Cardiac implantable device interrogation in left ventricular systolic dysfunction reveals physiologic abnormalities prior to symptom onset in COVID-19: a case series

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Background	COVID-19 has affected individuals across the globe, and those with cardiac implantable electronic devices (CIEDs) likely represent a high-risk group. These devices can be interrogated to reveal information about the patient activity, heart rate parameters, and respiratory rate.
Case summary	Four patients with CIEDs and left ventricular dysfunction were admitted to a single institution for COVID-19 infection. Each patient survived hospitalization, and none required intensive care. Retrospectively, CIED interrogation revealed each patient had decreased activity level prior to their reporting COVID-19 symptoms. Similarly, respiratory rate increased before symptom onset for three of the patients, while one did not have these data available. Of the three patients with heart rate variability (HRV) available, two had decreased HRV before they developed symptoms. After hospital discharge, these parameters returned to their baseline.
Discussion	This case series suggests physiologic changes identifiable through interrogation of CIEDs may occur prior to the reported onset of COVID-19 symptoms. These data may provide objective evidence on which to base more sensitive assessments of infectious risk when performing contact tracing in communities.
Keywords	COVID-19 • Contact tracing • Cardiac internal electronic device • Systolic dysfunction • Case report
ESC Curriculum	5.9 Pacemakers • 9.9 Cardiological consultations • 5.10 Implantable cardioverter defibrillators • 6.2 Heart failure with reduced ejection fraction

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Learning points

- Patients exposed to SARS-CoV-2 may begin to have altered activity level, respiratory rate, and heart rate variability prior to reporting symptoms of COVID-19.
- Data from cardiac implantable electronic devices in patients with systolic dysfunction can be monitored remotely for physiologic changes after exposure to SARS-CoV-2 virus, which may improve current contact tracing methods.

Introduction

The COVID-19 pandemic has affected individuals across the globe, and a vulnerable subgroup may be those with cardiac implanted electronic devices (CIEDs). Nonetheless, CIEDs record a host of patient clinical data in an ongoing fashion, including heart rate, heart rate variability (HRV), respiratory rate, and patient activity level.[1] Many patient characteristics and serum markers have been shown to be predictive of certain COVID-19 outcomes.[2] While CIEDs have been used to determine the patient activity level during regional lock-downs, the data from CIEDs have not yet been thoroughly examined as a predictive measure, nor as an instrument to be used for contact tracing.[3,4] Here, four patients with CIEDs from a single centre who were admitted for acute COVID-19 infection between March and May 2020 are described. Their devices were interrogated as part of their clinical management. As COVID-19 continues to spread across the globe with new variants and variable vaccination rates, CIEDs may represent an opportunity for contract tracing, which remains important.[2,5] Knowledge of how CIEDs can be leveraged to anticipate and mitigate the spread of COVID-19 may improve outcomes within communities.

Timeline

Patient 1, CRT-D (Boston Scientific)

Three weeks prior to admission	Respiratory rate increased
Five days prior to admission	Activity level decreased, heart rate, and heart rate variability decreased
Three days prior to admission	**Symptoms began**
Day 1	Hospital admission
Day 11	Hospital discharge
One week after discharge	Heart rate variability increased and respiratory rate decreased
One month after discharge	Activity level increased

Patient 2, CRT-D (Boston Scientific)

Three weeks prior to admission	Activity level decreased
One- and one-half weeks prior to admission	Respiratory rate increased and heart rate variability decreased
One week before admission	**Symptoms began**
Day 1	Hospital admission
Day 7	Hospital discharge
One day after discharge	Respiratory rate decreased
One week after discharge	Heart rate variability decreased and activity level increased

Patient 3, CRT-D (Boston Scientific)

Two weeks prior to admission	Activity level decreased
One week prior to admission	Respiratory rate increased
Two days prior to admission	**Symptoms began**
Day 1	Hospital admission
Day 2	Hospital discharge

Continued

Continued

Patient 1, CRT-D (Boston Scientific)

One day after discharge	Respiratory rate decreased
One week after discharge	Activity level increased

Patient 4, CRT-D (Boston Scientific)

One month prior to admission	Activity level decreased
Four days prior to admission	**Symptoms began**
Day 1	Hospital admission.
Day 2	Hospital discharge.
One day after discharge	Activity level increased and heart rate variability increased.

Outlined cells delineate changes in device measures that preceded the onset of reported symptoms.
CRT, cardiac resynchronization therapy; ICD, implanted cardioverter defibrillator.

Patient 1

A 73-year-old man with a history of non-ischaemic cardiomyopathy, left bundle branch block (LBBB), New York Heart Association (NYHA) Class III functional class, and a primary prevention cardiac resynchronization therapy-defibrillator (CRT-D) (Momentum®, Boston Scientific, implanted 2019) with subsequent recovery of left ventricular ejection fraction (LVEF) presented with several days of a dry cough, diarrhoea, and lightheadedness. His home medications included aspirin, atorvastatin, carvedilol, telmisartan, spironolactone, and furosemide. Admission vital signs and laboratory results are noted in *Table 1*. Due to his hypoxia, the patient was admitted to the hospital, where he received corticosteroids, tocilizumab, and supplemental oxygen via nasal cannula, and he was enrolled in a blinded trial studying the effects of anti-inflammatory drug (group assignment unknown).

Routine remote device interrogation of his device performed after his admission demonstrated increased respiratory rate, increased mean heart rate, decreased activity level, and reduction in HRV in the days leading up to his hospital presentation. Furthermore, his mean daily and nocturnal heart rates increased over this same time period.

