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Research paper

## Arrhythmia patterns during and after hospitalization for COVID-19 infection detected via patch-based mobile cardiac telemetry<sup>☆</sup>

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### ABSTRACT

**Background:** Coronavirus infection is the cause of the current world-wide pandemic. Cardiovascular complications occur in 20–30% of patients with COVID-19 infection including myocardial injury and arrhythmias. Current understanding of specific arrhythmia type and frequency is limited.

**Objective:** We aimed to analyze arrhythmia type and frequency in patients with COVID infection, identifying arrhythmia patterns over time during hospitalization and post discharge utilizing a patch based mobile cardiac telemetry system.

**Methods:** A prospective cohort study during the COVID-19 pandemic was performed. We included in our study patients hospitalized with COVID-19 infection who had a patch-based mobile telemetry device placed for cardiac monitoring.

**Results:** Quantitative reports for 59 patients were available for analysis. Arrhythmias were detected in 72.9% of patients and at a consistent frequency throughout the monitoring period in 52.9%–89.5% of patients daily. The majority of arrhythmias were SVT (59.3% of patients) and AF (22.0%). New onset AF was noted in 15.0% of all patients and was significantly associated with older age (OR 1.4 for 5 yrs. difference; 95% CI 1.03–2.13). Of 9 patients who were discharged with continued patch monitoring, 7 (78%) had arrhythmic events during their outpatient monitoring period.

**Conclusion:** In COVID-19 patients arrhythmias were observed throughout hospitalization with a consistent daily frequency. Patients continued to exhibit cardiac arrhythmias after hospital discharge of a type and frequency similar to that seen during hospitalization. These findings suggest that the risk of arrhythmia associated with COVID infection remains elevated throughout the hospital course as well as following hospital discharge.

### 1. Introduction

Coronavirus infection is the cause of the present world-wide pandemic, which has dramatically impacted global public health and surpassed 170 million cases worldwide [1]. Rapid spread of the infection has overwhelmed health-care facilities in multiple countries. Despite being asymptomatic in a majority of cases, a number of patients are at risk for developing severe respiratory symptoms and viral pneumonia, as well as multiorgan system damage. Cardiovascular complications have

been reported to occur in 20–30% of patients with COVID-19 infection. The most common cardiovascular complications include myocardial injury and arrhythmias. The presence of cardiac injury is associated with higher mortality in patients with COVID-19 infection [2,3]. Based on various reports the incidence of arrhythmia in hospitalized patients is 7–16.7% and in up to 44.4% in patients requiring ICU level of care [4–6].

Suggested underlying mechanisms for arrhythmogenicity during COVID-19 infection include myocardial injury, strain or ischemia,

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hypoxia, electrolyte and volume imbalance, inflammation or abnormal host immune response [2]. Furthermore, in addition to these potential mechanisms, medication effects can place these patients at a distinctly higher risk of arrhythmia. Initial COVID-19 treatment strategies included hydroxychloroquine and azithromycin that are known to have pro-arrhythmic effects, including an increased risk of Torsades de Pointes. Therefore during the initial phase of the pandemic, a large proportion of patients hospitalized with COVID infection met guideline recommendations for QT- interval monitoring with serial ECGs or telemetry monitoring [7].

In view of the potential for increased viral exposure to staff and limited access to ICU and telemetry hospital beds in the face of the pandemic, alternative methods of monitoring, such as mobile cardiac telemetry (MCT) devices were found to be useful in this setting [8,9]. The ambulatory monitoring system MCT received emergency use Food and Drug Administration (FDA) approval for inpatient cardiac monitoring during the COVID-19 pandemic. A Heart Rhythm Society (HRS) practice update highlighted that an MCT approach could be utilized when telemetry capacity of the hospital is overwhelmed by the number of patients [10]. Our research group previously reported that such mobile telemetry systems could be successfully implemented during the COVID-19 pandemic and was useful for patient management in such situations [8].

