ORIGINAL ARTICLE

Pericardial Effusion in COVID-19 Hospitalized Patients in ICU: Prevalence, Related Factors, and Outcomes

Maryam Heidari Sooreshjaani [1], Taraneh Faghihi Langroudi [1], Hamed Norouzi [2*], Atefeh Tahmasebzadeh [3]

[1] Department of Radiology, Shahid Modarres Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

[2] Radiology Assistant, Department of Radiology, Shahid Beheshti University of Medical Science, Tehran, Iran

[3] Student Research Committee, Department of Medical Physics, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

*Corresponding Author: Hamed Norouzi
Email: hamednorouzi7337@gmail.com

Received: 23 December 2022 / Accepted: 14 March 2023

Abstract

Purpose: COVID-19 disease is associated with pericardial effusion through both direct invasions of myocardial tissue and activation of inflammatory processes and oxidative stress. However, its exact mechanism and related implications are unclear. We aimed to evaluate the pericardial effusion in hospitalized patients with a definite diagnosis of COVID-19 and finally to determine underlying factors related to this cardiac event. Finally, the hospital outcome of patients with and without pericardial involvement was compared.

Materials and Methods: The hospital records of 1824 patients suffering from COVID-19 were reviewed with respect to pieces evidence of pericardial effusion. Baseline characteristics, cardiovascular risk profiles, laboratory and echocardiography parameters as well as hospital outcomes were reviewed.

Results: Out of 1824 patients hospitalized with COVID-19 in our medical center in Intensive Care Unit (ICU) sections, a total of 300 cases (16.4%) (P value <0.05) had evidence of pericardial effusion. Patients with pericardial effusion had much higher mean age, higher mean heart rate and also a higher prevalence of hypertension, diabetes mellitus, and a history of ischemic heart disease compared to those without this complication. The changes in some echocardiography parameters, including left ventricular end-diastolic diameter, E/A ratio, E/Ep ratio, and tricuspid annular plane systolic excursion were more prominent in those with pericardial effusion. Those with pericardial effusion experienced longer hospitalization and ICU admission and the death rate was significantly higher in such patients.

Conclusion: The occurrence of pericardial effusion is predictable in about 16.4% of patients with COVID-19, which occurs mainly in older people and people with a history of cardiovascular risk profiles. Pericardial effusion in COVID-19 patients leads to poorer in-hospital outcome.

Keywords: COVID-19; Pericardial Effusion; Outcome.

DOI: https://doi.org/10.18502/fbt.v11i3.15887

1. Introduction

COVID-19 disease, the pandemic of the present century, was reported in 216 countries and led to approximately 6.3 million deaths whole of the world [1, 2]. Although respiratory symptoms are the most obvious clinical manifestations of COVID-19, serious cardiovascular damages such as acute coronary syndrome, pulmonary embolism, arrhythmias, heart failure, and cardiogenic shock are also serious complications of the disease [3-5]. Various mechanisms have been proposed for heart damage following COVID-19, including direct invasion of the virus to the cardiac tissue directly and injuries mediated by cytokine storm and oxidative stress activity indirectly [6]. The same mechanisms have been proposed in the development of pericardial effusion following COVID-19. In fact, ACE II receptors are located on various cells such as cardiomyocytes and vascular endothelium, vascular smooth muscle cells, and cardiac fibroblasts. The virus binds to these cells and activates the ACE II signalling pathways, causing myocardial damage and cardiomyopathy that eventually also leads to pericardial effusion [7]. Therefore, one of the most important and life-threatening manifestations in patients with COVID-19 is pericardial effusion, which can occur in the primary form or after pericarditis or myocarditis in isolation or with acute respiratory distress syndrome. Although the incidence of this heart condition has been reported in studies, mainly reported cases of the disease [8, 9], comprehensive community-based studies, especially in communities such as Iran (which has experienced successive waves of COVID-19 disease and with a relatively high incidence of disease in the world) have not been reported. Also, factors such as risk factors for pericardial effusion in COVID-19 have not been properly elucidated so far, as almost all published studies have been based on case reports. Therefore, this study attempted to provide statistics on the prevalence of pericardial effusion in the field of COVID-19 to address the underlying factors associated with the occurrence of this cardiac complication. Also, by examining and following up with patients, the hospital consequences of patients with this cardiac complication will be examined.

