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**Brief Report**

**Epidemiology of Acute Heart Failure in Critically Ill Patients With COVID-19: An Analysis From the Critical Care Cardiology Trials Network**

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**ABSTRACT**

**Background:** Acute heart failure (HF) is an important complication of coronavirus disease 2019 (COVID-19) and has been hypothesized to relate to inflammatory activation.

**Methods:** We evaluated consecutive intensive care unit (ICU) admissions for COVID-19 across 6 centers in the Critical Care Cardiology Trials Network, identifying patients with vs without acute HF. Acute HF was subclassified as de novo vs acute-on-chronic, based on the absence or presence of prior HF. Clinical features, biomarker profiles and outcomes were compared.

**Results:** Of 901 admissions to an ICU due to COVID-19, 80 (8.9%) had acute HF, including 18 (2.0%) with classic cardiogenic shock (CS) and 37 (4.1%) with vasodilatory CS. The majority (n = 45) were de novo HF presentations. Compared to patients without acute HF, those with acute HF had higher cardiac troponin and natriuretic peptide levels and similar inflammatory biomarkers; patients with de novo HF had the highest cardiac troponin levels. Notably, among patients critically ill with COVID-19, illness severity (median Sequential Organ Failure Assessment, 8 [IQR, 5–10] vs 6 [4–9]; P = 0.025) and mortality rates (43.8% vs 32.4%; P = 0.040) were modestly higher in patients with vs those without acute HF.

**Conclusions:** Among patients critically ill with COVID-19, acute HF is distinguished more by biomarkers of myocardial injury and hemodynamic stress than by biomarkers of inflammation. (J Cardiac Fail 2022;28:675–681)

**Key Words:** heart failure, COVID-19, biomarkers.
Since the beginning of the coronavirus disease 2019 (COVID-19) pandemic, acute heart failure (HF) has been recognized as an important complication of severe acute respiratory syndrome-coronavirus 2 (SARS-CoV2) infection.1,2 Multiple mechanisms are potential drivers of acute HF in COVID-19, including myocarditis, systemic inflammation, catecholamine toxicity (ie, takotsubo cardiomyopathy), and myocardial ischemia/infarction; however, cardiovascular histopathology and imaging studies have not identified a single clear mechanistic culprit.3 Furthermore, epidemiological data comparing patients who develop COVID-19-related HF syndromes to noncritically ill patients with COVID-19 have made it difficult to discern whether their clinical characteristics are related specifically to the development of acute HF or more broadly to critical illness. Therefore, our objective was to describe the clinical features and hospital courses of patients critically ill with COVID-19 with and without acute HF syndromes in a multi-institutional cohort of patients in intensive care units (ICUs).

Methods
We analyzed consecutive admissions to ICUs of patients with COVID-19 from March 2020 to December 2020 across 6 academic medical centers in the United States using data from the Critical Care Cardiology Trials Network.4 Participating centers entered comprehensive clinical data into a central case-report form for patients with primary diagnoses of COVID-19 who had been admitted to all ICUs at their institutions. All patients admitted to the ICUs with cardiogenic shock (CS) (either classic or vasodilatory) or with acute HF without CS were classified as having an acute HF syndrome and were compared to patients without acute HF. CS was defined by sustained hemodynamic impairment (systolic blood pressure < 90 mmHg) and evidence of end-organ hypoperfusion due to low cardiac output.5 The distinction between classic and vasodilatory CS was based on high vs low systemic vascular resistance by using either invasive hemodynamic or history CS was based on high vs low systemic vascular resistance according to presenting HF categories. Categorical features and ICU resource use were summarized at each center.

Informed consent were approved by the Institutional Review Board at Mass General Brigham. The study was conducted according to the ethical principles stated in the Declaration of Helsinki and in accordance with the guidelines of the Clinical Research Ethics Committee. This study was supported by the Harvard Clinical Research Center and the National Heart, Lung, and Blood Institute (R01 HL151471 to J.J.R.)

