Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Arrhythmias and Intraventricular Conduction Disturbances in Patients Hospitalized With Coronavirus Disease 2019

Nishi H. Patel, MD[a,*], Josh Rutland, MD[b], and Kristen M. Tecson, PhD[b]

Cardiac arrhythmias have been observed in patients hospitalized with coronavirus disease (COVID-19). Most analyses of rhythm disturbances to date include cases of sinus tachycardia, which may not accurately reflect true cardiac dysfunction. Furthermore, limited data exist regarding the development of conduction disturbances in patients hospitalized with COVID-19. Hence, we performed a retrospective review and compared characteristics and outcomes for patients with versus without incident arrhythmia, excluding sinus tachycardia, as well as between those with versus without incident conduction disturbances. There were 27 of 173 patients (16%) hospitalized with COVID-19 who developed a new arrhythmia. Incident arrhythmias were associated with an increased risk of intensive care unit admission (59% vs 31%, p = 0.0045), intubation (56% vs 20%, p <0.0001), and inpatient death (41% vs 10%, p = 0.0002) without an associated increase in risk of decompensated heart failure or other cardiac issues. New conduction disturbances were found in 13 patients (8%). Incident arrhythmias in patients hospitalized with COVID-19 are associated with an increased risk of mortality, likely reflective of underlying COVID-19 disease severity more than intrinsic cardiac dysfunction. Conduction disturbances occurred less commonly and were not associated with adverse patient outcomes. **(Am J Cardiol 2022;162:111−115)**

Mounting evidence shows that patients with coronavirus disease (COVID-19) are at risk of developing arrhythmias.[1-5] Several early publications include sinus tachycardia in their definitions.[6-9] Given that sinus tachycardia is often reflective of systemic disease rather than intrinsic cardiac dysfunction, including it in the definition of arrhythmia may bias such analyses. It is also still unclear if mortality associated with arrhythmias in COVID-19 is driven by disease severity versus primary cardiac dysfunction. Furthermore, limited data exist on conduction disturbances and other electrocardiographic (ECG) abnormalities in COVID-19. Hence, the purpose of this study is to report the incidence of atrioventricular arrhythmias and other ECG abnormalities in patients hospitalized with COVID-19 and to examine their associations with mortality.

All inpatient adults aged 18 years or older hospitalized for COVID-19 from March 2020 through June 2020 were included in this retrospective study. Only those with a confirmed nasopharyngeal polymerase chain reaction test were considered positive for COVID-19. Charts were reviewed for demographic information and medical comorbidities present on admission. ECG and telemetry data were reviewed for abnormalities throughout hospitalization. Any arrhythmia or other abnormality was defined according to standard accepted criteria.[10] Atrial arrhythmias included atrial fibrillation, atrial flutter, frequent atrial premature complexes, and other supraventricular tachycardias such as atrioventricular nodal re-entrant tachycardia or atrioventricular re-entrant tachycardia. Ventricular arrhythmias were defined as ventricular fibrillation, ventricular tachycardia (VT), and ventricular premature complexes in a bigeminal or trigeminal pattern. Sinus bradycardia was considered significant at a heart rate <40 beats/min.[11] Conduction disturbances were defined and analyzed per standard criteria[12] and included atrioventricular conduction defects such as first, second, and third-degree atrioventricular block and intraventricular conduction delays such as right bundle branch block and left bundle branch block. Lesser degrees of intraventricular conduction delays, such as left anterior fascicular block or right anterior fascicular block, were also included. This study was approved by the Institutional Review Board of the Baylor Scott & White Research Institute.

Categorical variables are presented as frequencies and percentages. Continuous variables are presented as median (quartile 1, quartile 3). We compared continuous characteristics of patients with versus without incident arrhythmia using the two-sample *t* test and the Wilcoxon rank sum test, depending on normality. We compared discrete characteristics using the chi-square and Fisher's exact test, depending on the expected cell count. Variables found to be associated with incident arrhythmia were considered for inclusion in a multivariable logistic regression model to assess the joint effect on the outcome of inpatient mortality. We created the adjusted (multivariable) logistic regression model using a data-driven stepwise selection process, which resulted in

[a]WellSpan Health, York Hospital, York, Pennsylvania; and [b]Baylor Heart and Vascular Institute, Baylor Scott & White Research Institute, Dallas, Texas. Manuscript received May 31, 2021; revised manuscript received and accepted August 31, 2021.

