Association between regional distributions of SARS-CoV-2 seroconversion and out-of-hospital sudden death during the first epidemic outbreak in New York

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BACKGROUND Increased incidence of out-of-hospital sudden death (OHSD) has been reported during the coronavirus 2019 (COVID-19) pandemic. New York City (NYC) represents a unique opportunity to examine the epidemiologic association between the two given the variable regional distribution of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in its highly diverse neighborhoods.

OBJECTIVE The purpose of this study was to examine the association between OHSD and SARS-CoV-2 epidemiologic burden during the first COVID-19 pandemic across the highly diverse neighborhoods of NYC.

METHODS The incidences of OHSD between March 20 and April 22, 2019, and between March 20 and April 22, 2020, as reported by the Fire Department of New York were obtained. As a surrogate for viral epidemiologic burden, we used percentage of positive SARS-CoV-2 antibody tests performed between March 3 and August 20, 2020. Data were reported separately for the 176 zip codes of NYC. Correlation analysis and regression analysis were performed between the 2 measures to examine association.

RESULTS Incidence of OHSD per 10,000 inhabitants and percentage of SARS-CoV-2 seroconversion were highly variable across NYC neighborhoods, varying from 0.0 to 22.9 and 12.4% to 50.9%, respectively. Correlation analysis showed a moderate positive correlation between neighborhood data on OHSD and percentage of positive antibody tests to SARS-CoV-2 (Spearman ρ 0.506; P <.001). Regression analysis showed that seroconversion to SARS-CoV-2 and OHSD in 2019 were independent predictors for OHSD during the first epidemic surge in NYC ($R^2 = 0.645$).

CONCLUSION The association in geographic distribution between OHSD and SARS-CoV-2 epidemiologic burden suggests either a causality between the 2 syndromes or the presence of local determinants affecting both measures in a similar fashion.

KEYWORDS Arrhythmias; COVID-19 pandemic; Epidemiologic burden; Out-of-hospital sudden death; SARS-CoV-2 antibodies

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Introduction

Reports of increased incidence of out-of-hospital sudden death (OHSD) during the coronavirus 2019 (COVID-19) pandemic have raised the question of a possible association between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and malignant arrhythmias, traditionally considered the common mechanism of sudden death.[1,2]

In addition to the previously reported temporal association between COVID-19 and OHSD during the epidemic surge,[1,2] a similar association in the regional distribution of their incidence is expected. New York City (NYC) represents a unique opportunity to examine the epidemiologic association between the two given the variable regional distribution of SARS-CoV-2 in its highly diverse neighborhoods.[3]

Methods

Serologic testing of the population post epidemic outbreak is a reliable surrogate for viral epidemiologic burden that is less likely to be affected by inherent limitations of assessing COVID-19 incidence during the epidemic crisis, including limited testing, poor access to care, and inaccurate documentation. Therefore, we used the results of all antibody tests reported to the NYC Department of Health between March 3 and August 20, 2020, in NYC. We analyzed results for 176 NYC zip codes after excluding 8 zip codes that represented commercial districts. Testing was voluntary and free of charge for all NYC residents.[4] The NYC Department of Health requires mandatory reporting of serologic testing results, and data presented here are reflective of all reported electronic laboratory results in NYC.

In order to examine potential confounders of socioeconomic characteristics of each zip code on the rate of testing, we used data from the American Community Survey (5-year estimates) 2014–2018 conducted by the United States Census Bureau. We used the following 5 socioeconomic characteristics for our comparisons—percentage of population with (1) age over 65; (2) black race or Hispanic ethnicity; (3) no medical insurance; (4) education less than high school; and (5) immigration status of noncitizen.

Incidence of OHSD was obtained from the Fire Department of New York (FDNY) during the COVID-19 epidemic outbreak in NYC (period between March 20 and April 22, 2020). We define OHSD as patients who were pronounced dead on the scene by emergency medical personnel responding to a call that was classified as sudden cardiac arrest according to FDNY criteria.[1] An historical cohort was also obtained for the same time period a year earlier.

