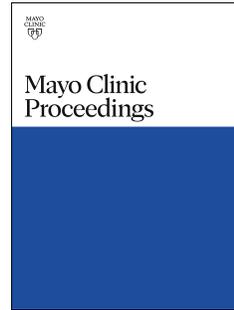


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Trends in Heart Failure Outcomes From a Large, Geographically Diverse Cohort During the COVID-19 Pandemic

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The evolving coronavirus disease-2019 (COVID-19) pandemic has presented extraordinary challenges to the health of populations globally. As our understanding of the virus continues to grow at a rapid pace, it has become increasingly clear that the clinical manifestations of SARS-CoV-2 infection range widely, and are in large part dictated by age, underlying comorbidities, and vaccination status. Robust epidemiologic data over the past years have underscored that individuals with chronic health conditions including cardiovascular disease (CVD), diabetes mellitus, immunosuppression, tobacco use, and obesity carry a significantly greater risk of falling critically ill with SARS-CoV-2.¹ As an example, in a study of nearly 5 million adults hospitalized with SARS-CoV-2 from March 2020 to March 2021, half (50.4%) of patients carried a diagnosis of hypertension, and those with obesity and diabetes were 30% and 26% more likely to succumb to the disease, respectively, after adjustment for confounding risk factors.²

While the impact of chronic diseases on susceptibility to SARS-CoV-2 must not be understated, it is perhaps equally as important to recognize the indirect effects the pandemic has had on other causes of death. From March 2020 to October 2021, during the height of the COVID-19 pandemic, heart disease (20.1%) and cancer (17.5%) remained the leading causes of mortality in the United States, with SARS-CoV-2 accounting for 12.2% of deaths nationwide.³ Across a similar time period, deaths attributed to heart disease, stroke, diabetes, accidents, and Alzheimer's disease, all markedly increased.⁴ These numbers speak to the wide-ranging consequences of SARS-CoV-2 that span beyond the immediate ramifications of the disease itself, and include, but are not limited to, delayed access to emergent and routine medical care, racial inequities in the availability of healthcare resources, increased stress and anxiety levels, greater alcohol consumption, and reduced physical activity.

In the decade leading up to the pandemic, the volume of patients hospitalized annually with a diagnosis of heart failure (HF) has progressively risen, from 1,060,540 in 2008 to 1,270,360 in 2018; additionally, the median age of patients has fallen modestly, from 76 to 73, according to one study of over 11 million adults with HF.^{5, 6} Patients with HF are particularly at risk for severe SARS-CoV-2, not only because of their high likelihood of carrying comorbid, risk-enhancing diagnoses, but also due to renin-angiotensin system dysregulation which may possibly potentiate complications of infection with SARS-CoV-2.⁷ Most recently, a 2021 report by Bhatt and colleagues evaluated outcomes in over 1 million patients with HF hospitalized with SARS-CoV-2 from April to September of 2020. In this study, the authors identified that, remarkably, HF patients hospitalized with SARS-CoV-2 carried a 24.2% in-hospital mortality rate, compared to just 2.6% in those hospitalized with acute HF (without SARS-CoV-2 infection).⁸

In this issue of *Mayo Clinic Proceedings*, Yousufuddin and colleagues add to the growing body of literature describing how outcomes in patients with HF have been affected by the COVID-19 pandemic.⁹ The authors present a cohort of 8,989 cumulative HF hospitalizations, 2,341 occurring during the COVID-19 pandemic (March 2020 through October 2020) and 6,648 occurring prior to the pandemic (October 2018 through February 2020). They demonstrate that: 1) adjusted 30-day readmission rates were lower during the pandemic compared to preceding years (10% vs. 13.1%, aHR 0.77, [0.66-0.89], $P < 0.001$); 2) all-cause mortality rates were higher during the pandemic compared to prior years (11.3% vs. 9.7%, aHR 1.19, [1.02-1.39], $P = 0.03$); and 3) disease severity, heart failure subtypes, and treatment patterns (pacemaker, ICD, and LVAD implantation, coronary revascularization, and heart transplantation) remained similar

before and during the pandemic. The study cohort was geographically diverse, spanning 3 states and 16 hospitals, predominately White (91%), with a mean age of 74 years.

Broadly, the data presented by Yousufuddin and colleagues are in agreement with the prevailing literature. Large, multicenter studies from Germany and England have previously demonstrated marked reductions in HF admissions and 30-day readmission rates at the nascence of the COVID-19 pandemic^{10, 11}, likely reflecting, principally, an aversion to seeking hospital-based care due to the perceived risk of contracting SARS-CoV-2; other factors contributing to this decrease include increased telemedical care, strict “stay-at-home” directives, reduced triggers for decompensation due to historically low levels of other viruses, and potential (mis)-classification of true HF admissions as SARS-CoV-2 admissions. In regard to the increased all-cause mortality among HF patients observed during the COVID-19 pandemic, these data reinforce the alarming vulnerability of this patient population and high risk for complications, with some studies quoting a nearly one in four chance of dying if hospitalized with SARS-CoV-2 and HF early in the COVID-19 pandemic.⁸ As outlined in the article, this trend in all-cause mortality is likely due to a constellation of factors, most notably severe SARS-CoV-2 infection, rise in out-of-hospital cardiac arrest¹², reduction in percutaneous revascularization¹³, systemic racial disparities, and disproportionate access to care during the COVID-19 pandemic.¹⁴ Last, the stability of treatment patterns before and during the pandemic, including rates of pacemaker, ICD, and LVAD implantation, guideline-directed medical therapy, coronary revascularization, and heart transplantation, represent a departure from previously published studies detailing a sharp decline in these interventions during the COVID-19 pandemic.^{13, 15} One may speculate that this difference is indicative of the robust, well-resourced hospital system from which Yousufuddin and colleagues obtained their cohort. Notwithstanding, as the authors discussed, the

lack of a statistically significant change in the use of these therapies does not necessarily signify that these trends were not clinically significant, especially for heart transplantation and LVAD implantation, which were performed in much lower numbers than other therapies.

While re-affirming important epidemiologic trends in HF patients during the COVID-19 pandemic, Yousufuddin and colleagues do not provide data to better characterize what may be driving the elevated mortality rates in this vulnerable population. It is not clear whether most patients are succumbing to SARS-CoV-2 infection, or whether there may be concurrent cardiovascular processes at play, for instance myocarditis, accelerated atherosclerosis, arrhythmias, thrombosis, and/or myocardial injury. Expanding these outcome measures will be a valuable next step in investigation. Second, as the study was performed prior to January 2021, the role of vaccination against SARS-CoV-2 could not be assessed. There is compelling evidence to suggest that vaccination reduces both hospitalization and mortality rates in patients with HF, and this important variable merits inclusion in future studies.¹⁶ Finally, given the well-described racial disparities in SARS-CoV-2 outcomes¹⁴, the homogeneity of the study population (91% White patients) presents a major limitation to the generalizability of the findings; while efforts to recruit diverse study cohorts are ongoing, they must be intensified in order to ensure equitable representation from all members of our society.

The COVID-19 pandemic continues to present extraordinary challenges to the health of medically vulnerable populations including those with HF. Yousufuddin and colleagues admirably add to the growing body of literature describing the concerning mortality rates in these patients. Further research is needed to more comprehensively characterize the drivers of these outcomes, and determine what measures may be taken to mitigate their impact on people living with HF.

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