ASSOCIATION OF ATRIAL FIBRILLATION AND LEFT ATRIAL VOLUME INDEX WITH MORTALITY IN PATIENTS WITH COVID-19 PNEUMONIA

Antonello D'Andrea[1], Vincenzo Russo[2], Gianluca Manzo[1], Valerio Giordano[1], Marco Di Maio[1], Fabio Crescibene[1], Michele D'Alto[2], and Eduardo Bossone[3]

[1]Umberto I Nocera Inferiore Hospital District
[2]AORN Ospedali dei Colli
[3]AORN Cardarelli

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Abstract

Information on atrial arrhythmias in patients with COVID-19 pneumonia is limited, and we aimed to explore the possible association of left atrial (LA) involvement and of atrial fibrillation (AF) occurrence with mortality in patients with COVID-19 pneumonia. A total of 140 hospitalized patients with COVID-19 pneumonia were included in the analysis; mean age was 66.6 years (range, 20-89 years), and 56 (40%) were female. A total of 35 patients had cardiac injury (increased troponin levels), and these patients were older, had more frequently systemic hypertension, had higher levels of C-reactive protein and of D-Dimer, and a higher proportion of multiple ground-glass opacities in computed tomography findings. By echocardiography, LA diameters and volume index (LAVI) injury (33.9± 27.2±8.7 ml/m2; P<0.001) were significantly increased in patients with cardiac. Greater proportion of patients with cardiac injury showed AF occurrence (14 of 35 [40.0%] vs 11 of 105 [10.4%]; P < 0.0001). Patients with cardiac injury had higher mortality than those without cardiac injury (17 of 35 [48.5 %] vs 9 of 105 [8.5%]; P < 0.0001). In a Cox regression model, in the overall population of COVID pneumonia patients, troponin levels (Hazard Ratio, 4.29 [95% CI, 1.85-8.43] P< 0.001), LA volume index (HR 3.6 [95% CI, 1.15-7.48; p<0.001], PASP (HR: 3.9; [95% CI, 1.72-6.39] P< 0.001) and AF occurrence (HR: 2.5; [95% CI, 1.22-5.4] P< 0.001) emerged as independent predictors of in-hospital death. Assessment of both LA morphology and function during the recovery of COVID patients with cardiac injury may represent key points in the prognostic stratification

ABSTRACT

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Greater proportion of patients with cardiac injury showed AF occurrence (14 of 35 [40.0%] vs 11 of 105 [10.4%]; P < 0.0001). Patients with cardiac injury had higher mortality than those without cardiac injury

(17 of 35 [48.5 %] vs 9 of 105 [8.5%]; $P < 0.0001$). In a Cox regression model, in the overall population of COVID pneumonia patients, troponin levels (Hazard Ratio, 4.29 [95% CI, 1.85-8.43] P< 0.001), LA volume index (HR 3.6 [95% CI, 1.15-7.48; p<0.001], PASP (HR: 3.9; [95% CI, 1.72-6.39] P< 0.001) and AF occurrence (HR: 2.5; [95% CI, 1.22-5.4] P< 0.001) emerged as independent predictors of in-hospital death. Assessment of both LA morphology and function during the recovery of COVID patients with cardiac injury may represent key points in the prognostic stratification.

