

Arrhythmias in COVID-19: clinical significance and management

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Abstract

Worldwide spread of coronavirus disease (COVID-19) caused overwhelming mortality rate during preceding half of the year 2020. Although coronavirus infection was known for mostly respiratory tract involvement, novel COVID-19 pandemic showed excessive cardiac mortality and arrhythmic complications. We aimed to summarize current literature and emphasize on underlying pathological mechanisms and global point of view to coronavirus and arrhythmia relationship.

Key words: Coronavirus, COVID-19, arrhythmia

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Introduction

Since December 2019, whole world is threatened by a new pandemic respiratory tract infection (coronavirus disease 2019 or COVID-19) caused by the novel coronavirus (SARS-CoV-2) (1). New pandemic firstly occurred in Wuhan, China (2) and as of this writing total worldwide infected cases has reached over ten millions (3). Although major complications of viral infections are acute respiratory distress syndrome and pneumonia, severe cardiac sequelae were also described (4). There is a surge in serum proinflammatory mediators in SARS-CoV-2 infection and this situation may contribute to pathophysiology of cardiac complications. Cardiac injury was observed in 19% of hospitalized COVID-19 patients and it was found to be associated with high risk for in-hospital mortality (5). It is not gratuitous to speculate arrhythmic complications of SARS-CoV-2, because more and more electrophysiological findings are described such as, an early report from China notified that overall arrhythmia incidence was 17% in hospitalized COVID-19 patients whereas a recent study reported 44% arrhythmia incidence in critically ill cases (6). We sought to bring out a plain, direct and easy to track mini-review about arrhythmia and COVID-19 relationship. While preparing this work, authors utilized online databases in order to find relevant literature; PUBMED and EMBASE, by using following key words: tachyarrhythmia, bradyarrhythmia,

arrhythmia, SARS2-COV and COVID-19.

Historical perspective and arrhythmia data from previous coronavirus pandemics

In 2002, the first human infection due to SARS-CoV was reported. Possible manifestations of disease are listed as hypotension, arrhythmia and sudden cardiac death (7). Sinus tachycardia was claimed to be the most frequently encountered cardiac finding in this patient group in a cohort of 121 patients (8). Mean tachycardia duration was nearly 12 days and mean heart rate was 117 beats/minute. Besides, significant transient sinus bradycardia was also seen in 14.9% of patients. Interestingly, transient atrial fibrillation, which is frequent in critically ill patients, was seen in only one patient. Authors suggested that autonomic imbalance and/or cardiac/pulmonary/circulatory deconditioning were underlying reasons. When it comes to sudden cardiac death, some possible mechanisms were put forward: lung injury leading to hypoxemia that precedes myocardial electrical instability, direct viral damage to myocardial cells and conduction system, previously documented cardiac diseases that were aggravated by infection, increased endogenous catecholamine production leading further to myocardial electrical instability (9).

In 2012, another subtype of coronavirus family, Middle

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East respiratory syndrome coronavirus (MERS-CoV) caused another pandemic with an overall 35% mortality rate, which was more than during previous coronavirus pandemic (10). A meta-analysis documented that overall cardiac arrhythmia incidence was 15.7% (11). Due to MERS-CoV infection occurrence was higher in patients with underlying chronic heart disease; literature is not rich with specific arrhythmia complications in pandemic term.

Global perspective of arrhythmia in current pandemic

In their recent analysis, Bhatla et al. reported a series of 700 COVID-19 cases (12). They sought to evaluate risk of cardiac arrhythmias including incident atrial fibrillation, bradyarrhythmias and nonsustained ventricular arrhythmias in the largest population published until today. They identified 53 arrhythmia-related events including 9 cardiac arrests, 25 incident atrial fibrillation cases, 9 clinically significant bradyarrhythmias, and 10 nonsustained ventricular arrhythmias. Among the assessment of selected variables that included age, sex, race, body mass index (BMI), history of heart failure, coronary heart disease, diabetes, hypertension, chronic renal disease, and intensive care unit (ICU) status on admission, only ICU status emerged as having an association with each arrhythmia category. In unadjusted analysis, admission to the ICU was associated with greater than 10-fold odds of developing each arrhythmia. After adjustment of other parameters, ICU status remained independently associated with incident atrial fibrillation and nonsustained ventricular tachycardia; however, the odds for bradyarrhythmias were rendered insignificant. Only prevalent heart failure was found to be independently associated with bradyarrhythmias. In addition, cardiac arrests were preceded by non-shockable rhythms such as pulseless electrical activity and asystole. In a rather smaller case series, it was detected that patients with abnormal serum troponin levels tend to have a higher rate of mortality and cardiac complications, including ventricular arrhythmias (11.5% vs. 6.2%) (13).

