Tachyarrhythmias in COVID19 Patients: A Systematic Review and Meta-Analysis

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Abstract

Background: Studies have shown that cardiovascular disease is associated with an increased risk of mortality in patients with COVID-19. The incidence of tachyarrhythmias and how it affects prognosis is not well determined. This systematic review and meta-analysis aimed to evaluate the incidence of tachyarrhythmias in patients with COVID-19 and their implications on patient prognosis.

Methods: We performed a search PubMed, and BVS Salud databases. The primary endpoint of the study was poor outcomes including mortality, tachyarrhythmias, and COVID-19.

Results: A total of 6 studies including 2232 patients were analyzed. The incidence of tachyarrhythmias in patients with COVID-19 was 7.9% (95% CI: 15.39, 143.26; I2: 0%). Supraventricular tachycardia was common, occurring in 5% (OR: 40.79, [95% CI: 11.18, 148.83, I2: 0%]). All-cause mortality had an (OR: 27.96, [95% CI: 7.59, 102.98, I2: 37%]) and arrhythmia-related mortality had an (OR: 4.21, [95% CI: 0.91, 19.45, I2: 8%]).

Conclusion: Tachyarrhythmia incidence and tachyarrhythmia-related mortality appears to be low in patients with COVID-19.

Keywords: Arrhythmias; Covid-19; Rhythm; Disorders; SARS-CoV-2; Cardiovascular Disease

Introduction

Coronavirus was identified as the cause of a cluster of pneumonia cases in Wuhan, a city in the Hubei Province of China, in December 2019, being later designated the disease COVID-19, which stands for coronavirus disease 2019 [1]. Current numbers since it has been identified and declared a pandemic is now over 84 million confirmed cases, with almost 2 million deaths, according the World Health Organization and European Centre for Disease Prevention and Control data, updated on the last week of December 2020.

The spectrum of symptoms may vary from asymptomatic to mildly symptomatic in about 80 percent of the cases, severe and critical disease in 14 and 5 percent of the cases, respectively [2]. Among pediatric patients, severe and critical forms of the disease appear to be less frequent [3,4]. It is now recognized, that cardiovascular disease among other comorbidities increase the risk of severe illness and hence the mortality [2,6]. However, little is known about the role of cardiac arrhythmias (tachyarrhythmias) and how it affects mortality among patients with COVID-19. We conducted a systematic review and meta-analysis, to investigate the incidence of tachyarrhythmias among the patients with COVID-19 infection.

Methods

We searched the PubMed, and BVS Salud databases through July 25 2020 using the MeSH term ['ventricular tachycardia' and 'CO-VID19'] infection according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement, PRISMA [6]. Two investigators working independently screened all titles and abstracts of the studies for eligibility. Duplicate citations were discarded after the preliminary search results were obtained. Furthermore, the references lists of all included studies and relevant review studies were also manually searched.

Inclusion criteria

The inclusion criteria were based on (i) Research article with 10 patients or more; (ii) Study population included patients with confirmed COVID-19 infection; (iii) Arrhythmic events were reported in the study.

Exclusion criteria

We excluded the following studies: (i) articles other than original research articles; (ii) studies with a sample of less than 10 or case reports; (iii) non-English language articles.

Data extraction

Data extraction was performed independently by two of the authors. We used standardized extraction forms that included author, year, study design, age, sex, cardiovascular diseases, history of hypertension and diabetes mellitus, respiratory comorbidities, follow-up duration, arrhythmia and mortality. The primary outcomes were all-cause mortality, arrhythmia-related mortality. Secondary outcomes included overall incidence of tachyarrhythmias and incidence of different types of ventricular, and supraventricular arrhythmia.

Quality appraisal

The quality appraisal was established according to Le Floch and colleagues criteria [7]. This tool appraises the quality of the study based on the following questions: Did this article give an answer to the research question? Did the article focus clearly on the research question? Was the methodology appropriate? Do you believe the results? (Can it be due to chance, bias or confounding?). To be included, the article had to score "yes" on every question.

Statistical analysis

All comparisons were estimated on an intention-to-treat basis. The categorical variables were described as percentages and estimated by odds ratio (OR) with a two-tailed 95% confidence interval (CI). Continuous variables were described as mean and standard deviation and analyzed by weighted mean difference (WMD). Statistic value I^2 assessed by Q test was used to quantify the degree of interstudy heterogeneity. Considering the intrinsic variation in study design, we calculated the OR and WMD estimates using random-effects model for all comparisons. All P values were two-tailed, and the statistical significance was set at 0.05. Statistical analyses were performed using the Revman software package (Review Manager, Version 5.4. Copenhagen, The Nordic Cochrane Centre, the Cochrane Collaboration).