See page 114 for disclosure information.

*Corresponding author: Tel: 478-320-8422; fax: 972-982-7128.
E-mail address: nishi.h.patel@gmail.com (N.H. Patel).

0002-9149/
https://doi.org/10.1016/j.amjcard.2021.08.052

Table 1
Baseline patient characteristics by incident arrhythmia status

Variable	Incident arrhythmia		
	Yes (n=27)	No (n=146)	P-value
Age (years)	79 [66, 91]	60 [47, 71]	<0.0001
Men	17 (63%)	82 (56%)	0.5119
Body mass index (kg/m^2)	27 [21.2, 30.0]	29 [24.8, 35]	0.0382
Type 2 diabetes mellitus	9 (36%)	47 (32%)	0.7077
Coronary artery disease	5 (19%)	10 (7%)	0.0623
Systemic hypertension	11 (41%)	42 (29%)	0.2150
Chronic kidney disease	2 (7%)	12 (8%)	1.0000
Congestive heart failure	8 (31%)	9 (6%)	0.0009
Peripheral vascular disease	6 (22%)	5 (3%)	0.0023
Prior atrial arrhythmia	7 (26%)	8 (6%)	0.0028
Prior ventricular arrhythmia	0	1 (1%)	1.0000
Prior conduction disturbance	6 (22%)	16 (11%)	0.1194
QTC prolongation	2 (7%)	5 (3%)	0.2999
Prior CIED	1 (4%)	5 (3%)	1.0000

Other EKG abnormalities include acute pericarditis, ST-segment changes.
CIED = cardiovascular implantable electronic device.

the minimum Akaike information criterion, indicating that the final model was both information-rich and simplistic. This resultant data-driven model provides insight into the relation between incident arrhythmia and inpatient mortality whereas jointly accounting for age and congestive heart failure (HF). Analyses were performed in SAS version 9.4 (Cary, North Carolina).

There were 173 patients hospitalized with COVID-19 included. Baseline traits are listed in Table 1; incident arrhythmia and ECG abnormalities are reported in Figure 1. There were 27 patients (16%) with incident arrhythmia. Such patients were older and had a higher comorbidity burden (e.g., higher rates of type 2 diabetes mellitus, congestive heart failure, and peripheral vascular disease) than those without an incident arrhythmia (Table 1). Patients with an incident arrhythmia were also more likely to have had a previous atrial arrhythmia. Of these 27 patients, 10 (6%) had new atrial fibrillation, 1 (<1%) had new atrial flutter, 2 (1%) had other new supraventricular tachycardias, 6 (4%) had new atrial premature complexes, 5 (3%) had new monomorphic VT, 1 (<1%) had new ventricular fibrillation, and 2 (1%) had new ventricular premature complexes. We did not detect a significant relation between the use of proarrhythmic drugs and the onset of arrhythmia (Table 2). Patients with incident arrhythmia were more likely to be admitted to the intensive care unit (ICU) and be intubated than patients without an incident arrhythmia. Additionally, the inpatient mortality rate was significantly higher for patients who had incident arrhythmia compared with those who did not (41% vs 10%, p = 0.0002; Figure 2). After adjusting for age and congestive HF, the effect of incident arrhythmia remained significant, with an adjusted odds ratio 3.2 (95% confidence interval 1.06 to 9.76, p = 0.0393). Additionally, the combination of these 3 risk factors yielded an area under the receiver operating characteristic curve = 0.8, indicating a moderately strong discriminatory ability. Further, the 6-month mortality rates of the patients who survived to discharge showed a similar, but nonsignificant trend (19% vs 9%, p = 0.2180; including all patients: 52% vs 17%, p = 0.0013).

