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JACC: CARDIOVASCULAR IMAGING
VOL. ■, NO. ■, 2020

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER

Right Ventricular Function and Pulmonary Pressures as Independent Predictors of Survival in Patients With COVID-19 Pneumonia

Coronavirus 2019 (COVID-19) disease, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), can lead to cardiac impairment, with increased troponin levels, left ventricular (LV) dysfunction and myocarditis (1,2). Information for right ventricular (RV) involvement and pulmonary pressures in these patients is limited, and this study aimed to explore the possible association between these factors and mortality. This study was conducted from February 20, 2020, to April 2020 in 4 centers. The final follow-up date was April 20, 2020. All consecutive patients with test results positive for SARS-CoV-2, as well as laboratory and computed tomography-confirmed interstitial pneumonia were included. Clinical, laboratory, radiological, and ultrasonographic data were collected. Cardiac injury was defined by measuring blood concentrations of high-sensitivity troponin I (hs-TnI) using the 99th percentile upper reference limit of the electrochemiluminescence immunoassay method. RV end-diastolic chamber size was assessed by using basal-tract and mid-tract diameters in apical 4-chamber view. Tricuspid annular plane systolic excursion (TAPSE) was calculated as a bedside-feasible index of RV longitudinal systolic function by aligning an M-mode cursor parallel with the RV free wall as it met the tricuspid annulus.

Pulmonary artery systolic pressure (PASP) was calculated by adding the value of right atrial pressure to the systolic transtricuspid gradient. Mean pulmonary artery pressure (mPAP) was calculated as $0.6 \times \text{PASP} + 2$ mm Hg (3). Outcomes of patients with cardiac involvement were compared to those in patients without cardiac involvement. An ethics committee approved the study, and all individuals gave written informed consent.

A total of 115 patients with COVID-19 pneumonia were included in the analysis. The mean age was 64.6 years (range 20 to 88 years of age), and 45 (40%) were female. Twenty-six patients had cardiac injury, and those patients were older (mean age: 73.5 years of age [range 37 to 88] vs. 55.3 years of age [range 20 to 78], respectively; $p < 0.001$). They also more frequently had systemic hypertension (16 of 26 patients [61.5%] vs. 26 of 89 patients [29.2%], respectively; $p < 0.001$). They also had higher levels of C-reactive protein (mean: 98.8 [range 45.8 to 130.4] mg $\cdot$ l^{-1} vs. 38.9 [range 22.2 to 96.3] mg $\cdot$ l^{-1}, respectively; $p < 0.001$); higher D-Dimer (mean: 4.8 [3.2 to 7.1] vs. 2.1 [0.5 to 3.4], respectively; $p < 0.001$); a higher proportion of multiple ground-glass opacities in computed tomography (CT) findings (18 of 26 patients [69.2%] vs. 30 of 89 patients [33.7%], respectively; $p < 0.001$); and multiple consolidations by lung ultrasonography (20 of 26 patients [76.6%] vs. 34 of 89 patients [38.2%], respectively; $p < 0.001$). Lower-limb compression ultrasonography (CUS) was positive (proximal deep vein thrombosis of the common femoral vein and/or popliteal vein) only in 3 patients with cardiac injury and in 3 other patients without cardiac injury. A single echocardiograph for each hospital was identified, portably to facilitate sanitation, and the examination was performed by a single operator, reducing patient contact with the device. RV end-diastolic diameters and mPAP values were significantly increased in patients with cardiac injury, whereas the tricuspid inflow E/A ratio (the ratio of peak velocity blood flow from LV relaxation in early diastole [E wave] to peak velocity flow in late diastole caused by atrial contraction [A wave]) and TAPSE were reduced (Table 1). All patients were treated with oxygen, and the percentages of use of noninvasive ventilation and invasive mechanical ventilation were 16.5 % (19 patients) and 9.5 % (11 patients), respectively. A greater proportions of patients with cardiac injury required invasive or noninvasive mechanical ventilation (17 of 26 [65.4%] vs. 20 of 89 [22.4%], respectively; $p < 0.001$). The common complication in patients with cardiac injury was acute respiratory distress syndrome (14 of 26 [63.5%] vs. 15 of 89 [16.8%], respectively; $p < 0.001$). Patients with cardiac injury had higher mortality than those without cardiac injury (13 of 26 [50%] vs. 8 of 89 [7.8%], respectively; $p < 0.0001$). In a Cox regression model in COVID-19 patients, troponin levels (hazard ratio [HR]: 4.33 [95% confidence interval [CI]: 1.87 to 8.49]; $p < 0.001$), partial pressure of oxygen (Pao_2) at admission (HR: 0.26 [95% CI: 0.15 to 0.74; $p < 0.01$]; mPAP (HR: 3.8 [95% CI: 1.72 to 6.39] $p < 0.001$), and RV TAPSE (HR: 0.5 [95% CI: 0.22 to 0.74] $p < 0.001$) emerged as the only independent predictors of in-hospital death.