Results

Study selection

A flow diagram of study selection is shown in figure 1. A total of 29 papers were initially identified, of which 18 were excluded for not meeting the inclusion criteria. After review of the full texts of the 11 remaining studies, 5 were excluded based on the absence of data and duplicates. Thus, six articles published in 2020 with a total of 2232 patients were included in this systematic review [8-13].
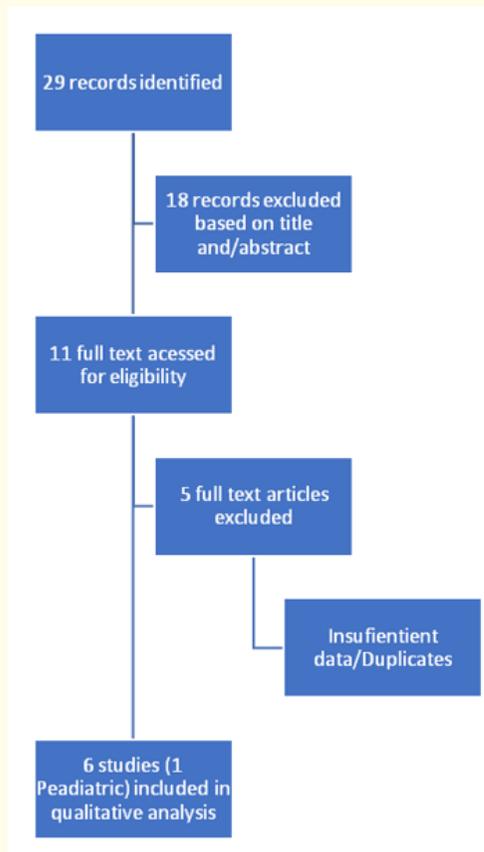
Figure 1: PRISMA (PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-analyses).

