

Short term Prognostic value of tricuspid annular plane systolic excursion / pulmonary arterial systolic pressure ratio in patients with COVID-19 ARDS

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Abstract

SARS-CoV-2 infection can lead to the development of ARDS, which is associated with high mortality rates. COVID-19 has also been linked to myocardial injury and alterations in RV strain, which have been identified as independent predictors of poor prognosis. This study investigated the prevalence and prognostic significance of right heart failure and right ventricular-arterial uncoupling in patients with COVID-19 complicated by ARDS. The research comprised a total of ninety-four individuals with acute respiratory failure caused by COVID-19. Using complete transthoracic echocardiography, the link between right ventricular function and pulmonary circulation was investigated, with an emphasis on the ratio of TAPSE to PASP. TAPSE was substantially higher in the group of survivors, but PASP was significantly higher in the group of the dead. LVEF, LVESD, frequency of tricuspid regurgitation, and LAD also differed considerably between the surviving and dying groups. There was no statistically significant difference between the two groups in terms of LVEDD. In conclusion, COVID-19-induced ARDS is linked with a considerable and early separation of right ventricular function from pulmonary circulation. Evaluation of this uncoupling by noninvasive echocardiography using the TAPSE/PASP ratio has been shown to be a significant predictor of patient outcome.

Keywords: COVID-19, ARDS, Right ventricular-arterial uncoupling, Echocardiography, outcome.

1. Introduction

SARS-CoV-2 infection can result in ARDS, with mortality rates ranging from 26% to 61% [1]. Moreover, COVID-19 is linked to myocardial injury and altered strain in the right ventricle (RV), which is an independent predictor of poor prognosis [2]. Acute cor pulmonale, characterized by right heart failure, is a recognized complication of ARDS, influenced by disease severity and ventilatory strategies that cause lung hyperinflation and permissive hypercapnia [3].

We hypothesized that COVID-19-induced cardiac damage and inflammatory alterations may contribute to the development of acute right heart failure in ARDS based on these results. This research sought to determine the prevalence and prognostic importance of right heart failure and the decoupling of right ventricular function from pulmonary circulation in COVID-19 and ARDS patients.

To accomplish this objective, we conducted bedside transthoracic echocardiography, specifically evaluating the TAPSE to PASP ratio. This assessment allowed us to examine the relationship between RV function and the pulmonary circulation.

2. Patients and methods

2.1. Study design:

It will be a Single center, prospective observational study that will be conducted at Benha University Hospital.

2.2. Patients:

A total of ninety-four individuals diagnosed with COVID-19 complicated by ARDS were included in this study. These patients will undergo evaluations upon admission and will be followed up for a duration of one month to assess the short-term predictive value of the TAPSE/PASP ratio in COVID-19 ARDS patients.

2.3. Inclusion criteria:

Patients of both genders were presented with covid-19 complicated by ARDS.

Patients with adequate imaging quality by trans thoracic echocardiography.

2.4 Exclusion criteria:

Patients are excluded for Unwilling or unable to provide written informed conse, Poor Echo window, previous right ventricular systolic dysfunction, previous pulmonary arterial hypertension, ARDS due to COPD or lung disease other than covid -19, Chronic thromboembolic pulmonary hypertension.

2.5. Patient's characteristics:

Demographics:

- Age
- Gender
- **Admission details:**
- Risk factors (hypertension, diabetes mellitus, smoking, obesity
- Diagnosis of ARDS (PaO₂/FIO₂ ratio)
- Type of ventilation (Nasal oxygen, Noninvasive ventilation, Intubation.)
- Investigations: Laboratory investigations: including Cardiac troponin I, Serum creatinine, D-dimer, C-reactive protein.
- Trans Thoracic ECHO: for assessment of TAPSE \ PASP ratio, LVEDD , LVESD , LVEF , LA volume index, degree of tricuspid regurge).

2.6. Statistical analysis:

Using the Kolmogorov-Smirnov test, the distribution of variables was examined. Continuous data with a normal distribution were represented by mean SD, whereas skewed continuous variables were represented by median and IQR. Variables representing categories like counts and percentages. Both paired and unpaired data were analyzed using two-tailed t-tests to determine group differences. Using regression analysis and Pearson's partial correlation test, the relationships between variables were investigated. To assess the relationship between the covariates and the result, which was mortality, Cox proportional hazard regression analysis were undertaken. Utilizing univariate and

multivariate linear models, we identified potential outcome determinants.

3. Results and discussion

The patient group was largely older and male, with a significant frequency of pulmonary comorbidities and cardiovascular risk factors, as shown in Table 1. Non-survivors were six years older than survivors on average and had greater rates of smoking and obesity. In addition, non-survivors displayed higher cardiac troponin I, blood creatinine, and CRP levels, as well as poorer PaO₂/FIO₂ ratios. Table 2 summarizes the echocardiographic findings, demonstrating a significant increase in PASP and a decrease in the TAPSE/PASP ratio in non-survivors compared to survivors. Univariate analysis revealed significant associations between most biological and echocardiographic differences and survival, as shown in Table 3. However, in multivariate analysis, only the PaO₂/FIO₂ ratio and TAPSE/PASP ratio were identified as independent predictors of outcome, as indicated in Table 3.