Coronavirus 2019 disease (COVID-19), caused by SARS-CoV-2, can lead to cardiac impairment. Possible expressions of cardiac injury include increased troponin levels, left ventricular dysfunction, and arrhythmias (1-3). Atrial fibrillation (AF) is a common sequela of critical illness, with an estimated prevalence of almost 10% in ICU patients, and several studies report worse outcomes in patients with new-onset AF as compared with their non-AF counterparts (3). Information on AF and on left atrial (LA) involvement in patients with COVID-19 pneumonia is limited, and we aimed to explore the possible association with mortality in these patients. This study was conducted from February 20, 2020 to May 2020, in 4 centers (Umberto Ideg; M.Scarlato; Cardarelli and Monaldi hospitals); the final date of follow-up was May 10, 2020. All consecutive patients with positive SARS-CoV-2 test result and laboratory- and TC-confirmed interstitial pneumonia were included. Clinical, laboratory, radiological and ultrasound data were collected. Cardiac injury was defined as blood levels of cardiac biomarkers (high sensitivity Troponin I – ECLIA method; hs-TNI) above the 99th-percentile upper reference limit. eft atrial volume. LA volume was calculated using the biplane area-length method at the apical 4-chamber and apical 2-chamber views at ventricular end-systole (maximum LA size) and indexed for body surface area. Pulmonary artery systolic pressure (PASP) was calculated by adding the value of right atrial pressure to the systolic transtricuspid gradient. Clinical and instrumental variables and outcomes of patients with and without cardiac involvement were compared. The local Ethics committee approved the study and all individuals gave written informed consent.

A total of 140 hospitalized patients with COVID-19 pneumonia were included in the final analysis; mean age was 66.6 years (range, 20-89 years), and 56 (40%) were female. A total of 35 patients had cardiac injury, and these patients were older (mean age 74.5 [38-89] vs 56.3 [20-79] years; $P < 0.001$); had more frequently systemic hypertension (20 of 35 [57.5%] vs 31 of 105 [29.2%]; $P < 0.001$); had higher levels of C-reactive protein (mean 99.8 [45.8-130.4] vs 37.9 [22.2-96.3] mg*L^{-1}; $P < 0.001$), and of D-Dimer (mean 4.9 [3.2-7.3] vs 2.1 [0.5-3.4]; P< 0.001); had a higher proportion of multiple ground-glass opacities in computed tomography (CT) findings (25 of 35 patients [71.2%] vs 36 of 105 patients [34.7%]; $P < 0.001$) and multiple consolidations by lung ultrasound (26 of 35 patients [75.6%] vs 31 of 105 patients [38.2%]; $P < 0.001$). By echocardiography, LV diameters and ejection fraction were comparable between the two groups. Conversely, LA volume index was significantly increased in patients with cardiac injury (Table 1). Greater proportion of patients with cardiac injury showed AF occurrence (14 of 35 [40.0%] vs 11 of 105 [10.4%]; $P < 0.0001$) and required invasive or noninvasive mechanical ventilation (22 of 35 [66.4%] vs 20 of 105 [21%]; $P < 0.001$). The more common complication in patients with cardiac injury was acute respiratory distress syndrome (23 of 35 [66.5%] vs 17 of 105 [17.8%]; $P < 0.001$). Patients with cardiac injury had higher mortality than those without cardiac injury (17 of 35 [48.5 %] vs 9 of 105 [8.5%]; $P < 0.0001$). In a Cox regression model, in the overall population of COVID pneumonia patients, troponin levels (Hazard Ratio, 4.29 [95% CI, 1.85-8.43] P< 0.001), LA volume index (HR 3.6 [95% CI, 1.15-7.48; p<0.001], PASP (HR: 3.9; [95% CI, 1.72-6.39] P< 0.001) and AF occurrence (HR: 2.5; [95% CI, 1.22-5.4] P< 0.001) emerged as independent predictors of in-hospital death.

Cardiac arrhythmias are frequent clinical manifestations in patients with COVID-19 pneumonia; however, there is a paucity in the emerging literature with regard to the nature and classification of these arrhythmogenic events (4). Arrhythmias are complex and multifactorial in a COVID-19 patient and may result from metabolic derangements, hypoxia, acidosis, intravascular volume imbalances, neurohormonal, and catecholaminergic stress. Sepsis is characterized by a systemic process involving inflammatory cytokines and autonomic dysfunction. Postulated mechanisms of this arrhythmogenesis include autonomic nervous system -induced calcium entry into cardiac myocytes as well as a spontaneous release of calcium from the sarcoplasmic reticulum (5). Tachycardia and myocardial injury may themselves increase atrial arrhythmias

and contribute to worse outcomes (1-2).