2. Materials and Methods

This cross-sectional study was performed on all patients with a definitive diagnosis of COVID-19 that were hospitalized between 2020 and 2021 in our referral hospital in Tehran. In CT scans, evidence of pericardial effusion was evident in patients. The aim was to evaluate cases with evidence of pericardial effusion among these patients. In this regard, by referring to the hospital archives as well as the electronic patient data registration system (HIS), comprehensive information related to COVID-19 patients was extracted. After reviewing the relevant information, patients with evidence of cardiac involvement were identified as pericardial effusion cases. In addition to determining the frequency of these patients compared to all patients with COVID-19, demographic information, clinical manifestations, laboratory and imaging findings, cardiovascular manifestations, and also the patient's hospital outcomes (mortality, ICU admission, and length of hospital stay) were also collected. The severity of pulmonary involvement was also scored as follows: each lung is scored between 0 and 4 based on the extent of involvement with the grand glass opacity or consolidation, so that a score of 0 for the absence of involvement, a score of 1 for the involvement of less than 25%, score 2 for involvement between 25 to 50%, score 3 for involvement between 50 to 75% and score 4 for involvement above 75%. The total score was obtained by summing the scores for two lung involvements. Finally, by comparing the underlying characteristics of patients with COVID-19 with and without pericardial effusion involvement, the underlying factors associated with the occurrence of this complication and its severity were identified.

Also, echocardiography was performed for the patients, and parameters such as Left Ventricular End-Diastolic Diameter (LVEDD), E/A ratio, E/Ep ratio, and the value of Tricuspid Annular Plane Systolic Excursion (TAPSE) left ventricular ejection fraction or Left Ventricular End-Systolic Diameter (LVESD) were examined.

For statistical analysis, results were presented as mean ± Standard Deviation (SD) for quantitative variables and were summarized by frequency (percentage) for categorical variables. Continuous variables were compared using t-test or Mann-Whitney U test

whenever the data did not appear to have normal distribution or when the assumption of equal variances was violated across the study groups. The categorical variables were compared using the Chi-Square test. P-values of ≤ 0.05 were considered statistically significant. For the statistical analysis, the statistical software SPSS version 23.0 for Windows (IBM, Armonk, New York) was used.

3. Results

Out of 1824 samples with the diagnosis of COVID-19 admitted in our medical center, a total of 300 cases (16.4%) had evidence of pericardial effusion. Comparing baseline characteristics of patients with and without pericardial effusion (Table 1) showed significantly higher mean age in the subjects with pericardial effusion. Also, the overall prevalence of underlying cardiovascular risk profiles, including hypertension, diabetes mellitus, and history of cardiac ischemic events was significantly higher in those with pericardial effusion. However, there was no difference in symptoms of COVID-19 disease between the two groups with and without pericardial effusion. With regard to vital signs, those with pericardial effusion experienced more tachycardia as compared to the group without pericardial effusion. We showed no difference in baseline laboratory parameters, including blood cell count, hemoglobin, serum troponin, serum creatinine, or even C-reactive protein between the two study groups. With regard to echocardiography parameters, we found significant changes in most diastolic functional parameters, including left ventricular end-diastolic diameter (LVEDD), E/A ratio, E/Ep ratio, and the value of TAPSE with no significant changes in other parameters, including left ventricular ejection fraction or left ventricular end-systolic diameter (LVESD).

The groups with pericardial effusion experienced longer hospitalization (Table 2). The rates of hospital death in the two groups with and without pericardial effusion were 32.0% and 9.4%, respectively, which was significantly higher in the first group (P = 0.001). Also, admission to the intensive care unit ward was reported more in the group with pericardial effusion (64.0% versus 24.9%, p = 0.001).