Another brief case series demonstrated exemplary situations of patients with high-grade atrioventricular block, atrial fibrillation, polymorphic ventricular tachycardia and pulseless electrical activity (14). Authors concluded that reported arrhythmia complications did not correlate with severity of lung infection on chest radiograph.

Finally, an online survey, which was sent to worldwide electrophysiology professionals by Heart Rhythm Society (15), demonstrated the severity of arrhythmia complications. Attendants' response showed that nearly 75% of them had COVID-19 patients in their hospitals and the most frequently reported tachyarrhythmia was atrial fibrillation. Most common bradyarrhythmias were severe sinus bradycardia and complete atrioventricular block. Arrest rates due to ventricular arrhythmias and pulseless electrical activity were reported as 4.8% and 5.6%.

Accumulating data point out that there is an increased risk of cardiovascular death in patients with COVID-19 (16). At first glance, underlying mechanism seemed simple: direct viral myocardial tissue invasion and hypoxemia due to critical lung disease that led to further myocardial damage and arrhythmia. Cardiac injury is reflected by elevated serum troponin levels; however, despite the high frequency of arrhythmias in ICU patients only half of them showed increased markers (16). There are likely other mechanisms in charge both related and unrelated to viral infection. First of all, during COVID-19 there is a surge in immune mediators such as interleukin (IL-6). Increased inflammatory cytokines not only induce cardiac sympathetic system and trigger arrhythmias but also, specifically IL-6, can inhibit cytochrome p450 and thereby increase bioavailability of QT-prolonging medications (17).

At this point, the values of immune response dampening medications prevail. Monoclonal antibody treatment with tocilizumab blocks the IL-6 pathway and has potential beneficial effect on COVID-19 survival (16). Other factors for arrhythmia risk are severe electrolyte imbalance of these patients and use of QT prolonging drugs such as hydroxychloroquine and azithromycin. The worldwide survey (15) shows that there is 12.3% discontinuation of these two drugs due to QT prolongation. It is important to remember that most drugs, which are frequently used in intensive care units such as antiemetics, proton pump inhibitors, also prolong QT interval.

Treatment of arrhythmias and reducing arrhythmia risk: what to do or not to do?

As mentioned above, widespread use of hydroxychloroquine and azithromycin in COVID-19 pandemic is a fact. However, current recommendations for use of these drugs are based on small number case series (18) rather than randomized clinical trials. It would be proper for physicians to be vigilant for immediate electrocardiographic changes and be eager to regulate drug dose when needed. Other drugs which are still in use, namely lopinavir and ritonavir, have limited cardiac effects and found to be of small value for COVID-19 treatment, however they may also cause bradyarrhythmias and sinus arrest in COVID-19 patients (19, 20).

On the other hand, when it comes to management of arrhythmias, which are not related with COVID-19 treatment drugs, we are short of options. In a recent commentary, it was suggested to use amiodarone if there was a life-threatening arrhythmia and utilize wearable defibrillators or implantable cardioverter-defibrillators in case of low ejection fraction heart failure at hospital discharge (21).

Conclusion

We suggest that successful struggle with arrhythmias include improving hypoxemia and lung reserve and diminishing anti-inflammatory response and meticulous usage of additional drug therapy.

