, with cardiovascular risk factors and older age being frequently identified as major risk factors for poor survival in COVID-19 patients, our knowledge remains limited on the pooled prevalence of shock and its effect on predicting mortality in COVID-19 infection. Although the predominant complication of COVID-19 is acute respiratory illness that could lead to acute respiratory distress syndrome, COVID-19 patients with cardiovascular complications and sepsis have a heightened risk of developing shock with potential inhospital mortality during the disease course. Acute cardiac injury has been reported to range from 12% to 16.7% in COVID-19 patients.

To our knowledge, this is the first pooled estimate of the prevalence of shock in COVID-19 patients with age-based variation (mean age <50 versus >50 years). Random-effects models were obtained to perform a meta-analysis, and I^2 statistics were used to measure interstudy heterogeneity. After a thorough review of the literature from PubMed, Scopus, and Google Scholar, data were collected from 5 studies (4/5 septic shock) reported from China until March 2020.[1-5] Among 1,578 COVID-19 patients, the pooled prevalence of shock was 6.3% (95% confidence interval 4.0% to 16.8%) and I^2=96%, with the cohort older than 50 years (mean age) showing significantly higher prevalence of shock (9.5%; 95% confidence interval 2.4% to 20.5%) compared with the younger cohort (mean age <50 years) (3.3%; 95% confidence interval 0% to 11.4%) (Figure).

In this meta-analysis, the elderly population had a higher burden of shock compared with the younger cohort. The predilection of elderly patients toward sepsis and a higher burden of cardiovascular diseases owing to higher comorbidities could be a major reason for the observed age-related disparity in the prevalence of shock. This warrants stricter precautions and social distancing for the geriatric population.

A potential link for shock in COVID-19 could be due to elevated cytokine levels. During a viral illness, the up-regulation of cytokines such as interferon gamma and interleukin (IL)-10 potentiates the vasodilation leading to shock. Similarly, IL-1β, 6, and 8; monocyte chemoattractant protein-1; and plasminogen activator inhibitor-1 levels are increased in the acute phase of sepsis,

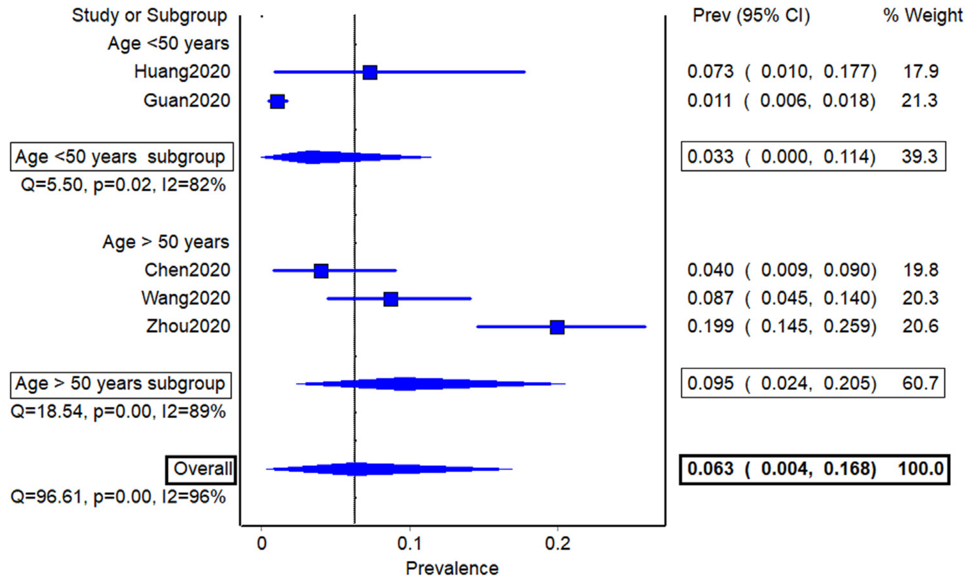

Figure. Random-effects pooled prevalence of shock among COVID-19 patients stratified by mean age.

reflecting endothelial injury. Viral infections could trigger a hyperinflammatory state, such as cytokine-storm syndrome, as featured in COVID-19 patients, which could contribute to developing shock with a potential for multiorgan dysfunction.