In our meta-analysis overall tachyarrhythmias incidence was 7.9%, RR: 46,95, [95% CI: 15.39, 143.26, P = 0.88, I^2: 0%] (Figure 2). Regarding different types of arrhythmia, the present analysis showed that ventricular tachycardia accounted for 0,95% of the cases, OR: 9.38, [95% CI: 2.53, 34.8, P = 0.91, I^2: 0%] (Figure 3) and the incidence of supraventricular tachycardia, including both atrial fibrillation and atrial flutter was 5,04%, OR: 40.79, [95% CI: 11.18, 148.83, P = 0.73, I^2: 0%] (Figure 4).
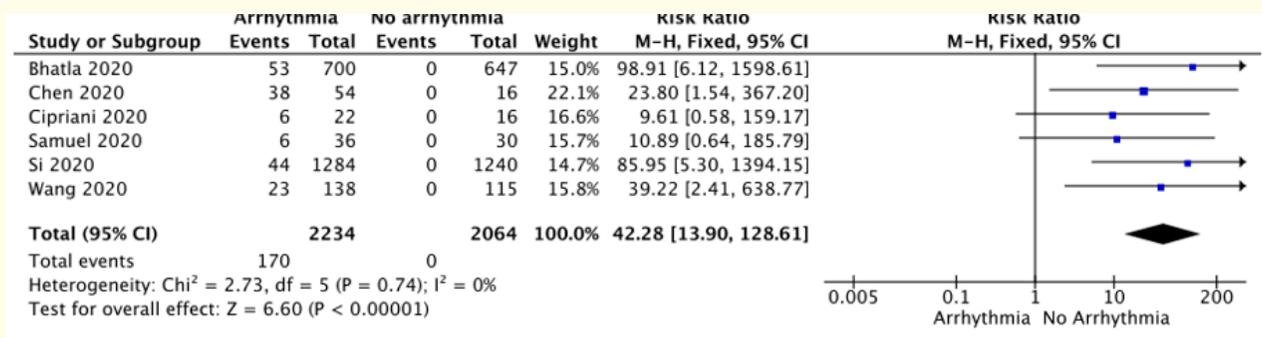
Figure 2: Forrest plot-overall arrhythmias.
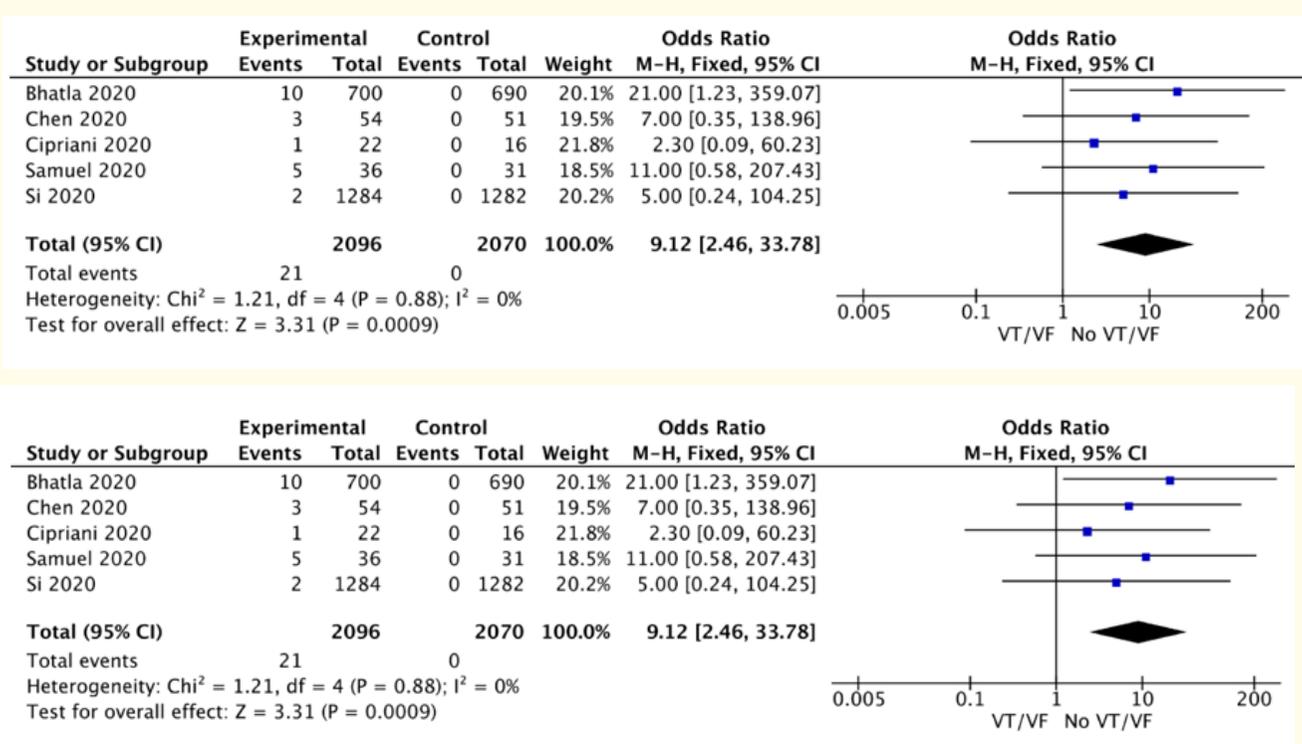
Figure 3: *Forrest plot-Arrhythmia type-ventricular tachycardia/fibrillation.*
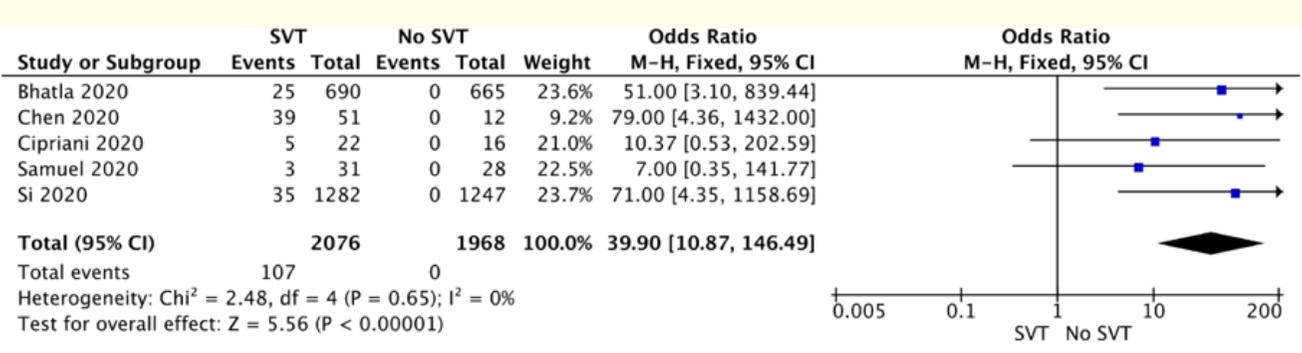
Figure 4: *Forrest plot-Arrhythmia type-supraventricular tachycardia.*