In a retrospective study that evaluated medical history and ECG abnormalities of patients with COVID-19 infection admitted to a large center in New York, atrial fibrillation and atrial flutter was found to be associated with a two times higher 30-day mortality risk [11]. However, a detailed characterization of arrhythmia type and frequency in patients hospitalized with COVID-19 remains limited. The aim of the present study was to examine and characterize in detail arrhythmia patterns including type, frequency and time course identified by patch-based cardiac monitor in patients hospitalized with COVID-19 infection.

## 2. Materials and methods

The design of the study has previously been reported [8]. In brief, in response to the COVID-19 pandemic, we recognized that critical care and telemetry resources of our institution will be overwhelmed. We developed a system to provide cardiac monitoring using the MCT (Zio AT Patch, iRhythm Technologies Inc., San Francisco, CA, USA) for high risk COVID-19 patients who would qualify for cardiac monitoring but due to crisis limitations were unable to be placed in the telemetry capable units. This system allowed for cardiac telemetry and daily QT monitoring on hospital floors while limiting high-risk viral exposure of the staff.

We performed a prospective cohort study that included patients undergoing inpatient treatment during the COVID-19 pandemic in our urban academic medical center who had the patch-based MCT placed. A device was placed for patients on non-ICU and non-telemetry capable hospital units meeting at least one of the following criteria: Prolonged QT on admission ECG defined as QTc >470 ms for males or >480 ms for females and considered for treatment with agents which might prolong the QT interval, history of QT prolongation in the past with pharmacologic therapy, anticipated therapy with two or more agents known to prolong QT (e.g. hydroxychloroquine + azithromycin or methadone), high oxygen supplementation requirements, or history of or concern for arrhythmias. The decision of MCT device placement for patients was at the discretion of the treating physicians.

In the current analysis we included patients who had a positive SARS-CoV-2 test result and who underwent patch-based MCT device placement. Baseline demographic and clinical data were collected from the Epic EMR system including age, sex, race/ethnic group, anti-arrhythmic and other QT prolonging medication use prior to admission. Medical history included history of hypertension, diabetes, heart failure, arrhythmias, chronic kidney disease and use of renal replacement therapy and presence of cardiac implantable electronic devices.

Patients with devices not returned for quantitative analysis were excluded from the analysis.

Hospital employed ECG technicians who had prior experience with the cardiac monitoring technology fitted the MCT device on the patients. The cardiac monitoring includes a 1-lead adhesive patch monitoring device and a cellular transmitter. Once in place, monitoring device continuously recorded and analyzed cardiac telemetry [8]. Per discretion of the treating physicians, patients could be discharged with the MCT to continue monitoring outside of the hospital settings (e.g. at home or rehabilitation centers).

Final reports from MCT devices containing detailed arrhythmia counts were analyzed after completion of the wear time. Arrhythmia episodes noted during the hospitalization as well as following hospital discharge were included in the analysis. Criteria for episode detection included: Ventricular Tachycardia (VT)  $\geq 100$  bpm for 4 beats, any Torsades de Pointes (TdP)/Ventricular Fibrillation (VF), any Atrial Fibrillation (AF)/Atrial Flutter for  $\geq 30$  s, Supraventricular Tachycardia (SVT)  $\geq 90$  bpm for  $\geq 4$  beats, any complete heart block, any Mobitz I or II atrioventricular block (AVB), and pauses  $\geq 3$  s. Clinically significant arrhythmia criteria included: SVT  $\geq 200$  bpm for  $\geq 30$  s, AF  $\geq 1$  min, any 3rd degree AVB, pause  $\geq 6$  s, VT  $\geq 170$  bpm and  $\geq 30$  s in duration, any VF. New onset AF was defined as AF  $\geq 30$  s and not previously documented in the patient's medical records. Patients were followed up until the time of completion of the monitor wear period, discharge, or death.

The primary aim of the present study was to perform a quantitative analysis of arrhythmia events including type, frequency, and duration of detected arrhythmias. Primary outcomes included arrhythmic episodes detected according to the final report criteria above. Secondary aims included comparison of the arrhythmia incidence during inpatient and outpatient monitoring periods, as well as identification of risk factors associated with new onset of AF.

The flow chart in the Fig. 1 delineates the design of the study.

