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REVIEW

Cardiac arrhythmias associated with COVID-19 infection: state of the art review

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ABSTRACT

Introduction: COVID-19 infection is associated with many different systemic complications. Among these, cardiovascular system complications are particularly important as these are associated with significant mortality. There are many different subgroups of cardiovascular complications, with Arrhythmias being one of them. Arrhythmias are especially important as there are a substantial percentage of patients who have arrhythmia after a COVID-19 infection, and these patients are seen with an increased mortality rate. The main interest of this review is understanding some of the specific post-COVID-19 arrhythmic complications and their predisposing factors.

Areas covered: This paper will highlight the findings of studies on cardiovascular system disease after COVID-19 infection, different specific arrhythmic complications of COVID-19, and changes in electrophysiologic interventions post-COVID-19 outbreak in different centers around the world. An extensive literature search was made to find pertinent articles.

Expert Opinion: Studies show us that a significant percentage of COVID-19 patients have arrhythmia. Many distinct types of arrhythmias are associated with COVID-19 infection, and specific risk factors of these arrhythmias are important as this information can be used to detect and prioritize certain at-risk patients for early treatment, which can mean life or death in some cases.

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1. Introduction

In late December 2019, there were clustered cases of pneumonia originating in Wuhan, China[1]. This disease brought about a novel virus later named by WHO as COVID-19[2]. After an exponential increase in disease spread and severity, WHO made an assessment that characterized COVID-19 as a pandemic on 11 March 2020[3]. There were more than 115 million confirmed cases and 2.5 million reported deaths to WHO[4]. To this day, the disease is still a major public health concern.

The virus that causes the COVID-19 infection is named severe acute respiratory syndrome. Coronaviruses are positive-stranded RNA viruses[5]. They can cause many different systemic complications, with cardiovascular systems being one of them. The processes that set off the cardiovascular manifestations of COVID-19 have not been completely known and most likely have multiple explanations. Both indirect and direct mechanisms are likely causes of cardiovascular injury[6]. One of the suspected pathways for the virus is direct damage inflicted to the body by using ACE2 receptors to enter cells[7]. ACE2 gene expression is found in many organs such as lung, heart, and kidney[7]. Many studies found that there is an increased mortality rate for patients with cardiovascular complications [8–10]. One of the important subgroups of cardiovascular complications is arrhythmic complications.

The aim of this review is to summarize studies mainly on different post-COVID-19 arrhythmic complications and their risk factors so that clinicians can better detect certain at-risk populations of patients.

2. Post-COVID-19 cardiovascular disease

Meta-analysis of 12 comparative studies on 1845 hospitalized patients shows that deaths from the COVID-19 infection were related to cardiovascular disease-associated laboratory biomarkers such as cardiac troponin I (OR = 25.5, p = <0.0001), LDH (OR = 11.8, p = 0.03), and CK (OR = 2.3, p = 0.04)[9]. Meta-analysis of 28 studies on 6,270 patients, which separated patients into severe or nonsevere group, shows that some comorbidities were linked with severe COVID-19 like cerebrovascular disorder (OR 4.85, 95% CI: 3.11–7.57), cardiovascular disorders (OR 4.81, 95% CI: 3.43–6.74), hypertension (OR 2.37, 95% CI: 1.80–3.13), and diabetes (OR 2.61, 95% CI: 2.02–3.39) [11]. A retrospective cohort study of 2877 hospitalized patients with verified COVID-19 found that the mortality rate was 4% for the hypertension group and 1.1% for the nonhypertension group (crude HR 3.75, 95% CI 2.19–6.41; P < 0.001). Even after adjusting for confounders, hypertension has remained related

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Article highlights

- Increase in COVID-19 disease severity was associated with an increased arrhythmia prevalence.
- History of atrial fibrillation, male sex, age, and hypoxia on presentation were separately related to arrhythmias. Any type of arrhythmia was separately related to a 30-day all-cause mortality.
- Existence of thorax CT diffuse lung infiltration was the biggest separate parameter related to new-onset atrial fibrillation formation.
- Combination of high-sensitivity cardiac troponin T ≥20 ng/L and abnormal ECG was related to a rise in the 30-day mortality rate relative to normal ECG and high-sensitivity cardiac troponin T <20 ng/L.
- Different studies from many centers around the world reported that they had decreased numbers of electrophysiological procedures.

with increased risk for mortality (adjusted HR 2.12, 95% CI 1.17–3.82; P = 0.013). Also, this study found a 7.9% mortality rate for hypertension patients without treatments, relative to (3.2%) the mortality rate for hypertensive patients with treatment (HR 2.52, 95% CI 1.23–5.17; P = 0.012). After adjusting for confounders, mortality for patients without antihypertensive treatments was higher (HR 2.17, 95% CI 1.03–4.57; P = 0.041) [12]. A single-center cohort study of 416 consecutive patients found that comorbidities like hypertension (59.8% vs 23.4%, P < .001), diabetes (24.4% vs 12.0%, P < .001), coronary heart disease (29.3% vs 6.0%, P < .001), cerebrovascular disease (15.9% vs 2.7%, P < .001), and chronic heart failure (14.6% vs 1.5%) were higher in patients with cardiac damage.Table 1

Table 1. Post-COVID-19 cardiovascular diseases.

