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Prevalence and Clinical Correlates of Echo-Estimated Right and Left Heart Filling Pressures in Hospitalized Patients With Coronavirus Disease 2019

Objectives: The prevalence of elevated right and left heart filling pressures in coronavirus disease 2019 is not well characterized. We aimed to characterize the prevalence of pulmonary hypertension and concurrent elevated left heart filling pressure in hospitalized patients with coronavirus disease 2019. We hypothesized that a significant proportion of coronavirus disease 2019 patients has evidence of pulmonary hypertension associated with elevated left heart filling pressure on transthoracic echocardiography.

Design: Retrospective cohort study.

Setting: Academic tertiary-care center.

Patients: Hospitalized coronavirus disease 2019 patients who underwent clinical transthoracic echocardiography.

Interventions: None.

Measurements and Main Results: The exposure variable of interest was right ventricular systolic pressure, calculated using the American Society of Echocardiography guidelines. Pulmonary hypertension was defined as right ventricular systolic pressure greater than 40 mm Hg. Left heart filling pressure was estimated with Nagueh's method for pulmonary artery occlusion pressure using E/e' ratio, and normal was considered pulmonary artery occlusion pressure less than 16 mm Hg. Clinical characteristics and outcomes were compared between the patients with and without pulmonary hypertension. A total of 73 patients (median age 66 yr [57–75 yr]; 46% women) were included. Median right ventricular systolic pressure was 39 mm Hg (interquartile range, 32–50 mm Hg), and 36 patients (49.3%) had evidence of pulmonary hypertension. Patients with pulmonary hypertension were more likely to require ICU admission (86% vs 65%; $p = 0.035$) and have acute respiratory distress syndrome (72% vs 49%; $p = 0.0053$) than those without. In-hospital mortality was 26% for those with pulmonary hypertension compared with 14% for those without ($p = 0.19$). Patients with pulmonary hypertension had higher median-estimated pulmonary artery occlusion pressure (17.4 mm Hg [12.7–21.3 mm Hg] vs 12.1 mm Hg [10.0–14.1 mm Hg]; $p = 0.0008$), and elevated left heart filling pressure was present in 59% of those with pulmonary hypertension.

Conclusions: Pulmonary hypertension is common in hospitalized patients with coronavirus disease 2019 and is associated with poor

clinical outcomes. Left ventricular filling pressure is elevated in over half of those with pulmonary hypertension and may represent a target to reduce right ventricular afterload and potentially improve outcomes in coronavirus disease 2019.

Key Words: coronavirus disease 2019; coronavirus; critical illness; pulmonary occlusion pressure; right ventricular function

To the Editor:

Coronavirus disease 2019 (COVID-19) results in critical illness with respiratory failure. Pulmonary vascular dysfunction and pulmonary hypertension (PH) are common in critical illness, and COVID-19 can be associated with severe right heart failure and acute cor pulmonale (1, 2). Because COVID-19 pulmonary disease involves the pulmonary vessels, understanding the prevalence and prognostic impact of pulmonary vascular dysfunction in COVID-19 is important (3). Additionally, although right ventricular (RV) dysfunction is common and associated with adverse outcomes in COVID-19, the prevalence of elevated left heart filling pressures (LHFPs) in this patient population is unclear (4). Elevated LHFP contributes to PH and RV dysfunction and represents a treatable target to reduce RV afterload (5). Given that very few COVID-19 patients undergo pulmonary artery catheterization, echocardiography is an important noninvasive method to estimate biventricular filling pressures (6, 7). We characterized the prevalence of PH and concurrent elevated LHFP in hospitalized patients with COVID-19, using transthoracic echocardiography (TTE). We hypothesized that a significant proportion of COVID-19 patients has PH associated with elevated LHFP on TTE.

MATERIALS AND METHODS

This study was approved by the Johns Hopkins Institutional Review Board (IRB00249051). Hospitalized COVID-19 patients who underwent clinical TTE were included if they had adequate imaging windows and detectable tricuspid regurgitation (TR) velocity. Echocardiographic measurements were performed by a dedicated research sonographer. All measures including the exposure variable of interest, estimated RV systolic pressure (RVSP), were acquired and calculated per guidelines (7). PH was defined as RVSP greater than or equal to 40 mm Hg. LHFP was estimated using the E/e' ratio and with the Nagueh's method to estimate pulmonary artery occlusion pressure (PAOP) (8). Clinical and demographic variables were compared across PH categories using the Mann-Whitney test for continuous variables and the Pearson chi-square for categorical variables. Linear regression was used to assess the relationship between LHFP and RVSP. The assumptions of linear regression were verified by the inspection of the residuals versus predicted value plot and inspection of the residuals for normal distribution using Q-Q plots. Analyses were performed using

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Stata Version 14.0 (StataCorp, College Station, TX). A *p* value of less than 0.05 was considered statistically significant.

