Left atrial pressure in patients with respiratory failure due to SARS-CoV-2 infection and supraventricular arrythmias

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To the Editor

One of the most common complications of Coronavirus Disease 19 (COVID-19) is the development of supraventricular arrhythmias (SA).[1–4] COVID-19 patients developing SA are at higher risk of worse prognosis, because of the development of hemodynamic instability, of the difficult management of the rhythm and rate control and of the related treatments (i.e. anticoagulants drugs) further causing adverse events (i.e. bleedings).[3] The aim of this study was to detect clinical, and echocardiographic parameters useful for the identification of an increased risk of SA development in COVID-19 patients.

Methods

The 'Pro-thrombotic status in patients with severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) infection' (ATTAC-Co) study[5–7] is an investigator-initiated single-center prospective study recruiting critically ill COVID-19 patients admitted to University Hospital of Ferrara, Italy for moderate-to-severe respiratory failure. The full protocol of the study has been previously reported (NCT04343053).[6–8] All patients enrolled underwent comprehensive transthoracic echocardiogra-phy (TTE) within 96 h from the hospitalization.[9,10] Dia-stolic disfunction (DD) was assessed following the last American Society of Echocardiography/European Association of Cardiovascular Imaging algorithm;[10] normal left atrial pressure (LAP) was considered in case of DD grade 0 or 1, increased LAP in case of DD 2 or 3. Only patients with sinus rhythm detected at the hospital admission and at the time of TTE and without a previous history of atrial fibrillation/flutter were included in the study. TTE was performed with GE Vivid q with M4S-RS transducers. The main outcome of the study was to identify predictors of SA defined as the onset during hospitalization of atrial fibrillation, atrial flutter, atrial tachycardia, and any paroxysmal supraventricular tachycardia. Values were compared with the *t*-test, Mann-Whitney *U* test, and the two-tailed Fisher exact test as appropriate. Variables listed in Table 1 were evaluated by univariate logistic regression. Those with $P < 0.05$ were included in the multivariate model. The odds ratio (OR) with 95% confidence intervals (CIs) was used. All statistical analyses were performed using Stata/SE version 16 software (Stata Corp, College Station, Texas).

Results

Overall, 76 patients were included in the analysis (mean age 64.8 ± 10 years, 26% female). SA occurred in 18 patients (24%). The median interval between TTE and onset SA was 4 (1–7) days. Patients who developed SA showed increased LAP (67% vs 15%, $P < 0.001$), lower left ventricle ejection fraction (LVEF) (55% vs 60%, $P = 0.002$), higher prevalence of dilated right atrium (56% vs 24%, $P = 0.012$), increased systolic pulmonary arterial pressure (36 ± 8vs32 ± 6 mmHg, $P = 0.028$) and increased prevalence of history of arterial hypertension and of smoking habit (Table 1). Considering serum biomarkers, the C-reactive protein levels and the platelet counts were higher in patients who developed SA (Table 1). At univariate analysis hypertension, smoking habit, LVEF, increased filling pressure, and dilated right atrium were significantly associated with SA (Table 2). After multivariate analysis only increased LAP (OR 5.61, 95% CI 1.35–23.31, $P = 0.018$) and hypertension (OR 6.32, 95% CI 1.22–32.7, $P = 0.028$) were shown to be independent predictors of SA (Table 2).

Comment

In this analysis, we found that LAP assessed at TTE together with a history of hypertension can predict SA development in patients with moderate-to-severe respiratory failure due to SARS-CoV-2 infection. Hypertensive patients had more DD.[11,12] Increased LAP is closely associated with electro-anatomical remodeling of left

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Table 1 Study population characteristics