There were 13 patients (8%) who experienced a new conduction disturbance during the hospitalization. Three patients (2%) had first-degree atrioventricular block, 6 (4%) had new left anterior fascicular block, 2 (1%) had new RBBB and 2 (1%) had new incomplete RBBB. The only significant difference in patient characteristics was a higher

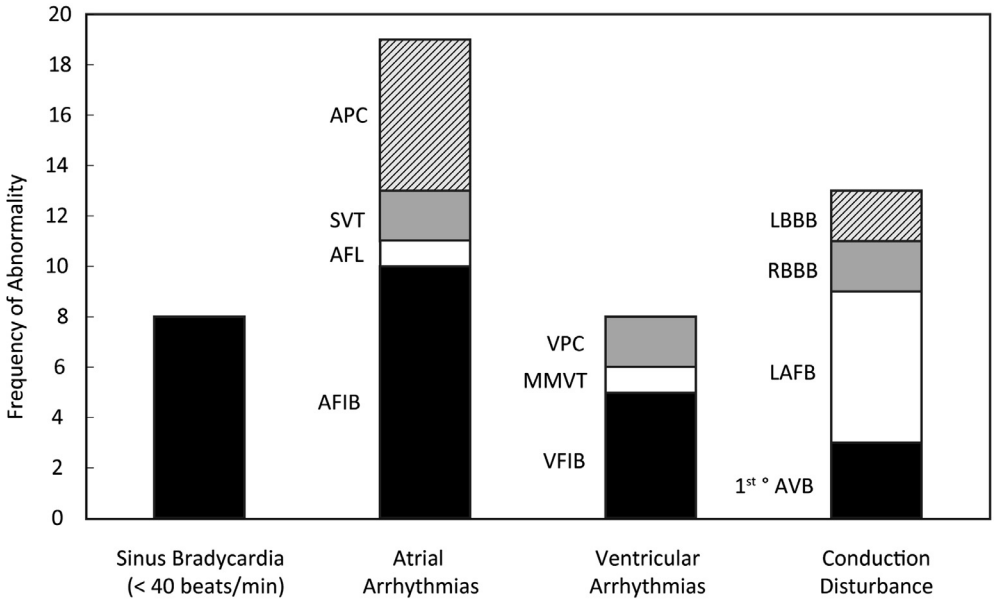

Figure 1. Frequency of incident arrhythmias and new conduction disturbances in patients hospitalized with coronavirus disease 2019. 1st AVB = 1st atrioventricular block, AFIB = atrial fibrillation, AFL = atrial flutter, APC = atrial premature complex, LAFB = left anterior fascicular block, LBBB = left bundle branch block, MMVT = monomorphic ventricular tachycardia, SVT = other supraventricular tachycardia, VFIB = ventricular fibrillation, VPC = ventricular premature complex

Table 2
Hospital course and patient outcome by incident arrhythmia status

Variable	Incident arrhythmia		
	Yes (n=27)	No (n=146)	P-value
Azithromycin use	14 (52%)	70 (48%)	0.7091
Ciprofloxacin use	0	6 (4%)	0.5917
Hydroxychloroquine use	4 (15%)	19 (13%)	0.7618
Remdesivir use	8 (30%)	34 (23%)	0.4801
Decompensated heart failure	2 (7%)	14 (10%)	1.0000
New conduction disturbance	2 (7%)	11 (8%)	1.0000
New QT prolongation	2 (7%)	2 (1%)	0.1154
Other EKG abnormality	0	7 (5%)	0.5978
Intensive Care Unit admission	16 (59%)	45 (31%)	0.0045
Intubation	15 (56%)	29 (20%)	<0.0001
Length of stay (days)	10 [4, 19]	9 [5, 20]	0.9716
Death during hospitalization	11 (41%)	14 (10%)	0.0002
Death at 6 months	14 (52%)	26 (18%)*	0.0013

* 3 patients without incident arrhythmia were lost to follow-up 6 months after their diagnosis.

prevalence of lung disease for those who experienced a new disturbance (39% vs 13%, p = 0.0287; Table 3). The only difference in the clinical course and/or outcomes of these patients was a higher rate of myocarditis (15% vs 1%, p = 0.0288; Table 3).

Of note, a small number of patients had other ECG abnormalities such as QTc interval prolongation (2%), ST-segment changes (2%), and evidence of pericarditis (2%).

In this study of 173 patients hospitalized with COVID-19, we found that 16% of patients developed a new arrhythmia in the hospital and that this development was not associated with proarrhythmic medications. Those with a new arrhythmia were at a higher risk of intubation and death than those without a new arrhythmia; this association remained after accounting for age and HF. New conduction disturbances occurred in 8% of this cohort and were associated with an increased risk of myocarditis but not death.