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References

- Centers for Disease Control and Prevention. Interim clinical guidance for management of patients with confirmed 2019 novel coronavirus (2019-nCoV) Infection. 2020. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-managementpatients.html>.
- Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* 2020; 579: 270-3.
- Coronavirus cases. Worldometer. 2020. www.worldometers.info/coronavirus/.
- Fried JA, Ramasubbu K, Bhatt R, Topkara VK, Clerkin KJ, Horn E, et al. The variety of cardiovascular presentations of COVID-19. *Circulation* 2020; 141: 1930-6. doi: 10.1161/CIRCULATIONAHA.120.047164.
- Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMA*. 2020. <https://doi.org/10.1001/jamacardio.2020.0950>
- Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020; 323: 1061-9. doi: 10.1001/jama.2020.1585
- Xiong TY, Redwood S, Prendergast B, Chen M. Coronaviruses and the cardiovascular system: acute and long-term implications. *Eur Heart J* 2020; 41:1798-800.
- Yu CM, Wong RS, Wu EB, Kong SL, Wong J, Yip GWK, et al. Cardiovascular complications of severe acute respiratory syndrome. *Postgrad Med J*. 2006; 82: 140-4.
- Pan SF, Zhang HY, Li CS, Wang C. Cardiac arrest in severe acute respiratory syndrome: analysis of 15 cases. *Zhonghua Jie He He Hu Xi Za Zhi*. 2003; 26: 602-5.
- Badawi A, Ryoo SG. Prevalence of comorbidities in the Middle East respiratory syndrome coronavirus (MERS-CoV): a systematic review and meta-analysis. *Int J Infect Dis*. 2016; 49:129-133.
- Saad M, Omrani AS, Baig K, Bahloul A, Elzein F, Matin MA, et al. Clinical aspects and outcomes of 70 patients with Middle East respiratory syndrome coronavirus infection: a single-center experience in Saudi Arabia. *Int J Infect Dis* 2014; 29: 301-6.
- Bhatla A, Mayer MM, Adusumalli S, Hyman MC, Oh E, Tierney A, et al. COVID-19 and cardiac arrhythmias. *Heart Rhythm* 2020; S1547-5271(20)30594-4.
- Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA Cardiol* 2020; 5:1-8.
- Kochav SM, Coromilas E, Nalbandian A, Ranard LS, Gupta A, Chung MK, et al. Cardiac arrhythmias in COVID-19 infection. *Circ Arrhythm Electrophysiol* 2020; 13:e008719.
- Gopinathannair R, Merchant FM, Lakkireddy DR, Etheridge SP, Feigofsky S, Han JK, et al. COVID-19 and cardiac arrhythmias: a global perspective on arrhythmia characteristics and management strategies. *J Interv Card Electrophysiol* 2020: 1-8.
- Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Biondi-Zoccai G, et al. Cardiovascular considerations for patients, health care workers, and health systems during the coronavirus disease 2019 (COVID-19) pandemic. *J Am Coll Cardiol* 2020; 75: 2352-71.
- Lazzerini PE, Capocchi PL, Laghi-Pasini F. Systemic inflammation and arrhythmic risk: lessons from rheumatoid arthritis. *Eur Heart J* 2017; 38: 1717-27.
- Gautret P, Lagier JC, Parola P, Hoang VT, Meddeb L, Mailhe M, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label nonrandomized clinical trial [e-pub ahead of print]. *Int J Antimicrob Agents* 2020; 56: 105949.
- Cao B, Wang Y, Wen D, Liu W, Wang J, Fan G, et al. A trial of lopinavir-ritonavir in adults hospitalized with severe Covid-19 [e-pub ahead of print]. *N Engl J Med* 2020; 382: 1787-99.
- Tlegenova Zh.Sh., Zholdin B, Kurmangazin M.S., Khamidulla B.K., Zhailybaev Zh.E. Severe bradyarrhythmia requiring temporary pacemaker in a COVID-19 patient receiving lopinavir/ritonavir treatment: a case report. *Heart Vessels Trasplant* 2020; 4: 79-84.
- Kuck KH. Arrhythmias and sudden cardiac death in the COVID-19 pandemic. *Herz* 2020; 45: 325-6.



The lake in Kiel, Near North Sea. Kiel, Germany, 2013. Marjan Aikimbaeva, Bishkek, Kyrgyzstan