4. Discussions

COVID-19 disease is associated with myopericarditis and ultimately pericardial effusion through both direct invasions of myocardial tissue and indirect activation of inflammatory processes and oxidative stress. Obviously, the occurrence of such events will be associated with a worsening of the clinical outcome of patients with COVID-19. However, given that most published studies on the occurrence of pericardial effusion in the disease have been reported in the form of case reports, it will be difficult to determine the exact prevalence of this disorder or the underlying factors associated with it. Therefore, what we did in the present study was to evaluate the prevalence of pericardial effusion in patients with a history of COVID-19 and finally to determine underlying factors related to this cardiac event. Finally, the hospital outcome of patients with and without pericardial involvement was compared.

In this regard, out of 1824 samples of patients with a diagnosis of COVID-19 admitted to our referral center, 300 samples had evidence in favor of pericardial effusion, indicating a prevalence of 16.4%. Similarly, in a study conducted by Eihab Ghantous *et al.* in 2022 [10], 14% had conclusive evidence of this complication, which was close to our prevalence.

Comparing the clinical and underlying features between the two groups with and without pericardial effusion, we found that firstly, patients with this complication had a much higher mean age than patients without this complication and also a higher prevalence of cardiovascular risk factors, including hypertension, diabetes mellitus, and a history of ischemic heart disease were evident in those with pericardial effusion. But there was no difference in sex distribution, body mass index, or even the severity of COVID-19 underlying disease between the two groups. In other words, even the severity of COVID-19 does not predict the occurrence of pericardial effusion, and whether patients with mild or moderate disease may develop this cardiac complication. The pathophysiology of pericardial effusion appears to be independent of the severity and extent of COVID-19 disease.

As a second finding, among the vital signs, the higher heart rate in patients with pericardial effusion

Table 1. Baseline characteristics of study population

Characteristics	Group with pericardial effusion (n= 300)	Group without pericardial effusion (n=1524)	P value
Mean age, year	66.92±4.18	55.00±7.85	0.001
Mean body mass index, kg/m^2	26.63±1.72	26.60±1.85	0.792
Male gender, %	77.7%	76.4%	0.630
COVID-19 severity, %			0.171
Mild to moderate	68.0%	71.9%	
Severe	32.0%	28.1%	
History of hypertension, %	68.0%	35.4%	0.001
History of diabetes mellitus, %	40.0%	32.3%	0.010
History of heart disease, %	37.3%	11.2%	0.001
History of brain stroke, %	5.0%	5.6%	0.656
History of renal failure, %	2.7%	2.8%	0.931
Mean body temperature, °C	36.92±0.53	36.90±0.53	0.549
Mean heart rate, /min	80.96±3.81	78.37±3.91	0.001
Mean respiratory rate, /min	17.13±0.79	17.11±0.79	0.637
Mean arterial oxygen saturation, %	92.37±0.84	92.34±0.80	0.939
Mean systolic blood pressure, mmHg	135.47±6.07	134.79±6.36	0.826
Mean diastolic blood pressure, mmHg	82.28±5.83	81.07±5.24	0.656
Mean serum hemoglobin level, g/dl	11.84±0.67	11.86±0.68	0.707
Mean white blood cell count, /mm^3	8005.33±610.04	8526.30±623.72	0.253
Mean platelet count, /mm^3	221.18±22.18	256.79±19.72	0.226
Mean serum BUN level, mg/dl	21.43±2.25	20.42±2.22	0.947
Mean serum creatinine level, mg/dl	1.27±0.17	1.22±0.18	0.854
Mean serum D-dimer level, mg/dl	1.84±0.17	1.22±0.18	0.815
Mean serum troponin level, mg/dl	84.27±2.42	84.15±2.47	0.253
Mean serum CRP level, mg/dl	58.39±5.17	56.46±5.25	0.820
Mean LVEF	53.79±3.22	53.73±3.23	0.794
Mean LVEDD	43.15±1.79	42.56±1.86	0.002
Mean LVESD	26.99±1.26	27.10±1.30	0.164
Mean TAPSE	1.85±0.12	2.36±0.07	0.001
Mean E/A ratio	1.06±0.04	1.08±0.07	0.001
Mean e/e’ ratio	11.85±0.73	9.82±0.85	0.001

