

Cardiac Arrhythmias and COVID-19 – a Meta-analysis of Recent Reports

Husam M. I. Salah

Department of Internal Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas
<https://orcid.org/0000-0002-9549-7907>

Jawahar L. Mehta (✉ MehtaJL@uams.edu)

Department of Medicine, Cardiology Division, University of Arkansas for Medical Sciences, Little Rock, Arkansas

Research Article

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Abstract

Introduction: The 2019 novel coronavirus disease (COVID-19) is a current pandemic. Cardiovascular manifestations of COVID-19 have been described in many studies; however, no studies have examined the prevalence and characterizations of cardiac arrhythmias among patients with COVID-19 infection. The aim of this meta-analysis was to examine the prevalence of cardiac arrhythmias among patients with COVID-19 infection.

Method: PubMed, Google Scholar, and ResearchGate databases were searched for relevant articles from inception until June 14, 2020. Inclusion criteria were: 1) Cohort studies or case series studies; 2) Study population included individuals with confirmed COVID-19 infection; 3) Arrhythmic events were reported in the study. All other studies were excluded. MedCalc software was used to analyze the pooled data. The random-effect model was utilized to obtain the prevalence of arrhythmia among the included patients and its 95% confidence interval. Cochran's Q and I² index were used for heterogeneity measurements. The main planned outcome was the prevalence of arrhythmia among patients with COVID-19 infection.

Results: Thirteen studies with a total of 2861 patients met our inclusion criteria. The prevalence of arrhythmia among patients with COVID-19 infection was 8.1% (95% CI [6.10, 10.37]). 82.8% of the patients who had arrhythmia has severe illness (95% CI [70.916, 92.124]).

Conclusion: The prevalence of arrhythmias among patients with COVID-19 infection is 8.1%, which is much higher than in the general population (2.35%).

Introduction

In December 2019, an outbreak of new viral illness called the 2019 novel coronavirus disease (COVID-19) occurred in Wuhan, China.¹ On March 11, 2020, the World Health Organization characterized COVID-19 infection as a pandemic. Most of the manifestations of COVID-19 infection are related to the respiratory system; however, COVID-19 infection appears to be a systemic disease. Extra-respiratory manifestations, such as cardiovascular, renal, gastrointestinal, neurological, olfactory, gustatory, ocular, cutaneous, and hematological manifestations, have been reported in various studies.² Cardiac manifestations of COVID-19 infection include myocardial injury, myocarditis, heart failure and cardiac arrhythmias. The prevalence and characterizations of cardiac arrhythmias in COVID-19 infection has not been well-studied. In this study, we show the prevalence of cardiac arrhythmias among patients with COVID-19 infection. To the best of our knowledge, this is the first systematic review and meta-analysis to examine this.

Method

We searched the PubMed, Google Scholar, and ResearchGate databases for relevant articles from inception until June 14, 2020. Inclusion criteria were: 1) Cohort studies or case series studies; 2) Study population included individuals with a confirmed COVID-19 infection; 3) Arrhythmic events were reported

in the study. The prevalence of arrhythmias among the included patients was calculated. As studies reported different definitions of the disease severity, we formed two groups in our analysis: 1) patients with severe illness, defined as patients with an intensive care unit (ICU) level of care, or patients who met the severe or critical illness criteria based on the trial version 7 or who experienced death during hospitalization; 2) patients with non-severe illness, defined as patients who did not meet the criteria for inclusion in the severe illness group. A random effect model was utilized. Results were reported with 95% confidence interval (CI). Cochran's Q and I² index were used for heterogeneity estimation.

Results

The initial search yielded 387 articles. After careful assessment, only 13 studies with a total of 2861 patients were included. Of those, 235 patients had an arrhythmic event. The prevalence of arrhythmia among patients with COVID-19 infection was 8.1% (95% CI [6.10, 10.37]). The I² index was 71.29%. (*Figures 1.*) The pooled mean age was 61.8 years. The pooled sample had a slight male predominance (56%). The type of arrhythmia was reported in 2 studies only. Atrial arrhythmias were the most common and occurred in 96% of the cases. Further classification of the atrial arrhythmia types was only reported in one study, and atrial fibrillation was the most common type of atrial arrhythmias as it occurred in 90% of the atrial arrhythmia cases.

