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EDITORIAL COMMENTARY

Excess out-of-hospital sudden deaths during the COVID-19 pandemic: A direct or indirect effect of SARS-CoV-2 infections?

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Since its emergence from Wuhan, China, in December 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus responsible for coronavirus disease 2019 (COVID-19), has claimed the lives of >1.7 million individuals worldwide and >317,000 individuals in the United States alone (as of December 21, 2020, 1 PM CST).[1,2] Although the acute respiratory and thrombotic complications of COVID-19 seem to explain much of the observed morbidity and mortality, cardiac involvement, including myocardial infarction, myocarditis, and life-threatening ventricular arrhythmias,[3–5] seems to be relatively common.[6]

Of note, areas such as New York City (NYC),[7] the Lombardy region of Italy,[8] and Paris, France,[9] hit hardest during the early pandemic (defined classically as March and April 2020) all have reported a marked rise in the incidence of out-of-hospital cardiac arrest/out -of-hospital sudden death (OHCA/OHSD) suggesting a possible causal link between COVID-19 and OHCA/OHSD. However, aside from the French study of Marijon et al,[9] these initial reports detailed a compelling temporal association but failed to establish any sort of causal link between the burden of COVID-19 infections and the precipitous rise in OHSDs observed during the early pandemic.[7,8]

In this context, the report by Coleman et al[10] in this issue of *Heart Rhythm Journal* serves as a welcome and important extension of the work Mountantonakis et al[7] that clearly illustrates a positive correlation between regional COVID-19 infection burden, as determined by the percentage of positive SARS-CoV-2 antibody tests (aka seroconversion), and the incidence of OHSD observed at the neighborhood level.

Although the report by Coleman et al[10] provides another piece of evidence suggesting that the direct effects of COVID-19, including ventricular arrhythmias potentiated by hypoxia, systemic inflammation, electrolyte disturbances, and perhaps the indiscriminate use of ineffective QTc-prolonging COVID-19–directed pharmacotherapies are responsible,[11] at least in part, for the observed rise in OHSD across Europe and North America during the early pandemic, there likely is more to this particular puzzle.

Of note, unlike the recent reports of Marijon et al[9] (Paris metropolitan area) and Baldi et al[12] (Italian provinces of Cremona, Lodi, Pavia, and Mantova), the brief report by Coleman et al[10] does not attempt to differentiate the proportion of excess OHSDs attributable directly to COVID-19 infection vs indirect effects of the pandemic, such as (1) deferment of routine ambulatory care; (2) reluctance of patients to utilize emergency medical services and/or present to the emergency department; (3) OHCA/OHSD circumstance; and (4) rate of bystander cardiopulmonary resuscitation/automatic external defibrillation, which also may be subject to geographic variability.

Furthermore, in light of the finding that the OHSD incidence in 2019 was also an independent predictor of OHSD incidence during the early pandemic, it is somewhat perplexing that neighborhood-specific socioeconomic factors such as age > 65 years, race/ethnicity, educational attainment, and uninsured rate that are associated with worse clinical outcomes in patients with and without COVID-19 were not found to be independent predictors of OHSD incidence in the study by Coleman et al.[10]

Regardless of the ultimate breakdown of causality between the direct and indirect effects of COVID-19 on OHSD incidence, the precipitous rise in OHSD in NYC and other metropolitan areas during the early COVID-19 pandemic seems to be indisputable.[7–10] Unfortunately, despite the rapid development and ongoing deployment, of a slate of highly efficacious SARS-CoV-2 vaccines, it seems increasingly likely that most areas are poised to endure an additional surge(s) before the benefit of widespread vaccination takes hold. Therefore, it is more important than ever that we as health care providers lead by example and advocate strongly for efforts to reduce the spread of COVID-19 via appropriate masking, social distancing, and hygiene. Until a SARS-CoV-2 vaccine(s) is widely available, these

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precautions seem to be our only means of assuring that health care systems are not once again overwhelmed.

Similarly, with the knowledge of the direct and indirect effects of the COVID-19 pandemic on OHSD incidence provided by studies such as Coleman et al,[10] there is hope that (1) the maintenance of safe access to routine and emergency health care services, (2) the avoidance of ineffective and likely proarrhythmic treatment strategies,[13,14] and (3) improvements in how COVID-19 patients are monitored and treated in the outpatient setting (ie, so-called COVID care packages) may help reduce the incidence of OHSD during subsequent COVID-19 surges. With any luck, history will not repeat itself, and these and additional efforts will reduce the number of excess OHCAs/OHSDs observed in late 2020 and early 2021 in what all of us hope will one day be referred to as the late COVID-19 pandemic period.

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