Results
Among 901 admissions to an ICU due to COVID-19, 80 (8.9%) had acute HF, including 18 (2.0%) with classic CS and 37 (4.1%) with vasodilatory CS. In our cohort, patients critically ill with COVID-19 and with acute HF had a median age of 64 (25th–75th percentile, 55–76) years and were predominantly male (70.0%). More than half were de novo presentations of HF (n = 45).

Compared to patients critically ill due to COVID-19 but without acute HF, those with acute HF were more likely to have prior HF (43.8% vs 8.8%; P < 0.001), coronary artery disease (26.3% vs 9.5%; P < 0.001), atrial fibrillation (27.5% vs 8.8%; P < 0.001), or chronic kidney disease (32.5% vs 14.6%) (P < 0.001) (Table 1). These comorbidities were more common in acute-on-chronic HF than in de novo HF (Table 2).

Presentations with acute HF were most commonly due to left ventricular-predominant failure. Among patients with acute HF who had available presenting data for left ventricular ejection fraction (n = 67), 65.6% had left ventricular systolic dysfunction (LVEF < 50%), which was more common in patients with de novo (74.3%) vs acute-on-chronic HF (56.3%; P = 0.03) (Fig. 1). Of patients with acute HF, 16% had concurrent acute coronary syndromes (Table 1). Pulmonary vascular disease (eg, pulmonary hypertension, pulmonary embolism) was identified as a contributor in a minority of patients with biventricular (n = 5; 31.3%) and isolated right ventricular failure (n = 4; 25.0%). Acute myocarditis was not strictly defined or captured in this dataset. As compared to those without acute HF, patients with acute HF had significantly higher circulating biomarkers of myocardial injury (median baseline cardiac troponin (Ctn): 3.2x [1.6x–8.7x] vs 1.0x [0.4x–2.6x], the 99th percentile upper reference limit [URL]; median peak Ctn 12.7x [4.1x–53.3x] vs 2.1x [0.7x–7.0x] 99th percentile URL; P < 0.001 for both) and hemodynamic stress (median baseline N-terminal pro-B-type natriuretic peptide [NT-proBNP]: 2391 [976–7357] vs 381 [114–1459] pg/mL; median peak NT-proBNP: 5146 [2319–23,446] vs 742 [186–3510] pg/mL; P < 0.001 for both) (Table 1). Although peak NT-proBNP concentrations were similar in de novo and acute-on-chronic HF (median 4518 [1230–23,446] vs 5589 [2505–23,977] pg/mL; P = 0.39), Ctn was significantly higher in patients...
Table 1. Clinical Characteristics, Biomarker Profiles and Outcomes of Patients Critically Ill With COVID-19 and With vs Without Acute Heart Failure

