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# Frequency of pericardial effusion on COVID-19 patients in Rasht, Iran

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## ABSTRACT

Pericardial involvement is a rare extra-pulmonary manifestation of coronavirus disease 2019 (COVID-19). This study aimed to determine the frequency of pericardial effusion (PE) on patients with COVID-19. In this cross-sectional study, 582 patients with COVID-19 were investigated between March and May, 2020. Using high-resolution computed tomography (HRCT), patterns of pulmonary involvement and existence of PE were evaluated by a team including a radiologist, an emergency medicine specialist and a cardiologist. Other information such as laboratory tests, clinical symptoms, underlying comorbidities and a history of contact with COVID-19 patients was extracted from the patient's records. A total of 582 COVID-19 cases were investigated, of which 350 (60.14%) cases were women and 232 (39.86%) cases were men. Mean age of patients was 60.38±16.12 years. The most common symptoms were cough (58.93%), myalgia (52.74%), sweating (49.31%) and fever (44.32%). Among 582 COVID-19 patients, 2.7% (16 cases) had PE (95% CI; -4.5-1.6). Furthermore, 81% of the patients had mild PE (95% CI; 1.57-3.89). Also, 92% of the patients with PE had underlying comorbidities. By comparison, 74.5% of the patients without PE had comorbidities (P=0.047). There was no significant difference in the pattern of pulmonary involvement between the patients with PE and without PE (P>0.05). Prevalence of PE in COVID-19 patients is low. Underlying comorbidities, respectively, HTN and DM and ischemic heart diseases play an important role in occurrence of PE in COVID-19 patients. Our study revealed that it is not necessary for all patients to undergo an echocardiography.

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## 1. Introduction

Coronavirus disease 2019 (COVID-19) is the result of infection by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2 ( reported as a pneumonia of unknown cause in Wuhan, China, on December 30, 2019 for the first time in WHO (1). As of December 12, 2021, nearly 270 million confirmed cases and nearly 5.3 million deaths have been reported globally (2).

The most common symptoms of COVID-19 include fever, dry cough, myalgia or fatigue like other viral infections. We should understand the interaction of COVID-19 and cardiovascular disease (CVD) because the severity of COVID-19 disease correlates with cardiovascular manifestations (3). Clinical cardiovascular manifestations of COVID-19 include elevation of cardiac biomarkers (ischemic or non-ischemic etiology), cardiac arrhythmia, arterial and venous thromboembolism (VTE), and cardiogenic shock and arrest (4). COVID-19 patients with underlying CVD were more likely to have cardiac injury (troponin elevation) compared with patients without CVD (54.5% vs 13.2%) (3). One study revealed that the presence of underlying comorbidities such as DM, chronic lung disease, and CVD, was associated with a higher risk of developing severe COVID-19 associated disease (5). COVID-19 may exacerbate underlying CVD and may also give rise to new cardiovascular injuries (3).

Pericardial involvement is a rare extra-pulmonary manifestation of COVID-19. The main pericardial syndromes include pericarditis (acute, subacute, chronic and recurrent), pericardial effusion (PE), cardiac tamponade, constrictive pericarditis and pericardial masses. PE is a life-threatening condition that must be diagnosed as soon as possible for correct course of treatment and management (6). There is no set of laboratory parameters to help distinguish COVID-19-related PE from other etiologies (7). PE is often associated with known or unknown medical conditions. In about 60% of cases, the PE is associated with a known disease and the essential treatment is that of the underlying disease. According to a study, 15-30% PEs are because of infections (8). TB is believed to be the most common etiology of PE in developing countries (9).

Pericardial syndromes include different clinical presentations. Signs and symptoms of significant PE include tachycardia, raised jugular venous pressure, orthopnea, chest pain and/or fullness pulses paradoxes and pericardial rub. Hypotension and bradycardia will appear ultimately before cardiac arrest (10). PE is classified according to its onset (acute or subacute vs. chronic when lasting for 3 months), distribution (circumferential or loculated), hemodynamic impact (none, cardiac tamponade, effusive-constrictive), composition (exudate, transudate, blood, rarely air or gas from bacterial infections) and in particular, by its size based on a simple semi quantitative echocardiographic assessment as mild (10 mm), moderate (10–20 mm) or large (20 mm) (11).

The diagnosis of PE is generally performed by echocardiography, which also enables semi-quantitative assessment of the PE size and its hemodynamic effects. The use of high-resolution computed tomography (HRCT) has also helped in the diagnosis and management of pericardial disease and it is strongly recommended in suspected COVID-19 cases because of respiratory involvement of COVID-19 (12). A systematic review study found the characteristic patterns and distribution of CT manifestations including ground glass opacification (GGO) (88.0%), bilateral involvement (87.5%), peripheral distribution (76.0%), and multi-lobar involvement (78.8%). According to a number of studies, the most common pattern of lung involvement is GGO (13-15). Due to the COVID-19 pandemic and the importance of PE and its various complications in these patients, the present study aimed to evaluate frequency of PE in COVID-19 patients in Rasht, Iran.