AUTHOR	STUDY DESIGN	SAMPLE SIZE	RESULTS
Shoar et al. [9]	Meta-analysis	1,845	Some cardiovascular disease-associated biomarkers related to mortality like cardiac troponin I (OR = 25.5, p = <0.0001), LDH (OR = 11.8), and CK (OR = 2.3).
Honardoost et al. [11]	Meta-analysis	6,270	Certain comorbidities were related to serious COVID-19 presentation like cardiovascular disease (OR 4.81), cerebrovascular disease (OR 4.85), hypertension (OR 2.37), and diabetes (OR 2.61).
Gao et al. [12]	Retrospective cohort study	2,877	Hypertension patients had increased risk for mortality. Hypertension patients without antihypertensive treatment had an increased mortality rate than patients with antihypertensive treatment.
Shi et al. [13]	Single-center cohort study	416	Comorbidities like hypertension, cerebrovascular disease, diabetes, chronic heart failure, and coronary heart disease were more common in patients with cardiac damage. A higher mortality rate was seen in patient with cardiac damage.
Chen et al. [14]	Retrospective case series	274	Cerebrovascular disease, hypertension, and cardiovascular disease were more common with deceased patients compared to recovered patients. In deceased patients, N-terminal pro-brain natriuretic peptide and cardiac troponin I concentrations were elevated.
Rosenberg et al. [15]	Retrospective cohort study	1438	No significant changesin in-hospital mortality related to treatment of azithromycin and hydroxychloroquine or using these drugs together relative to using none of these treatments.
Kim et al. [16]	Meta-analysis	49,569	Randomized controlled trials of hydroxychloroquine were not related to better clinical results. Also, the study found that remdesivir and corticosteroids might successfully improve the clinical results of COVID-19[16].

Table 2. Post-COVID arrhythmia.

AUTHOR	STUDY DESIGN	SAMPLE SIZE	RESULT
Wang et al. [17]	Single-center case series	138	Arrhythmia incidence was 16.7%.
Liao et al. [18]	Meta-analysis	17,435	Patients' overall arrhythmia incidence with COVID-19 was 16.8%. The mortality rate of those who developed arrhythmia was 20.3%.
Pranata et al. [19]	Meta-analysis	784	Arrhythmia incidence was 19%. Also, 48% of poor outcome patients had arrhythmia.
Wen et al. [20]	Meta-analysis	1553	30.09% of severe COVID-19 patients had arrhythmia. 2.82% of nonsevere COVID-19 patients had arrhythmia.
Guan et al. [21]	Retrospective study	463	18.4% of patients had arrhythmia. The all-cause mortality rate was higher with arrhythmia patients (25.9% vs 10.1%; p < o.001).
Zylla et al. [22]	Retrospective cohort study	166	20.5% of patients had arrhythmia during hospitalization. In-hospital fatality was increased with arrhythmia patients (OR 3.02).
Rav-Acha et al. [23]	Single-center cohort study	390	Important rise in prevalence of arrhythmia with growing illness severity [9.5% 13.5%, and 23.5% for moderate, severe, and critical severity, in that order]. 7.2% of these patients developed new-onset arrhythmia during hospitalization.
Peltzer et al. [24]	Retrospective observational cohort study	1053	Age (adjusted odds ratio [aOR], 1.04), male sex (aOR, 2.49), previous record of atrial fibrillation (aOR, 6.03), and hypoxia on presentation (aOR, 2.17) were separately associated with the arrhythmia. Any arrhythmia was separately associated with 30-day all-cause mortality (aOR, 2.01).
Amirhossein Hessami a, b, c et al. [8]	Meta-analysis	159,698	In ICU patients, second most, prevalent cardiovascular complication was arrhythmia (33%) behind hypertension (43%).
Li et al. [26]	Systemic review and meta-analysis	4,631	Arrhythmia was in 3.1% of patients with non-severe disease/non-ICU relative to 43.8% in the severe disease/ICU group. New-onset arrhythmia patients were at increased risk of severe disease/ICU admission (RR 13.09).
Keikha et al. [25]	Cross-sectional study	123	hsa-miR-126-3p expression was decreased with the rise of COVID-19 disease grade.