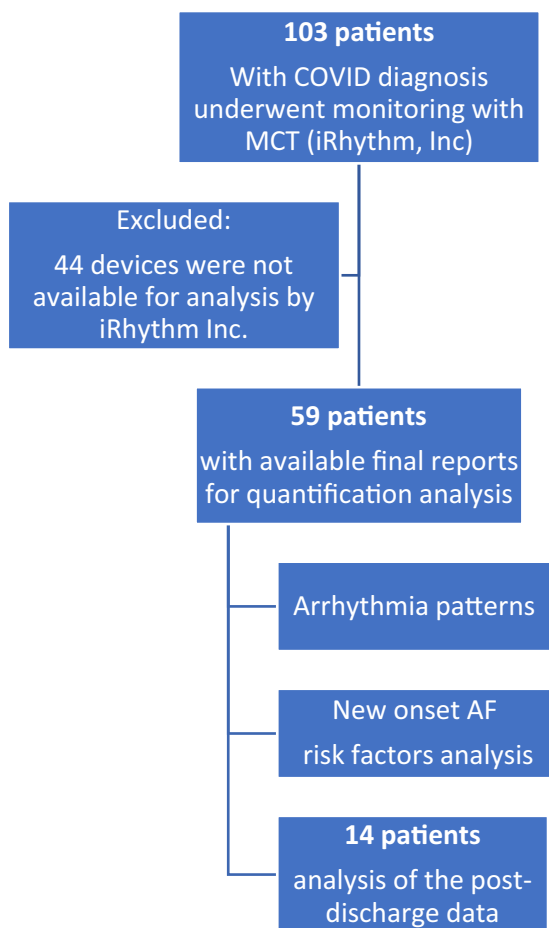
Normality of distribution of continuous variables was determined by visual assessment of histograms. Mean and standard deviation (SD) was reported for normally distributed data, median and interquartile range (IQR) - for non-parametric data. Categorical variables are presented as n (%). For bivariate analysis of association between continuous variables, we used Student's *t*-test and Pearson correlation for normally distributed data, Mann-Whitney and Spearman correlation tests for non-normally distributed data. For analysis of the association between categorical or dichotomized variables we used Chi square test or Fisher exact test, as appropriate.

We evaluated association of new onset AF with risk factors by constructing a multivariable logistic regression model. In the multivariable model we selected the variables that were significantly associated with new onset of AF in the bivariate analysis with  $p < 0.25$ , clinically relevant demographic variables (race, sex, BMI) were included regardless of statistical significance of their association with new onset AF. We tested all variables in the model for the first order interaction with our independent variable of interest – new onset of AF. We tested the assumption of linearity with Lowess curves. Logistic regression diagnostics performed with Hosmer and Lemeshow Goodness of Fit Test.

A *p*-value  $< 0.05$  denoted statistical significance. Statistical analysis was performed using STATA software, version 16.1. The institutional review board at Montefiore Medical Center/Albert Einstein College of Medicine approved this study in April 2020.

## 3. Results

A total of 103 patients hospitalized with COVID-19 diagnosis underwent cardiac monitoring. Fifty-seven percent ( $n = 59$ ) of monitors were returned and had final reports available for quantitative analysis and are the subject of this report. The baseline clinical characteristics did not differ significantly between the whole cohort of 103 and the 59 patients with final report data available for analysis. Monitors from the majority of the patients who died were not returned for analysis,



**Fig. 1.** Flowchart of the study design. AF – atrial fibrillation, MCT – mobile cardiac telemetry system.

however the difference in mortality between the cohorts of patients was not statistically significant (Table 1). The predominant cause of death in our cohort of patients was acute respiratory failure resulting in non-shockable rhythms and all deaths occurred while patients were hospitalized.

Among 59 patients included in this study 35 (59%) were males, median age 65 (IQR 56–76) years. Mean wear time was 6.8 ± 5.0 days. Number of monitored patients decreased from 59 on day 1 to 13 patients at the end of the monitoring period at 14 days.

At least 1 arrhythmic episode was detected in 72.9% (n = 43) of patients and clinically significant arrhythmias as defined in the methods section were detected in 33.9% (n = 20) of patients in our study (Fig. 2).