Table 3
Patient characteristics and outcomes by occurrence of new conduction disturbance

Variable	New conduction disturbance		
	Yes (n=13)	No (n=160)	P-value
Age (years)	62 [42, 69]	61 [48, 73.5]	0.611
Men	8 (62%)	91 (57%)	0.7438
Body mass index (kg/m^2)	30 [25.7, 34]	28 [24, 34.2]	0.598
Type 2 diabetes mellitus	4 (31%)	52 (33%)	1
Coronary artery disease	2 (15%)	13 (8%)	0.3133
Systemic hypertension	3 (23%)	50 (31%)	0.7566
Chronic kidney disease	0	14 (9%)	0.6036
Congestive heart failure	2 (15%)	15 (9%)	0.6209
Lung disease	5 (39%)	21 (13%)	0.0287
History of peripheral vascular disease	2 (15%)	9 (6%)	0.1949
Prior atrial arrhythmia	1 (8%)	14 (9%)	1
Prior ventricular arrhythmia	0	1 (1%)	1
Prior conduction disturbance	4 (31%)	18 (11%)	0.065
QTC prolongation	0	7 (4%)	1
Prior CIED	0	6 (4%)	1
Decompensated heart failure	0	16 (10%)	0.613
Myocarditis	2 (15%)	2 (1%)	0.0288
Intensive care unit admission	6 (46%)	55 (34%)	0.3852
Intubation	3 (23%)	41 (26%)	1
Length of stay (days)	13 [8, 16]	9 [5, 20]	0.4501
Death during hospitalization	2 (15%)	23 (14%)	1
Death at 6 months	2 (15%)	38 (24%)*	0.7907

* 3 patients without new conduction disturbances were lost to follow-up 6 months after their diagnosis.
CIED = cardiovascular implantable electronic device.

Virtually every form of arrhythmia has been observed in patients with COVID-19.[1-9] Our findings are correlative with several of these studies regarding frequency and type of incident arrhythmias.[2,4,13-15] A meta-analysis from Liao et al[16] indicated that patients hospitalized with COVID-19 who had cardiac arrhythmia had an overall mortality of 20%. Another study by Peltzer et al[17] reported similar findings in patients with new atrial arrhythmias. Our study

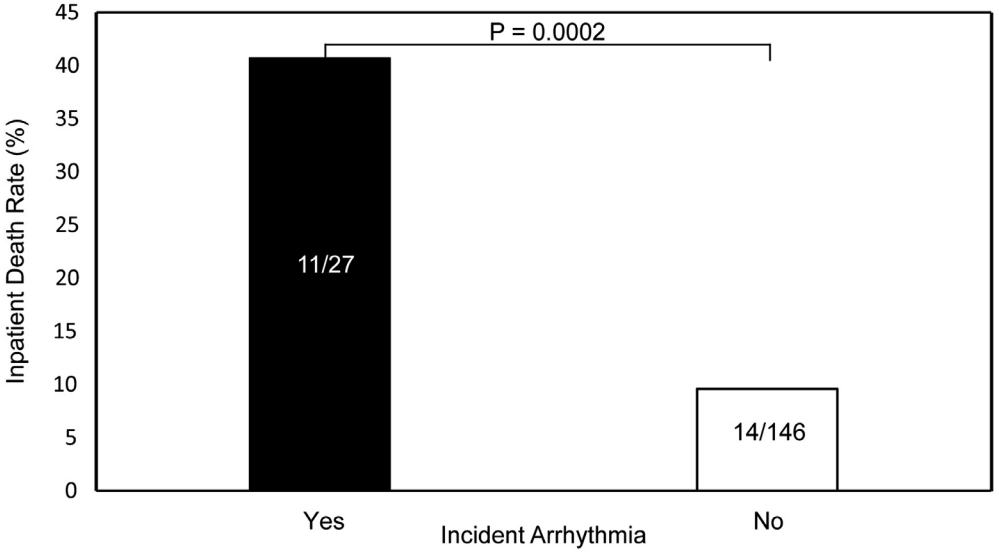

Figure 2. Inpatient hospital mortality rate according to the development of incident arrhythmia.

validated the association between true incident arrhythmia and increased risk of ICU admission and death during hospitalization and 6 months after diagnosis.