Table 3. Post-COVID-19 atrial arrhythmia/flutter.

AUTHOR	STUDY DESIGN	SAMPLE SIZE	RESULTS
Elias et al. [28]	Retrospective cohort study	850	Sinus rhythm was the most common rhythm in ECG (65.6%) after that sinus tachycardia (25.9%) and then atrial fibrillation or flutter (4.9%).
Mccullough et al. [29]	Retrospective observational cohort study	756	A majority of patients had sinus rhythm (94.4%), and 5.6% of patients had atrial fibrillation/flutter.
Mountantonakis et al. [30]	Retrospective cohort study	9,564	17.6% of patients experienced atrial fibrillation 12.5% of which was new-onset atrial fibrillation. In-hospital mortality of patients with atrial fibrillation was higher (54.3% vs 37.2%).
Guan et al. [21]	Retrospective study	463	Multivariate logistic regression analyses shows that atrial tachycardia/atrial fibrillation/atrial flutter (OR, 5.23) were separate risk factors for serious disease. Patients with elevated IL-10 levels had significantly more frequent atrial arrhythmia than patients who have physiological levels. The adjusted odds ratio of death during hospitalization for atrial arrhythmia was 3.51.
Kelesoglu et al. [31]	Single-center study	658	5% of patients had onset atrial fibrillation. Existence of thorax CT diffuse lung infiltration was biggest separate factor related to new-onset atrial fibrillation formation.
Peltzer et al. [32]	Observational cohort study	1053	14.6% of patients had atrial fibrillation, and 3.8% of them had atrial flutter/tachycardia; among these patients, 61% of them no history of atrial fibrillation or atrial flutter/tachycardia. Overall, in-hospital mortality was greater among patients with atrial fibrillation or atrial flutter/tachycardia than those without (39.2% vs. 13.4%; p < 0.001). Multivariable regression analysis shows that male sex, age, previous atrial fibrillation, hypoxia, and renal disease were separately related to incidence of atrial fibrillation and atrial flutter/tachycardia.
Bertini et al. [33]	Multicentric cross-sectional retrospective cohort	431	22% of patients had atrial fibrillation or flutter, and it was more common with patients older than 74 years (31% vs. 15%).
Russo et al. [34]	Retrospective multicenter observational study	414	Atrial fibrillation recurrence (RR:7.09) was related to ventricular tachycardia. Atrial fibrillations separate predictors who were male gender, were of older age, and hadCAD and HF. The atrial fibrillation event was substantially related to event ventricular tachycardia.
Linschoten et al. [35]	Cohort	3011	Most common cardiac complication was atrial fibrillation (4.7%).
Poterucha et al. [36]	Retrospective cohort	887	The mortality rate within 30 days was 59% for patients who had atrial fibrillation/atrial flutter relative to 21% of patients with other rhythm. The mortality rate was similar between patients with previous atrial fibrillation/atrial flutter compared to newly diagnosed ones (56% vs 62%).
Wei et al. [37]		135	Atrial fibrillation patients had lower levels of miR-126 relative to controls (P < 0.01). [37]

Patients with cardiac damage required more invasive ventilation relative to patients without cardiac damage (22.0% vs 4.2%; P < .001). Some complications were higher in patients with cardiac damage relative to patients without cardiac damage like ARDS (58.5% vs 14.7%; P < .001), acute kidney injury (8.5% vs 0.3%; P < .001), and electrolyte disturbances (15.9% vs 5.1%; P = .003). The fatality rate was higher in patients with cardiac damage relative to patients without cardiac damage (51.2% vs 4.5%; P < .001)[13]. Retrospective case series of 274 patients in Wuhan, China, found that hypertension (48% vs 24%), cardiovascular disease (14% vs 4%), and cerebrovascular disease (4% vs 0%) were higher among deceased patients compared to recovered patients. 44% of patients who died had an arterial pressure of more than 140 mm Hg relative to 20% of patients who had recovered. Also, cardiac troponin I (72% vs 14%) and N-terminal probrain natriuretic peptide concentrations (85% vs 18%) were higher in deceased patients[14].Table 2 A retrospective cohort study performed with 1438 hospitalized patients in New York found that there are no significant chances in-hospital mortality related to treatment of azithromycin, hydroxychloroquine, or using these drugs together relative to using none of these treatments[15]. Meta-analysis of pharmacological treatments perfomed with 70 observational studies and 40 randomized controlled trials on 49,569 COVID-19 patients found that at randomized controlled trials of hydroxychloroquine were not related to better clinical results, but the same study also found that remdesivir and corticosteroids might successfully improve the clinical results of COVID-19[16] Table 3.