The results reveal an early and considerable dissociation between right ventricular function and pulmonary circulation in COVID-19-induced ARDS. In addition to the PaO₂/FIO₂ ratio, the TAPSE/PASP ratio has prognostic value in these individuals. As shown by echocardiographic assessments of PASP, the pulmonary hypertension seen in this investigation was mostly mild to moderate in severity. Notable is that a PASP of 40 mmHg in non-survivors would still fall within the normal upper range after adjusting for age, gender, and body weight. In addition, TAPSE levels in non-survivors remained above the normal lower limit despite a decline [5]. In accordance with previous studies, survivors demonstrated a slight decrease in the TAPSE/PASP

ratio, with a value of 0.89 ± 0.29 . This finding is consistent with a study involving 209 individuals aged over 60, where the TAPSE/PASP ratio was reported as 1.11 ± 0.03 [5]. Conversely, non-survivors exhibited a significant reduction in the TAPSE/PASP ratio, measuring at 0.51 ± 0.22 mm/mmHg. These values are near or below the 0.50 mm/mmHg threshold, which has previously been associated with a poor prognosis in heart failure and severe pulmonary hypertension [6].

Recent research involving 200 hospitalized COVID-19 patients in non-ICU departments revealed that 12.5% of patients had a PASP greater than 35 mmHg, while 14.5% had a TAPSE 17 mm. Interestingly, the study revealed that an elevated PASP, rather than a decreased TAPSE, was indicative of an unfavorable outcome [7]. The TAPSE/PASP ratio was first designed as a measurement for assessing the relationship between RV myocardial length and tension, and it has shown predictive utility in cases of heart failure [7]. Subsequent research has confirmed its prognostic importance not only in heart failure [8], but also in pulmonary arterial hypertension [9] and in patients with chronic lung diseases [10]. TAPSE served as a load-dependent surrogate for end-systolic elastance (Ees) in these investigations [8-10], while PASP provided an indirect estimate of arterial elastance (Ea). When assessing the coupling between the RV and PA, the TAPSE/PASP ratio has been shown to be a superior indicator compared to other composite echocardiographic indices. Studies have shown a high connection between the TAPSE/PASP ratio and invasive measures, the gold standard [11]. Additionally, this ratio has also been found to correlate with indirectly assessed ratios of Ees to arterial Ea [8].

Table (1) Alive and dead patients affected by COVID-19

	Alive (n = 69)	Dead (n = 25)	p
Age (year)	62 ± 13	68 ± 12	0.033
Sex M (%)	53 (77)	17 (68)	0.549
Disease duration (day)	7.7 ± 3.3	7.7 ± 3.1	0.942
Lung disease (%)	17 (25)	11 (44)	0.079
Coronary artery disease (%)	14 (20)	3 (12)	0.545
Cardiovascular comorbidities			
Hypertension (%)	44 (64)	19 (76)	0.362
Diabetes (%)	11 (16)	5 (20)	0.99
Smoke (%)	7 (10)	8 (32)	0.021
Obesity (%)	18 (26)	13 (52)	0.025
Type of ventilation			
Nasal oxygen (%)	35 (51)	0 (0)	< 0.001
Noninvasive ventilation (%)	22 (32)	0 (0)	< 0.001
Intubation (%)	12 (17)	25 (100)	< 0.032
Biochemistry			
Creatinine (mg/dl)	1.3 ± 1.3	2.8 ± 1.4	< 0.001
Cardiac Troponin I (pg/l)	365 ± 644	1245 ± 2049	< 0.002
D-dimer (ng/ml)	317 ± 557	919 ± 974	< 0.001
C-reactive protein (mg/dl)	10.6 ± 19.9	22.8 ± 27.3	< 0.023
PaO ₂ /FiO ₂ ratio (mmHg)	270 ± 104	117 ± 56	< 0.00

PaO₂ arterial partial pressure of oxygen, FiO₂ fraction of inspired O₂

Table (2) Echocardiographic features

	Alive (n = 69)	Dead (n = 25)	p
LVEDD (mm)	48 ± 5	49 ± 4	0.388
LVESD (mm)	29 ± 7	31 ± 5	0.059
LAD (mm)	38 ± 6	40 ± 5	0.082
LVEF (%)	60 ± 7	58 ± 8	0.209
TR	2 (3)	3 (12)	0.084
TAPSE (mm)	25 ± 4	19 ± 4	< 0.001
PASP (mmHg)	30 ± 7	42 ± 12	< 0.001
TAPSE/PASP	0.89 ± 0.29	0.51 ± 0.22	< 0.001

P-value < 0.05 is considered statically significant.