## 2. Materials and Methods

This cross-sectional study was conducted on COVID-19 cases who were referred to Razi hospital, the only general hospital in Guilan province, Iran, between March and May, 2020. Among all patients admitted in 3 months period in Razi Center in Rasht, Iran, 582 patients who had COVID-19 infection based on clinical symptoms, PCR test and radiological findings of HRCT images, were investigated in the study by randomized sampling method.

The general CT manifestation was assessed based on the definition in the Fleischner Society Recommendation (16). Types of pulmonary involvement (Ground-glass opacity (GGO), consolidation lesion and pleural effusion) and existence of PE in HRCT were evaluated by a radiologist, an emergency medicine specialist, and a cardiologist. Other information such as laboratory tests, clinical symptoms, underlying cormorbidies and a history of contact with COVID-19 patients was extracted from the patients' records. All the patients who had a history of previous PE or heart failure or valve diseases before COVID-19 infection, patients who performed chest CT-Scan in another center, hospitalized patients without chest CT-Scan records, patients who died before doing CT-Scan, and pregnant women, were excluded from this study.

To investigate the frequency of PE on COVID-19 patients, qualitative data were presented as frequency (percent), while quantitative data were presented as mean and standard deviation (SD). Chi-square, T-test and Mann-Whitney U test were used. All data analyses were performed using the SPSS version 24. Any P value of $<0.05$ was considered statistically significant.

## 3. Results

A total of 582 COVID-19 cases were investigated, of which 350 (60.14%) cases were women and 232 (39.86%) cases were men. Mean age of patients was 60.38±16.12 years old. Among all 582 COVID-19 cases, 2.7% of the patients (16 cases) had PE (95% CI; 4.5-1.6). Evaluating the severity of PE, 81% of the patients had mild (95% CI; 95.1, 53.7), 12.5% of the patients had moderate (95% CI; 39.6-2.2) and just one case (6.2%) had severe PE (95% CI; 32, 2-0.3). Demographic, clinical, and laboratory information are presented in Table 1. There was no significant difference in terms of age (P=0.083) and there was significant difference in terms of gender (P=0.038) between the COVID-19 patients with and without PE. Among all COVID-19 cases, 92% of COVID-19 patients with PE had underlying comorbidities such as congestive heart failure (CHF), ischemic heart disease (IHD), chronic pulmonary obstructive disease (COPD), and old tuberculosis (TB). By comparison, 74.5 % of the patients without PE had comorbidities (P=0.047). Also Underlying comorbidities, respectively, HTN and DM and ischemic heart diseases play an important role in occurrence of PE in COVID-19 patients (Table2).

**Table1.** Demographic, clinical and laboratory characteristics of the participants.

| Variable | Group | Pericardial effusion | | P value |
|---|---|---|---|---|
| | | With | Without | |
| Age in year | <40 | 1 (6.24%) | 61 (11.21%) | 0.083* |
| | 40-60 | 3 (18.75%) | 187 (34.38%) | |
| | 60-80 | 9 (56.25%) | 216 (39.71%) | |
| | >80 | 3 (18.75%) | 80 (14.71%) | |
| Gender | Men | 13 (82.25%) | 330 (59.25%) | 0.038* |
| | women | 3 (18.75%) | 227 (40.75%) | |
| Ejection fraction mean±SD (median) | | 33.7 ±16( 33) | 42.2 ±13.8(45) | 0.032** |
| Comorbidity disease | CHF | 1 (6%) | 3 (0.54%) | 0.040** |
| | IHD | 2 (12%) | 33 (5.92%) | 0.043 |
| | COPD | 2 (12%) | 16 (2.87%) | 0.012 |
| | Old TB | 2 (12%) | 4 (0.072%) | <0.001 |
| CRP | +1 | 8 (50%) | 393 (70.68%) | 0.035 |
| | +2 | 4 (25%) | 108 (19.42%) | |
| | +3 | 4 (25%) | 55 (9.89%) | |
| WBC counts (μ/L) mean±SD (median) | | 4185.26±8168.74(6900.0) | 3807±8532.01(8500.0) | 0.582*** |
| ESR (mm/h) mean±SD (median) | | 22.27±57.12(60.0) | 17.28±61.18( 60.0) | 0.549*** |