3. Post-COVID-19 arrhythmia

3.1. Post-COVID-19 arrhythmia mortality

A retrospective single-center case series of 138 hospitalized patients in Wuhan, China, found that the arrhythmia incidence was 16.7%[17]. Meta-analysis of 56 studies from 11 different countries on 17,435 patients, where a vast majority of them were hospitalized, found that arrhythmia incidence with COVID-19 patients was 16.8% and the mortality rate of patients who developed arrhythmia was 20.3%[18].Meta-analysis of 4 studies (most of them from China and retrospective) on 784 patients showed that that arrhythmia incidence was 19%. Arrhythmia was associated with poor outcomes (RR 7.96 [3.77, 16.81], p < 0.001; I2: 71.1%). Arrhythmia was seen with 48% of patients with poor outcomes[19]. Meta-analysis of five studies on 1553 patients, which separated patients into a severe or nonsevere group shows that 22.47% of patients had severe COVID-19 and 77.53% had nonsevere COVID-19. Of these patients, arrhythmia complications were 30.09% and 2.82%, respectively[20]. A retrospective study of 463 patients shows that 18.4% had arrhythmia and 81.6% had no arrhythmia. The all-cause mortality rate was higher with arrhythmia patients (25.9% vs 10.1%; p < 0.001)[21]. The hort study of 166 patients found that 20.5% of them had arrhythmia during hospitalization. Of these patients, 13.3% showed new-onset arrhythmia, which is either without past arrhythmia 9.6% or in addition to previous diagnosed arrhythmia. In-hospital fatality was increased in COVID-19 patients with arrhythmia (OR 3.02; 95% CI 1.22–7.46; p = 0.02)[22]. A single-center cohort study

performed with 390 patients showed an important rise in arrhythmia prevalence with escalating disease severity [9.5%, 13.5%, and 23.5%)for moderate, severe, and critical severity, P < 0.001] and 2% prevalence of arrhythmia with mild COVID-19 disease. In this study, 7.2% of these patients developed new +onset arrhythmia during hospitilization[23]. A retrospective observational cohort study of 1053 patients on multivariable regression analysis found that age (adjusted odds ratio [aOR], 1.04; P < 0.001), male sex (aOR, 2.49; P < 0.001), past record of atrial fibrillation (aOR, 6.03; P < 0.001), and hypoxia on presentation (aOR, 2.17; P < 0.001) were separately related to arrhythmia. Patients with arrhythmia compared with those without arrhythmia had greater in-hospital mortality (34.8% versus 11.5%; P < 0.001). Following adjustment for age, race, comorbidities, and any arrhythmia were separately linked with 30-day all-cause mortality (aOR, 2.01 [95% CI, 1.34–3.03])[24] A cross-sectional study performed with 123 patients in Iran found that hsa-miR-126-3p expression was decreased with the rise of COVID-19 disease grade. Also, that hsa-miR-126-3p expression decreases seen with hospitalized patients who did not respond to treatment[25].

4. Post-COVID-19 arrhythmia ICU/ventilator Use

Meta-analysis of 254 studies on 159,698 adult hospitalized patients shows that in ICU patients, the second most prevalent cardiovascular complication was arrhythmia, 33% behind hypertension 43%[8]. Systemic review and meta-analysis of 23 high-quality retrospective studies on 4631 patients found that arrhythmia was 3.1% of the nonsevere disease/non-ICU relative to 43.8% in the severe disease/ICU group. Patients with new-onset arrhythmia were at increased risk of severe disease/ICU admission (RR 13.09, 95% CI 7.00 to 24.47, P < 0.001; I2 = 42.0%)[26]. In a cohort study of 166 patients, multiple regression analyses after correcting for variances in baseline variables show that arrhythmia incidence is a stronger predictive factor for the hospitalization length and the necessity for mechanical ventilation than prevalence of cardiovascular disease and age; nonetheless, preceding cardiovascular disease had a stronger predictive implication than cardiac arrhythmia concerning in-hospital mortality [22]. The study performed with retrospective analysis of 319 patients' multivariate logistic regression also showed that atrial fibrillation (OR = 6.9, 95% CI 2.683–18.213, p < 0.001) and sinus tachycardia (OR = 6.2, 95% CI 2.920–13.222, p < 0.001) were separate risk factors for ventilator use[27]. 'The cohort study performed with 390 patients revealed that ICU patients had more arrhythmic prevalence than non-ICU patients (21% vs 5.7%; p 0.003)[23].