		Supraventricular arrhythmia		
	Total $N=76$	No $N=58$	Yes $N=18$	*P*-value
Age – years, mean ± sd	64.87 ± 10.42	63.69 ± 11.16	68.67 ± 6.69	0.075
Female sex, *n* (%)	20 (26)	12 (21)	8 (44)	0.046
BMI – kg/mq, mean ± sd	26.78 ± 4.19	26.88 ± 4.30	26.45 ± 4.05	0.706
SBP – mmHg, mean ± sd	133.49 ± 29.33	129.96 ± 20.97	144.44 ± 47.00	0.07
DBP – mmHg, mean ± sd	77.78 ± 11.77	75.75 ± 10.30	84.11 ± 14.35	0.007
History				
Hypertension, *n* (%)	36 (47)	22 (38)	14 (78)	0.003
Dyslipidemia, *n* (%)	10 (13)	6 (10)	4 (22)	0.193
Smoking habit, n (%)	22 (29)	12 (21)	10 (56)	0.004
Diabetes, *n* (%)	12 (16)	8 (14)	4 (22)	0.39
Chronic coronary syndrome, *n* (%)	2 (3)	2 (3)	0 (0)	0.42
Heart failure, *n* (%)	0 (0)	0 (0)	0 (0)	
Stroke, *n* (%)	0 (0)	0 (0)	0 (0)	
PAD, *n* (%)	6 (8)	6 (10)	0 (0)	0.15
COPD, *n* (%)	8 (11)	4 (7)	4 (22)	0.064
Medications				
RAAS inhibitors, *n* (%)	22 (33)	16 (30)	6 (50)	0.18
Diuretics, *n* (%)	6 (9)	4 (7)	2 (11)	0.31
B-blockers, *n* (%)	10 (15)	8 (15)	2 (11)	0.87
Aspirin, *n* (%)	4 (5)	4 (7)	0 (0)	0.33
p2y12 inhibitors, *n* (%)	4 (5)	4 (7)	0 (0)	0.33
Anticoagulant, *n* (%)	4 (5)	2 (4)	2 (11)	0.09
Respiratory drugs, *n* (%)	2 (3)	2 (4)	0 (0)	0.49
Inotropes, *n* (%)	24 (32)	20 (34)	4 (22)	0.32
Laboratory tests				
GFR – mL/min, mean ± SD	94.02 ± 66.42	100.16 ± 73.91	74.22 ± 26.59	0.15
PLT – 10^3/mmc, mean ± SD	254.63 ± 117.90	239.83 ± 108.84	302.33 ± 139.53	0.047
D-dimer – μg/mL, mean ± sd	2.33 ± 3.98	2.40 ± 4.61	2.12 ± 1.15	0.82
HS TnI – pg/mL, mean ± SD	67.64 ± 121.52	86.44 ± 150.54	33.80 ± 21.02	0.27
BNP – pg/mL, mean ± SD	146.29 ± 114.40	145.80 ± 107.81	147.50 ± 147.80	0.97
C-reactive protein – mg/mL, mean ± SD	15.50 ± 11.02	16.78 ± 10.91	11.66 ± 11.04	0.09
Echo				
EDV – mL/mq, mean ± SD	56.59 ± 12.31	54.85 ± 6.12	62.19 ± 22.87	0.025
LVEF – %, mean ± SD	59.30 ± 6.76	60.63 ± 5.15	55.04 ± 9.59	0.002
Increased filling pressure, *n* (%)	30 (26)	8 (15)	12 (67)	<0.001
SVi – mL/mq, mean ± SD	35.76 ± 10.34	36.11 ± 8.54	34.81 ± 14.85	0.65
Dilated RA, *n* (%)	24 (32)	14 (24)	10 (56)	0.012
TAPSE – mm, mean ± SD	24.57 ± 3.70	24.50 ± 3.17	24.78 ± 5.26	0.78
sPAP – mmHg, mean ± SD	33.50 ± 6.82	32.57 ± 6.05	36.75 ± 8.71	0.028
Severe valve disease, *n* (%)	0 (0)	0 (0)	0 (0)	
Pericardial effusion, *n* (%)	2 (3)	2 (3)	0 (0)	0.57
Average LVGLS – %, mean ± SD	−17.78 ± 2.72	−18.80 ± 1.78	−16.42 ± 3.29	0.44
Average RVS – %, mean ± SD	−24.65 ± 8.69	−26.35 ± 9.63	−22.95 ± 8.15	0.84
Average PALS – %, mean ± SD	30.72 ± 12.51	35.20 ± 15.57	26.23 ± 7.03	0.05
Type of arrythmias developed				
Atrial fibrillation, *n* (%)	16 (21)	–	16 (88)	–
Atrial flutter, *n* (%)	1 (1)	–	1 (6)	–
Paroxysmal supraventricular tachycardia, *n* (%)	1 (1)	–	1 (6)	–

BMI, body mass index; BNP, brain natriuretic peptide; COPD, chronic obstructive pulmonary disease; DBP, diastolic blood pressure; EDV, end-diastolic volume; GFR, glomerular filtration rate; HS TnI, troponin I high sensitivity; LVEF, left ventricle ejection fraction; LVGLS, left ventricle global longitudinal strain; MRA, mineralocorticoid receptor antagonists; PAD, peripheral artery disease; PALS, peak atrial longitudinal strain; PLT, platelets; RA, right atrium; RAAS, renin-angiotensin aldosterone system; RVS, rightventricle strain; SBP, systolicblood pressure; sPAP, systolic pulmonaryarterial pressure; SVi, strokevolumeindexed; TAPSE, tricuspid annularplane excursion.

