Review Article

Electrocardiographic features of patients with COVID-19: One year of unexpected manifestations

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1. Introduction

Coronavirus Disease 2019 (COVID-19) is the clinical manifestation of infection with Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) [1 -3]. COVID-19 is frequently characterized by symptoms and signs of respiratory tract infection which may progress to pneumonia, acute respiratory distress syndrome (ARDS) and shock. [1, 2, 4] Thus, much of the focus has been on the respiratory system.

Nonetheless, COVID-19 can also cause a variety of cardiovascular complications including myocardial injury, myocarditis, acute myocardial infarction, stress cardiomyopathy, heart failure, dysrhythmias, and thromboembolic events [5 14]. In this context, standard electrocardiography (ECG) showed to be a crucial test in the diagnosis of cardiac complications in patients with SARS-CoV-2. A study of 756 patients hospitalized with COVID-19 in New York, documented a range of COVID-19-related ECG findings including atrial fibrillation (5.6%), atrial and ventricular premature beats (7.7% and 3.4%, respectively), right bundle branch block (7.8%), left bundle branch block (1.5%), T-wave inversion (10.5%), and nonspecific repolarization abnormalities (29.0%) [15]. These manifestations are believed to be the result of several pathogenetic mechanisms including cytokine and Angiotensin II storms, activation of coagulation cascade, hypoxic injury, endothelial and myocardial injuries, and atherosclerotic plaque destabilization and rupture [5, 7, 16, 17].

Several evidences of uncommon ECG manifestations of COVID-19 have been recently accrued. A paper from our group [18] published in the 2020 August issue of the European Journal of Internal Medicine [18] was one of the first studies to report a wide spectrum of unexpected ECG features of COVID-19 which exhibited a late onset and mostly occurred after recovery from the acute phase. In patients hospitalized for COVID-19 pneumonia, we found a 6% incidence of atrial fibrillation, a 2% incidence of brady-tachy syndrome, a 2% incidence of persistent ST-T changes not associated with increase in troponin I levels nor pericardial effusion, and a 12% incidence of ST-T changes associated with acute pericarditis [18].

The main aim of this narrative review was to explore incidence and pathogenesis of ECG features of COVID-19, with particularly emphasis to “unexpected” manifestations.

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Our review was performed according to standard methods. [19] We searched for eligible studies or case reports using research methodology filters [20]. We used PubMed, Scopus, and Web of Science for literature searches. The following search terms were used: “ECG”, “electrocardiography”, “EKG”, “COVID-19”, “SARS-CoV-2”, and “coronavirus”.

2. “Typical” ECG features of COVID-19 complications

At the beginning of the pandemic, much attention has been focused on ECG features of “common” cardiovascular complications of SARS-CoV-2 infections [8, 11]. Several reports described “typical” features of COVID-19 complications including arrhythmias, ischemic ST-T abnormalities (spanning from acute coronary syndromes to Takotsubo syndrome), pulmonary embolism, acute heart failure, and myocarditis [8, 11]. Remarkably, ECG abnormalities are common, being present up to 93% of critically ill patients [21]. For these conditions, interpretation of the ECG is unchanged from the non-COVID-19 patient [16].

2.1. Sinus tachycardia

It is the most common ECG manifestation overall in patients with COVID-19. It may reflect several underlying mechanisms including intrinsic sinus node hyperactivity, autonomic dysfunction and a hyperadrenergic state (fever, hypovolemia, hypoxia, pain, anxiety, and hypoperfusion) [22]. Nonetheless, inflammatory cytokines released by patients with COVID-19 may affect the function of myocardial ion channels and perpetuate the sinus tachycardia [23]. As in the general population, other etiologies of sinus tachycardia should be considered (i.e. pulmonary embolism) [24].

2.2. Atrial arrhythmias

Atrial arrhythmias are the most commonly reported features in patients with COVID-19. Specifically, atrial fibrillation is commonly observed among COVID-19 patients (as detected in 19% to 21% of all cases) [25, 26].

The etiology of atrial arrhythmias remains to be fully elucidated. However, a reduction in angiotensin-converting enzyme 2 (ACE2) receptor availability, CD147- and sialic acid-spik protein interaction, enhanced inflammatory signaling, direct viral endothelial damage, metabolic derangements, electrolytes and acid-base balance abnormalities in the acute phase of COVID-19 have been suggested as putative mechanisms [27].

