Remote monitoring temporal trends during COVID-19 pneumonia in patients with implanted defibrillators

Giosuè Mascioli (MD)\textsuperscript{a,b,*}, Elena Lucca (MD)\textsuperscript{a}, Lucia Annunziata (MSc)\textsuperscript{b}, Daniele Giacopelli (MSc)\textsuperscript{b,c}

\textsuperscript{a}Humanitas Gavazzeni, Via Mauro Gavazzeni, 21, 24125 Bergamo, BG, Italy
\textsuperscript{b}BIOTRONIK Italia, Vimodrone, Italy
\textsuperscript{c}Department of Cardiac, Thoracic, Vascular Sciences & Public Health, University of Padova, Padua, Italy

\section*{Introduction}

Patients with concomitant cardiac disease and coronavirus disease 2019 (COVID-19) have an extremely poor prognosis [1]. Many of them are cardiac implantable electronic device (CIED) recipients and could be followed with remote monitoring (RM) systems that are widely used in clinical practice. Beyond technical data for device functioning surveillance, these systems provide a wide range of clinical diagnostics, such as mean heart rate, heart rate variability, physical activity, and thoracic impedance. It is unknown whether some of these parameters could show recurrent patterns during COVID-19 infection to be potentially used for early diagnosis, isolation, and treatment. In this case series, we describe RM temporal trends for one patient with cardiac resynchronization therapy defibrillator (CRT-D) and one with implantable cardioverter defibrillator (ICD) who developed severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).

\section*{Case 1}

A 65-year-old woman with chronic ischemic disease, hypertension, and diabetes underwent CRT-D implantation in November 2018 due to symptomatic severe left ventricular dysfunction and left bundle branch block. The implanted device was equipped with the Home Monitoring system (Biotronik, Berlin, Germany), a well-known RM technology characterized by daily and automatic transmissions through a mobile patient unit. Daily diagnostics data are available in a protected website for physician reviewing.

She presented at the emergency room of our hospital on March 9th, 2020 for dyspnea onset. She was tachypneic, but afebrile and denied any recent travel or sick contacts during the past 20 days.
The electrocardiogram demonstrated sinus rhythm with CRT pacing and the echocardiography confirmed a dilated cardiomyopathy without signs of pleural effusion. Laboratory analysis included C-reactive protein 6.29 mg/dL, lactic acid dehydrogenase 1057 U/L, troponin level 401 ng/L, and white blood cell count 300/mm³. The radiological and computed tomography (CT) images of the chest were compatible with pulmonary edema, but did not exclude bilateral interstitial pneumonia (Fig. 1A).

The patient was hospitalized and tested for COVID-19 that resulted positive. She was started on oral hydroxychloroquine 200 mg daily for 7 days. A bladder catheter was inserted to monitor fluid balance. During hospitalization her respiratory status required oxygen therapy at high flows without mechanical intubation.

On March 18th, after 9 days of hospital stay, the patient was discharged. She was permanently afebrile, with discrete oxygen saturation (94% on room air) and with a clinical and radiological trend of continuous improvement of the inflammation and pulmonary edema status. The patient died suddenly the next day at home from unknown cause and with no evidence of arrhythmia transmitted by the RM system.

Fig. 2 depicts the daily temporal trends of RM diagnostics over the 1-month period before last transmission (March 19th). The gap of transmissions covered the hospital stay since the patient did not bring her mobile patient unit to the hospital. In the preceding period, the patient activity decreased progressively and continuously starting from February 27th, 11 days before emergency room admission, showing an almost complete inactivity in the last days (values lower than 5% per day in the last week). With the same timing, increases in the mean (from 60 bpm to 70 bpm) and nocturnal (from 54 to 70 bpm) heart rates were observed. Differently from the progressive decrease of patient activity, heart rate suddenly increased 11 days before hospitalization. Heart rate variability appeared to be affected by the disease progression a few days later (starting from March 2nd), showing values around 30 ms much lower than the average value of 80 ms observed in the preceding period, except for a higher outlier value just before admission. Interestingly, the thoracic impedance had a less evident trend. Starting from values above 60 Ohm, it had a progressive decrease from February 21st (17 days before emergency room admission) to February 25th. After this variation, thoracic impedance values remained quite stable until hospitalization.

**Case 2**

A 78-year-old woman was implanted in June 2017 with a dual-chamber ICD with the Home Monitoring system due to dilated cardiomyopathy with severe left ventricular dysfunction, brady-tachy syndrome and heart failure symptoms (New York Heart Association class III) during atrial arrhythmic episodes. A few months later, due to the progression of the atrial arrhythmia to persistent forms, we decided to set the device in DDI pacing mode and apply a rate control approach. The ventricular rate was well controlled without episodes of worsening heart failure reported in the following period.

On March 25th, 2020, the husband of the patient died from acute respiratory distress syndrome in hospital with positive COVID-19 testing. In the same week, the patient started to present cough, shortness of breath, and intermittent fever, but she refused hospitalization. Due to resources limitation, the pharyngeal swab for the detection of SARS-CoV-2 antigen was not performed and the patient was followed remotely as a highly suspected case of COVID-19, but without specific therapy for the infection. The dyspnea and low tolerance to physical efforts persisted for the following period, but the patient decided to accept the hospitalization only two months later, on May 21st, when the pandemic peak in the region was terminated. Intravenous diuretics and isotropic agents were administrated as acute intervention for heart failure. At hospital admission COVID-19 testing was negative, but the CT showed a “crazy-paving” pattern of the lungs, which is a clinical picture of previous SARS-CoV-2 pneumonia with concomitant pleural effusion (Fig. 1B). The clinical picture of the patient improved with hospital therapy and she was discharged on June 5th.

