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Excess of heart failure-related deaths during the 2020 COVID-19 pandemic in Unites States

Marco Zuin, MD FESC FACC FANCMO[a,b,*], Gianluca Rigatelli, MD PhD FACC FSCAI[c], Claudio Bilato, MD PhD[a]

[a] Department of Cardiology, West Vicenza Hospital, Arzignano, Italy
[b] Department of Translational Medicine, University of Ferrara, Ferrara, Italy
[c] Department of Cardiology, Madre Teresa Hospital, Schiavonia, Padova, Italy

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ABSTRACT

Background: HF can be encountered at different stages in the course of COVID-19 disease. However, data regarding the HF-related mortality during COVID-19 pandemic are scant
Objective: We investigate the heart failure (HF)-related mortality rate in the US among patient with or without COVID-19 infection during the first two pandemic waves in 2020 and to compare them to those of previous years (2014–2019).
Methods: Age-adjusted mortality rates (AAMR) per 100.000 person-years, with relative 95% confidence interval (CI) were determined using the free-available dataset for Multiple cause-of-death, provided by the Center for Disease Control.
Results: Throughout the 2020, the first year of the COVID-19 pandemic, 522.848 HF-related deaths were registered (461.594 and 61.254 in subjects without and with COVID-19 infection, respectively). The overall HF-related AAMR was 124.6 (65% CI 123.4–125.6), reflecting an increased HF-related mortality of 13.2% and 25.9% compared to 2019 and 2018 ($p < 0.0001$). HF-related AAMR was 111.0 (95% CI: 110.7–111.4) and 14.8 (95% CI: 14.6–14.9) per 100.000 population for decedents without and with COVID-19 disease, respectively. The proportionate mortality of HF in COVID-19 patients was 11.7%. HF-related AAMR in COVID-19 patients was higher in men (18.0 per 100.000, 95% CI: 17.8–18.2), in patients aged more 65 years (104.0 per 100.000, 95% CI: 103.1–104.9), in African Americans (22.5 per 100.000, 95% CI: 22.0–22.3) and in those living in rural counties (18.4 per 100.000, 95% CI: 18.0–18.7).
Conclusions: A significant increase in the HF-related mortality during the 2020 was observed synchronously with the COVID-19 pandemic

Introduction

Heart failure (HF) represents one of the leading cardiovascular disease and cause of hospitalizations in the US.[1] HF can be encountered at different stages in the course of COVID-19 disease. However, few investigations have reported epidemiological population-based estimated of HF mortality using contemporary data. To this regard, previous studies have demonstrated that an history of HF confers a higher risk for in-hospital mortality among adults hospitalized with COVID-19, especially in those age more than 65 years and with comorbid conditions.[2] To this regard, some investigations have also highlighted a higher incidence of HF in critically ill patients.[3] Furthermore, SARs-CoV-2 infection may, per se, induce HF through a variety of pathophysiological mechanisms.[4] However, nationwide data regarding the HF-related mortality rate in COVID-19 patients are lacking. To fill this gap, we assess the HF-related mortality rate in the US among subjects with and without COVID-19 infection during the pandemic and compare them to those before the pandemic using a large national administrative database from 2014 to 2020.

Methods

Data source

De-identified data regarding the HF-related mortality were obtained from the online publicly available Multiple cause-of-death database, provided by the Center for Disease Control (CDC) (CDC

Abbreviations: AAMR, Age-adjusted mortality rates; CDC, Center for Disease Control; HF, Heart failure

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* Corresponding author: Department of Translational Medicine, University of Ferrara, Via Aldo Moro 8, 44124 Ferrara, Italy.
E-mail address: zuinml@yahoo.it (M. Zuin).

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WONDER).[5] Given that data were obtained from a publicly available, deidentified database, the study did not require ethics approval.

Data extraction

We identified all decedents between 2014 and 2020 (last year of confirmed results), using the International Classification of Diseases, 10th Revision [ICD-10] listing a HF (I11.0, I13.0, I13.2, I50.0, I50.1 and I 50.9) or COVID-19 infection (U07.1) in any position of the death certificate.