One-way analysis of variance was used to detect the influence of the 5 socioeconomic characteristics on serologic testing. Correlation analysis (Spearman ρ) was used to show correlation at a significance level of 0.05. Linear regression analysis was used to identify independent predictors of OHSD in 2020. Statistical analyses were performed using SPSS Version 27.0 (IBM, Armonk, NY). The research reported in this study adhered to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Results

Between March 3 and August 20, 2020, a total of 1,763,251 people had a serologic test for SARS-CoV-2 in NYC. Distribution of testing per 10,000 inhabitants varied significantly across the 176 zip codes, varying from 1231 to 5387 (12.3%–53.9% of the population). One-way analysis of variance failed to detect significant differences in testing rate among quartiles of the 5 socioeconomic characteristics. Among those tested, 457,956 (24.7%) were reported to be
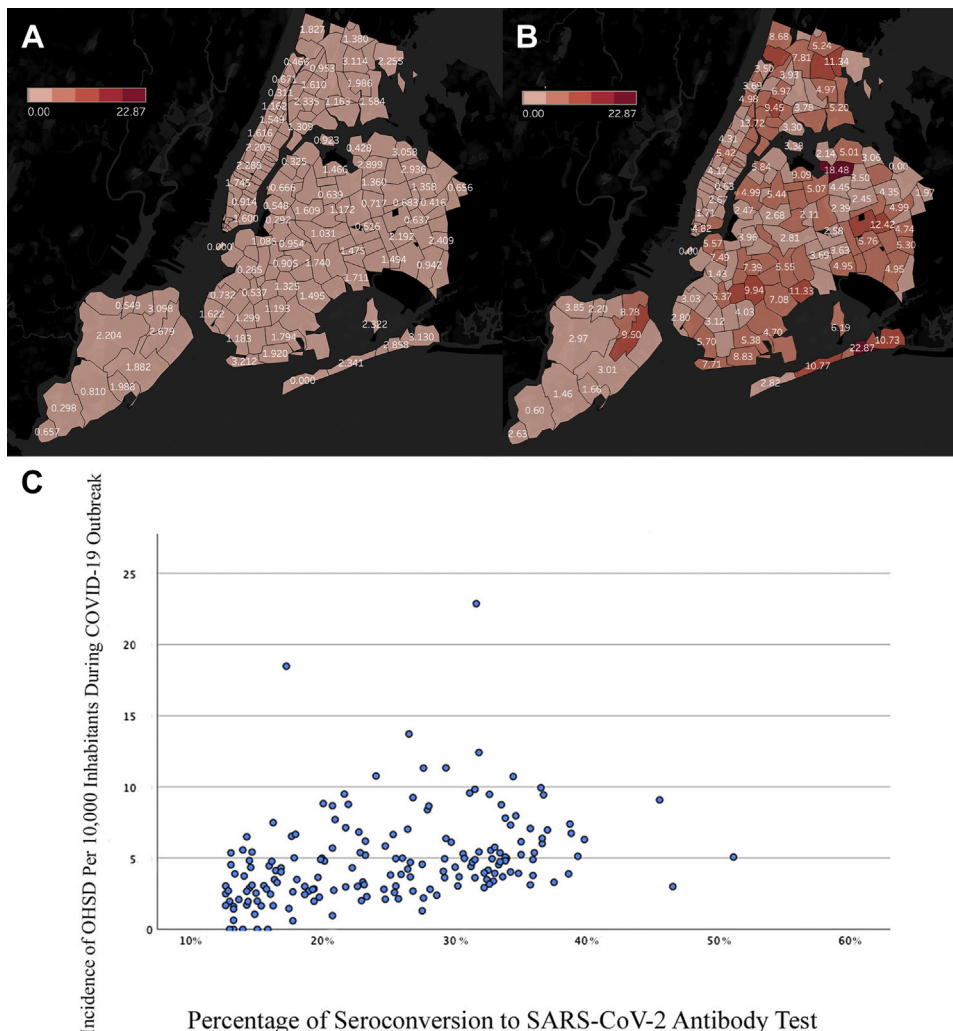
Figure 1   A: Geographic distribution of incidence of out-of-hospital sudden death (OHSD) per 10,000 inhabitants (historical control) (March 22 to April 22, 2019) in New York City. **B:** Geographic distribution of incidence of OHSD per 10,000 inhabitants during coronavirus 2019 (COVID-19) outbreak (March 22 to April 22, 2020) in New York City. **C:** Scatterplot depicting neighborhood-level association between OHSD during the COVID-19 outbreak and percentage of positive tests for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies.

seropositive to SARS-CoV-2 antibody test. Percentage of seroconversion also was highly variable across NYC neighborhoods, varying from 12.4% to 50.9 %.