As shown in figure 5 and 6, all-cause mortality had an OR: 27.96, [95% CI: 7.59, 102.98, P = 0.18, I^2: 37%] and arrhythmia-related mortality had an OR: 4.21, [95% CI: 0.91, 19.45, P = 0.35, I^2: 8%], respectively.
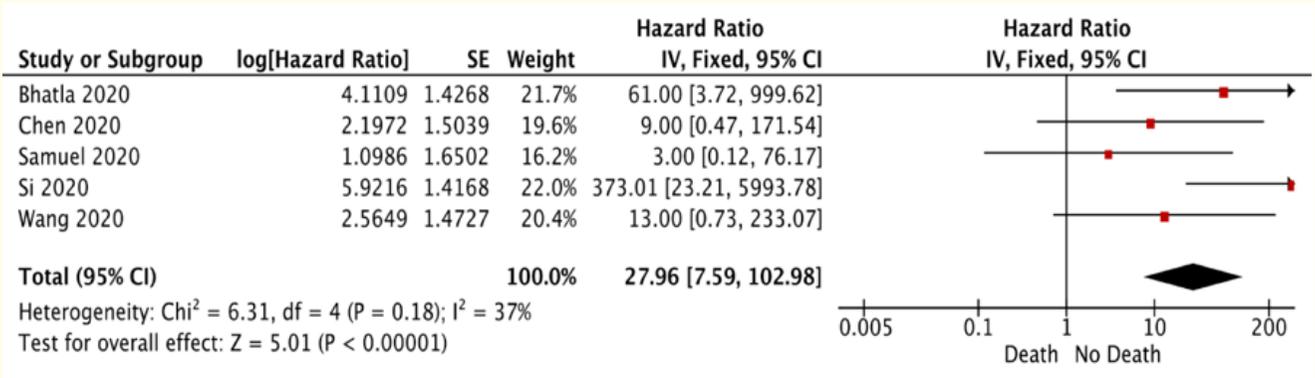
Figure 5: *Forrest plot-All-cause mortality.*
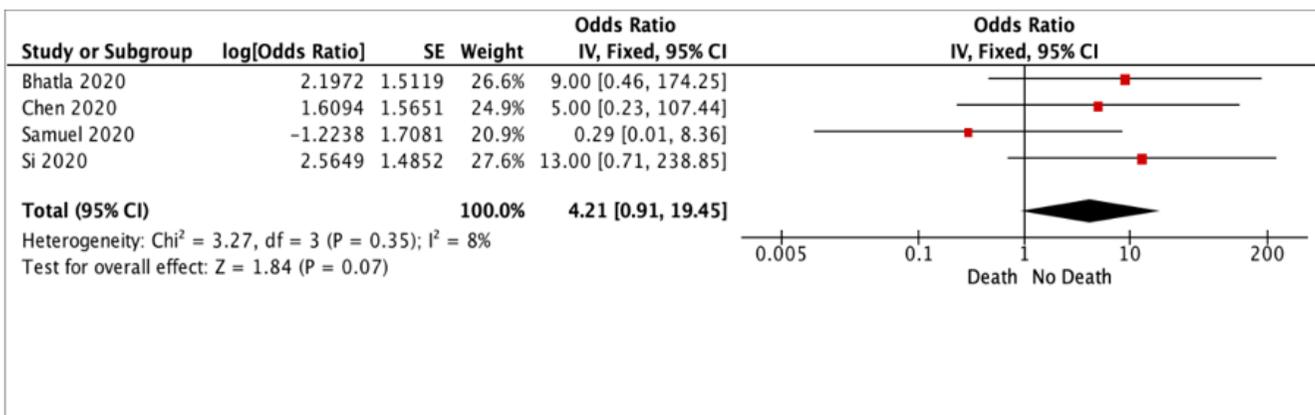
Figure 6: *Forrest plot-Arrhythmia-related mortality.*

