
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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## Myocardial Impairment and Acute Respiratory Distress Syndrome in Hospitalized Patients With COVID-19

The ECHOVID-19 Study

Acute respiratory distress syndrome (ARDS) is the primary complication observed in coronavirus disease-2019 (COVID-19)-related deaths (1). Additionally, studies have found cardiac biomarkers to be increased in a significant proportion of patients, emphasizing COVID-19-related cardiac injury (2,3).

We aimed to assess the prevalence and value of assessing myocardial impairment using echocardiography and cardiac biomarkers in hospitalized patients with COVID-19.

The Echocardiographic COVID-19 (ECHOVID-19) study is a prospective multi-center cohort study of hospitalized patients with laboratory-confirmed COVID-19 at 8 hospitals of eastern Denmark (March 30 to June 1, 2020). Inclusion criteria are as follows: laboratory-confirmed Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) and ≥18 years. All patients independent of their health status underwent echocardiography (including two-dimensional-speckle tracking) according to a predetermined protocol and cardiac biomarkers were obtained. Investigators were blinded to the health status of the patients prior to inclusion. The endpoint was ARDS defined according to the Berlin Definition (4). All participants gave written informed consent and the study was performed in accordance with the 2nd Declaration of Helsinki and approved by the regional ethics committee. The study is registered at Clinicaltrials.gov (NCT04377035). Echocardiographic examinations were performed using the portable Vivid IQ Ultrasound System and analyzed off-line using EchoPAC version 203 (GE Healthcare). Elevated troponins were defined as troponins greater than the 99th percentile upper limit reference. A clinical cutoff value of ≥300 ng/l for N-terminal pro-B-type natriuretic peptide was used.

A total of 174 patients were included (mean age: 68 ± 15 years, 55% males). Of the included patients, 14% had prevalent heart disease. Median time from hospital admission to echocardiography was 4 days (interquartile range: 2 to 8). During follow-up (median: 16 days [interquartile range: 6 to 24]), 27 (16%) patients developed ARDS. Patients developing ARDS were older, more frequently men, smokers, hypertensive, and had prevalent heart disease, elevated N-terminal pro-B-type natriuretic peptide, troponin, and C-reactive protein. In addition, they had more impaired systolic function assessed using echocardiography (lower left ventricular ejection fraction [LVEF]: 51% vs. 59%, and global longitudinal strain (GLS): 13.7% vs. 16.9%). Among the 129 patients who had all biochemical and echocardiographic parameters available, 79.1% had myocardial impairment (decreased systolic function as assessed using echocardiography and/or elevated cardiac biomarkers). In this group, 20 developed ARDS, whereas only 2 in the nonmyocardial impairment group developed ARDS.

In Cox regression analysis adjusted for age, sex, body mass index, C-reactive protein, time to echocardiography, hypertension, diabetes, hyperlipidemia, and smoking, both LVEF and GLS were associated with ARDS (**Figure 1A and 1B**). Cardiac biomarkers and systolic parameters were assessed separately. These results did not change when restricting our analysis to patients without prevalent heart disease from the fully adjusted model. Cardiac biomarkers were not significantly associated with ARDS in multivariable models. Patients with preserved systolic function and cardiac biomarkers within the normal range had a low risk of ARDS (specificity: 28%; sensitivity: 96%; positive predictive value: 23%; negative predictive value: 97%).

In this multi-center study, we found that myocardial impairment is a common finding in hospitalized patients with COVID-19 and that it is associated with a higher risk of developing ARDS. We do not propose that impaired systolic function due to COVID-19 infection is a causal agent of ARDS development. Although we found that a combination of cardiac biomarkers and echocardiographic measures could rule out patients at high risk of developing ARDS, the results were based on a low number of events, which are reflected in the low specificity and positive predictive value. A limitation to the study is that patients presenting with myocardial impairment in the study may already have had unacknowledged myocardial impairment prior to infection. Therefore, we do not claim that the COVID-19 infection directly impairs myocardial function because this would require control for previous myocardial performance.

Nonetheless, although our results suggest that echocardiographic examination and cardiac biomarker assessment could potentially identify patients at low risk of in-hospital development of ARDS, routine echocardiography does not appear to provide sufficient value in a clinical setting.

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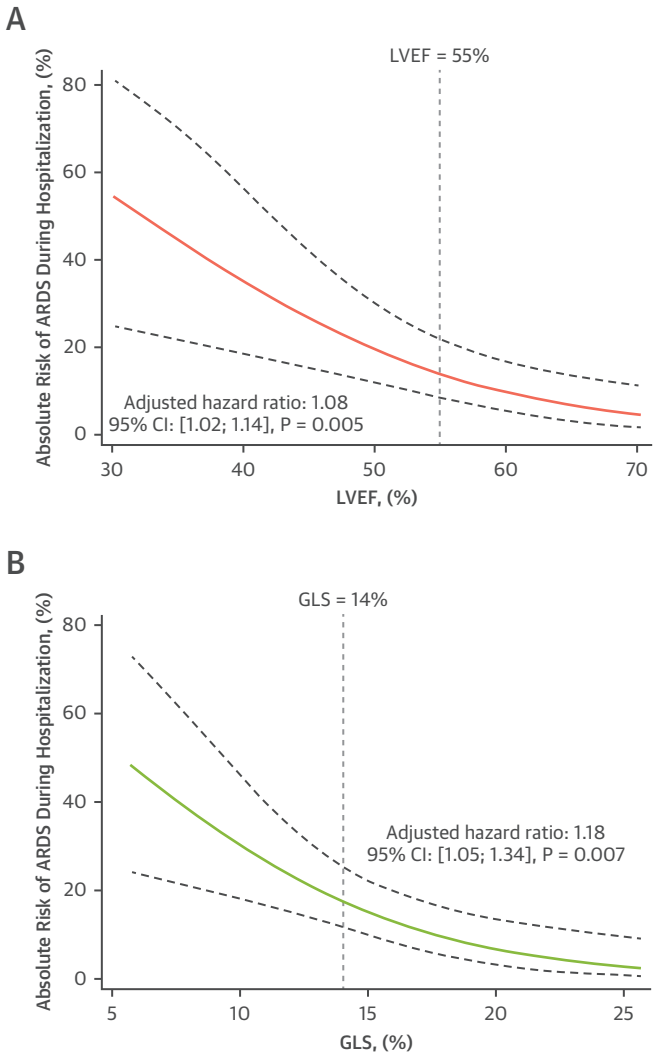
**FIGURE 1 Association Between Echocardiography-Assessed Myocardial Impairment and Risk of Acute Respiratory Distress Syndrome**