The majority of arrhythmias were SVT identified in 35 patients (59.3%), in 6 patients (10%) detected SVTs were longer than 30 s in duration. First occurrences of SVT were noted on the first day of monitoring for the majority of patients, however some patients had first events detected later during the course (Fig. 3). AF episodes were noted in 13 patients (22.0%), AF with a duration >30 min was detected in 12 patients (20%). Median daily AF burden in patients with AF during the monitoring period was 25.6% (IQR 3.7–100%). Anticoagulation was initiated when appropriate.

Brady arrhythmias (2nd and 3rd degree AVB, pause ≥ 3 s) were detected in 18.7% of patients. Second and third degree AVB were detected in 4 patients (7%). Daily frequency of various types of AVB increased throughout the monitoring period. First episodes of AVB were detected on days 1, 2, 5 and 9 throughout the monitoring period (Fig. 4). Pauses longer than 3 s were detected in 5 patients (8.5%), out of those, 4 patients (6.85) had pauses longer than 6 s in duration and were noted to

**Table 1**

Baseline clinical characteristics of the patients in the study.

Characteristics	Study cohort (N = 59)	Total (N = 103)	P value
Age, years	64 (55–76)	68 (57–78)	0.17
Male	35 (59.3)	63 (61.2)	0.81
BMI	27.5 ± 6.5	27.9 ± 6.6	0.51
Race/ethnic group			
White (non-Hispanic)	5 (8.5)	7 (6.8)	0.69
Black/African American	19 (32.2)	34 (33.0)	0.92
Hispanic	23 (39.0)	45 (43.7)	0.56
Other/Unknown	15 (20.3)	17 (16.5)	0.54
Medical history			
Hypertension	44(74.6)	81 (78.6)	0.56
Diabetes	33 (55.9)	54 (52.4)	0.67
Coronary Artery Disease	11 (18.6)	22 (21.4)	0.67
Heart Failure	12 (20.3)	19 (18.5)	0.78
Atrial Fibrillation	9 (15.3)	15 (14.5)	0.89
Ventricular arrhythmias	2 (3.4)	2 (1.9)	0.55
CKD	12 (20.3)	20 (19.4)	0.89
ESRD on Renal Replacement therapy	3 (5.1)	4 (3.9)	0.72
CIED	2 (3.4)	3 (2.9)	0.86
Indication for mobile telemetry device use			
Hydroxychloroquine use	15 (26.3)	30 (30.6)	0.56
Prolonged QT	9 (15.8)	17 (17.4)	0.79
Arrhythmia	26 (45.6)	38 (38.8)	0.40
Hypoxia	22 (38.6)	44 (44.9)	0.44
Use of other QT prolonging medications	5 (8.8)	7 (7.1)	0.70
Death	12 (20.3)	31 (30.1)	0.18

Values are n (%), mean ± SD or median (IQR).

BMI – body mass index; CIED - Cardiac Implantable Electronic Device; CKD – Chronic kidney disease; ESRD - End-stage Renal Disease.

occur either during cardiac arrest or prior to death due to respiratory failure.

Fifteen patients (25%) had at least one episode of non-sustained VT (NSVT). One patient had episode of sustained VT (>30 s) along with pauses and it occurred during cardiac arrest due to severe respiratory failure in the setting of COVID-19 pneumonia. No VT or VF noted in patient population in this analysis or the original 103 patients cohort who wore the monitor.

In the study population arrhythmic events of any type were detected throughout the monitoring period with a similar daily frequency ranging from 52.9% to 89.5% of patients (Fig. 5).

New onset AF occurred in 9 patients (15.0%). In a multivariable logistic regression analysis adjusted for sex, race, and BMI, new onset atrial fibrillation was statistically significantly associated with age (OR 1.4 for 5 years difference; 95% CI 1.02–1.99, p = 0.04).