Although our study is smaller than several published reports, we have examined 6-month mortality which has not been previously reported. We found a nonsignificant trend toward increased mortality in patients with incident arrhythmias who survived to discharge. Also, unlike several previous reports, we did not include sinus tachycardia in our analysis; we suspect that hypoxia and increased oxygen demand are the primary drivers of new-onset sinus tachycardia in patients with COVID-19 rather than true underlying cardiac disease. Other mediators of sinus tachycardia may include hemodynamic compromise, pain, and/or anxiety.[14]

Several mechanisms have been proposed to explain the propensity for new arrhythmias in patients with COVID-19, direct myocardial inflammatory damage.[3,5,14] Myocardial injury and inflammation in these patients have been demonstrated using biomarkers and cardiac magnetic resonance imaging.[14,18] In our study patients with incident arrhythmias were no more likely to develop clinical signs of myocardial injury and inflammation compared with those without incident arrhythmia, suggesting that an inflammatory effect may not be a major risk factor. Incident arrhythmia was associated with preexisting cardiovascular comorbidities of heart failure, peripheral vascular disease, and previous atrial arrhythmia, suggesting that underlying cardiovascular disease provides a substrate for arrhythmogenesis. Drug interactions have also been reported as a contributing factor to arrhythmias in COVID-19 patients. Specific drugs that have been studied include azithromycin, hydroxychloroquine, remdesivir, and other antibiotics.[13,19,20] Such studies have produced inconclusive results; we did not find an association between medications and the onset of new arrhythmia. Other causal mechanisms for cardiac manifestations include changes in autonomic tone, electrolyte imbalances, increased myocardial wall strain, cytokine-mediated effects, endothelial dysfunction, and vascular inflammation.[21,22] The association of incident arrhythmia with intubation may shed light on the multifactorial causes of the cardiac effects of COVID-19. Because most of the incident arrhythmias found were benign, and COVID-19-negative patients with these arrhythmias generally do not require intubation, severe infection is likely the key factor driving the need for intubation. Incident arrhythmias, much like sinus tachycardia, may be a marker for underlying COVID-19 severity rather than a marker of myocardial damage. In this context, it is not surprising that incident arrhythmias were associated with increased risk of ICU admission, intubation, and death—sicker patients will have worse outcomes. This is supported by the finding that those with preexisting arrhythmia—the majority of which were also benign atrial arrhythmias—did not have a higher risk of ICU admission, intubation, or death.

Myocardial inflammation could explain the occurrence of conduction disturbances and pericarditis observed in our patients. This is consistent with the stronger association of myocarditis in patients with new conduction disturbance compared with those without (15% vs 1%). Patients with previous lung disease were nearly 3 times more likely to develop a conduction disturbance, suggesting that chronic hypoxia may also play a role in their development. However, patients with a new conduction disturbance were no more likely to be intubated, admitted to the ICU, or to die compared with those without any conduction disturbances. Unlike incident arrhythmias, the severity of COVID-19 illness may be less important in the development of new conduction disturbances.

This study has all the limitations inherent to a small, observational, retrospective study. We observed several differences in patient characteristics between those who did versus did not have an incident arrhythmia, yet the small event count precluded a fully adjusted statistical model and a more detailed analysis of events based on the subtype of incident arrhythmia. However, we created an optimally adjusted model to make our conclusions more robust. Furthermore, not all patients had follow-up ECG or continuous cardiac monitoring, so arrhythmia and ECG abnormalities may be under-reported. However, the percentages reported in our data are consistent with other studies and err on the conservative side.

In conclusion, we found that 16% of patients hospitalized with COVID-19 developed an incident arrhythmia, and conduction disturbances occurred in 8%. Development of an incident arrhythmia, but not conduction disturbance, was associated with an increased risk of intubation, ICU admission, and death and is likely more reflective of a severe disease state of COVID-19 rather than intrinsic cardiac dysfunction.

Disclosures

The authors have no conflicts of interest to disclose.

1. Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Bondi-Zoccai G, Brown TS, Der Nigoghossian C, Zidar DA, Haythe J, Brodie D. Cardiovascular considerations for patients, health care workers, and health systems during the COVID-19 pandemic. *J Am Cardiol* 2020;75:2352–2371.
2. Bhatla A, Mayer MM, Adusumalli S, Hyman MC, Oh E, Tierney A, Moss J, Chahal AA, Anesi G, Denduluri S, Domenico CM, Arkles J, Abella BS, Bullinga JR, Callans DJ, Dixit S, Epstein AE, Frankel DS, Garcia FC, Kumareswaram R, Nazarian S, Riley MP, Santangeli P, Schaller RD, Supple GE, Lin D, Marchlinski F, Deo R. COVID-19 and cardiac arrhythmias. *Heart Rhythm* 2020;17:1439–1444.
3. Dherange P, Lang J, Qian P, Oberfeld B, Sauer WH, Koplan B, Tedrow U. Arrhythmias and COVID-19: a review. *JACC Clin Electrophysiol* 2020;6:1193–1204.
4. Kochav SM, Coromilas E, Nalbandian A, Ranard LS, Gupta A, Chung MK, Gopinathannair R, Biviano AB, Garan H, Wan EY. Cardiac arrhythmias in COVID-19 infection. *Circ Arrhyhthm Electrophysiol* 2020;13:579–585.
5. Elsaid O, McCullough PA, Tecson KM, Williams RS, Yoon A. Ventricular fibrillation storm in coronavirus 2019. *Am J Cardiol* 2020;135:177–180.
6. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020;323:1239–1242.
7. Kui L, Fang YY, Deng Y, Liu W, Wang MF, Ma JP, Xiao W, Wang YN, Zhong MH, Li CH, Li GC, Liu HG. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei province. *Chin Med J (Engl)* 2020;133:1025–1031.
8. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, the Northwell COVID-19 Research Consortium, Barnaby DP, Becker LB, Chelico JD, Cohen SL, Cookingham J, Coppa

K, Diefenbach MA, Dominello AJ, Duer-Hefele J, Falzon L, Gitlin J, Hajizadeh N, Harvin TG, Hirschwerk DA, Kim EJ, Kozel ZM, Marrast LM, Mogavero JN, Osorio GA, Qiu M, Zanos TP. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in New York City. *JAMA* 2020;323:2052–2059.

9. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, Zhao Y, Li Y, Wang X, Peng Z. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020;323:1061–1069.
10. O'Keefe JH, Hammill SC, Freed M, Pogwizd SM. *The complete guide to ECGs: a comprehensive study guide to improve ECG interpretation skills*. Boston, MA: Jones and Bartlett Publishers; 2008.
11. Kusumoto FM, Schoenfeld MH, Barrett C, Edgerton JR, Ellenbogen KA, Gold MR, Goldschlager NF, Hamilton RM, Joglar JA, Kim RJ, Lee R, Marine JE, McLeod CJ, Oken KR, Patton KK, Pellegrini CN, Selzman KA, Thompson A, Varosy PD. 2018 ACC/AHA/HRS guideline on the evaluation and management of patients with bradycardia and cardiac conduction delay: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice guidelines, and the Heart Rhythm Society. *J Am Coll Cardiol* 2019;74:932–987.
12. Surawicz B, Childers R, Deal BJ, Gettes LS, Bailey JJ, Gorgels A, Hancock EW, Josephson M, Kligfield P, Kors JA, Macfarlane P, Mason JW, Mirvis DM, Okin P, Pahlm O, Rautaharju PM, van Herpen G, Wagner GS, Wellens H. American Heart Association Electrocardiography and Arrhythmias Committee. Council on Clinical Cardiology. American College of Cardiology Foundation. Heart Rhythm Society. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part III: intraventricular conduction disturbances: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. Endorsed by the International Society for Computerized Electrocardiology. *J Am Coll Cardiol* 2009;53:976–981.
13. Manolis AS, Manolis AA, Manolis TA, Apostolopoulos EJ, Papatheou D, Melita H. COVID-19 infection and cardiac arrhythmias. *Trends Cardiovasc Med* 2020;30(8):451–460.
14. Coromilas EJ, Kochav S, Goldenthal I, Biviano A, Garan H, Goldbarg S, Kim JH, Yeo I, Tracy C, Ayanian S, Akar J, Singh A, Jain S, Zimerman L, Pimentel M, Osswald S, Twerenbold R, Schaerli N, Crotti L, Fabbri D, Parati G, Li Y, Atienza F, Zatarain E, Tse G, Leung KSK, Guevara-Valdivia ME, Rivera-Santiago CA, Soejima K, De Filippo P, Ferrari P, Malanchini G, Kanagaratnam P, Khawaja S, Mikhail GW, Scanavacca M, Abrahão Hajjar L, Rizerio B, Sacilotto L, Mollazadeh R, Eslami M, V Laleh Far, Mattioli AV, Boriani G, Migliore F, Cipriani A, Donato F, Compagnucci P, Casella M, Russo A, Coromilas J, Aboyme A, O'Brien CG, Rodriguez F, Wang PJ, Naniwadekar A, Moey M, Kow CS, Cheah WK, Auricchio A, Conte G, Hwang J, Han S, Lazzerini PE, Franchi F, Santoro A, Capecchi PL, Joglar JA, Rosenblatt AG, Zardini M, Bricoli S, Bonura R, Echarte-Morales J, Benito-González T, Minguito-Carazo C, Fernández-Vázquez F, Wan EY. Worldwide survey of COVID-19–associated arrhythmias. *Circ Arrhythm Electrophysiol* 2021;14:e009458.
15. Cho JH, Namazi A, Shelton R, Ramireddy A, Ehdaie A, Shehata M, Wang X, Marban E, Chugh SS, Cingolani E. Cardiac arrhythmias in hospitalized patients with COVID-19: a prospective observational study in the western United States. *PLoS One* 2020;15:e0244533.
16. Liao SC, Shao SC, Cheng CW, Chen YC, Hung MJ. Incidence rate and clinical impacts of arrhythmia following COVID-19: a systematic review and meta-analysis of 17,435 patients. *Crit Care* 2020;24:690.
17. Peltzer B, Manocha KK, Ying X, Kirzner J, Ip JE, Thomas G, Liu CF, Markowitz SM, Lerman BB, Safford MM, Goyal P, Cheung JW. Outcomes and mortality associated with atrial arrhythmias among patients hospitalized with COVID-19. *J Cardiovasc Electrophysiol* 2020;31:3077–3085.
18. Chen Q, Xu L, Dai Y, Ling Y, Mao J, Qian J, Zhu W, Di W, Ge J. Cardiovascular manifestations in severe and critical patients with COVID-19. *Clin Cardiol* 2020;43:796–802.
19. Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC, Hohmann E, Chu HY, Luetkemeyer A, Kline S, Lopez de Castilla D, Finberg RW, Dierberg K, Tapson V, Hsieh L, Patterson TF, Paredes R, Sweeney DA, Short WR, Touloumi G, Lye DC, Ohmagari N, Oh M, Ruiz-Palacios GM, Benfield T, Fätkenheuer G, Kortepeter MG, Atmar RL, Creech CB, Lundgren J, Babiker AG, Pett S, Neaton JD, Burgess TH, Bonnett T, Green M, Makowski M, Osinusi A, Nayak S, Lane HC, ACTT-1 Study Group Members. Remdesivir for the treatment of COVID-19 — final report. *N Engl J Med* 2020;383:1813–1826.
20. RECOVERY Collaborative Group, Horby P, Mafham M, Linsell L, Bell JL, Staplin N, Emberson JR, Wiselka M, Ustianowski A, Elmahi E, Prudon B, Whitehouse T, Felton T, Williams J, Faccenda J, Underwood J, Baillie JK, Chappell LC, Faust SN, Jaki T, Jeffery K, Lim WS, Montgomery A, Rowan K, Tarning J, Watson JA, White NJ, Juszczak E, Haynes R, Landray MJ. Effect of hydroxychloroquine in hospitalized patients with COVID-19. *N Engl J Med* 2020;383:2030–2040.
21. Zhang J, McCullough PA, Tecson KM. Vitamin D deficiency in association with endothelial dysfunction: Implications for patients with COVID-19. *Rev Cardiovasc Med* 2020;21:339–344.
22. Zhang J, Tecson KM, McCullough PA. Endothelial dysfunction contributes to COVID-19 associated vascular inflammation and coagulopathy. *Rev Cardiovasc Med* 2020;21:315–319.