

Mortality from acute myocarditis between 2007 to 2022: Insights from a US nationwide registry

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To the Editor,

Recent evidence has been provided that the number of hospitalizations for myocarditis may have increased between the years 2007 and 2022 in Germany, although the death rate of this pathology remained almost unchanged [1]. Interestingly, it was also found that mortality for coronavirus disease 2019 (COVID-19)-related myocarditis was more than five times that of non-COVID-19 myocarditis (i.e., 12.5 vs. 2.3%). Therefore, to provide further insight on the trend of mortality for acute myocarditis in the US, we present here real-world data on acute myocarditis deaths between 2007 and 2022. We accessed the WONDER (Wide-Ranging, Online Data for Epidemiologic Research) repository, an open-access, nationwide database maintained by the US Centers for Disease Control and Prevention (CDC) that includes a wide-ranging query system for allowing analysis of public health data, including individual causes of death in US residents [2]. Our search was based on the specific ICD-10 (10th revision of the International Classification of Diseases) codes I40* (acute myocarditis) and I40.0 (acute infective myocarditis) between 2007-2022, and data were downloaded as age-adjusted death rate ($\times 100,000$) with 95% confidence intervals (95%CI). This study was conducted in accordance with the Declaration of Helsinki. WONDER is an anonymized and publicly available data set, so this study is exempt from Institutional Review Board review. The results of our analysis are summarized in Figure 1. According to the information from the US

nationwide WONDER database, the age-adjusted mortality rate for all types of acute myocarditis (ICD-10 code I40*) remained almost stable between 2007 ($0.097 \times 100,000$) and 2016 ($0.086 \times 100,000$), but then showed a marked decline in the following years, stabilizing at $0.058-0.061 \times 100,000$ between 2018 and 2021, and then sharply decreasing to $0.028 \times 100,000$ in 2022 (Figure 1a). The mortality for all cases of acute myocarditis appears to have fallen by 71% in 2022 compared to 2007. The age-adjusted mortality rate for acute infective myocarditis (ICD-10 code I40.0) also gradually decreased over time, from $0.067 \times 100,000$ in 2007 to $0.007 \times 100,000$ in 2022 (-90%). Nevertheless, the trend was not linear, with notable peaks in 2013, 2016 and 2020. In particular, the peak of mortality for acute infective myocarditis in 2020 was more than three times higher than the mortality in 2019 (i.e., 0.046 vs. $0.014 \times 100,000$). The results of our analysis based on the US nationwide death registry maintained by the CDC do not exactly match those found in other countries [1]. Notwithstanding the different population characteristics, the different approach to collecting mortality data, and the different epidemiologic impact of infectious diseases potentially causing acute myocarditis in the two countries, we found that the age-adjusted mortality rate for all types of acute myocarditis decreased by 71% between 2007 and 2022 in the US. Correspondingly, the age-adjusted death rate for acute infective myocarditis has actually decreased by approximately 90%. However, in line with previous data [1], we also found a notable peak of mortality for acute infective myocarditis in 2020,

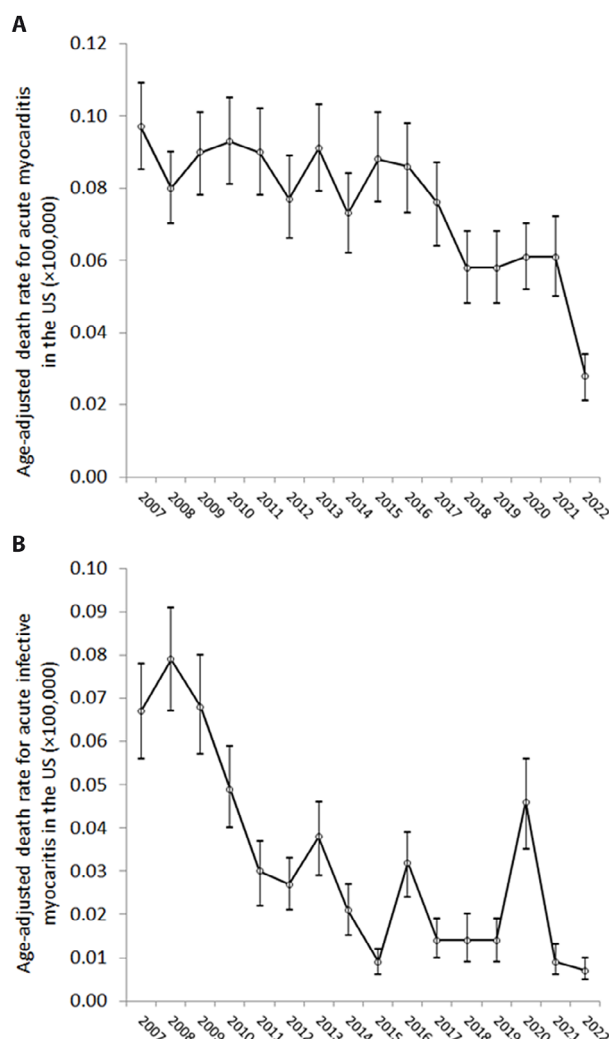


Figure 1. Mortality for acute myocarditis in the US between the years 2007 and 2022. Data are shown as age-adjusted death rate $\times 100,000$. (a) All forms of acute myocarditis (ICD-10 code I40*); (b) Acute infective myocarditis (ICD-10 code I40.0).

which is likely due to the impact of COVID-19, as acute myocardial injury is a relatively common complication in patients with a severe form of the disease [3], and this risk is magnified (i.e., up to seven times higher) in unvaccinated individuals [4]. This is consistent with the decline in acute infective myocarditis that we have seen in 2021 and especially in 2022, as all US states opened COVID-19 vaccine eligibility by

April 19, 2021. The other two peaks (2013 and 2016) in acute infective myocarditis mortality are also not surprising, as these winter seasons were dominated by the H3N2 strain, which caused an increased number of severe and fatal forms of the disease, some of which likely caused by acute infective myocarditis [5]. In summary, with the exception of the first COVID-19 wave in 2020, mortality from acute (infective or non-infective) myocarditis has decreased significantly over the period 2007–2022 in the US, probably due to improved surveillance, more efficient diagnosis and better clinical management.

Ethics Statement: WONDER is an anonymized and publicly available data set, so this study is exempt from Institutional Review Board review.

Patients Consent: Not applicable.

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