Studies	Bhatla., *et al.* 2020	Chen., *et al.* 2020	Cipriani., *et al.* 2020	Samuel., *et al.* 2020	Si., *et al.* 2020	Wang., *et al.* 2020
Sample size, n	700	54	126	36	1282	138
Mean age (yrs)	50	57.6	64	12.6	61.5	56
Male, n (%)	314 (45)	36 (66.7)	22 (82)	20 (57.5)	-	75 (54.3)
Hypertension, n (%)	347 (50)	16 (29,6)	12 (55)	-	-	43 (31.2)
Diabetes, n (%)	182 (26)	25 (46.2)	6 (27)	-	-	14 (10.1)
CAD, n (%)	76 (11)	6 (11,1)	N/A	-	-	20 (14.5)
CKD, n (%)	63 (9)	0	1 (5)	-	-	4 (2.9)
CPOD, n (%)	80 (11)	0	1 (5)	-	-	4 (2.9)

Table 1: *Clinical characteristic of the patients.*

Discussion

Pneumonia complicated by acute respiratory distress syndrome (ARDS), appears to be the most frequent critical manifestation of infection. As a systemic disease, patients may develop cardiac involvement, manifested or not, by conduction system disease and subsequently arrhythmias [14].

The present meta-analysis involving 2232 patients show that the overall tachyarrhythmia incidence in patients with confirmed COVID infection was lower than reported in other two meta-analysis [15,16]. In the meta-analysis reported by Pranata., *et al.* the authors found that the incidence of arrhythmia in patients with COVID-19 was 19% but in this study, the authors only report the global incidence of arrhythmias without discriminating its different types [16]. Liao., *et al.* reports an overall incidence of arrhythmia in patients with COVID-19 of 16,9%. In contrast with our study (that included only patient with tachyarrhythmia), Liao., *et al.* included patients with all types of arrhythmia and conduction disorders [16].

We found that the incidence of supraventricular arrhythmias (including atrial fibrillation and flutter) was quite similar to those reported by Liao., *et al.* (8.2%) [16]. In other hand, in critically ill patients requiring mechanical ventilation the incidence of atrial arrhythmias can reach 17.7% as reported in a cohort of 393 patients with Covid-19, in New York city [17].

Regarding ventricular arrhythmias in a study reported by Cho., *et al.* the authors found an incidence of ventricular tachycardia and ventricular fibrillation in 1.4 and 0.7 percent, respectively [18]. This finding is consistent with our meta-analysis, where the incidence of ventricular tachycardia and/or fibrillation were 0,95%. Although, our results contradict with those reported by Liao., *et al.* where the incidence of VT/VF was 3,3% [16]. In a study conducted in patients with myocarditis an incidence of VT and VF were found in 24% and 7%, respectively [19].

The mechanisms of this arrhythmia are not yet clarified but concurrent factors such as acute myocarditis, and drug-related (hydroxychloroquine and azithromycin) may play an important role [19,20].

All-cause mortality had an OR: 27.96, (95% CI: 7.59, 102.98, P = 0.18)]. Although with some degree of heterogeneity I^2 = 37%, the analysis showed a significantly lower overall mortality (P = 0.00001). Several studies have reported mortality rates between 10 - 25 percent [18,21,22]. Arrhythmia-related mortality was found to have an OR: 4.21, (95% CI: 0.91, 19.45, P = 0.35, I^2: 8%], however it was no significant (P = 0.07).

Study Limitations

This analysis has limitations. In the present analysis we did not adjust mortality to factors such as age and comorbidities. Studies included in the present analysis were mostly retrospective and were not intended to directly evaluate the effects of arrhythmias in this population, nor as to compare its effects on mortality. Some studies had small population samples, and because we used a fixed-effect model, the results of the present study may not be extrapolated to the general population. However, the present analysis may shad a light on an ongoing COVID-19 pandemic, and the role it plays on prognosis.

Conclusion

In conclusion, the present meta-analysis included 6 studies (one of which of paediatric population) that reported arrhythmias in COVID 19 patients. Supraventricular arrhythmias were the most frequent in these patients. Arrhythmia-related mortality appears to be low in this group of patients. This is still an ongoing pandemic and more studies need to be conducted, as to acquire more data and establish a direct cause-effect relationship, as well as the long-term effect of the disease in the conduction system.

Conflict of Interests

None to declare.

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None.

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