For atrial fibrillation, it is worth mentioning that epicardial fat has been linked to atrial electrical remodeling and the progression of atrial fibrillation [28, 29]. Although it is likely that atrial fibrillation may be related to COVID-19 infection (systemic hyperinflammation, fever, hypoxia, adrenergic tone), the involvement of epicardial adipocytes (as demonstrated by ECG signs of pericarditis and development of pericardial effusion) during SARS-CoV-2 infection could predispose to the development of atrial fibrillation [18].

2.3. Ventricular arrhythmias

These arrhythmias may occur among COVID-19 patients with myocarditis, metabolic abnormalities, or treated with QT interval prolonging medications [5, 16, 30].

Abrams and co-workers reviewed demographics, laboratory and cardiac tests, medications, and cardiac rhythm proximate to death or initiation of comfort care for patients hospitalized with a positive SARS-CoV-2 reverse-transcriptase polymerase chain reaction in three New York City hospitals between March 1 and April 3, 2020. They documented that the last cardiac rhythm recorded was ventricular tachycardia or fibrillation in 5.3% of all cases [31].

Furthermore, life threatening ventricular arrhythmias are reported to be more common in patients with elevated serum levels of cardiac troponins [30, 32].

2.4. Myocardial ischemia and injury

A plethora of ischemic and myocardial injuries manifestations have been documented among hospitalized patients with COVID-19 [5, 32, 34].

In a retrospective observational study including patients with COVID-19 admitted at the Wuhan Asia General hospital, ST-T abnormalities (40%) were the most common ECG feature [35].

Of note, myocardial injury during the acute phase of COVID-19 demonstrates ST segment deviations (both elevation or depression), pathological Q waves, and T wave inversion at standard ECG [21, 36, 38]. Although the distinction between a ST-elevation myocardial infarction and myocarditis remains difficult, diagnosis of acute myocardial infarction is suggested with focal ST-segment elevations; conversely, myocardial injury demonstrates diffuse or widespread ST-segment elevation [39].

It has been proposed that mechanisms of SARS-CoV-2 myocardial injury may be explained by a combination of direct cell injury and T-lymphocyte-mediated cytotoxicity [40, 41].

2.5. Pulmonary embolism

A high prevalence of venous thromboembolism (VTE) is reported during hospitalization for COVID-19 [42]. The most common ECG finding in the setting of a pulmonary embolism is sinus tachycardia [43]. This associated ECG condition is also confirmed among COVID-19 patients [16, 44]. The S1Q3T3 sign (prominent S wave in lead I, Q wave and inverted T wave in lead III) is a classic sign of acute cor pulmonale (acute pressure and volume overload of the right ventricle because of pulmonary hypertension) with increased right ventricular strain [45].

Nonetheless, a single center, retrospective observational cohort study of COVID-19 patients diagnosed with pulmonary embolism showed that the S1Q3T3 sign was present in less than 10% of cases and that non-specific ST-T abnormalities or T wave changes were the most common ECG findings of pulmonary embolism [44].

3. “Unexpected” ECG features of COVID-19

Evidences on unexpected ECG features of COVID-19 have been recently accrued, showing that uncertainties still overshadow our clinical knowledge in the field [16, 36].

Interestingly, in our previous report of ECG features of patients with COVID-19 pneumonia, we documented that the development of ECG abnormalities during hospitalization was unrelated to the severity of respiratory function [18]. Moreover, abnormal serum levels of high sensitivity troponin I were recorded in the 38% of cases and ECG abnormalities showed a late onset from hospitalization and initiation of COVID-19 symptoms. The average time for development of ECG abnormalities was 20 and 30 days from admission and onset of symptoms, respectively [18]. Notably, a large proportion of patients (54%) experienced ECG abnormalities immediately before the scheduled discharge from hospital and after 2 consecutive negative nasopharyngeal swabs [18].