Table (3) Single predictor models of Cox proportional hazard analysis

variables	HR	95% (CL)	P
Age (year)	1.04	1.003–1.078	0.035
Sex (female)	0.00	0.000–0.216	0.006
Hypertension	1.767	0.706–4.429	0.224
Diabetes	1.525	0.571–4.072	0.40
Smokers	3.050	1.313–7.086	0.10
Obesity	2.252	1.027–4.936	0.044
Nasal oxygen	0.019	0.001–0.512	0.018
Noninvasive ventilation	0.031	0.001–1.386	0.073
Intubation	223.89	4.81–10.415	0.006
PaO ₂ /FiO ₂ ratio (mmHg)	0.986	0.981–0.992	0.001
Creatinine (mg/mL)	1.236	1.067–z 1.432	
Troponine (pg/l)	1.000	1.000–1.000	
D-dimer (ng/ml)	1.000	1.000–1.001	
C-reactive protein (mg/dl)	1.014	1.004–1.024	
LVEDd (mm)	1.031	0.948–1.121	0.473
LVESd(mm)	1.039	0.99–1.091	0.123
LAD (mm)	1.066	0.995–1.143	0.068
LVEF (%)	0.972	0.934–1.011	0.151
Severe TR	2.671	0.798–8.95	0.111
TAPSE (mm)	0.796	0.727–0.871	<0.001
PASP (mm Hg)	1.085	1.054–1.118	<0.001

TAPSE/PASP (mm/mmHg) 0.013 0.002-0.069 <0.001

4. Conclusion

COVID-19-induced ARDS is linked with right ventricular-arterial uncoupling, and noninvasive evaluation of this state utilizing the TAPSE/PASP ratio

provides useful and independent prognostic information in addition to the PaO₂/FIO₂ ratio. The necessity of incorporating bedside echocardiography into the

assessment and treatment of COVID-19 patients in the ICU is highlighted by these results.

References

- [1] G. Grasselli, A. Zangrillo, A. Zanella, COVID-19 lombardy ICU network. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy region, Italy. *JAMA*, vol. 323, 1574–81, 2020.
- [2] Y.Li, H.Li, S.Zhu, Prognostic value of right ventricular longitudinal strain in patients with COVID-19. *JACC Cardiovasc Imaging*, 2020.
- [3] A.Vieillard-Baron, LC.Price, MA.Matthay, Acute cor pulmonale in ARDS. *Intens Care Med.*, vol.39, pp.1836–8, 2013.
- [4] BM.McQuillan, MH.Picard, M.Levitt, AE.Weyman, Clinical correlates and reference intervals for pulmonary artery systolic pressure among echocardiographically normal subject. *Circulation*, vol.104, pp.2797–802, 2001.
- [5] F.Ferrara, LG.Rudski, O.Vriz, L.Gargani, J.Afilalo, A.D'Andrea, M.D'Alto, E.Acri, AA.Stanziola, Physiologic correlates of tricuspid annular plane systolic excursion in 1168 healthy subjects. *Int J Cardiol.*, 39, pp.223:736–43, 2016.
- [6] M.Guazzi, Use of TAPSE/PASP ratio in pulmonary arterial hypertension: an easy shortcut in a congested road. *Int J Cardiol.*, vol.4, pp.266:242, 2018..
- [7] M.Guazzi, F.Bandera, G.Pelissero, S.Castelvecchio, L.Menicanti, S.Ghio, Tricuspid annular plane systolic excursion and pulmonary arterial systolic pressure relationship in heart failure: an index of right ventricular contractile function and prognosis. *Am J Physiol Heart Circ Physiol.*, vol.305, pp.1373-1381, 2013.
- [8] M.Guazzi, D.Dixon, V.Labate, L.Beussink-Nelson, F.Bandera, MJ.Cuttica, RV contractile function and its coupling to pulmonary circulation in heart failure with preserved ejection fraction: stratification of clinical Phenotypes and outcomes. *ACC Cardiovasc Imaging.*, vol.10, pp.1211–21, 2017.
- [9] K.Tello, J.Axmann, HA.Ghofrani, R.Naeije, N.Narcin, A.Rieth, W.Seeger, H.Gall, Relevance of the TAPSE/PASP ratio in pulmonary arterial hypertension. *Int J Cardiol.*, vol. 35, pp.266:229, 2018.
- [10] K.Tello, HA.Ghofrani, C.Heinze, K.Krueger, R.Naeije, C.Raubach, W.Seeger A simple echocardiographic estimate of right ventricular-arterial coupling to assess severity and outcome in pulmonary hypertension on chronic lung disease. *Eur Respir J.*, vol.54, pp.1802435, 2019.,
- [11] K.Tello, J.Wan, A.Dalmer, R.Vanderpool, HA.Ghofrani, R.Naeije, F.Roller, E.Mohajerani, W.Seeger, Validation of the tricuspid annular plane systolic excursion/systolic pulmonary artery pressure ratio for the assessment of right ventricular-arterial coupling in severe pulmonary hypertension. *Circ Cardiovasc Imaging.*, vol.12, pp.009047, 2019.