Of 59 patients included in the study, 14 were discharged after hospitalization with continued monitoring by a patch device. Nine of these patients had MCT placed during hospital stay 1 to 9 days prior to discharge and were discharged with continued monitoring to finish a 14-day monitoring period. Mean total wear time in this group was 12.1 ± 3.7 days, mean wear time as outpatient was 9.1 ± 4.4, mean age was 69.1 ± 14.2 years, 33% were males. Of these 9 patients, 7 (78%) had arrhythmic events during hospitalization and 7 (78%) patients had events post-discharge (counts restarted after patients were discharged) (Fig. 6). In this cohort five patients (36%) had episodes of AF > 30 min. Median duration of the longest SVT episodes was 14.6 s (IQR 7.4–48.2). Mean duration of the longest VT episodes was 5.5 ± 3.4 s. Arrhythmia type distribution in this patient group presented in Fig. 6.

#### 4. Discussion

In our cohort study of patients with COVID-19 infection, 73% of patients had arrhythmias detected by patch-based MCT during the monitoring period. Importantly, arrhythmias were observed throughout

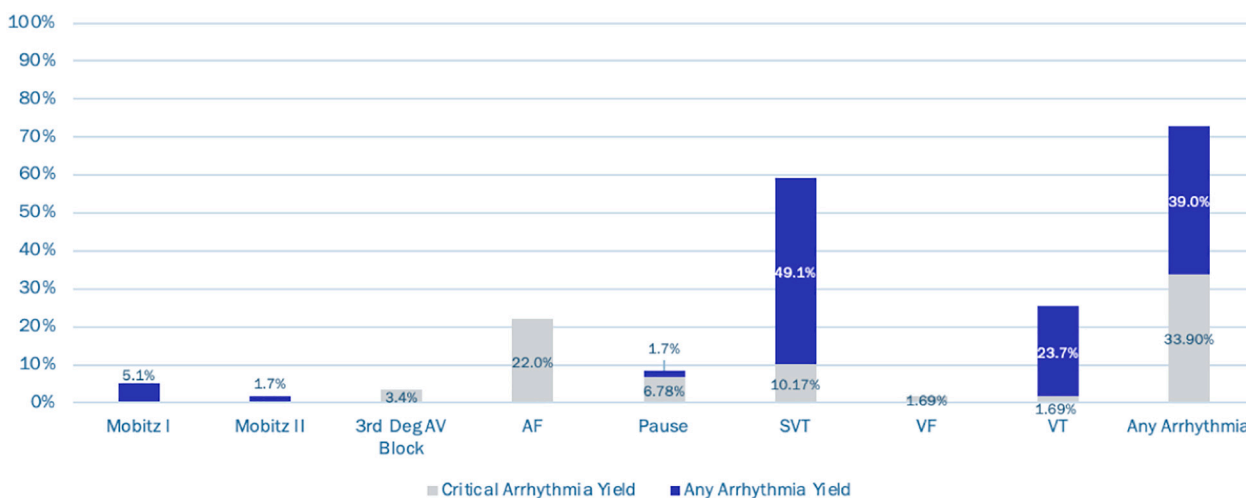


Fig. 2. Arrhythmia types frequencies in the study patient population (n = 59) during the monitor wear time of COVID-19 admission. AF – atrial fibrillation ≥30 s VT – supraventricular tachycardia ≥90 bpm for ≥4 beats, VT – ventricular tachycardia ≥100 bpm for 4 ventricular beats, pause >3 s. Clinically significant arrhythmias: SVT ≥200 bpm and ≥30 s, AF ≥ 1 min, any 3rd degree atrioventricular block (AVB), pause ≥6 s, VT ≥ 170 bpm and ≥30 s, any VF.