Fig. 3 depicts the daily temporal trends of RM diagnostics over the 6-month period before hospital discharge (June 5th). Starting from the week of symptoms onset (March 9th–16th), the patient activity had a strong decrease with low values until hospitalization (May 21st). The mean and nocturnal ventricular heart rate increased progressively from symptoms onset reaching peak values of 140 and 130 bpm, respectively. The heart variability started to be more variable a few weeks after symptoms, while the thoracic impedance had a continuous decreasing trend until hospitalization.

**Discussion**

Daily RM provides a wide spectrum of continuous information from CIED patients that has been demonstrated to improve clinical outcomes for patients with heart failure [2]. In the COVID-19 pandemic scenario, this may be a useful tool for patients predisposed to the infection. This hypothesis is still more meaningful considering that patients with cardiovascular diseases who are infected by the virus have an elevated risk of adverse outcomes [1,3,4].

Further research could be addressed on the potential use of RM for early diagnosis, isolation, and treatment of infection in CIED patients. The feasibility of this approach should be tested preliminarily to understand if some of the available parameters show recurrent patterns during infection. In this paper, we described RM temporal trends for two CRT-D/ICD patients with confirmed or highly suspected COVID-19.
Fig. 2. Remote monitoring temporal trends during COVID-19 infection for case 1. Red dashed line represents the day of emergency room admission, while missing transmissions covered the period of hospital stay. Graph represents daily values.

Fig. 3. Six-month remote monitoring temporal trends of case 2. Red dashed line represents the day of emergency room admission, while missing transmissions covered the period of hospital stay. Graph represents mean values per week with standard deviation.
The first case showed a significant and sudden increase in mean and nocturnal heart rate. Interestingly, this jump occurred almost 2 weeks in advance of hospital admission. Nocturnal and mean heart rates had their peak the first day of the increasing trend with an overlapping value greater than 70 bpm. The effect of COVID-19 on heart rate is not completely clear to date, but tachycardia is a quite common finding in community-acquired pneumonia [5]. In our case, a jump in mean/nocturnal heart rate was the first RM observation and was associated with a progressive and continuous decrease in physical activity that should reflect the increasing patient’s symptoms. These changes could be similar to what is observed also during other infectious disease and, therefore, it is possible to hypothesize a low specificity for the COVID-19. It is interesting to note the quite stable trend of thoracic impedance that could be associated with the absence of signs of pleural effusion and potentially be related to a fibrotic pneumonia.

In the second case, significant changes in RM trends appeared simultaneously with patient symptoms and, therefore, can be considered less promising in terms of early warning. However, it is impressive how all the parameters showed a picture that clearly characterized a profound decompensation that was later confirmed. In fact, it is known that decreased activity, increased heart rate, and decreased thoracic impedance before admission are consistent with the passage of time during exacerbation of heart failure. From these RM data, we cannot determine whether heart failure has been exacerbated in association with COVID-19 infection, because even if not infected with COVID-19, if heart failure worsens, this time course may be followed. However, the observed RM findings may be useful for early patient contact, particularly in suspected COVID-19 where early reversal of respiratory failure could lead to improvements in hemodynamics even in the absence of direct cardiac support.

In conclusion, patients with complications related to the COVID-19 infection appeared to show variations in the RM temporal trends of clinical variables daily transmitted from implanted cardiac devices. From only two cases, these changes cannot be considered characteristics of the infection and likely are not specific to COVID-19, but owing the severity of the pandemic, further research could be focused on exploring a potential use of these data for early diagnosis, isolation, and treatment of infected patients.

Declaration of Competing Interest

L.A. and D. G. are employees of BIOTRONIK Italia. All the remaining authors have no major conflicts of interest to disclose.

Acknowledgments

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

[1] Inciardi RM, Adamo M, Lupi L, Cani DS, Di Pasquale M, Tomasoni D, Italia L, Zaccone G, Tedino C, Fabricatore D, Curnis A, Faggiano P, Gorga E, Lombardi CM, Milesi G, et al. Characteristics and outcomes of patients hospitalized for COVID-19 and cardiac disease in Northern Italy. Eur Heart J 2020;41:1821–9.

[2] Hindricks G, Taborsky M, Glisovic M, Heinrich U, Schumacher B, Katz A, Brachmann J, Lewalter T, Götte A, Block M, Kautzner J, Sack S, Hussel D, Piorkowski C, Søgaard L. Implant-based multiparameter telemonitoring of patients with heart failure (IN-TIME): a randomised controlled trial. Lancet 2014;384:583–90.

[3] Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. Nat Rev Cardiol 2020;17:259–60.

[4] Iacopino S, Placentino F, Coletta J, Pesce F, Pardeo A, Filannino P, Artale P, De siro D, Sorrenti P, Campagna G, Fabiano G, Peluso G, Giacone P, Petretta A. New-onset cardiac arrhythmias during COVID-19 hospitalization. Circ Arrhythm Electrophysiol 2020;13:e009040.

[5] Kaysin A, Vieira AJ. Community-acquired pneumonia in adults: diagnosis and management. Am Fam Phys 2016;94:698–706.