RESULTS

Of 149 consecutive COVID-19 subjects who underwent TTE, 73 patients had TR velocity measured. Median age was 66 years (57–75 yr), and 45% were women. Median time to TTE was 4 days (2–7 d) from admission. Global left and RV function was normal in the majority of patients (Table 1). ICU admission was common (75.3%), and 60.3% had acute respiratory distress syndrome (ARDS). Two patients remained admitted at the time of analysis. Mortality was 21.1% for those with complete follow-up (*n* = 71). Median RVSP was 39.0 mm Hg (interquartile range, 32–50 mm

Hg) (Fig. 1), and 36 patients (49.3%) had evidence of PH. Patients with PH were more likely to require ICU admission (86% vs 65%; *p* = 0.035) and have ARDS (72% vs 49%; *p* = 0.04) compared with those without PH. Mortality and hospital length of stay were similar between the groups (Table 1). RV diameter was greater in patients with PH, and RV function assessed with tricuspid annular plane systolic excursion was similar. Patients with PH had higher LHFP than those without: *E/e'* 12.6 (8.7–15.7) versus 8.2 (6.6–9.9) and estimated PAOP 17.4 mm Hg (12.7–21.3 mm Hg) versus 12.1 mm Hg (10.0–14.1 mm Hg), *p* = 0.0008, for both (Table 1). Higher *E/e'* ratio was associated with higher estimated RVSP (Fig. 1) (standardized β = 0.41, *R*² = 0.17, and *p* = 0.002), with estimated LHFP responsible for approximately 17% of the variability in RVSP.

TABLE 1. Demographic and Clinical Variables in Coronavirus Disease 2019 Patients With and Without Echocardiographic Pulmonary Hypertension

Characteristics	Total Cohort (<i>n</i> = 73)	RVSP ≤ 40 mm Hg (<i>n</i> = 37)	RVSP > 40 mm Hg (<i>n</i> = 36)	<i>p</i>
Age, yr, median (interquartile range)	66 (57–75)	65 (57–77)	68 (57–74)	0.66
Female, <i>n</i> (%)	33 (45.2)	20 (54.1)	13 (36.1)	0.12
Body mass index, kg/m ²	29.5 (25.8–35.1)	28.1 (24.8–31.9)	29.9 (27.1–35.8)	0.06
Comorbidities				
Diabetes mellitus	31 (42.5)	13 (35.1)	18 (50.0)	0.20
Hypertension	47 (67.1)	22 (59.5)	27 (75.0)	0.16
Dyslipidemia	39 (53.4)	18 (48.7)	21 (58.3)	0.41
Coronary artery disease	14 (19.2)	4 (10.8)	10 (27.8)	0.066
Chronic obstructive pulmonary disease	10 (13.7)	5 (13.5)	5 (13.9)	0.96
Clinical events				
Time to echo, d	4 (2–7)	3 (1–5)	5 (2–9)	0.043
ICU admission	55 (75.3)	24 (64.9)	31 (86.1)	0.035
Total length of stay, d ^a	17 (9–30)	14 (6–25)	21 (11–31)	0.09
Acute respiratory distress syndrome	44 (60.3)	18 (48.6)	26 (72.2)	0.04
Death ^a	15 (21.1)	7 (18.9)	8 (23.5)	0.63
Echo parameters				
Left ventricular ejection fraction, %	60.0 (50.0–62.5)	62.5 (55.0–62.5)	58.8 (46.3–62.5)	0.66
Left ventricular end diastolic diameter, mm	43.0 (37.3–48.0)	42.0 (36.6–46.9)	43.0 (37.6–50.0)	0.55
Right ventricular end diastolic diameter (measured at base), mm (<i>n</i> = 59)	38.5 (33.1–42.4)	35.9 (32.8–39.8)	41.4 (35.8–45.0)	0.007
Tricuspid annular plane systolic excursion (<i>n</i> = 61)	1.8 (1.5–2.0)	1.8 (1.5–2.0)	1.9 (1.5–2.1)	0.38
<i>E/e'</i> (<i>n</i> = 57)	9.8 (7.6–13.0)	8.2 (6.6–9.9)	12.6 (8.7–15.7)	0.0008
Elevated <i>E/e'</i> ratio ^b	13 (22.8)	3 (10.0)	10 (37.0)	0.015
Estimated pulmonary artery occlusion pressure, mm Hg (<i>n</i> = 57)	14.0 (11.3–18.0)	12.1 (10.0–14.1)	17.4 (12.7–21.3)	0.0008

RVSP = right ventricular systolic pressure.

^a*n* = 71 patients with complete follow-up to death/discharge.

^bNormal *E/e'* ratio < 14.

Bold indicates significant *p* value < 0.05.