5. Post-COVID-19 atrial tachycardia/atrial flutter/atrial fibrillation

The study of 850 patients with COVID-19 ECG showed that most frequent rhythm is sinus rhythm (65.6%) after that sinus tachycardia (25.9%) then atrial fibrillation or flutter (4.9%)[28]. The retrospective observational cohort study of 756 patients found that a majority of patients had normal sinus rhythm (94.4%) and 5.6% of patients had atrial fibrillation/flutter[29]. The cohort study performed with 9564 patients shows that 17.6% of patients experienced atrial fibrillation, with 12.5% of those having new-onset atrial fibrillation. In-hospital mortality of patients with atrial fibrillation was higher (54.3% vs 37.2%). Atrial fibrillation, especially new-onset atrial fibrillation, was separately related with in-hospital mortality. Also, patients in the hospital experiencing atrial fibrillation are more likely to have mechanical ventilation treatment than those who do not (37.5% vs 15.9%; P < 0.0001)[30]. The retrospective study of 463 patients' multivariate logistic regression analyses shows that atrial tachycardia/atrial fibrillation/atrial flutter (OR, 5.23) were separate risk factors for critical disease. Patients with elevated IL-10 levels had significantly more frequent atrial arrhythmia than patients who had physiological levels. The adjusted odds ratio of death during hospitalization for atrial arrhythmia was 3.51 (95%CI, 1.74 to 7.08)[21]. A single-center study of 658 patients found that 5% of patients had onset atrial fibrillation. In this study, existence of diffuse lung infiltration on thorax CT was found to be the strongest separate factor related to new-onset atrial fibrillation formation[31]. In an observational cohort study of 1053 patients, 14.6% of them had atrial fibrillation and 3.8% of them had atrial flutter/tachycardia; among these patients, 61% had no known record of atrial fibrillation or atrial flutter/tachycardia. Overall, in-hospital mortality was greater among patients with atrial fibrillation or atrial flutter/tachycardia compared to those without (39.2% vs. 13.4%; p < 0.001). After adjusting for age, race, and gender, atrial fibrillation and atrial flutter/tachycardia had increased 30 days all-cause mortality (adjusted odds ratio [OR]: 1.93; 95% CI: 1.20–3.11; p = 0.007). This was the case even more so with new-onset atrial fibrillation or atrial flutter/tachycardia (adjusted OR: 2.87; 95% CI: 1.74–4.74; p < 0.001). Multivariable regression analysis shows that male sex, age, renal disease, prior atrial fibrillation, and hypoxia on presentation were separately related to incidence of atrial fibrillation and atrial flutter/tachycardia[32]. In a multicentric cross-sectional retrospective analysis of 431 patients, atrial fibrillation or flutter was detected in 22% of them and it was more common with patients older than 74 years of age (31% vs. 15%, P < 0.001) [33]. A retrospective multicenter observation study of 414 hospitalized patients with COVID-19 atrial fibrillation relapse (RR:7.09; P < 0.001) found a link with ventricular tachycardia. Incident sustained tachyarrhythmias did occur in 21% of the patients in this study, and atrial fibrillation was the most frequent arrhythmia seen with the patients (18.45%). Atrial fibrillations separate predictors who were male gender, of older age, and had coronary artery disease and heart failure. Atrial fibrillation was significantly related to incident ventricular tachycardia[34]. In a cohort study performed with 3011 patients found that the most common cardiac complication was atrial fibrillation (4.7%)[35]. A retrospective observational cohort study of 1053 patients showed that prevalence of atrial fibrillation/atrial flutter was in 15.8%, with (9.6%) of these being new diagnosis. Atrial fibrillation/atrial flutter had increased in-hospital mortality relative to the patients who did not have these conditions (39.2% versus 13.4%; P < 0.001)[32]. A retrospective cohort study with 887 patients showed that the mortality rate within 30 days was 59% for patients who had atrial fibrillation/atrial flutter relative to 21%

of patients with other rhythms. This study found that the mortality rate was similar between patients with previous atrial fibrillation/atrial flutter compared to the newly diagnosed ones (56% vs 62%)[36]. A study performed with 135 patients also found that atrial fibrillation patients had lower levels of miR-126 relative to controls ($P < 0.01$). Furthermore, patients with persistent atrial fibrillation also had substantially lower levels of miR-126 relative to proximal atrial fibrillation ($P < 0.05$)[37].

