Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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EDITORIAL COMMENT

Cardiovascular Complications Are Uncommon in Healthcare Workers With Mild or Asymptomatic COVID-19 Infection*

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Infection with severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) has the potential to be directly injurious to the cardiovascular system (1) and, because this is a novel virus, the incidence, nature, and severity of cardiovascular involvement in coronavirus disease-2019 (COVID-19) are uncertain. In this paper, the COVIDsortium describe a prospective case-control study of cardiovascular abnormalities in health care workers 6 months after mild COVID-19 infection (2). The study took place in 3 hospitals in London. Of 731 health care workers who underwent first wave weekly symptom, polymerase chain reaction testing, and serology assessment during a 4-month period, 157 (21.5%) had evidence of seroconversion. At 6 months after enrollment, 74 seropositive individuals (mean age: 37 years; range 18 to 63 years; 58% female) and 75 age-, sex-, and ethnicity-matched seronegative controls underwent cardiovascular phenotyping using biomarkers and cardiovascular magnetic resonance (CMR) imaging. COVID-19 infection was generally mild; only 1 person was hospitalized and 11 (15%) had been asymptomatic. There were no clinically meaningful differences in the CMR findings between seropositive and seronegative individuals. Specifically, the abnormalities included the following: reduced left ventricular ejection fraction (n = 2; minimum 50%), T1 elevation (n = 6), T2 elevation (n = 9), and late gadolinium enhancement (LGE) (n = 13; median: 1%; maximum: 5% of myocardium). Circulating concentrations of cardiac biomarkers were either normal in all individuals (N-terminal pro-B-type natriuretic peptide, reference: <400 pg/l) or in all but 4 individuals who had approximately normal circulating levels of troponin T (reference high sensitivity troponin T <14 ng/l). Overall, the observed abnormalities were very uncommon, and were distributed equally between seropositive and seronegative individuals. The investigators have previously reported that 30% of the seroconversions (n = 157) were asymptomatic (3).

The strengths of this study include the prospective design, open enrolment criteria, matched seronegative control individuals from the same population, serology status documented in all of the participants, use of state-of-the art automated acquisition and analyses techniques (artificial intelligence), high compliance with the imaging examination, and blinded analyses. The limitations include the lack of baseline information from cardiac imaging before COVID-19 infection, the lack of imaging at the time of infection, the focus on health care workers (rather than an unselected community population), and the limited sample size. Although CMR "abnormalities" are reported, these are not assessed using the Modified Lake-Louise Criteria (4), and they are investigator-reported, hence, potentially susceptible to ascertainment bias (positive or negative). These limitations are relevant. For example, myocardial involvement may have occurred in a higher proportion of patients at an earlier timepoint. However, as designed, the main aims of this study are achieved, and the aforementioned limitations are inherent to most cardiovascular imaging studies undertaken in COVID-19 to date.

This study population is restricted to health care workers; therefore, the findings may not necessarily be generalized to a community population. Healthcare workers do not reflect the population of

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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individuals most clinically affected by COVID-19 illness. The severity of acute COVID-19 infection is greatest in older individuals and those with pre-existing health problems. Healthcare workers are not representative of the wider, unselected, at-risk, community population. Cardiovascular risk factors and concomitant health problems may be more prevalent in an unselected community population than in health care workers, and prior studies have highlighted the clinical implications (interaction) for disease pathogenesis in COVID-19.

Some findings merit further comment. For instance, 62% of individuals were female. In most non-hospitalized COVID-19 populations, the sex distribution has included a higher proportion of male individuals. This may reflect a selection bias in the current study, or rather naturally reflect the fact that proportionately more women are asymptomatic or have milder forms of illness. Severe, hospitalized SARS-CoV-2 infection affects men to a greater degree (60% male in ISARIC [International Severe Acute Respiratory and Emerging Infection Consortium]) (5) whereas in hospitalizedopulations testing positive for SARS-CoV-2 there are proportionately more females than males affected (6,7). Considering the imaging findings, some of the LGE observed could be due to septal perforator arteries, as the authors mention. A limitation is that cross-sectional coronary computed tomography is not available. If obstructive coronary artery disease had been identified (implying scar due to chronic myocardial infarction), this would help with the interpretation of the LGE findings.

The COVIDsortium study provides as an excellent model to study the residual effects of COVID-19 at approximately 6 months post-infection, with minimal confounding effects of concomitant cardiovascular disease. Thus, the authors conclude that, in their population, the maximum prevalence of myocarditis may be <4% at 6 months. This is a reasonably reassuring result drawn from a healthy population, however, the sample size limits the precision of this estimate, and the prevalence of cardiovascular abnormalities (e.g., myocardial scar) would be expectedly higher in an unbiased community population including individuals from less-advantaged socioeconomic circumstances (e.g., unemployed) and with pre-existing health problems. Nonetheless, health care workers represent an important subgroup of the infected population, and dedicated research in this workforce is welcome.

Many of the cardiovascular imaging studies to date have involved selected patient populations, with retrospective recall of patients after discharge from hospital, and an imaging focus that lacked systematic evaluation of participants' disease or health status. Information gaps remain on the prevalence of cardiovascular and multisystem involvement in patients with symptomatic COVID-19 infection. This question is being prospectively investigated in the CISCO-19 (Cardiovascular Imaging in COVID-19) study (8). A further knowledge gap is the clinical significance of biochemical evidence of myocardial injury, as reflected by transient or sustained elevation of troponin, which is evident in about 1 in 10 survivors. This question is being investigated in the United Kingdom COVID-HEART study (ISRCTN58667920).

Future studies could target populations of patients who have already had cardiac imaging before COVID-19 infection (e.g., the United Kingdom Biobank study), however, the protocol did not include contrast imaging, hence, information on fibrosis, scar, and extracellular volume will be lacking. Other studies that did involve contrast imaging may be susceptible to selection bias. These issues highlight the challenges of undertaking clinical research in the context of an unheralded pandemic.

In conclusion, the COVIDsortium provides welcome, reassuring information that, in healthy individuals who experience mild infection with COVID-19, persisting evidence of cardiovascular complications is very uncommon. The results do not support cardiovascular screening in individuals with mild or asymptomatic infection with COVID-19.

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