Concisely, this meta-analysis highlights the worse effect of COVID-19 in an older age group (9.5% versus 3.3%) compared with the younger cohort. More data are required on the prevalence of shock, its predictors, and their effect on the survival of elderly COVID-19 patients to effectively maneuver supportive resuscitation measures on time. Furthermore, elderly survivors requiring prolonged nursing care and ventilator support might add to the magnitude of complications and economic liability during this global health care crisis.

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Fighting COVID-19 Hypoxia With One Hand Tied Behind Our Back: Blanket Prohibition of High-Flow Oxygen and Noninvasive Positive End-Expiratory Pressure in US Hospitals

To the Editor:

Before the coronavirus disease 2019 (COVID-19) pandemic, patients with hypoxia who were failing low-flow oxygen through nasal cannula were treated with noninvasive positive-pressure ventilation or high-flow nasal cannula oxygen, aimed at delivering higher concentration and flow of oxygen to match patient demand, decreasing anatomic dead space by preventing rebreathing, and recruiting alveoli by using positive end-expiratory pressure. Many emergency physicians began their fight against COVID-19 with neither of these options because of concerns about virus aerosolization exposure to staff and other patients. Instead, early intubation has been the suggested option for a patient failing nasal cannula. Often this is the correct answer, but not always.

There is a cost to staff and patients from overuse of intubation. It is an extremely high-aerosol-generating event. A systematic review of aerosol-generating procedures and their risk of transmission of severe acute respiratory syndrome to health care workers found intubation to have an odds ratio of 6.6 compared with 2.2 for noninvasive positive-pressure ventilation.[1] Also, many hospitals face the risk of running out of ventilators and ICU beds. Once intubated, COVID-19 patients tend to continue receiving mechanical ventilation for greater than 1 week, with poor outcomes. In vitro studies have demonstrated less airflow dispersal from high-flow nasal cannula or continuous positive airway pressure (CPAP) using sealed masks than from nasal cannula.[2]

Furthermore, data coming from overseas indicate an important role for noninvasive positive-pressure ventilation and high-flow nasal cannula in managing COVID-19 patients. Retrospective data from China demonstrate that approximately 21% of patients required high-flow nasal cannula and 14% required noninvasive positive-pressure ventilation.[3] Among admitted patients in Italy, approximately 30% required ventilation support beyond oxygen therapy. Of patients given ventilation support, 89% were assisted with noninvasive positive-pressure ventilation compared with 12% receiving invasive ventilation.[4] The *Handbook of COVID-19 Prevention and Treatment* recommends the use of high-flow nasal cannula for hypoxic patients not tolerating nasal cannula.[5]

We advocate early planning with colleagues from critical care, respiratory therapy, and nursing to develop protocols that mitigate risk associated with high-flow nasal cannula and noninvasive positive-pressure ventilation rather than prohibiting the use of these critical alternatives to intubation. Ideally, these interventions should be performed in negative-airflow rooms, but most emergency departments have a limited number of these. We are recommending use of these interventions in closed isolation rooms with staff in full airborne personal protective equipment. High-flow nasal cannula should be provided with a surgical mask over the patient's mouth, or high-flow oxygen could be provided with a nonvented sealed CPAP mask attached to a self-inflating bag plus viral filter with dual oxygen source (see https://emcrit.org/emcrit/covid-airway-management/). CPAP should be provided through a helmeted setup or nonvented CPAP masks with viral filter attached to the expiratory port. Policies can be rapidly adapted as more data emerge in regard to COVID-19, but it is already clear that we must find safe and creative ways to expand, not limit, our armamentarium during this pandemic.

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