LVEF: left ventricular ejection fraction; LVEDD: left-ventricular end-diastolic diameter; LVESD: left-ventricular end-systolic diameter; TAPSE: tricuspid annular plane systolic excursion

Table 2. Clinical outcome of patients with COVID-19

Characteristics	Group with pericardial effusion (n = 300)	Group without pericardial effusion (n=1524)	P value
Mean hospital stay, day	7.37±0.99	4.98±0.96	0.001
Death rate, %	32.0%	9.4%	0.001
Admission to intensive care unit, %	64.0%	24.9%	0.001

than in those without this complication was quite evident, which could be a prelude to the occurrence of pericardial effusion in patients with COVID-19. In other words, the occurrence of tachycardia as one of the obvious signs of pericardial effusion can be very helpful in predicting this event in the context of COVID-19. As a third finding, none of the laboratory markers was able to predict the occurrence of pericardial effusion in patients with COVID-19. As previously noted, even laboratory markers associated with myocardial infarction, such as serum troponin levels or BNP are not specific for the diagnosis and prognosis of pericardial effusion. In contrast to laboratory markers, early echocardiographic findings can be helpful in the early detection of pericardial effusion because, as our study found, abnormal changes in indices such as TAPSE, LVEDD, E/A ratio, and E/Ep ratio are traceable in the field of pericardial effusion and, therefore, can predict the occurrence of this complication in the field of COVID-19. Interestingly, essentially cardiac diastolic dysfunction (rather than systolic dysfunction) may be the precursor to pericardial effusion in these patients.

Overall, it seems that none of the clinical or laboratory findings can be specific to the early diagnosis of pericardial effusion in these patients, and perhaps the only means of predicting this event is echocardiographic evaluation, as well as imaging findings such as computed tomography scanning. In the study by Soewono *et al.* [11], a 30-year-old man with pleural chest pain was described whose electrocardiogram (ECG) assessment showed a sinus rhythm with an increase in ST-segment diffusion. Patient C-Reactive Protein (CRP) and dimer levels were also increased. Chest radiographs showed no evidence of involvement, but computed tomography angiography showed moderate pericardial effusion without pulmonary embolism. In a study by Foster *et al.* [12], a 44-year-old woman was described as having no changes in ECG evaluation and no evidence of pericardial effusion or pulmonary embolism on computed tomography angiography. But after hospitalization and in the secondary evaluation, evidence of NSTEMI was observed. Chest radiography was also normal. Following evaluation using cardiac MRI, acute hemorrhagic pericardial effusion was seen with evidence of delayed pericardial tamponade. In a study by Allam *et al.* [13], a 41-year-old woman was diagnosed with COVID-19, which showed no evidence of heart disease on the ECG. On echocardiography, extensive myocardial effusion was seen with mild symptoms of tamponade in the form of right atrial systolic collapse and cardiomegaly was also seen on chest radiographs. In a study by Eihab Ghantous *et al.* [10], similar to our study, the occurrence of pericardial effusion was completely independent of the severity of COVID-19 disease, BNP level, or right ventricular function.

Another important finding in our study was that the occurrence of pericardial effusion was associated with worsening clinical outcomes in patients with COVID-19, which increased the risk of mortality, increased ICU admission, and prolonged hospitalization. In other words, although the severity of COVID-19 disease is not a factor in predicting the occurrence of pericardial effusion, the occurrence of pericardial effusion will have a significant effect on the severity of adverse outcomes of COVID-19. As found in the study by Eihab Ghantous *et al.*, the occurrence of pericardial effusion was an important risk factor for mortality in patients following COVID-19 and increased the incidence of death in these patients by 1.8 times. However, due to the fact that few studies are available in the form of cross-sectional or retrospective studies in this field, determining the exact relationship of pericardial effusion with COVID-19 and related consequences still needs further study.