Statistical analysis

Age-adjusted mortality rates (AAMR) per 100.000 person-years, with relative 95% confidence interval (CI), also stratified by gender, were calculated using the annual national population totals from the US Census Bureau and the 2000 US standard population (Supplementary file 1). To calculate nationwide annual trends in HF-related mortality, we assessed the average annual percent change (AAPC). Dedicated subgroup analyses based on gender, race and urban status (urban versus rural), defined using the 2013 NHCS Urban-rural classification Scheme, were also performed to identify the characteristics of COVID-19 patients contributing to the excess mortality, if any. Deaths were subcategorized as premature HF in subjects < 65 years. Spearman's correlation coefficients were calculated between the COVID-19 and HF-related deaths in different subgroups (subjects with and without COVID-19 infection). Statistical analyses were performed using Joinpoint regression (Joinpoint, version 4.6.0.0, National Cancer Institute, USA) and SPSS package version 20.0 (SPSS, Chicago, IL, USA).

Results

Overall population

Between 2010 and 2020, 2.702.802 HF-related mortality occurred in the US. Over the years, the HF-related AAMR steadily increased [AAPC +3.4% (1.9–4.9, $p < 0.0001$)], both in males [AAPC +3.6% (95% CI: 2.6–4.7), $p < 0.0001$] and females [+3.5%, (95% CI: 2.1–4.9, $p < 0.0001$)] (Fig. 1, Panel A).

Impact of COVID-19 pandemic

Throughout the 2020, the first year of the COVID-19 pandemic, 522.848 HF-related deaths were registered (461.594 and 61.254 in subjects without and with COVID-19 infection, respectively). For that year the overall HF-related AAMR was 124.6 per 100.000 (65% CI 123.4–125.6), reflecting an increased HF-related mortality of 13.2% and 25.9% compared to 2019 and 2018, respectively, that was statistically significant as per Joinpoint analysis ($p < 0.0001$). More precisely, the HF-related AAMR of 111.0 (95% CI: 110.7–111.4) and 14.8 (95% CI: 14.6–14.9) per 100.000 population for decedents without and with COVID-19 disease, respectively. The relationship between COVID-19 and HF-related deaths is showed in Fig. 1, Panel B). The proportionate mortality of HF in COVID-19 patients was 11.7%. Spearman's rank tests demonstrated a significant positive correlation between COVID-19 deaths with COVID-19 cases ($p < 0.0001$) and all HF-related deaths over 2020 ($p = 0.001$) (Table 1).

Demographic and geographical patterns in COVID-19 patients

Further sub-analyses, performed to better describe the demographical features of decedents experiencing both HF and COVID-19 infection over the 2020, evidenced that the AAMR of these subjects was higher for men (18.0 per 100.000, 95% CI: 17.8–18.2) than for women (12.3 per 100.000, 95% CI: 12.1–12.4). Moreover, the HF-related AAMR resulted higher in individuals older than 65 years (104.0 per 100.000, 95% CI: 103.1–104.9) compared to those aged less than 65 years (1.8 per 100.000, 95% CI: 1.7–1.9) as well as in African Americans (22.5 per 100.000, 95% CI: 22.0–22.3) compared to white population (14.1 per 100.000. 95% CI: 14.0–14.3), Asians (6.5 per 100.000, 95% CI: 6.2–6.9) and American Indians/Alaska natives (17.3 per 100.000, 95% CI: 15.9–18.7). Furthermore, HF-related AAMR was higher for residents in rural (18.4 per 100.000, 95% CI: 18.0–18.7) compared with those living in urban (14.0 per 100.000, 95% CI: 13.9–14.1) counties.