| Variable | Acute Heart Failure (n = 80) | No Acute Heart Failure (n = 821) | P value |
|----------|-----------------------------|----------------------------------|--------|
| Demographics | | | |
| Age, median (IQR), years | 64 (55–76) | 60 (50–70) | 0.006 |
| Female sex | 24 (30.0%) | 308 (37.5%) | 0.184 |
| BMI, median (IQR), kg/m² | 29.5 (24.2–33.3) | 29.8 (25.8–34.9) | 0.196 |
| Comorbidities | | | |
| Prior heart failure | 35 (43.8%) | 72 (8.8%) | <0.001 |
| LV ejection fraction | | | |
| < 40% | 12 (34.3%) | 16 (22.2%) | 0.185 |
| 40% – 49% | 7 (20.0%) | 8 (11.1%) | |
| ≥ 50% | 12 (34.3%) | 40 (55.6%) | |
| Unknown | 4 (11.4%) | 8 (11.1%) | |
| Etiology (HFrEF only) | | | |
| Ischemic | 9 (45.0%) | 10 (43.5%) | 0.885 |
| Nonischemic | 4 (20.0%) | 6 (26.1%) | |
| Uncertain | 7 (35.0%) | 7 (30.4%) | |
| Diabetes mellitus | 34 (42.5%) | 328 (40.0%) | 0.657 |
| Hypertension | 46 (57.5%) | 459 (55.9%) | 0.784 |
| Coronary artery disease | 21 (26.3%) | 78 (9.5%) | <0.001 |
| Atrial fibrillation | 22 (27.5%) | 14 (1.7%) | <0.001 |
| Pulmonary hypertension | 4 (5.0%) | 14 (1.7%) | 0.044 |
| Chronic kidney disease | 26 (32.5%) | 120 (14.6%) | <0.001 |
| Chronic obstructive pulmonary disease | 8 (10.0%) | 42 (5.1%) | 0.069 |
| Admission Vital Signs | | | |
| Heart rate, bpm | 91 (74–115) | 94 (81–108) | 0.749 |
| Systolic blood pressure, mmHg | 115 (103–136) | 126 (111–142) | 0.005 |
| Diastolic blood pressure, mmHg | 66 (57–76) | 70 (61–81) | 0.023 |
| Respiratory rate, rpm | 22 (18–27) | 24 (20–29) | 0.080 |
| Presentation and illness severity | | | |
| Selected presenting symptoms | | | |
| Cough | 46 (57.5%) | 524 (63.8%) | 0.263 |
| Dyspnea | 63 (78.8%) | 589 (71.7%) | 0.181 |
| Fever | 35 (43.8%) | 567 (69.1%) | <0.001 |
| Concurrent acute coronary syndrome | 13 (16.3%) | 13 (1.6%) | <0.001 |
| STEMI | 6 (46.2%) | 8 (61.5%) | 0.695 |
| NSTEMI | 7 (53.8%) | 5 (38.5%) | |
| Unstable angina | 0 (0.0%) | 0 (0.0%) | |
| Primary/early PCI | 8 (61.5%) | 7 (53.8%) | 0.691 |
| SOFA score, median (IQR) | 8 (5–10) | 6 (4–9) | 0.025 |
| Clinical studies on presentation | | | |
| Interstitial infiltrates on CXR or CT | 64 (83.1%) | 653 (80.3%) | 0.553 |
| ECG abnormalities | | | |
| ST-segment elevation | 9 (11.3%) | 40 (4.9%) | 0.033 |
| ST-segment depression | 5 (6.3%) | 30 (3.7%) | 0.251 |
| Circulating biomarkers | | | |
| Procalcitonin, ng/mL | 1.2 (0.4–6.4) | 0.8 (0.3–3.5) | 0.078 |
| D-dimer, mg/mL | 4000 (1475–5238) | 3757 (1340–5408) | 0.587 |
| hsCRP, mg/L | 176 (43–280) | 123 (22–257) | 0.145 |
| Interleukin-6, pg/mL | 72 (54–304) | 91 (30–297) | 0.976 |
| Ferritin, mg/L | 1480 (575–3522) | 1375 (652–2798) | 0.600 |
| cTn, multiples of ULN | 12.7 (4.1–53.3) | 2.1 (0.7–7.0) | <0.001 |
| NT-proBNP, pg/mL | 5146 (2319–23,446) | 742 (186–3510) | <0.001 |
| Cardiac arrest | | | |
| Cardiac arrest prior to or during ICU admission | 24 (30.0%) | 89 (10.8%) | <0.001 |
| VT, VF or AED-shockable | 6 (25.0%) | 12 (13.5%) | 0.680 |
| PEA or asystole | 16 (66.7%) | 66 (74.2%) | |
| Unknown | 2 (8.3%) | 11 (12.4%) | |
| Respiratory failure characteristics | | | |
| PaO₂/FiO₂ ratio on ICU admission | 187 (119–307) | 134 (93–221) | <0.001 |
| Advanced respiratory therapy | 69 (86.3%) | 717 (87.3%) | 0.782 |
| Mechanical ventilation | 61 (76.3%) | 567 (69.1%) | 0.065 |
| Noninvasive PPV (BIPAP/CPAP) | 12 (15.0%) | 188 (22.9%) | 0.105 |
| High-flow nasal cannula | 5 (6.3%) | 51 (6.2%) | 0.989 |
| Other ICU resource utilization | | | |
| Renal replacement therapy | 16 (20.0%) | 125 (15.2%) | 0.262 |
| Pulmonary artery catheter | 13 (16.3%) | 8 (1.0%) | <0.001 |
| Invasive coronary angiography | 12 (15.6%) | 12 (15.5%) | <0.001 |
| Intravenous inotrope, vasopressor or vasodilator use | 68 (85.0%) | 520 (63.3%) | <0.001 |
| Mechanical circulatory support | 5 (6.3%) | 2 (0.2%) | <0.001 |

