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.

Brief Report

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

DAVID D. BERG, MD, MPH,[1] CARLOS L ALVIAR, MD,[2] ANKEET S. BHATT, MD, MBA,[1] VIVIAN M. BAIRD-ZARS, MPH,[1] CHRISTOPHER F. BARNETT, MD, MPH,[3,4] LORI B. DANIELS, MD, MAS,[5] ANDREW P. DEFILIPPIS, MD, MSC,[6] ANTONIO FAGUNDES JR, MD, PhD,[1] PRANEETH KATRAPATI, MD,[7] BENJAMIN B. KENIGSBERG, MD,[4] JIANPING GUO, MAS,[1] NORMA KELLER, MD,[2] MATHEW S. LOPES, MD,[1] ANIKA MODY,[5] ALEXANDER I PAPOLOS, MD,[4] NICHOLAS PHREANER, MD,[5] ROMTEEN SEDIGHI, BS,[5] SHASHANK S. SINHA, MD,[8] SANDEEP TOOMU, BS,[5] ANUBODH S. VARSHNEY, MD,[1] DAVID A. MORROW, MD, MPH,[1,*] and ERIN A. BOHULA, MD, DPhil[1,*]

Boston, Massachusetts; New York, New York; San Francisco, and La Jolla, California; Washington, D.C.; Nashville, Tennessee; Louisville, Kentucky; and Falls Church, Virginia

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.

From the [1]Levine Cardiac Intensive Care Unit, Cardiovascular Division, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts; [2]The Leon H. Charney Division of Cardiovascular Medicine, New York University Langone Medical Center, New York, New York; [3]Division of Cardiology, Department of Medicine, University of California San Francisco, San Francisco, California; [4]Medstar Heart and Vascular Institute, Medstar Washington Hospital Center, Washington, D.C.; [5]Division of Cardiovascular Medicine, Department of Medicine, University of California San Diego, La Jolla, California; [6]Division of Cardiology, Department of Medicine, Vanderbilt University Medical Center, Nashville, Tennessee; [7]Division of Cardiovascular Medicine, Department of Medicine, University of Louisville, Louisville, Kentucky and [8]Inova Heart and Vascular Institute, Inova Fairfax Medical Center, Falls Church, Virginia.

Manuscript received October 1, 2021; revised manuscript received December 8, 2021; revised manuscript accepted December 23, 2021.

Reprint requests: David D. Berg, MD, MPH, TIMI Study Group, 60 Fenwood Road, Suite 7022, Boston, MA 02115. E-mail: dberg1@bwh.harvard.edu

*Indicates cosenior authorship.

See page 680 for disclosure information.

1071-9164/$ - see front matter

https://doi.org/10.1016/j.cardfail.2021.12.020

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 clinical assessment. Classification of acute HF without CS was based on clinician assessment using local diagnostic standards and the entirety of the clinical record. Admissions for acute HF were further classified as de novo vs acute-on-chronic presentations based on the absence or presence of a prior diagnosis of HF, respectively. The protocol and waiver of informed consent were approved by the Institutional Review Board at Mass General Brigham and at each center.

Baseline patient characteristics, presenting clinical features and ICU resource use were summarized according to presenting HF categories. Categorical variables are presented as counts and percentages, and continuous variables are presented as medians with 25th−75th percentiles. Differences between groups were evaluated using the Pearson χ^2 test for categorical variables and the Wilcoxon rank sum test for continuous variables.

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/m^2	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[1]			
< 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%)	72 (8.8%)	<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[2]			
Procalcitonin, ng/mL	1.2 (0.4–6.4)	0.8 (0.3–3.5)	0.078
D-dimer, ng/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			
PaO_2/FiO_2 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 (1.5%)	<0.001
Intravenous inotrope, vasopressor or vasodilator use	68 (85.0%)	520 (63.3%)	<0.001
Mechanical circulatory support[3]	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,[4] median (IQR), days	10.4 (2.9–17.9)	8.0 (3.6–18.2)	0.975
In-hospital mortality[5]	35 (43.8%)	266 (32.4%)	0.040
CV mode of death	16 (45.7%)	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), TandemHeart 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	9 (20.0%)	4 (11.4%)	0.303
STEMI	6 (66.7%)	0 (0.0%)	0.070
NSTEMI	3 (33.3%)	4 (100.0%)	
Unstable angina	0 (0.0%)	0 (0.0%)	
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			
Interstitial 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

(*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			
PaO_2/FiO_2 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[2]	4 (8.9%)	1 (2.9%)	0.269
Hospital course and outcomes			
ICU LOS,[3] median (IQR), days	12.9 (3.5–16.0)	9.8 (1.8–24.2)	0.991
In-hospital mortality[4]	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

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; 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]Values indicate the worst levels (ie, peak or nadir, as appropriate) of the biomarker during ICU admission.

[2]Includes intra-aortic balloon pump counter-pulsation, Impella percutaneous ventricular assist systems (2.5, CP, 5.0, 5.5, RP), TandemHeart percutaneous ventricular assist systems, veno-arterial extracorporeal membrane oxygenation (VA-ECMO).