OHSD per 10,000 people during the epidemic outbreak in 2020 also followed a diverse geographic distribution in NYC, with rates between 0.0 and 22.9. As previously reported, there was a 2.89-fold increase in the incidence of OHSD in NYC compared to 2019 for the same period.[1] Correlation analysis suggested a similar geographic distribution in the incidence of OHSD throughout NYC neighborhoods (r = 0.715; P <.001) between 2019 and 2020. Regional distribution of OHSD during the COVID-19 outbreak correlated with that of seroconversion to SARS-CoV-2 antibody test (r = 0.506; P <.001). The geographic distribution of OHSD across the neighborhoods of NYC during the COVID-19 outbreak and the association between zip code–level OHSD and SARS-CoV-2 seroconversion are depicted in Figure 1. We used zip code–specific socioeconomic predictors (categorical variables), percentage of positive antibody tests, and OHSD during the control period in 2019 in regression models to identify predictors for OHSD during the pandemic. In our strongest model, seroconversion to SARS-CoV-2 (β = 0.757) and OHSD in 2019 (β = 2.88) were found to be independent predictors of OHSD during the first pandemic surge in NYC (R^2 = 0.645; P <.001).

Discussion

We report that the highly diverse regional distribution of OHSD during the COVID-19 pandemic surge follows the geographic distribution of seroconversion to SARS-CoV-2 in NYC. This finding adds to the previously reported temporal association between OHSD and COVID-19 presumed deaths[1] and further supports an association between OHSD and SARS-CoV-2 epidemiologic burden. Whether this association is causative or there are factors that affect similarly the geographic distribution of both is unclear. Malignant arrhythmias that have been reported in the inpatient setting[5] are potentiated by hypoxia, systemic inflammatory response, and metabolic disarray often seen with COVID-19.[6] In addition, the presence of regional myocardial inflammation is reported in patients who recovered from COVID-19, which can constitute a potential substrate for the development of ventricular arrhythmias.[7] Furthermore, the fulminant course of respiratory failure and thromboembolism as described in COVID-19 patients could result in the sudden demise of these patients.[8] Lai et al[9] reported a temporal relationship between emergency calls for viral-related symptoms and OHSD; however, the causative relationship between COVID-19 and OHSD cannot be proved because the COVID-19 status of those patients was unknown.

Conversely, regional socioeconomic factors are possible confounders that could affect both the virus spread and the increase of OHSD during a health care crisis. Lai et al[9] reported higher incidence of older age, nonwhite race/ethnicity, comorbidities, and physical limitations in patients with OHSD during the COVID-19 epidemic. These factors have

been shown to affect SARS-CoV-2 spread and outcomes, as well as patients' ability to access care in a timely fashion.[10–12]

The significant reduction in hospital admissions for myocardial infarctions and stroke has been widely published and postulated as the reason for the excess mortality not associated with COVID-19.[13] Failure to present to the emergency room due to fear may have had a detrimental impact on patients with myocardial infarction or stroke in either delaying or not seeking care altogether. We previously reported the relationship between an increase in OHSD and inpatient admissions for acute coronary syndromes.[1]

We present a moderate positive association between geographic dispersion of seroconversion to SARS-CoV-2 and rate of OHSD during the pandemic and acknowledge that future studies will need to explore a possible biological link or elucidate whether this relationship is due to other confounding variables.

Study limitations

There is an implicit selection bias in all reported Department of Health testing data related to availability of testing sites and disease severity in individuals seeking testing. Available data on the neighborhood level might not be able to detect differences in socioeconomic factors that might influence testing. Symptomatic individuals or those having close contact with a positive case may have preferentially sought out antibody testing. The use of seroconversion as a surrogate for COVID-19 could underrepresent the actual number of infected population due to a small percentage of nonresponders and reported rapid decline in antibody titers post initial infection.[14] In addition, results of seroconversion tests from outside the surge window are included in our analysis; as seroconversion is a marker of past infection from SARS-CoV-2, we feel this is appropriate. FDNY data may have underestimated the true incidence of OHSD for a minority of neighborhoods where secondary private emergency services are used.

Conclusion

There was a moderate positive association between geographic dispersion of seroconversion to SARS-CoV-2 and incidence of OHSD during the COVID-19 pandemic. This is a hypothesis-generating finding about the causal relationship or lack thereof between the 2 syndromes.

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