We found that increased LA volume and higher prevalence of AF are common conditions among patients with severe COVID-19 pneumonia and cardiac injury, associated with higher risk of in-hospital mortality. More definitive epidemiologic data is needed. Since some of the therapies empirically used to treat SARS-CoV-2 infections, such as chloroquine, have known effects on myocyte repolarization, resulting in increased risk of QT prolongation and subsequent arrhythmias, Given the high incidence of electrolyte abnormalities in ill patients (1-2), high vigilance by the treatment teams is required to avoid iatrogenic harm. Assessment of both LV and LA morphology and function during the recovery of these patients may represent key points in the prognostic stratification.

Disclosures : none.

REFERENCES

1. Shi S, Qin M, Shen B, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. JAMA Cardiol 2020. doi:10.1001/ jamacardio.2020.0950
2. Bonow RO, Fonarow GC, O'Gara PT, Yancy CW. Association of Coronavirus Disease 2019 (COVID-19) With Myocardial Injury and Mortality. JAMA Cardiol 2020. doi:10.1001/jamacardio.2020.1105
3. Goodman S, Weiss Y, Weissman C. Update on cardiac arrhythmias in the ICU. Curr Opin Crit Care. 2008;14:549-554.
4. Kuipers S, Klouwenberg PMK, Cremer OL. Incidence, risk factors and outcomes of new-onset atrial fibrillation in patients with sepsis: a systematic review. Crit Care. 2014;18:688.
5. Otake H, Suzuki H, Honda T, Maruyama Y. Influences of autonomic nervous system on atrial arrhythmogenic substrates and the incidence of atrial fibrillation in diabetic heart. Int Heart J. 2009;50:627-641.

Table 1. Echocardiographic structural and systolic/diastolic functional indices in COVID patients with and without cardiac injury.

Variables	Variables	**Without Cardiac Injury (n = 105)**	**W**
Septal wall thickness (mm)	Septal wall thickness (mm)	Septal wall thickness (mm)	1(
LV posterior wall thickness (mm)	LV posterior wall thickness (mm)	LV posterior wall thickness (mm)	9.
LV end-diastolic diameter (mm)	LV end-diastolic diameter (mm)	LV end-diastolic diameter (mm)	48
LV end-systolic diameter (mm)	LV end-systolic diameter (mm)	LV end-systolic diameter (mm)	33
Mitral peak A velocity (m/s)	Mitral peak A velocity (m/s)	Mitral peak A velocity (m/s)	0.
Mitral peak E/A ratio	Mitral peak E/A ratio	Mitral peak E/A ratio	0.
LV ejection fraction %	LV ejection fraction %	LV ejection fraction %	56
RV basal tract diameter (mm)	RV basal tract diameter (mm)	RV basal tract diameter (mm)	32
Tricuspid peak E velocity (m/s)	Tricuspid peak E velocity (m/s)	Tricuspid peak E velocity (m/s)	0.
Tricuspid peak A velocity (m/s)	Tricuspid peak A velocity (m/s)	Tricuspid peak A velocity (m/s)	0.
Tricuspid Peak E/A ratio	Tricuspid Peak E/A ratio	Tricuspid Peak E/A ratio	0.
TRV (m/s)	TRV (m/s)	TRV (m/s)	2.
PASP (mmHg)	PASP (mmHg)	PASP (mmHg)	3(
LA anterior-posterior diameter (mm)	LA anterior-posterior diameter (mm)	LA anterior-posterior diameter (mm)	38
LAVI (ml/m^2)	LAVI (ml/m^2)	LAVI (ml/m^2)	2(
TAPSE (mm)	TAPSE (mm)	TAPSE (mm)	2(

LV: left ventricle; RV = Right ventricle; LA: left atrium; TRV: tricuspid regurgitation velocity; PASP: pulmonary artery systolic pressure; LAVI: left atrial volume index; TAPSE: tricuspid annular systolic plane excursion.