(continued)
Table 1 (Continued)

| Variable | Acute Heart Failure (n = 80) | No Acute Heart Failure (n = 821) | P value |
|----------|-----------------------------|----------------------------------|---------|
| Hospital Course and Outcomes | | | |
| ICU LOS, median IQR, days | 10.4 (2.9 – 17.9) | 8.0 (3.6 – 18.2) | 0.975 |
| In-hospital mortality\(^1\) | 35 (43.8%) | 266 (32.4%) | 0.040 |
| CV mode of death | 16 (45.5%) | 44 (16.5%) | <0.001 |
| Respiratory mode of death | 19 (54.3%) | 191 (71.8%) | 0.034 |
| Other/unknown | 9 (25.7%) | 64 (24.1%) | 0.830 |

AED, automated external defibrillator; BIPAP, bilevel positive airway pressure; BMI, body-mass index; bpm, beats per minute; COVID-19, coronavirus disease 2019; CPAP, continuous positive airway pressure; CT, computed tomography; cTn, cardiac troponin; CV, cardiovascular; CXR, chest X-ray; FiO\(_2\), fraction of inspired oxygen; HFref, heart failure with reduced ejection fraction; hsCRP, high-sensitivity C-reactive protein; ICU, intensive care unit; IQR, interquartile range; kg, kilogram; L, liter; LOS, length of stay; LV, left ventricular; m\(^2\), meters-squared; mg, milligrams; ml, milliliter; mmHg, millimeters of mercury; ng, nanograms; NSTEMI, non-ST-segment elevation myocardial infarction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; PaO\(_2\), partial pressure of oxygen in arterial blood; PCI, percutaneous coronary intervention; PEA, pulseless electrical activity; pg, picograms; PPV, positive pressure ventilation; rpm, respirations per minute; SOFA, Sequential Organ Failure Assessment; STEMI, ST-segment elevation myocardial infarction; ULN, upper limit of normal; VF, ventricular fibrillation; VT, ventricular tachycardia.

\(^1\)Refers to historical LVEF in patients with previous diagnosis of heart failure

\(^2\)Values indicate the “worst” levels (ie, peak or nadir, as appropriate) of the biomarker during ICU admission.

\(^3\)Includes intra-aortic balloon pump counterpulsation, Impella percutaneous ventricular assist systems (2.5, CP, 5.0, 5.5, RP), Tandem-Heart percutaneous ventricular assist systems, and veno-arterial extracorporeal membrane oxygenation (VA-ECMO).

\(^4\)Among those surviving to ICU discharge.

\(^5\)Modes of death are not mutually exclusive categories.

Table 2. Clinical Characteristics, Biomarker Profiles, and Outcomes of Patients Critically Ill With COVID-19 With de novo vs Acute-on-Chronic Presentations of Heart Failure