* Chi-square
**Fishers exact test
***Mann-Whitney

**Table 2.** Pulmonary involvement in COVID-19 patients with and without PE (n=582).

| Variable | Group | Pericardial effusion | | P value* |
|---|---|---|---|---|
| | | Yes | No | |
| Pleural effusion | Yes | 1 (6%) | 12 (2.15%) | 0.541 |
| | No | 15 (94%) | 545 (97.85%) | |
| Consolidation lesions | Yes | 1 (6%) | 43 (7.72%) | 0.959 |
| | No | 15 (94%) | 514 (92.28%) | |
| Ground-glass opacity | Yes | 14 (88%) | 529 (94.97%) | 0.511 |
| | No | 2 (12%) | 28 (5.03%) | |

* Chi-square

## 4. Discussion

Findings of the current study, which aimed to evaluate frequency of PE on COVID-19 patients, showed that among all COVID-19 cases, a small percentage (2.7%) of them had PE. According to a review, a meta-analysis of 2676 hospitalized patients with confirmed COVID-19 also showed a pooled prevalence of pericardial effusion of 3% on chest CT, like the current study (17). Even though the cause of pericardial effusion was not identified, it is likely that most cases were because of pericardial inflammation (18).

According to a review, pericardial effusion is found in a significantly higher proportion of COVID-19 patients with severe/critical disease compared with the non-severe group, suggesting that it could be useful as a marker of poor outcome (19). However, in the current study, about 11.5% of COVID-19 patients were hospitalized in ICU (12% of patients with PE vs. 11.3% of patients without PE) (P=0.472); therefore, severity of COVID-19 seemed not to be associated with whether or not the patients had PE. In fact, the current study showed high prevalence of mild PE, but low prevalence of severe PE.

A systematic review showed that among comorbidities considered, hypertension and diabetes mellitus are present in 32% and 15% of the COVID-19 patients with PE, respectively (18). In the current study, the COVID-19 patients with PE had underlying comorbidities such as CHF, IHD and COPD. The difference in underlying cormorbidities between this study and the review may be due to a different lifestyle and cormorbidy frequency of the patients peculiar to regions and countries.

The typical early CT features of COVID-19 pneumonia are GGO (39.13%), and mixed GGO and cosolidation (60.83%), the lesions of which were located in peripheral or subpleural area (20). Jin YH, et al. reported that CT findings of the early stage of COVID-19 shows multiple scattered GGO, and light consolidation. After COVID-19 pneumonia gets exacerbated, consolidations with air-bronchogram inside, appears (21). In the current study, most of the patients had GGO pattern, not consolidation. Therefore, the stage of COVID-19 patients in the current study was thought to be early.

As mentioned above, the common symptoms of COVID-19 patients in the current study included cough, myalgia, sweating, and fever. However, there was no significant difference in frequency between COVID-19 patients with and without PE. The findings of the current study were not fully consistent with those of the previous study that the common symptoms include chest pain, fever, dyspnea and cough (19). However, in the currernt study, some peculiar symptpms such as loss of consciousness, vertigo and melena were significantly higher in COVID-19 patients with PE than without PE. Loss of consciousness, vertigo may be associated with the severity of COVID-19.

In the current study, C-reactive protein (CRP), were significantly higher in COVID-19 patients with PE than without PE. The significant association of PE with increased CRP levels indicates that pericardial inflammation plays an important role in the development of PE in COVID-19 patients (18, 19, 22-26).

One of the limitations of the study is the retrospective nature of the study. So that it was not possible to access the results of echocardiography and heart consultants in some patients. Also, the study was conducted in a single center, so that some patients had referred to the heart treatment center due to heart symptoms, and information about this group of patients was not available.

Our findings indicate that among 582 COVID-19 cases, 2.7% (16 cases) had PE. 92% of the COVID-19 patients with PE had underlying comorbidities such as CHF, IHD and COPD. Moreover, some peculiar symptpms such as, loss of consciousness, vertigo and melena were significantly higher in COVID-19 patients with PE than without PE. Therefore, clinicians should pay attention to aforementioned underlying cormorbidities and some peculiar symptoms as well as cough, myalgia, sweating, and fever, in order to diagnose rapidly COVID-19 patients with PE.

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## Authors' contributions

Supervision and conceptualization: SAFM and SMS. Original draft preparation: NNR, SR. Cooperated in study design and supervised: FSH, Data collection: PF, JN, SK. Critical revision and editing: YB. All authors read and approved the final version of manuscript.

## Conflict of interest

There are no conflicts of interest.

## Ethical declarations

This study was approved by the ethics committees at the Ministry of Health and Medical Education and the Guilan University of Medical Sciences (IR.GUMS.REC.1399.378)

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