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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.

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

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Mounting evidence shows that patients with coronavirus disease (COVID-19) are at risk of developing arrhythmias.\textsuperscript{1-3} Several early publications include sinus tachycardia in their definitions.\textsuperscript{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.\textsuperscript{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.\textsuperscript{11} Conduction disturbances were defined and analyzed per standard criteria\textsuperscript{12} and included atroventricular 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

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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).

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

### Table 1
Baseline patient characteristics by incident arrhythmia status

| Variable                      | Incident arrhythmia | 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/m²)       | 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.

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
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.

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.](image-url)
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.10

Several mechanisms have been proposed to explain the propensity for new arrhythmias in patients with COVID-19, direct myocardial inflammatory damage.13,14 Myocardial injury and inflammation in these patients have been demonstrated using biomarkers and cardiac magnetic resonance imaging.14,16 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.11–12. 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.

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