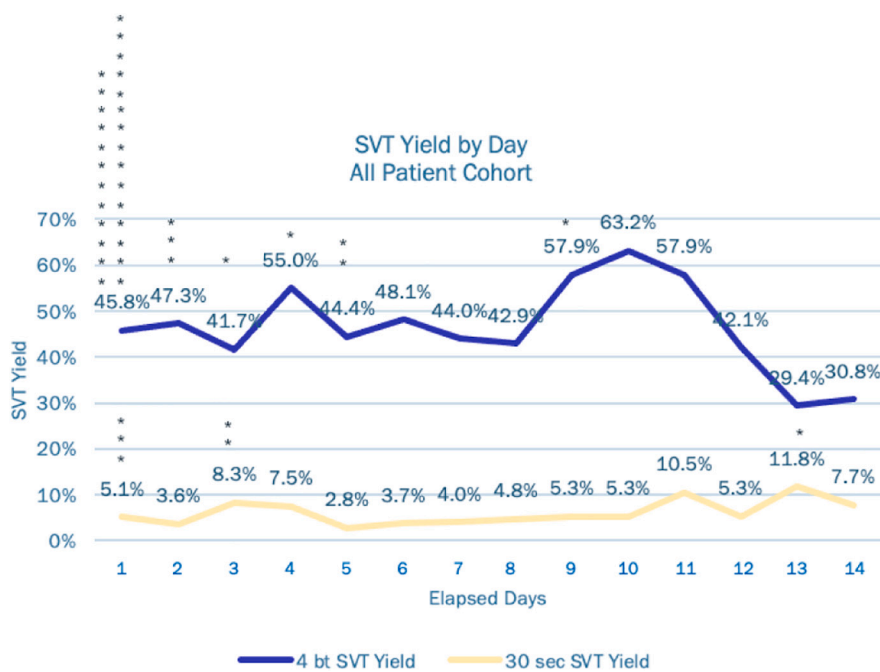


Fig. 3. Supraventricular Tachycardia (SVT) yield assessed daily based on different duration criteria: longer than 4 consecutive beats and longer than 30 s. \* First detection of SVT for an individual patient.

the hospitalization with a consistent daily frequency, ranging from 52.9 to 89.5% patients with arrhythmic episodes per day. Consistency of the arrhythmia episodes throughout the hospitalization suggests elevated arrhythmogenic risk in COVID-19 patients throughout the duration of the disease course, however our analysis was limited to 14 days of monitoring. The majority of the events recorded in our study represent subclinical arrhythmic episodes such as short SVT episodes, NSVT and Wenckebach. It is important to note that subclinical cardiac arrhythmias can exhibit important implications for outcomes and contribute to the increased rates of cardiovascular events [12–15]. Additionally, some types of subclinical arrhythmias like atrial high-rate episodes or NSVT often require further monitoring and careful evaluation [16]. Clinically significant arrhythmias were detected in 33.9% of patients in our study; this rate is higher than other reports on cardiovascular complications of COVID-19 infection that found arrhythmia events frequency varying

between 7 and 16.7% in hospitalized patients and the rate of arrhythmias in ICU patients reported to be up to 44.4% [4]. This disagreement in rates of arrhythmias may arise from the differences in the techniques used for cardiac monitoring, our study benefited from more detailed arrhythmia detection and quantification analysis by utilizing patch-based monitors.

In our study we did not observe a high rate of severe bradyarrhythmias. Rare severe bradycardia events that were recorded occurred near patients' demise from acute respiratory failure resulting in non-shockable rhythms that was the predominant cause of death in our cohort of patients. Bradyarrhythmias occurred at a rising rates throughout the cardiac monitoring period. In our subset of patients most likely it could be explained by worsening respiratory failure associated with the disease progression, however specific mechanisms remain unknown.