5. Conclusion

As a final conclusion, the occurrence of pericardial effusion is predictable in about 16.4% of patients with COVID-19, which occurs mainly in older people and people with a history of cardiovascular risk factors (hypertension, diabetes, or history of ischemic heart disease). Also, the occurrence of abnormalities in echocardiographic parameters, especially indicators related to cardiac diastolic dysfunction, can be predictable for the occurrence of pericardial effusion in patients with COVID-19.

5.1. Limitations

In this study, we faced some limitations, such as the unavailability of complete information of some patients, conducting research in an environment

completely infected with the corona virus, poor cooperation of departments, and a large number of people in the statistical community, and analyzing the results of echocardiography and the results of clinical tests.

References

1- Chen Chen, Spencer R Haupert, Lauren Zimmermann, Xu Shi, Lars G Fritsche, and Bhramar Mukherjee, "Global prevalence of post-coronavirus disease 2019 (COVID-19) condition or long COVID: a meta-analysis and systematic review." *The Journal of infectious diseases*, Vol. 226 (No. 9), pp. 1593-607, (2022).

2- Abdelmohcine Aimrane *et al.*, "Insight into COVID-19's epidemiology, pathology, and treatment." *Heliyon*, Vol. 8 (No. 1), (2022).

3- Shreya Sarkar and Rwik Sen, "Insights into Cardiovascular Defects and Cardiac Epigenome in the Context of COVID-19." *Epigenomes*, Vol. 6 (No. 2), p. 13, (2022).

4- Ivana Okor *et al.*, "COVID-19 myocarditis: an emerging clinical conundrum." *Current Problems in Cardiology*, Vol. 47 (No. 9), p. 101268, (2022).

5- Claudia Campanello *et al.*, "Cardiovascular manifestations in multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19 according to age." *Children*, Vol. 9 (No. 5), p. 583, (2022).

6- Melina Tangos *et al.*, "SARS-CoV-2 infects human cardiomyocytes promoted by inflammation and oxidative stress." *International Journal of Cardiology*, Vol. 362, pp. 196-205, (2022).

7- M Gul, S Ozyilmaz, Z Bastug Gul, C Kacmaz, and MH Satilmisoglu, "Evaluation of cardiac injury with biomarkers and echocardiography after COVID-19 infection." *J Physiol Pharmacol*, Vol. 73 (No. 1), pp. 89-95, (2022).

8- Waddah Aljaely Mohamed Osman, Abdelmuniem Siddig Mohamed Ahmed, Moh Mah Fadelallah Eljack, Khabab Abbasher Hussien Mohamed Ahmed, Mazin S. Haroun, and Yassin Abdelrahim Abdalla, "Acute pericarditis complicated with pericardial effusion as first presentation of COVID-19 in an adult sudanese patient: A case report." *Clinical Case Reports*, Vol. 10 (No. 3), p. e05570, (2022).

9- Nardine Abdelsayed, Benjamin Mckinney, and Mary Carter, "SARS-CoV-2 complicated by a large hemorrhagic pericardial effusion." *Cureus*, Vol. 14 (No. 2), (2022).

10- Eihab Ghantous *et al.*, "Pericardial involvement in patients hospitalized with COVID-19: prevalence, associates, and clinical implications." *Journal of the American Heart Association*, Vol. 11 (No. 7), p. e024363, (2022).

11- Kelvin Y Soewono, Kenneth C Raney III, and Manavjot S Sidhu, "Pericarditis with pericardial effusion as a delayed complication of COVID-19." in *Baylor University Medical Center Proceedings*, (2021), Vol. 34 (No. 5): *Taylor & Francis*, pp. 629-30.

12- Brian Foster, Adnan Liaqat, Anjula Chib, Scott S Bolton, Arthur C Kendig, and Arthur Kendig, "An unusual presentation of COVID-19: hemorrhagic pericardial effusion with tamponade physiology." *Cureus*, Vol. 13 (No. 2), (2021).

13- Hassan H Allam, Abdulhalim Jamal Kinsara, Tareq Tuaima, and Shadwan Alfakeh, "Pericardial fluid in a COVID-19 patient: is it exudate or transudate?" *European Journal of Case Reports in Internal Medicine*, (2020).