[3]Among those surviving to ICU discharge.

[4]Modes of death are not mutually exclusive categories.

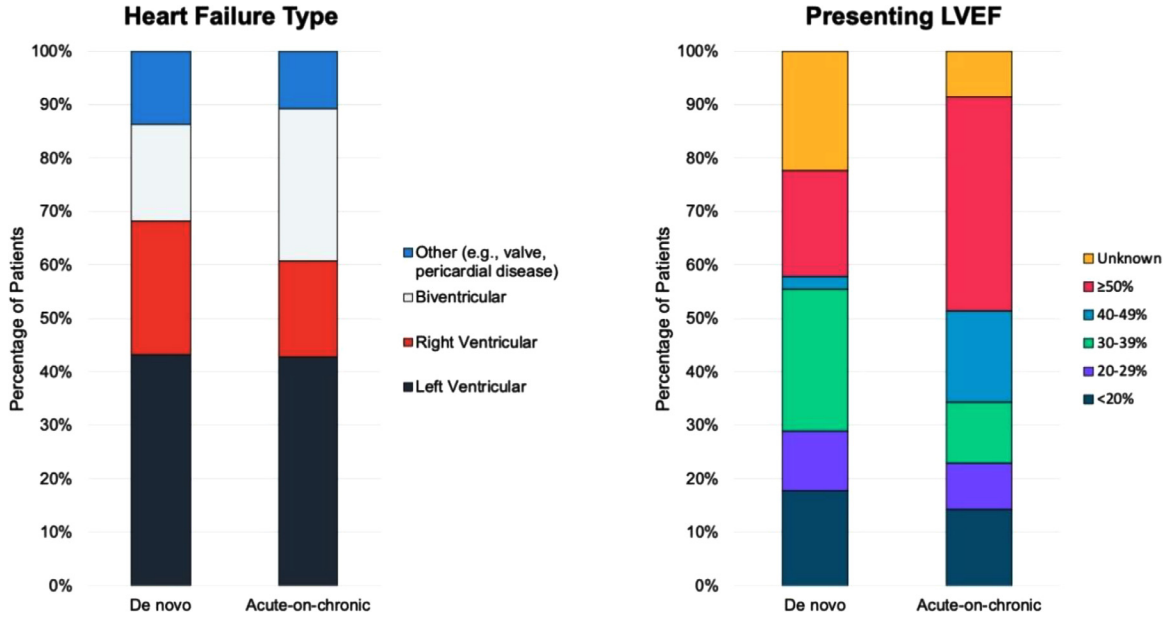

Fig. 1. Presenting heart failure syndrome of patients with de novo vs acute-on-chronic presentations of heart failure. LVEF, left ventricular ejection fraction.

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 inflamation 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 every 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.

References

1. Rey JR, Caro-Codon J, Rosillo SO, Iniesta AM, Castrejon-Castrejon S, Marco-Clement I, et al. Heart failure in COVID-19 patients: prevalence, incidence and prognostic implications. Eur J Heart Fail 2020;22:2205–15.
2. Bhatt AS, Adler ED, Albert NM, Anyanwu A, Bhadelia N, Cooper LT, et al. Coronavirus disease-2019 and heart failure: a scientific statement from the Heart Failure Society of America. J Card Fail 2022;28(1):93–112.
3. Atri D, Siddiqi HK, Lang JP, Nauffal V, Morrow DA, Bohula EA. COVID-19 for the Cardiologist: Basic Virology, Epidemiology, Cardiac Manifestations, and Potential Therapeutic Strategies. JACC Basic Transl Sci 2020;5:518–36.
4. Bohula EA, Katz JN, van Diepen S, Alviar CL, Baird-Zars VM, Park JG, et al. Demographics, care patterns, and outcomes of patients admitted to cardiac intensive care units: the Critical Care Cardiology Trials Network Prospective North American Multicenter Registry of Cardiac Critical Illness. JAMA Cardiol 2019;4:928–35.
5. Berg DD, Bohula EA, van Diepen S, Katz JN, Alviar CL, Baird-Zars VM, et al. Epidemiology of shock in contemporary cardiac intensive care units. Circ Cardiovasc Qual Outcomes 2019;12:e005618.
6. Tomasoni D, Inciardi RM, Lombardi CM, Tedino C, Agostoni P, Ameri P, et al. Impact of heart failure on the clinical course and outcomes of patients hospitalized for COVID-19: results of the Cardio-COVID-Italy multicentre study. Eur J Heart Fail 2020;22:2238–47.
7. Alvarez-Garcia J, Lee S, Gupta A, Cagliostro M, Joshi AA, Rivas-Lasarte M, et al. Prognostic impact of prior heart failure in patients hospitalized with COVID-19. J Am Coll Cardiol 2020;76:2334–48.
8. Alvarez-Garcia J, Jaladanki S, Rivas-Lasarte M, Cagliostro M, Gupta A, Joshi A, et al. New heart failure diagnoses among patients hospitalized for COVID-19. J Am Coll Cardiol 2021;77:2260–2.