Discussion

In this large nationally representative sample, we observed a significant excess mortality for HF during the 2020, synchronously with the first two COVID-19 pandemic waves. Decedents presenting HF and COVID-19 infection were mainly males, aged more 65-years old resident in rural counties. Moreover, our data demonstrated that the increase in HF-related mortality due to COVID-19 infection was also different between race subgroups. Indeed, African Americans, despite representing the 15% of HF- related deaths with COVID-19, showed a higher HF-related AAMR. Although hospitalizations for acute cardiovascular conditions declined during the outbreak,[6,7] cardiovascular mortality has risen substantially during the COVID-19 pandemic in the US.[8,9] Intriguingly, our results evidenced that existing disparities in the US healthcare system have been exacerbated by the COVID-19 pandemic.[10] The observed increased HF-related mortality is probably multifactorial. Indeed, several investigations have showed a significant reduction in HF hospitalizations during the pandemic, ranging from 30 to 66% in different countries and leading to a subsequent increase in HF-related mortality. The fear of being infected in the emergency department or during hospitalization or medical examinations may also have discouraged patients from seeking consultations with their general practitioner or their cardiologist.[11] Moreover, it has been demonstrated that pre-existing HF represents a risk factor for a more severe clinical course of COVID-19 as well as an independent predictor of in-hospital mortality.[12] Notably, the significant relationship between COVID-19 and all HF-related deaths may also represents the impact of the pandemic on cardiovascular diseases, and in this case on HF, due to national health system reorganization and changes in the behavior of individuals.

Previous analyses have demonstrated that patients hospitalized for COVID-19 may develop both an acute decompensation of chronic HF or a de-novo HF as a consequence of myocardial injury due to the acute infection. In these subjects, from a pathophysiological point of view, myocardial injury may be elicited by different mechanisms, including those generally observed in differ type of infections, such as tachycardia, fever, adrenergic stimulation, or mainly related to an exaggerated inflammatory response.[3]

Considering the increasing HF deaths observed during the first phase of COVID-19 pandemic, efforts to control medical comorbidities in infected patients as well as adequate treatment strategies and monitoring strategies are required to improve the reported epidemilolgi9cal trends. We cannot exclude that the higher HF-related AAMR observed in rural counties may be also due to the presence of less organized and developed health care systems which may have been early collapsed during the pandemic waves. Physicians must be aware of the potential squeal due to HF in patients with COVID-19 infection either in the short-and long-term period and especially in older subjects.[13] Appropriate diagnostic and monitoring strategies, as telemedicine interventions,[14,15] especially in rural populations, and appropriate follow-up programs for HF patients with COVID-19 infection must be promoted to reduce the mortality rate.