| Variable | De novo HF (n = 45) | Acute-on-Chronic HF (n = 35) | P value |
|----------|-------------------|-----------------------------|---------|
| Demographics | | | |
| Age, median (IQR), years | 64 (52 – 79) | 64 (57 – 73) | 0.771 |
| Female sex | 13 (28.9%) | 11 (31.4%) | 0.806 |
| BMI, median (IQR), kg/m\(^2\) | 27.5 (23.7 – 31.8) | 30.9 (25.1 – 35.0) | 0.193 |
| Comorbidities | | | |
| Diabetes mellitus | 16 (35.6%) | 18 (51.4%) | 0.154 |
| Hypertension | 21 (46.7%) | 25 (71.4%) | 0.026 |
| Coronary artery disease | 6 (13.3%) | 15 (42.9%) | <0.001 |
| Atrial fibrillation | 5 (11.1%) | 17 (48.6%) | <0.001 |
| Pulmonary hypertension | 0 (0.0%) | 4 (11.4%) | 0.020 |
| Chronic kidney disease | 9 (20.0%) | 17 (48.6%) | 0.007 |
| Chronic obstructive pulmonary disease | 1 (2.2%) | 7 (20.0%) | 0.009 |
| Admission vital signs | | | |
| Heart rate, bpm | 95 (78 – 119) | 90 (73 – 111) | 0.424 |
| Systolic blood pressure, mmHg | 111 (102 – 140) | 118 (105 – 135) | 0.803 |
| Diastolic blood pressure, mmHg | 66 (55 – 76) | 66 (58 – 80) | 0.634 |
| Respiratory rate, rpm | 22 (18 – 27) | 22 (18 – 27) | 0.771 |
| Presentation and illness severity | | | |
| Presenting symptoms | | | |
| Cough | 25 (55.6%) | 21 (60.0%) | 0.690 |
| Dyspnea | 33 (73.3%) | 30 (85.7%) | 0.179 |
| Fever | 18 (40.0%) | 17 (48.6%) | 0.443 |
| Concurrent acute coronary syndrome | | | |
| STEMI | 6 (66.7%) | 0 (0.0%) | 0.070 |
| NSTEMI | 3 (33.3%) | 4 (100.0%) | 0.001 |
| Unstable angina | 0 (0.0%) | 0 (0.0%) | 0.861 |
| Primary/early PCI | 6 (66.7%) | 2 (50.0%) | 0.569 |
| SOFA score, median (IQR) | 2 (5 – 10) | 8 (4 – 10) | 0.733 |
| Clinical studies on presentation | | | |
| Intestinal infiltrates on CXR or CT | 34 (79.1%) | 30 (88.2%) | 0.286 |
| ECG abnormalities | | | |
| ST-segment elevation | 9 (20.0%) | 0 (0.0%) | 0.004 |
| ST-segment depression | 3 (6.7%) | 2 (5.7%) | 0.861 |
| Circulating biomarkers\(^1\) | | | |
| Procalcitonin, ng/mL | 2.3 (0.4 – 8.0) | 0.8 (0.2 – 2.9) | 0.092 |
| D-dimer, ng/mL | 4000 (2689 – 8035) | 2976 (847 – 4000) | 0.003 |
| hsCRP, mg/L | 209 (101 – 295) | 83 (19 – 205) | 0.010 |
| Interleukin-6, pg/mL | 84 (56 – 347) | 62 (9 – 114) | 0.188 |
| Ferritin, mg/L | 1878 (1003 – 3522) | 844 (222 – 3072) | 0.019 |
| cTn, multiples of ULN | 21.6 (7.4 – 71.0) | 5.9 (2.1 – 26.2) | 0.004 |

\(^1\)Among those surviving to ICU discharge.

(continued)
### Table 2 (Continued)