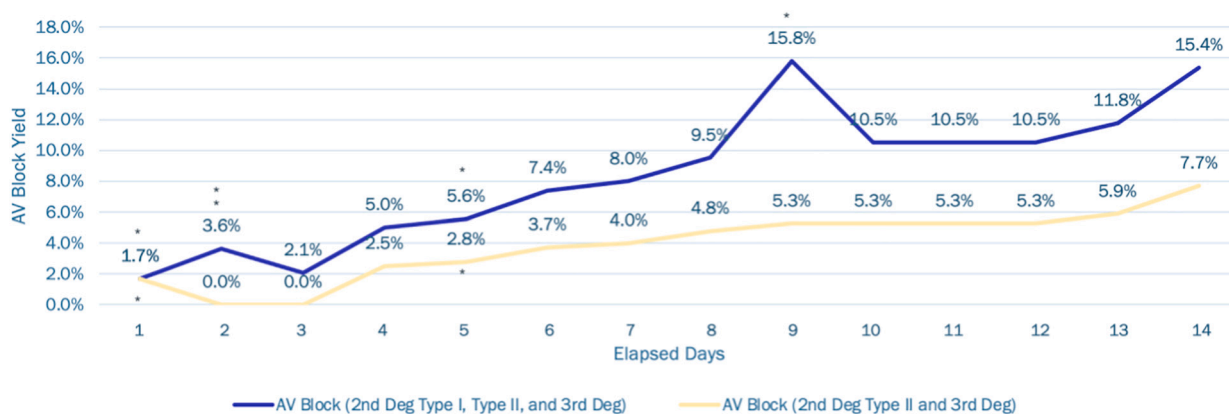


Fig. 4. Frequency of 2nd and 3rd degree atrioventricular block (AVB) in the study population. Four patients (6.8%) had 2nd and 3rd degree AVB. Two patients (3.4%) had high degree AVB (Mobitz type II and 3rd degree). \* First occurrence of AVB for an individual patient.

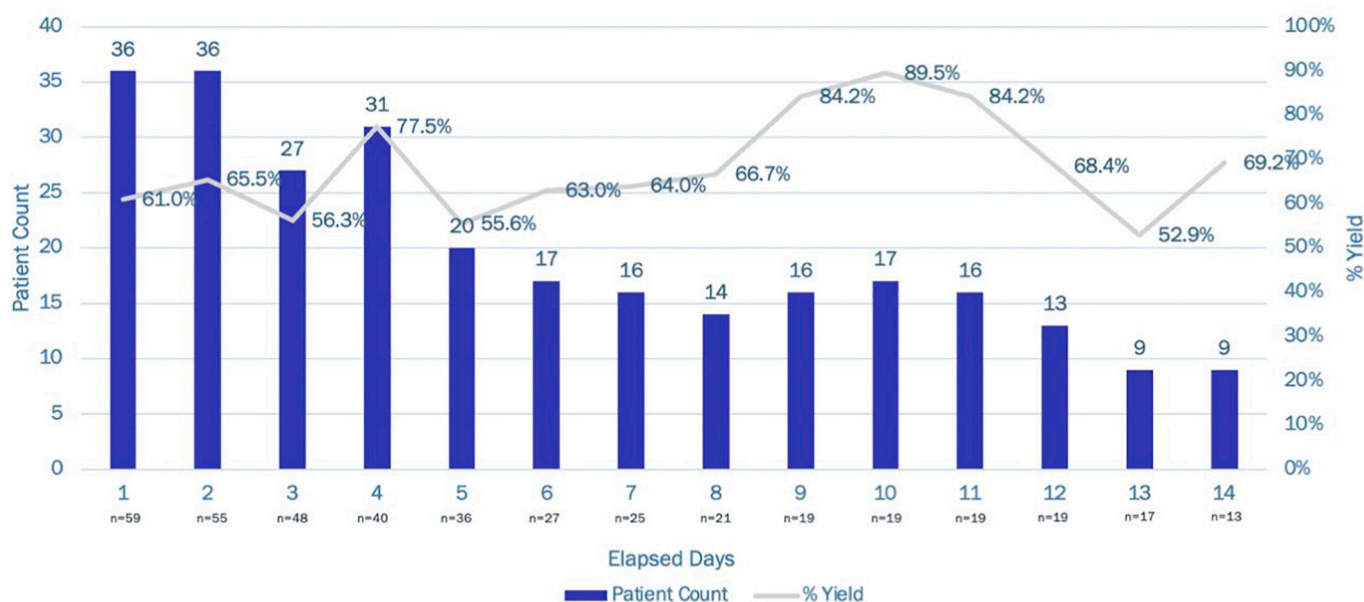


Fig. 5. Daily frequency of any arrhythmia detected by MCT described by number of patients with arrhythmic episodes per day.