Eleven studies were included for the analysis of the association between arrhythmia and illness severity; one of the 13 studies did not report illness severity and one only included fatal cases of COVID-19; therefore, both were excluded. 82.8% of the patients who had arrhythmia were classified in the severe illness group (95% CI [70.916, 92.124]). The I² index was 69.25%.

Discussion

Our meta-analysis shows that the prevalence of arrhythmia among patients with COVID-19 is 8.1%, which is a significantly higher prevalence compared to the general population. In the study by Khurshid et al⁴ in one-half million adults with a median age of 58 years, the prevalence of arrhythmia was 2.35%. In our study, 82.8% of patients with COVID-19 infection that exhibited arrhythmias had severe illness. We hypothesize that the high prevalence of arrhythmia among patients with COVID-19 infection compared to the general population may be related to:

1. Acute cardiac injury: Several studies have shown an association between COVID-19 infection and acute cardiac injury.⁴ The exact mechanism of cardiac injury in COVID-19 is unknown, and might be multi-factorial, such as direct viral invasion of the cardiac tissue by the virus, severe hypoxia, poor perfusion, formation of microthrombi in the coronary arteries, and cytokine-related inflammatory process.
2. Medications treat COVID-19 infection: Despite the lack of a clear evidence to support their benefits, hydroxychloroquine and azithromycin are widely used in the treatment of patients with COVID-19 infection.⁵ Both these medications can cause prolongation of the QT interval. However, QT interval

prolongation typically precipitates ventricular arrhythmias (e.g., Torsade de pointes). As observed in our study, the vast majority of the arrhythmias were atrial arrhythmias (96%), which makes a significant association between the use of these medications and our results less likely.

3. Electrolyte abnormalities: A pooled analysis by Lippi et al⁶ showed that COVID–19 infection can be associated with lower serum concentrations of sodium, potassium, and calcium.
4. Sympathetic system over-activation: Sepsis secondary to COVID–19 infection can lead to sympathetic system activation, which can lead to cardiac arrhythmias. Additionally, the use of vasopressors (e.g., dobutamine, norepinephrine) in patients with hypotension can increase the risks of arrhythmias. This may also explain the severe nature of illness in most patients with arrhythmias.

Conclusion

The prevalence of arrhythmias among patients with COVID–19 infection is 8.1%, which is much higher than in the general population. Atrial arrhythmias are more common than ventricular arrhythmias among these patients. Patients with concurrent COVID–19 and arrhythmias are more likely to have severe illness.

Declarations

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Conflicts of interest/Competing interests: none

Ethics approval: N/A **Consent to participate:** N/A **Consent for publication:** N/A

Availability of data and material: available upon request

Code availability: N/A

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Figures

Study	N	Proportion of arrhythmia (%)	95% CI	Weight (%)	
				Fixed	Random
Goyal et al	393	7.379	4.997 - 10.426	13.71	10.51
Ceo et al	102	17.647	10.807 - 26.448	3.58	7.13
Wang et al	339	10.324	7.297 - 14.066	11.83	10.24
Chen et al	51	3.922	0.478 - 13.459	1.81	5.00
Hou et al	101	6.931	2.832 - 13.760	3.55	7.10
Yu et al	226	9.292	5.844 - 13.853	7.90	9.36
Argenziano et al	1000	7.900	6.304 - 9.749	34.83	11.70
Jin et al	45	6.667	1.397 - 18.268	1.60	4.63
Zhang et al	221	10.860	7.083 - 15.727	7.72	9.30
Sun et al	63	3.175	0.387 - 11.002	2.23	5.63
Yang et al	205	2.439	0.797 - 5.600	7.17	9.12
Lei et al	34	23.529	10.746 - 41.171	1.22	3.86
Du et al	81	2.469	0.300 - 8.636	2.85	6.41
Total (fixed effects)	2861	8.099	7.127 - 9.157	100.00	100.00
Total (random effects)	2861	8.112	6.109 - 10.371	100.00	100.00

Test for heterogeneity

Q	41.7914
DF	12
Significance level	P < 0.0001
I ² (inconsistency)	71.29%
95% CI for I ²	49.60 to 83.64

Figure 1

Table summarizing the prevalence of arrhythmias in the included studies and the result of the pooled analysis of these studies with its heterogeneity measurements.