6. Post-COVID-19 ventricular fibrillation and ventricular tachycardia

A retrospective study of 463 patients found that elevated IL-10 levels had significantly more frequent ventricular arrhythmia than patients who had physiological levels. The adjusted odds ratio of death during hospitalization for ventricular arrhythmia was 3.41 (95%CI, 1.13 to 10.24)[21]. A cohort study of 800 patients found that the ones who died experienced more primary end point events of acute malignant arrhythmia such as ventricular tachycardia/ventricular fibrillation or atrioventricular block (17% versus 4%; $P = 0.01$) relative to those who were discharged[38]. A retrospective multicenter observational study of 414 hospitalized patients with COVID-19 atrial fibrillation incident found that they were significantly associated with incident ventricular tachycardia. Ventricular tachycardia occurred in 3.4% of patients and was independently related to recurrent atrial fibrillation. Ventricular tachycardia incident (RR: 2.55; P:0.003) was a predictor of in-hospital mortality[34]. A cohort study performed with 3011 patients found that malignant ventricular rhythm abnormalities were observed in 0.5% of patients[35]. A retrospective observational cohort study of 1053 patients found that prevalence of ventricular tachycardia/ventricular fibrillation was in 2.6% of patients. 1.2% of patients had cardiac arrest due to ventricular tachycardia/ventricular fibrillation. Patients who have tachycardia/ventricular fibrillation had increased in-hospital mortality relative to patients who did not have these conditions (59.3% versus 16.4%; $P < 0.001$,)[24]. Retrospective case series of 5 found that ARDS patients with severe COVID-19 who have normal baseline cardiac function died of ventricular arrhythmias[39] Table 4.

7. Post-COVID-19 premature atrial and ventricular beat

A retrospective study of 463 patients' multivariate logistic regression analyses showed that premature atrial beats (OR, 3.29) and premature ventricular beats (OR, 3.98) were separate risk factors for critical illness[21]. A retrospective observational cohort study of 756 patients found that atrial premature contractions occurred in 7.7% of patients and ventricular premature contractions occurred in 3.4% of patients. Atrial premature contractions were linked with a rise in mortality (OR 2.57, 95% CI 1.23–5.36, $P = 0.01$)[29]. In a retrospective observational cohort study of 1053 patients, premature ventricular contractions was found in 13% of patients[24].

8. Post-COVID-19 conduction disorders

A retrospective observational cohort study of 756 patients in New York found increased mortality with a right bundle branch block or wave inversion (OR 3.49, 95% CI 1.56–7.80, $P = 0.002$), also with an intraventricular conduction block (OR 2.61, 95% CI 1.32–5.18, $P = 0.002$). Atrioventricular block was prevalent in 2.6% of patients, 2.5% of them had a first-degree block, and 0.1% of them had sinus rhythm with complete heart block and a junctional escape rhythm. Aberrant intraventricular conduction was found in 11.8% of patients, with the right bundle branch block being in 7.8% of them, the left bundle branch block in 1.5% of them, and the nonspecific intraventricular conduction block in 2.5%[29]. A retrospective cross-sectional multicentric study with 431 patients found that 9% had incomplete RBBB and 11% had complete RBBB. Complete RBBB was more common with patients older than 74 years (16% vs. 8%, $P = 0.007$). Also, left anterior hemiblock was more common with patients older than 74 years (11% vs. 4%, $P = 0.01$)[33]. A cohort study performed with 3011 patients found that arrhythmia and conduction disorders occurred in 8.6% of patients[35]. A

Table 4. Post-COVID-19 ventricular arrhymia and ventricular tachycardia.

AUTHORS	STUDY DESIGN	STUDY SIZE	RESULTS
Guan et al. [21]	Retrospective	463	Elevated IL-10 levels had significantly more frequent ventricular arrhythmia than patients who had physiological levels. The adjusted odds ratio of death during hospitalization for ventricular arrhythmia was 3.41 (95%CI, 1.13 to 10.24).
Turagam et al. [38]	Cohort	800	Patients found that the ones who died experienced more primary end point events of acute malignant arrhythmia together with ventricular tachycardia/ventricular fibrillation or atrioventricular block (17% versus 4%; P = 0.01) than relative to those who are discharged.
Russo et al. [34]	Retrospective multicenter observation	414	Ventricular tachycardia occurred in 3.4% of patients and was independently related to recurrent atrial fibrillation. Ventricular tachycardia incident (RR: 2.55; P:0.003) was the predictor of in-hospital mortality.
Linschoten et al. [35]	Cohort	3011	Malignant ventricular rhythm abnormalities were observed in 0.5% of patients.
Peltzer et al. [24]	Retrospective observational cohort	1053	Ventricular tachycardia/ventricular fibrillation was in 2.6% of patients. 1.2% of patients had cardiac arrest due to ventricular tachycardia/ventricular fibrillation. These patients also had increased in-hospital mortality relative to the patients who do not have those conditions (59.3% versus 16.4%).
Abrams et al. [39]	Retrospective case series	5	ARDS patients with severe COVID-19 who have normal baseline cardiac function died of ventricular arrhythmias.