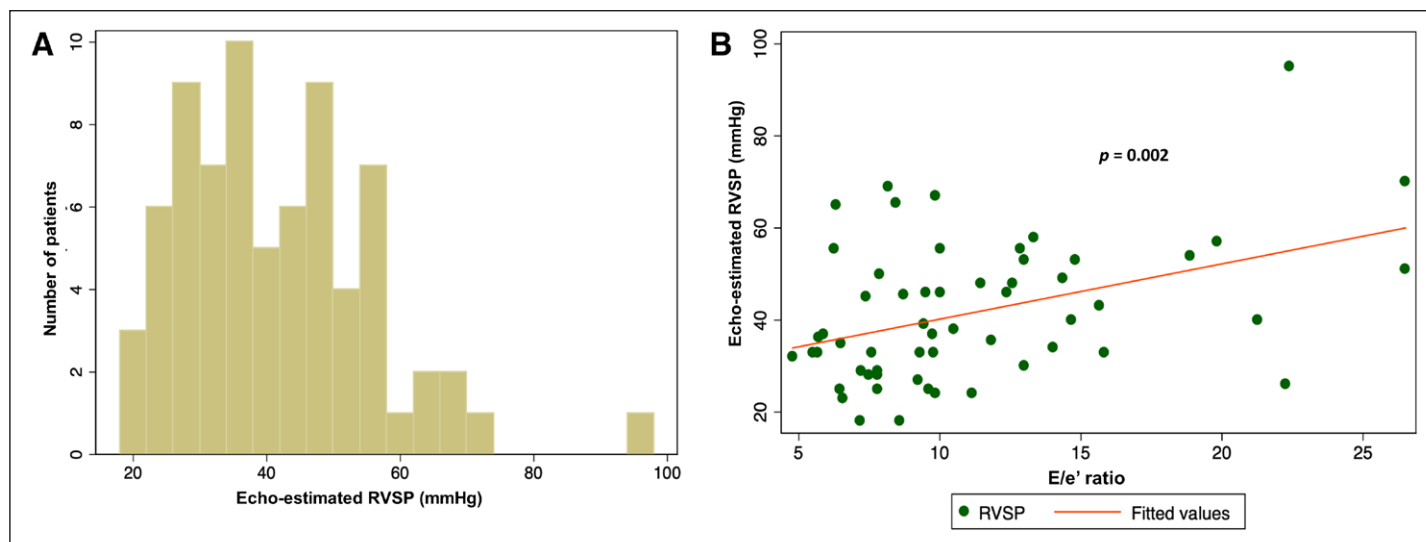


Figure 1. Distribution of estimated right ventricular systolic pressure (RVSP) and its relationship with E/e' in hospitalized patients with coronavirus disease 2019 (COVID-19). **A**, Distribution of estimated RVSP in hospitalized COVID-19 patients who underwent transthoracic echocardiography. **B**, Linear regression demonstrating the relationship between E/e' ratio, as an estimate of left heart filling pressure and estimated RVSP.

DISCUSSION

COVID-19 can be associated with acute cor pulmonale and RV failure; therefore, understanding contributors to RV afterload is of paramount importance (1). We demonstrate that PH is common in hospitalized patients with COVID-19 undergoing echocardiography and is associated with elevated LHFp in over one-third of patients assessed. Elevated LHFp contributes significantly to pulmonary arterial pressure in these patients and is known to contribute to PH and RV afterload (5). LHFp thus may represent a common, modifiable treatment target in COVID-19 to reduce RV afterload.

PH is common in critically ill patients and is an independent predictor of mortality, including in patients with ARDS (2). Our study suggests that echocardiographic findings of elevated RVSP are also common in COVID-19. These hemodynamic parameters are useful estimates of cardiac filling pressures and thus help guide volume management strategies.

Overt or subclinical RV failure is associated with worse outcomes in COVID-19 (1, 4). An RV protective strategy to treat ARDS has been advocated, which includes fluid conservative therapy (1, 9). Reducing LHFp in COVID-19 may, therefore, represent a mechanism to reduce PA pressure and RV afterload, and improve outcomes.

We also report that PH is associated with ICU admission and ARDS; although this study was not powered for mortality, PH has been associated with higher mortality in other ICU studies (10). Thus, these findings represent a higher risk COVID-19 phenotype.

Limitations include modest sample size and single-center retrospective design. We included only those patients undergoing TTE during admission, which could introduce bias. Another limitation is the requirement for adequate sonographic views, which are often compromised in the critically ill. RVSP is an imperfect estimation of pulmonary pressures and is dependent on some degree of TR. Similarly, E/e' is not an obtainable measurement in every patient.

CONCLUSIONS

PH is common in hospitalized patients with COVID-19 and is associated with elevated LHFp. Over one-third of those with PH have elevated LHFp, which may represent an important target to reduce RV afterload. Further investigation into RV protective treatment strategies in patients with COVID-19 is warranted.

Drs. Goerlich and Metkus contributed equally.

Research was performed at Johns Hopkins University School of Medicine, Baltimore, MD.

Dr. Metkus performs consulting unrelated to this subject matter for TelaDoc/BestDoctors and Oakstone/EBIX, and received royalties for a textbook publication for McGraw-Hill publishing, unrelated to this subject matter. The remaining authors have disclosed that they do not have any potential conflicts of interest.

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