3.1. Right ventricular strain

COVID-19 patients with acute respiratory failure may present QRS complex axis deviation with right ventricular strain (prominent R waves in leads V1 and V3, ST segment depression or T wave inversion in leads II, III, aVF, V1, V2, V3, and V4) [33]. Of note, right ventricular strain seems to be associated with an increased risk of death or need of mechanical ventilation during hospitalization [33, 46].
Fig. 1. A 79-year-old white woman who developed during hospitalization COVID-19 pneumonia, chest pain with ECG signs of acute pericarditis and significant pericardial effusion [18]. After 1 month after discharge from hospital, the patient was asymptomatic and the echocardiographic examination documented complete regression of pericardial effusion (upper panel). However, standard ECG revealed the persistence of signs of pericarditis (lower panel).
3.2. Brady-arrhythmias and atrioventricular blocks

Incidence of bradicardias, atrioventricular blocks, and brady-tachy syndromes is not well characterized among COVID-19 patients [16, 18, 47]. To date, these ECG manifestations are considered as disease-caused deterioration [47].

However, a recent case series by Dagher and co-workers [48] described four cases of COVID-19 patients who developed a transient high-degree atrioventricular block during the course of their hospitalization, not requiring permanent pacing [48]. Similar findings were also reported in our cohort [18] and by Eneizat Mahdawi and co-workers in a case series of heart blocks [49].

3.3. ECG features of pericardial disease

Postmortem studies have identified pericarditis in about 20% of the COVID-19 cases [50, 51] and several case reports reported acute pericarditis in patients with SARS-CoV-2 infection with typical ECG signs (diffuse ST elevation and PR depression) [52-56].

Data from 63,822 COVID patients attending 50 Spanish emergency departments during the COVID outbreak were used to analyze the frequency of (myo)pericarditis [57]. Compared with general emergency department population, COVID patients developed more frequently (myo)pericarditis (odds ratio [OR]: 1.45, 95% confidence interval [CI]: 1.07–1.97) [57]. Similarly, in a retrospective cohort study involving 718,365 patients with COVID-19, 10,706 (1.5%) patients developed new-onset pericarditis with a 6-months all-cause mortality of 15.5% (vs 6.7% in matched controls, OR: 2.55, 95% CI: 2.24–2.91) [40].

In our study cohort [18], ECG signs of acute pericarditis were the most common ECG manifestations of COVID-19. Notably, we diagnosed acute pericarditis by ECG evidence of new widespread concave ST elevation and PR depression throughout most of the limb (I, II, III, aVL, aVF) and precordial (V2–V6) leads, reciprocal ST depression, and PR...
inflammatory reaction (with cytokine storm), and endothelial damage coexists. On the other hand, several patients with acute pericarditis Furthermore, COVID-19 induced pericarditis might reflect the expression of ACE2 receptors in epicardial adipocytes (mediating the cell entry of SARS-CoV-2) [17, 61–65], and possibly triggering local inflammation of ACE2 receptors in epicardial adipocytes (mediating the cell entry of SARS-CoV-2) [17, 61–65], and possibly triggering local inflammation (63, 65, 70).

3.4. Brugada-like pattern

Two case reports documented Brugada patterns in patients with COVID-19 [71, 72]. In the first report [71], standard ECG revealed a Brugada-like pattern in a 61-year-old man presented with fever, shortness of breath, and chest pain (with coronary angiography demonstrating normal coronary arteries).

In the second, a 49-year-old Bangladeshi man without significant medical history and positive for COVID-19 showed a Brugada syndrome, with the combination of the Brugada ECG pattern and clinical symptoms [72].

4. Conclusions

COVID-19 impacts the cardiovascular system, causing a variety of cardiac complications and leading to a range of ECG abnormalities [73, 74] (Fig. 2). Cardiac injury is found in 7%–17% of COVID-19 patients, and it is associated with a higher risk of mortality [12, 14]. Therefore, clinicians must be aware of the ECG manifestations of COVID-19.

As the body of academic literature is expanding, it is also mandatory to understand uncommon ECG manifestations of COVID-19. Some patients with pericarditis may not have chest pain even with myocarditis coexists. On the other hand, several patients with acute pericarditis develop significant pericardial effusion necessitating pericardial drainage [53, 55, 75].

It’s now well established that several uncommon ECG manifestations of SARS-CoV-2 infection are associated with an increased risk of adverse outcome [16, 36, 76]. These conditions require an early diagnosis, a proper workup and specific management strategies based on organ involvement.

Declaration of Competing Interest

None of the authors of this study has financial or other reasons that could lead to a conflict of interest.

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