Table 5. Post-COVID-19 ECG changes.

AUTHOR	STUDY DESIGN	SAMPLE SIZE	RESULTS
Romero et al. [40]	Case series	195	Diffuse T wave inversion when the accompanying troponin elevation mortality rate was substantially increased than the absence of both (80% vs. 13%).
Mccullough et al. [29]	Retrospective observational cohort	756	There was increased mortality in patients with localized T- nonspecific repolarization abnormality (OR 2.31). In this study, 19.3% of patients had an abnormal axis and of those, 13.8% of patients had left axis and 5.5% of patients had a right or right superior axis deviation.
ertini et al. [33]	Multicentric cross-sectional retrospective analysis	431	Pathologically negative T waves were present in 14% of patients, and QT-corrected interval more than 460 ms were present in 38) of patients, both of which were more common in patients older than 74 years. The S1Q3T3 pattern was in separation or accompanied by the right bundle branch block (RBBB). Isolated RBBB (complete or incomplete) and S1Q3T3 patterns were deemed indicators of acute right ventricular pressure overload (RVPO) and 30% of patients had ECG showing signs of acute RVPO. 10% of patients had a just S1Q3T3 pattern, 9% had incomplete RBBB, and 11% had complete RBBB. RBBB associated with the S1Q3T3 pattern was more common in patients older than 74 years (7% vs. 1%).
Li et al. [41]	Retrospective observational	135	40% of patients had ST-T abnormalities, 37.8% of them had total arrhythmia, and 14.8% of them had left atrial abnormality. ICU patients were more likely to have ST-T abnormalities (65.2% vs 34.8), QTc interval prolongation (34.8% vs 8.9), and pathological Q wave (30.4% vs 3.6%; $p < 0.001$) than non-ICU patients.
Poterucha et al. [36]	Retrospective cohort	887	Combination of high-sensitivity cardiac troponin T ≥ 20 ng/L and abnormal ECG was related to the increase in 30-day mortality relative to normal ECG and high-sensitivity cardiac troponin T < 20 ng/L (49% vs 6%).

retrospective observational cohort study of 1053 patients found that atrioventricular block was in 0.4% of the patients[24].

9. Post-COVID-19 ECG changes

A case series of 195 patients found that diffuse T wave inversion with an accompanying troponin elevation mortality rate was notably higher than the absence of both (80% vs. 13%, p: 0.02)[40]. A retrospective observational cohort study of 756 patients in New York found increased mortality in patients with localized T-nonspecific repolarization abnormality (OR 2.31, 95% CI 1.27–4.21, P = 0.006). In this study, 19.3% of patients had an abnormal axis and of those patients, 13.8% had left axis and 5.5% had a right or right superior axis deviation[29]. A retrospective cross-sectional multicentric study with 431 patients showed that pathologically negative T waves were present in 14% of patients and the QT-corrected interval of more than 460 ms was present in 38% of patients, both of which were more common in patients older than 74 years. The S1Q3T3 pattern was in separation or accompanied by the right bundle branch block (RBBB). Isolated RBBB (complete or incomplete) and S1Q3T3 patterns were assumed as signs of acute right ventricular pressure overload (RVPO), and 30% of patients had ECG that showed signs of acute RVPO. 10% of patients had only a S1Q3T3 pattern, 9% had incomplete RBBB, and 11% had complete RBBB. RBBB associated with the S1Q3T3 pattern was more common in patients older than 74 years (7% vs. 1%, P = 0.002)[33]. A retrospective observational study in Wuhan, China, with 135 patients found that 40% of them had ST-T abnormalities and 37.8% of them had total arrhythmia and 14.8% of them had left atrial abnormality. Patients in ICU were more likely to have ST-T abnormalities (65.2% vs 34.8; p = 0.007), QTc interval prolongation (34.8% vs 8.9%; p = 0.003), and pathological Q waves (30.4% vs 3.6%; p < 0.001) than non-ICU patients[41]. A retrospective cohort study with 887 patients showed that combination of high-sensitivity cardiac troponin T ≥ 20 ng/L and abnormal ECG was associated with increased 30-day mortality relative to normal ECG and high-sensitivity cardiac troponin T < 20 ng/L (49% vs 6% P < 0.001)[36]. Also, many different studies found that drug combinations such as hydroxychloroquine and azithromycin are related to elongation of QT values with COVID-19 patients [42–45] Table 5.