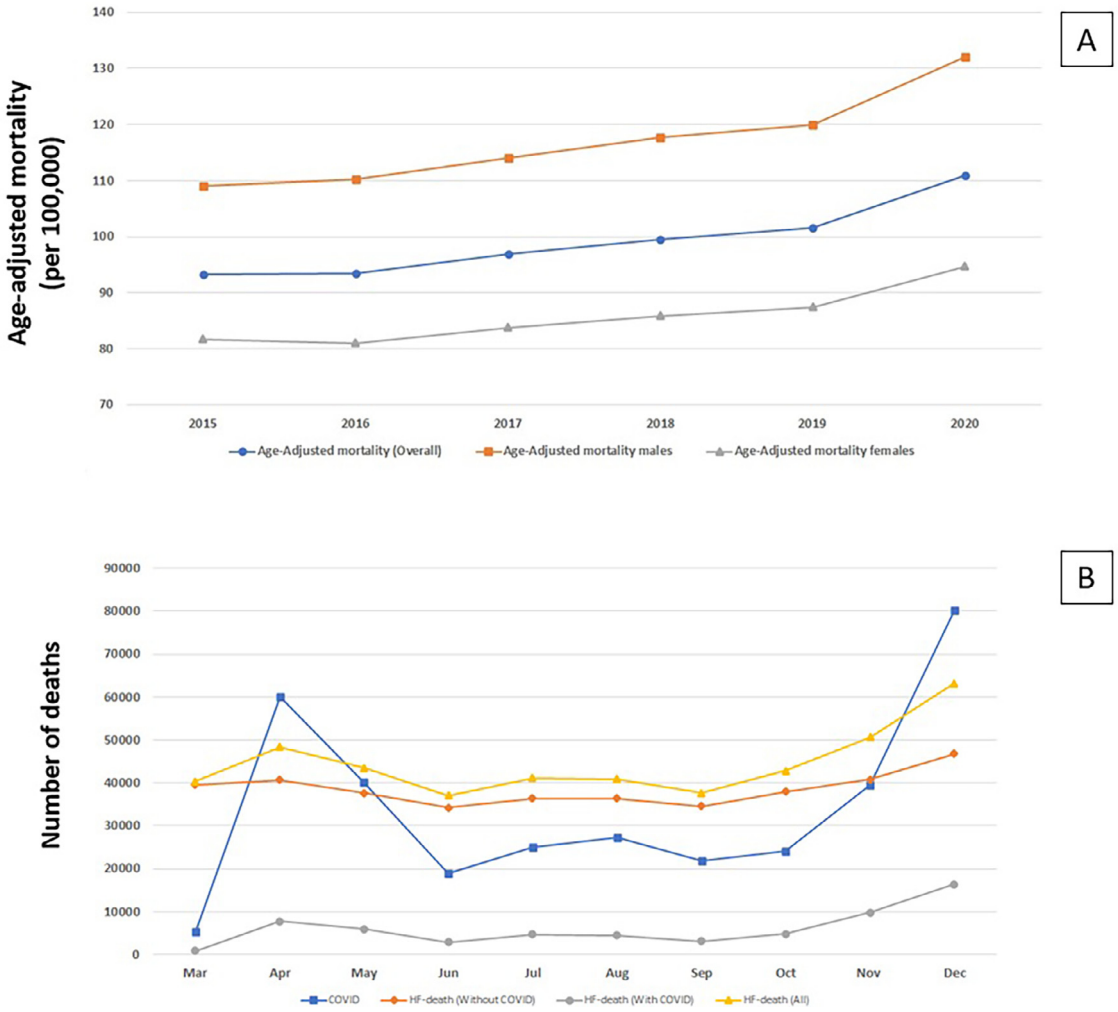

Fig. 1. Panel A: Age-adjusted mortality rates for heart failure in US between 2014 and 2020, also stratified by gender. Panel B: PE-related death count in 2020, per month, in the US in HF patients with and without COVID-19 infection.

Limitations

Our study has several limitations. We cannot exclude that possible undiagnosed COVID-19 cases, especially during the early phase of the pandemic, may have biased our results. Similarly, HF is frequently erroneously listed on death certificates, especially when the cause of death is not clear. The CDC wondering, being an administrative database, did not provide clinical data such as left ventricular ejection fraction, limiting us in differentiate HF patients with preserved or reduced ejection fraction. Doubtless, the rates of underling comorbidities, sex ratios and age distribution in US may be different from those present in other regions of the world, limiting the generalizability of our findings. Moreover, we were not able to assess the protective effect conferred by prior infection and vaccination against COVID-19, being the CDC wonder only a mortality dataset. Furthermore, no data were available regarding the HF-related mortality in patients with long-COVID syndrome. Moreover, we were not able to assess the trend of HF-related deaths in patients with COVID-19 infection over the following years since these data are still preliminary.

Table 1
Spearman's rank correlation coefficient rho and relative p-values between COVID-19 deaths and different subgroups of HF-related deaths. HF-deaths (All cases): defined as patients with and without COVID-19 infection.

	rho	p-value
COVID deaths*HF-deaths (without COVID-19)	0.600	0.67
COVID deaths*HF-deaths (with COVID-19)	0.915	<0.0001
COVID deaths*HF-deaths (All cases)	0.879	0.001

Conclusions

In conclusion, we observed a significant increase in the HF-related mortality during the 2020, synchronously with the first two COVID-19 pandemic waves. This increasing mortality was especially pronounced within male, aged more 65 years old, black individuals and residents in rural areas. It seems that the existing disparities in the US healthcare system have been exacerbated by the COVID-19 pandemic, also for patients with HF. Further investigations are needed to determine the causative mechanisms underlying the higher mortality rate in HF patients with COVID-19 infection.

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Declaration of Competing Interest

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