| Variable                                      | De novo HF (n = 45) | Acute-on-Chronic HF (n = 35) | P value |
|-----------------------------------------------|---------------------|------------------------------|---------|
| NT-proBNP, pg/mL (n=55)                      | 4518 (1230–23,446)  | 5589 (2505–23,977)           | 0.378   |
| Cardiac arrest                                |                     |                              |         |
| Cardiac arrest prior to or during ICU admission | 15 (33.3%)          | 9 (25.7%)                    | 0.461   |
| VT, VF or AED-shockable                       | 5 (33.3%)           | 1 (11.1%)                    | 0.479   |
| PEA or asystole                               | 8 (53.3%)           | 8 (88.8%)                    |         |
| Unknown                                       | 2 (13.3%)           | 0 (0.0%)                     |         |
| Respiratory failure characteristics           |                     |                              |         |
| PaO2/FiO2 ratio on ICU admission              | 193 (105–323)       | 185 (121–269)                | 0.707   |
| Advanced respiratory therapy                  | 37 (82.2%)          | 32 (91.4%)                   | 0.236   |
| Mechanical ventilation                        | 35 (77.8%)          | 26 (74.3%)                   | 0.716   |
| Noninvasive PPV (BIPAP/CPAP)                  | 4 (8.9%)            | 8 (22.9%)                    | 0.083   |
| High-flow nasal cannula                       | 3 (6.7%)            | 2 (5.7%)                     | 0.861   |
| Other ICU resource utilization                |                     |                              |         |
| Renal replacement therapy                     | 8 (17.8%)           | 8 (22.9%)                    | 0.573   |
| Pulmonary artery catheter                     | 11 (24.4%)          | 2 (5.7%)                     | 0.024   |
| Invasive coronary angiography                 | 10 (22.7%)          | 2 (6.1%)                     | 0.136   |
| Intravenous inotrope, vasopressor, or vasodilator use | 42 (93.3%)       | 26 (74.3%)                   | 0.018   |
| Mechanical circulatory support                | 4 (8.9%)            | 1 (2.9%)                     | 0.269   |
| Hospital course and outcomes                  |                     |                              |         |
| ICU LOS, median (IQR), days                  | 12.9 (3.5–16.0)     | 9.8 (1.8–24.2)               | 0.991   |
| In-hospital mortality                         | 19 (42.2%)          | 16 (45.7%)                   | 0.755   |
| CV mode of death                              | 8 (42.1%)           | 8 (50.0%)                    | 0.641   |
| Respiratory mode of death                     | 10 (52.6%)          | 9 (56.3%)                    | 0.831   |
| Other/unknown                                 | 5 (26.3%)           | 4 (25.0%)                    | 1.000   |

1Values indicate the worst levels (ie, peak or nadir, as appropriate) of the biomarker during ICU admission.
2Includes intra-aortic balloon pump counter-pulsation, Impella percutaneous ventricular assist systems (2.5, CP, 5.0, 5.5, RP), Tandem-Heart percutaneous ventricular assist systems, veno-arterial extracorporeal membrane oxygenation (VA-ECMO).
3Among those surviving to ICU discharge.
4Modes of death are not mutually exclusive categories.

**Fig. 1.** Presenting heart failure syndrome of patients with de novo vs acute-on-chronic presentations of heart failure. LVEF, left ventricular ejection fraction.
with de novo vs acute-on-chronic HF (median peak cTn 21.6x [7.4x–71.0x] vs 5.9x [2.1x–26.2x] 99th percentile URL; \( P = 0.004 \)) (Table 2). This pattern was consistent in a sensitivity analysis excluding patients with acute coronary syndrome or cardiac arrest prior to ICU admission (median peak cTn 16.9x [7.3x–29.2x] vs 5.2x [2.1x–13.0x] 99th percentile URL; \( P = 0.019 \)). In contrast to the distinct patterns observed with cardiovascular biomarkers, patients critically ill with COVID-19 with and without acute HF had similarly elevated biomarkers of systemic inflammation—median peak high-sensitivity C-reactive protein 176 (43–280) vs 123 (22–257) mg/L (\( P = 0.14 \)); median interleukin-6 (IL-6) 72 (54–304) vs 91 (30–297) pg/mL (\( P = 0.98 \)); and median ferritin 1480 (575–3,522) vs 1375 (652–2798) mg/L (\( P = 0.60 \)) (Table 1). However, patients with de novo HF tended to have more inflammation than those with acute-on-chronic HF (Table 2).

Patients who are critically ill due to COVID-19 and have acute HF had modestly higher indices of disease severity as compared to those without acute HF (median Sequential Organ Failure Assessment score 8 [5–10] vs 6 [4–9]; \( P = 0.025 \)), but similar patterns of ICU resource use, including mechanical ventilation (\( P = 0.22 \)) and acute renal replacement therapy (\( P = 0.26 \)). The median ICU length-of-stay among ICU survivors was similar in patients with and without acute HF (10.4 [2.9–17.9] vs 8.0 [3.6–18.2] days; \( P = 0.98 \)) (Table 1).