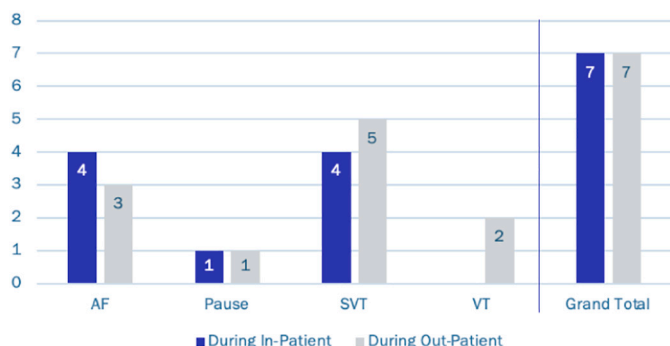


Fig. 6. Distribution of arrhythmia types among 9 patients with COVID-19 infection who wore the MCT monitor after hospital discharge.

Despite the fact that the majority of patients received hydroxychloroquine during the hospitalization, we did not observe a high incidence of VT in the cohort and no patients died from primary arrhythmic events, including the whole cohort of 103 patients. Recent analysis of 700 patients by Bhatla et al. also reports low numbers of VT/VF in

patients with COVID even when hydroxychloroquine is included in the treatment [17].

An important finding of our study was the comparison of inpatient and outpatient arrhythmia rates. A small subset of our study population (9 patients) was discharged with MCT monitors and we observed continued manifestation of arrhythmic episodes similar in type and frequency to hospitalization period (78%). These results support the hypothesis of possible subclinical myocardial injury and long-term cardiovascular consequences of COVID infection suggested by Puntman et al. in a study describing myocardial involvement detected by MRI in 78% of patients who recovered from COVID-19 infection. These results were independent of the severity of the disease [18]. In our study inpatient application of an MCT with continued monitoring as outpatient was shown to be feasible and effective in detecting occult arrhythmias in patients with COVID infection and when new onset of AF detected can trigger treatment initiation to prevent stroke. Further investigation of long-term arrhythmia prevalence in patients with COVID-19 infection warrants additional research.

Atrial fibrillation was one of the most commonly detected arrhythmias among our study patient population (22% of patients) similar to prior reports detecting AF in 19–21% of COVID-19 patients [19,20]. This

rate of AF reported in COVID-19 patients is similar to the rate seen in acutely ill patients with sepsis [21], acute respiratory distress syndrome (ARDS) [22]. New onset AF was recorded in 14% of patients in our patient cohort and was associated with traditional risk factors such as older age and history of heart failure in agreement with previously demonstrated data for COVID patients [17]. In a recent study conducted in Spain 7.5% of patients were noted to have new onset AF and it was associated with higher rates of cardiovascular outcomes especially thromboembolism and as in our cohort of patients, new onset AF was associated with older age [23]. A recent retrospective study from New York found a new onset AF rate to be 4%, which increased when charts were manually reviewed. The frequency of AF was found to be similar in hospitalizations for COVID and for Influenza [24]. The differences in detected new AF in COVID patients among all the recently published data may be related to the adjudication of arrhythmia and methods of detection. Underlying mechanisms of AF in COVID-19 infection are proposed to include myocardial injury, inflammatory cytokine storm, direct viral endothelial damage, electrolytes disbalance, increased adrenergic drive and hypoxia [20]. However, the exact mechanisms are still unknown and further studies with long term follow up are required for better characterization of arrhythmias in COVID.

## 5. Limitations

The study population was limited to patients with COVID infection who were admitted to the medicine floors. Patients who were eligible for ICU or continuous telemetry were not included in the study. No control group was used, all patients in our analysis had a cardiac monitor placed. This limited the comparison of arrhythmia occurrence in selected patients who wore the monitor with the ones who didn't.

A significant number of patients who underwent monitoring with MCT did not have their monitors returned for the final analysis. This was a consequence of the demanding clinical circumstances of the initial phases of the pandemic. Only a small number of patients wore an MCT both as an inpatient and outpatient. Outpatient wear time of the MCT was limited. Additional studies are warranted to investigate long-term arrhythmic events in the patients discharged after COVID-19 hospitalization.

## 6. Conclusions

Arrhythmia episodes including subclinical events were noted to occur throughout the hospitalization for COVID-19 infection with consistent daily frequency. These findings extended to post-discharge where detected abnormal heart rhythms were similar in type and frequency to those seen during hospitalization. New onset atrial fibrillation occurred in 15% of study cohort and was associated with older age.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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