10. Electrophysiology-related interventions post-COVID-19 outbreak

A cross-sectional descriptive study performed by using the database of the largest national reference hospital in Peru found a decrease of pacemaker implant by 73% (95% CI: 33–113; P < .001) during the COVID-19 pandemic period. Also, after social restrictions, implant procedures reduced by 82% relative to the past 3 years in the same period[46]. A survey performed with doctors from 84 arrhythmia centers in Italy found that over half of the centers reported more than a 50% decrease in elective pacemaker implantation. Only 4.8% of centers reported no significant changes. Also, 92.9% of partaking centers stated a substantial decrease in implantable cardioverter-defibrillator (ICD) implantations for primary prevention in the same period and 65.5% of these centers describe a decrease in the number of implantations by more than half. Only 7.1% of centers reported no significant changes. 70.0% of partaking centers describe a substantial decrease in cardiac implantable electronic devices implemented in emergency conditions like temporary and definitive pacemaker insertions for severe life-threatening bradyarrhythmia and ICD implantations that are used for secondary prevention through the pandemic period relative to the same time of the preceding year. No substantial changes were reported at 22.6% of centers. 10.0% of centers reported a substantial rise. 54.8% of centers reported a substantial decrease of ablation procedures in the emergency setting for the duration of the COVID-19 pandemic period relative to the same time of the previous

year. 40.5% of centers reported no substantial change. Only 4.8% reported a significant rise[47]. Data from eleven counties in the Philadelphia region found that up to six weeks before versus six weeks after the local COVID-19 outbreak, arrhythmia ablation procedures reduced by 80%. Device implantations were also reduced by 47% after the regional COVID-19 outbreak. Permanent pacemakers decreased by 56%, ICD procedures decreased by 78%, and generator replacement decreased by 40%[48]. A study performed with data from two cardiac catheterization laboratories in New Zealand found that a decreased number of electrophysiological procedures were largely caused by the reduced number of elective procedures. The number of inpatient electrophysiology procedures was relatively constant[49]. An observational study performed in Catalonia found that after lockdown was declared on 14 March 2020, there was a 54.7% decrease in the number of pacemaker implantations compared to the pre-COVID-19 period[50].

11. Expert opinion

More than a year later, our understanding of COVID-19 showed that the disease has had many adverse cardiovascular risk factors and complications. Substantial numbers of patients were adversely affected by this. At this point, one of the most important considerations in assessing patients with COVID-19 is to determine the burden on each patient's cardiovascular system. Many studies found that cardiovascular system problems before the infection or secondary to infection are related to mortality and ICU/ventilator use. Therefore, it is imperative for clinicians to have high clinical suspicion of any adverse effects with these patients. There are still not enough studies for some of the specific arrhythmic complications of COVID-19. Atrial arrhythmia was the most studied and most common arrhythmia caused by COVID-19 infection. Atrial arrhythmia was associated with mortality and ICU/ventilator use. Diffuse infiltration on thorax CT, certain conditions, IL-10, cardiac troponin I, and other biomarkers were associated with atrial arrhythmia. Patients with these findings can have close follow-up for atrial arrhythmia, and its complications before more serious adverse effects can occur. Ventricular arrhythmia is also associated with an increase in mortality. One study found that ventricular tachycardia was independently associated with atrial fibrillation and ventricular tachycardia was a predictor of in-hospital mortality. Atrial and ventricular premature beats were associated with critical illness, and atrial premature beat was associated with an increase in mortality. Increases in mortality were also seen with different types of conduction blocks. There were many different ECG changes associated with COVID-19 infection. Changes like ST-T abnormalities and pathological Q waves were related to the rise in mortality and ICU treatment. Also, one study found that abnormal ECG and high-sensitivity cardiac troponin T were related to a rise in mortality. Many studies from different regions of the world found that electrophysiological procedures decreased in numbers although some of them were related to fewer elective procedures. These findings raise important questions about inadequate interventions in some patients. Considering the significant relationship of COVID-19 with cardiac arrhythmias, these short comings in our healthcare systems may cause avoidable adverse outcomes. Also, with this disease being relatively new, there should be in-depth studies for long-term effects of COVID-19 infections specifically but not limited to the cardiovascular system. All these different studies show us that there are many distinct types of arrhythmias that can be seen with COVID-19 patients and certain at-risk patients for these arrhythmias are an important subpopulation of patients who require an in-depth understanding so they can be prioritized for treatment.

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