Patients critically ill with COVID-19 and with acute HF were more likely than patients without acute HF to experience cardiac arrest either before or during ICU admission (30.0% vs 10.8%; \( P < 0.001 \)). In-hospital mortality was moderately higher in patients with vs without acute HF (43.8% vs 32.4%; \( P = 0.040 \)). Patients with acute HF were more likely to have a cardiovascular (eg, acute myocardial infarction, HF, stroke, arrhythmia) mode of death (45.7% vs 16.5%; \( P < 0.001 \)) and less likely to have a respiratory mode (54.3% vs 71.8%; \( P = 0.034 \)) (Table 1).

**Discussion**

Prior HF is an important prognostic indicator in COVID-19.\(^6^,^7\) Our analysis extends this observation by demonstrating that pre-existing HF is also an important risk factor for the development of severe acute HF syndromes in patients critically ill with COVID-19. At the same time, more than half of admissions to ICUs for acute HF occurred in patients without prior diagnoses of HF, highlighting the clinically important risk of de novo myocardial dysfunction and HF in this population. In a single-center analysis of hospitalized (critically ill and noncritically ill) patients with COVID-19, 37 were identified as having de novo HF, 8 of whom had no prior cardiovascular disease or known risk factors.\(^8\) The point prevalence of de novo HF in our cohort was > 8-fold higher than that observed in that study (5.0% vs 0.6%), probably related to the higher overall risk of our exclusively ICU-based population. Nevertheless, we also observed that many patients with de novo HF had no known prior cardiovascular disease or risk factors. Collectively, these findings underscore the importance of recognizing this subset of patients and investigating the mechanisms of myocardial injury so we can tailor acute and chronic therapies and future preventive interventions.

The biomarker profiles observed in our study also offer potentially important and clinically relevant insights. Both cTn and natriuretic peptide concentrations were strongly associated with acute HF presentation in critically ill patients with COVID-19; however, cTn was particularly elevated in de novo compared with acute-on-chronic HF, suggesting more acute myocardial injury in this group. Notably, although patients with COVID-19 in ICUs and with acute HF had elevated inflammatory markers, the degree of inflammation was comparable to those without acute HF, suggesting that the hyperinflammatory phenotype may not distinguish presentation with acute HF. Whether these biomarker patterns reflect the underlying mechanisms driving acute HF syndromes in critically ill patients with COVID-19 warrants further investigation (eg, correlation with cardiac MRI, endomyocardial biopsy).

Finally, although mortality rates were high in patients critically ill with COVID-19, both with and without acute HF, those with acute HF had higher risks of cardiac arrest and of dying from a cardiovascular cause, which may have implications for optimal triage of these patients (eg, to cardiac ICUs). It is important to note that mortality estimates from our study period may be higher than contemporary estimates due to subsequent adoption of effective therapies (eg, corticosteroids).

In conclusion, acute HF is an important complication in patients critically ill with COVID-19, occurring in approximately 1 in 11 such patients. Although the risk of acute HF is higher in patients with prior HF, > 50% of acute HF syndromes in patients critically ill with COVID-19 are de novo presentations of HF. Among critically ill COVID-19 patients, presentation with acute HF is characterized more by elevations in biomarkers of myocardial injury and hemodynamic stress than by elevations in biomarkers of inflammation, and myocardial injury appears to be a particularly distinguishing feature of patients with de novo HF.

**Disclosures**

The present analysis was supported by Evergrande COVID-19 Response Fund Award from the...
Massachusetts Consortium on Pathogen Readiness (DDB, DAM, EAB). DDB is supported by Harvard Catalyst KL2/Catalyst Medical Research Investigator Training (National Center for Advancing Translational Sciences grant UL 1TR002541). SS reports receiving personal fees from Abiomed outside the submitted work. ASV is supported by the National Heart, Lung, and Blood Institute T32 postdoctoral training grant T32HL007604 and the Daniel Pierce Family Fellowship in Advanced Heart Disease. All other authors report no disclosures relevant to the contents of this paper.

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