Table 2 Univariate and multivariate analysis for the occurrence of supraventricular arrythmias

	Univariate		Multivariate	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Female	0.33 (0.11–1.01)	0.051	–	–
Diastolic blood pressure	1.07 (0.99–1.13)	0.052	–	–
Hypertension	5.73 (1.67–19.62)	0.005	6.32 (1.22–32.7)	0.028
Smoking habit	4.79 (1.55–14.77)	0.006	2.63 (0.60–11.59)	0.199
PLT	1 (0.99–1.01)	0.06	–	–
EDV	1.05 (0.99–1.09)	0.08	–	–
LVEF	0.88 (0.81–0.97)	0.006	0.90 (0.81–1.01)	0.057
Incremented filling pressure	12.5 (3.64–42.84)	<0.001	5.61 (1.35–23.31)	0.018
Dilated RA	3.93 (1.29–11.89)	0.015	3.74 (0.86–16.27)	0.078
sPAP	1.09 (0.99–1.19)	0.055	–	–

EDV, end-diastolic volume; LVEF, left ventricle ejection fraction; PLT, platelets; RA, right atrium; sPAP, systolic pulmonary arterial pressure.

atrium[13,14] that progressively facilitate the development of arrythmias. In COVID-19 patients with history of hypertension, it seems to be of paramount importance to closely monitor LAP, aiming to reduce the burden of new-onset SA. Nevertheless, this study is based on a single-center experience, cases are very limited, and additional analyses are needed to confirm their consistence and transferability in clinical practice, defining which pharmacological or interventional strategy may reduce SA occurrence.

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Conflicts of interest

There are no conflicts of interest.

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References

1 Inciardi RM, Adamo M, Lupi L, Metra M. Atrial fibrillation in the COVID-19 era: simple bystander or marker of increased risk? *Eur Heart J* 2020; **41**:3094.
2 Paris S, Inciardi RM, Lombardi CM, *et al.* Implications of atrial fibrillation on the clinical course and outcomes of hospitalized COVID-19 patients: results of the Cardio-COVID-Italy multicentre study. *Europace* 2021; **23**:1603–1611.
3 Musikantow DR, Turagam MK, Sartori S, *et al.* Atrial fibrillation in patients hospitalized with COVID-19: Incidence, predictors, outcomes, and comparison to influenza. *JACC Clin Electrophysiol* 2021; **7**:1120–1130.
4 Karamchandani K, Quintili A, Landis T, Bose S. Cardiac arrhythmias in critically ill patients with COVID-19: a brief review. *J Cardiothorac Vasc Anesth* 2020; **35**:3789–3796.
5 Campo G, Contoli M, Fogagnolo A, *et al.* Over time relationship between platelet reactivity, myocardial injury and mortality in patients with SARS-CoV-2-associated respiratoryfailure. *Europace* 2020; **22**:1848–1854.
6 Spadaro S, Fogagnolo A, Campo G, *et al.* Markers of endothelial and epithelial pulmonary injury in mechanically ventilated COVID-19 ICU patients. *Crit Care* 2021; **25**:74.
7 Contoli M, Papi A, Tomassetti L, *et al.* Blood interferon-α levels and severity, outcomes, and inflammatory profiles in hospitalized COVID-19 patients. *Front Immunol* 2021; **12**:74–83.
8 Lang RM, Badano LP, Mor-Avi V, *et al.* Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging* 2015; **16**:233–270.
9 Nagueh SF, Smiseth OA, Appleton CP, *et al.* Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging* 2016; **17**:1321–1360.
10 Bertini M, Ferrari R, Guardigli G, *et al.* Electrocardiographic features of 431 consecutive, critically ill COVID-19 patients: an insight into the mechanisms of cardiac involvement. *Europace* 2020; **22**:1848–1854.
11 Baltabaeva A, Marciniak M, Bijnens B, *et al.* How to detect early left atrial remodelling and dysfunction in mild-to-moderate hypertension. *J Hypertens* 2009; **27**:2086–2093.
12 Messerli FH, Rimoldi SF, Bangalore S. The transition from hypertension to heart failure: contemporary update. *JACC Heart Fail* 2017; **5**:543–551.
13 Hoit BD. Left atrial remodeling: more than just left atrial enlargement. *Circ Cardiovasc Imaging* 2017; **10**:e006036.
14 Park J, Joung B, Uhm JS, *et al.* High left atrial pressures are associated with advanced electroanatomical remodeling of left atrium and independent predictors for clinical recurrence of atrial fibrillation after catheter ablation. *Heart Rhythm* 2014; **11**:953–960.