Despite the high prevalence of normal CUS, it was found that increases in mPAP and RV dysfunction

TABLE 1 Echocardiographic Structural and Systolic/Diastolic Functional Indices in COVID-19 Patients With and Without Cardiac Injury

	Without Cardiac Injury (n = 89)	With Cardiac Injury (n = 26)	p Value
Septal wall thickness, mm	10.7 ± 2.3	11.5 ± 2.3	NS
LV posterior wall thickness, mm	9.8 ± 1.2	10.8 ± 1.1	NS
LV end-diastolic diameter, mm	48.7 ± 4.8	49.9 ± 6.7	NS
LV end-systolic diameter, mm	33.4 ± 3.8	35.4 ± 5.2	NS
Mitral peak A velocity, m/s	0.72 ± 0.32	0.73 ± 0.3	NS
Mitral peak E/A ratio	0.91 ± 0.3	0.88 ± 0.3	NS
LV ejection fraction %	56.2 ± 4.4	54.4 ± 4.6	NS
RV basal tract diameter, mm	31.2 (2.6)	35.8 (4.2)	<0.01
RV mid-tract diameter, mm	28.6 (3.7)	32.4 (3.9)	<0.01
Tricuspid peak E velocity, m/s	0.15 ± 0.08	0.12 ± 0.06	<0.01
Tricuspid peak A velocity, m/s	0.13 ± 0.08	0.16 ± 0.06	<0.01
Tricuspid peak E/A ratio	1.1 ± 0.6	0.77 ± 0.5	<0.01
TRV, m/s	2.9 ± 0.5	3.4 ± 0.6	<0.001
PASP, mm Hg	36.1 ± 5.3	46.8 ± 4.8	<0.001
MPAP, mm Hg	23.6 ± 2.7	29.6 ± 2.9	<0.001
TAPSE, mm	20.3 ± 4.7	15.4 ± 3.2	<0.001

Values are mean ± SD or n (%). COVID-19 = coronavirus 2019; E/A = ratio of peak velocity blood flow from LV relaxation in early diastole [E wave] to peak velocity flow in late diastole caused by atrial contraction [A wave]); LV = left ventricle; MPAP = mean pulmonary artery pressure; NS = not significant; PASP = pulmonary artery systolic pressure; RV = right ventricle; TAPSE = tricuspid annular systolic plane excursion; TRV = tricuspid regurgitation velocity.

were common conditions among patients with COVID-19 pneumonia and cardiac injury, associated with higher risk of in-hospital mortality. Use of empiric therapeutic anticoagulation in certain COVID-19 patients who did not have deep vein thrombosis has been advocated, but this remains controversial because of the risk of major bleeding and lack of data about the true incidence of pulmonary embolism (4). However, assessment of RV function and of pulmonary pressures during the recovery of these patients may represent a key point in the prognostic stratification.

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https://doi.org/10.1016/j.jcmg.2020.06.004

Please note: The authors have reported that they have no relationships relevant to the contents of this paper to disclose.
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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