Displaying the unadjusted absolute risk of developing acute respiratory distress syndrome (ARDS) during hospitalization (with 95% confidence intervals [CIs]) according to left ventricular ejection fraction (LVEF) **(A)** and global longitudinal strain (GLS) **(B)**. Optimal cutoff values in relation to ARDS for LVEF and GLS are displayed as **dashed grey lines**. Adjusted hazard ratios per 1% decrease are displayed.

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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 *JACC: Cardiovascular Imaging* author instructions page.

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## Patients Recovered From COVID-19 Show Ongoing Subclinical Myocarditis as Revealed by Cardiac Magnetic Resonance Imaging

The cardiovascular complications of coronavirus disease-2019 (COVID-19) are still being established (1). Expert guidelines recommend the use of cardiac imaging in the management of patients with COVID-19 (2), and cardiac magnetic resonance (CMR) has shown utility in the noninvasive detection of myocardial inflammation (3). We present a case series of 16 patients who recovered from COVID-19 who underwent CMR to assess for evidence of myocardial involvement or ongoing myocarditis.

Ethics approval was obtained from the Hong Kong West Cluster (UW20-359) Institutional Review Board for this retrospective study. Inclusion criteria were COVID-19 patients admitted as inpatients to Queen Mary Hospital, referred for outpatient CMR post-recovery for raised troponin levels or electrocardiogram changes during the acute illness. Exclusion criteria were poor-quality CMR preventing assessment of ventricular function and late gadolinium enhancement (LGE). COVID-19 was diagnosed based on reverse transcription polymerase chain reaction test results of nasopharyngeal and throat swabs. Recovered COVID-19 status was based on: 1) 2 negative nasopharyngeal swab reverse transcription polymerase chain reaction results >24 h apart; and 2) absence of fever and improvement in respiratory symptoms. COVID-19 disease severity was defined according to World Health Organization criteria (4). CMR performed at 1.5-T (GE Healthcare Systems, Chicago, Illinois) included cine, native T1-mapping ($SMART_1$), T2-mapping, and LGE. T1/T2-mapping were analyzed in the mid-ventricular slice for an average value per patient. Images were reviewed independently by 3 cardiac radiologists.

Sixteen patients were identified (median age 68 years [interquartile range: 53 to 69 years]; 7 female subjects). Fifteen (94%) of the 16 patients had mild/moderate World Health Organization–defined disease severity. On admission, 14 (88%) had electrocardiogram changes, and 7 (44%) had raised troponin levels. At ≥2 weeks' post-discharge, 11 (69%) patients were asymptomatic. Five (31%) had symptoms such as cough, shortness of breath, and mild chest pain.

CMR was performed at a median of 56 days' post-recovery. Three (19%) patients had nonischemic LGE with elevated global T2-mapping values (57 to 62 ms), fulfilling the Lake Louise criteria for myocardial inflammation (3): 1 had chest discomfort with mildly elevated C-reactive protein (CRP) levels; 1 was asymptomatic but with elevated troponin levels (**Figure 1**); and 1 was asymptomatic with no blood biomarkers of inflammation. The fourth patient with LGE had a known history of non-ST-segment elevation myocardial infarction with circumflex artery stenting, showing a lateral wall infarct but no myocarditic changes. In the remainder (all 12 without LGE), 4 patients had elevated T1 only, 1 had elevated T2 only, and 1 had both elevated T1 and T2. Of these, 4 of 6 had blood biomarkers of inflammation (high white blood cell count, CRP, or troponin), and 3 of 6 had ongoing symptoms (1 cough, 1 cough/shortness of breath, and 1 shortness of breath/chest discomfort). The remaining 6 had normal T1 and T2 and no LGE; 5 of 6 were asymptomatic. Two of these 5 patients still had elevated troponin levels, 1 of 5 had elevated CRP levels, and 2 of 5 had normal blood test results. None had pericardial thickening or effusion.

Our study describes subclinical ongoing or resolving myocardial inflammation in patients recovered from COVID-19, as revealed by CMR. A study from Wuhan, China, reported that 58% of patients who recovered from COVID-19 had abnormal CMR findings but all had cardiac symptoms (5). In contrast, our study extends that although 69% (11 of 16) of patients who recovered from COVID-19 were asymptomatic, a majority (56% [9 of 16]) exhibited abnormal CMR findings (high T1 and/or T2, ± nonischemic LGE), 67% (6 of 9) of whom had accompanying blood biomarkers of ongoing inflammation, even if asymptomatic (3 of 6). In asymptomatic patients, 45% (5 of 11) had abnormal CMR findings; 27% (3 of 11) of asymptomatic patients also had