He was hospitalized for 11 days in a non-intensive care COVID unit, during which time he had no arrhythmias, required a maximum of 2 L oxygen via nasal cannula, and he was discharged home. His respiratory rate and heart rate both returned towards normal values over the course of the inpatient stay. His activity level slowly increased over subsequent months, as did his HRV.

Patient 2

A 57-year-old man with ischaemic cardiomyopathy (ICM) and LVEF 20%, LBBB, primary prevention CRT-D (Inogen®, Boston Scientific, implanted 2019), HIV, and paroxysmal atrial fibrillation presented with 1 week of fever, cough, and progressively worsening shortness of breath and found to have COVID-19 pneumonia. Home medications included aspirin, atorvastatin, carvedilol, and lisinopril. Admission vital signs and laboratory results are noted in *Table 1*. He was treated with corticosteroids, and he did not require supplemental oxygen.

Remote device interrogation after his admission revealed that for 4 days prior to his reported symptoms (and 10 days prior to admission), his respiratory rate increased, his activity level and HRV declined, and

Table 1 Admission vital signs

Patient	Length of hospital admission (days)	Troponin I (ng/mL)	C-reactive protein (mg/dL)	Temperature (°C)	Blood pressure (mmHg)	Oxygen saturation on room air (%)	Respiratory rate (r.p.m.)	Heart rate (b.p.m.)
1	11	0	3.7	36.6	117/74	90	18	91
2	7	0.1	NA	39.6	132/97	97	18	84
3	2	0.047	8.5	36.9	110/73	92	20	92
4	2	0	7.8	37.5	160/65	95	16	67

NA, not available.

mean and maximum heart rates increased. He was discharged home after 7 days without supplemental oxygen or complications, after which time his respiratory rate, activity level, and HRV improved towards normal, but his mean heart rate continued to slowly increase over the next several days after discharge.

Patient 3

A 57-year-old man with ICM and LVEF 20%, prior coronary artery bypass graft, bioprosthetic mitral valve, chronic kidney disease, dual-chamber secondary prevention implanted cardioverter defibrillator (ICD) (Dynagen EL®, Boston Scientific, implanted 2017), and paroxysmal atrial fibrillation presented with 2 days of shortness of breath, cough, lightheadedness, nausea, vomiting, and diarrhoea. He had seen his primary care doctor initially, who referred him for outpatient COVID-19 testing. When the results returned positive, given his constellation of ongoing symptoms, he was directly admitted. His home medications included aspirin, atorvastatin, carvedilol, sacubitril-valsartan, spironolactone, isosorbide mononitrate, hydralazine, furosemide, and amiodarone. Admission vital signs and laboratory results are noted in Table 1. He was treated with corticosteroids, and he was discharged after 1 day without any complications or the need for supplemental oxygen.

Seven days leading up to symptom onset, his respiratory rate increased and activity level decreased. The transmission report is missing several days of respiratory rate immediately before symptoms reportedly began, which can occur with poor respiratory excursion and shallow breathing.[6] There were insufficient data to determine HRV (as in this device, heart rate data are only collected when the patient atrial senses >70% of the time, and this patient was predominantly atrially paced).[6] After his discharge, his activity level increased and his respiratory rate remained elevated for several weeks.

Patient 4

A 75-year-old man with a history of ICM, LVEF of 20%, dual-chamber ICD for secondary prevention after sustained ventricular tachycardia (Evera XT®, Medtronic, implanted 2014), diabetes mellitus, and hypertension presented with 4 days of non-productive cough and diffuse myalgias. His home medications include rosuvastatin, metoprolol tartrate, losartan, furosemide, amiodarone, and apixaban. His admission vital signs and laboratory results are noted in Table 1, and his COVID-19-specific therapies included corticosteroids. He required no supplemental oxygen.

Twenty-six days leading up to his COVID-19 symptoms, which preceded his admission by 4 days, he had decreased measured activity yet stable HRV when compared with previous months. Respiratory rate

was not available as his device did not include a respirometer. Additionally, he had a significant increase in average heart rate (and a decrease in the percentage of atrial pacing) in the days leading up to hospital admission. The day after discharge, his activity level and his HRV increased.

Discussion

A registry of 500 consecutive inpatients with COVID-19 was queried for those with CIEDs; 19 individuals were identified, of which 4 had remote interrogations within 3 months after their admission. Here, we describe these patients with CIEDs and COVID-19, and how remote device interrogation revealed measurable changes in physical activity, heart rate, HRV, and respiratory rate days prior to reported symptom onset of COVID-19. The patients were hospitalized from March to May 2020, prior to the rise of the multiple SARS-CoV-2 variants. Similarly, all infections occurred after local lockdown restrictions were in place, and therefore, physical activity data are not representative of changes that would correspond to these enforcements. The data described here were collected retrospectively; however, CIEDs are able to be monitored in near real time as well. The physiologic data trends may have value in contact tracing, even beyond simply using patient-reported symptoms or last known SARS-CoV-2 exposure, the current standards.[7] All changes in physiologic parameters in this case series were based on visual assessment and were not statistically analysed. This visual approach to identifying trends in data accurately reflects everyday clinical practice for physiologic data in CIED interrogations. The techniques used in this case series may therefore be widely applicable to everyday practice and do not require special tools.

Each patient described is a high risk for a severe course of COVID-19, based on the presence of systolic dysfunction.[2] From their remote device interrogations collected after their COVID-19 admissions, those patients with available respiratory rate data demonstrated an increased respiratory rate in the days leading up to their admissions. All patients were less active leading up to not just hospital admission, but also prior to reported symptom onset—in Patient 4, as many as ~30 days prior (suggesting his hospitalization occurred towards the end of his illness). Heart rate variability decreased in two out of three patients for whom such data were available, as much as ~10 days prior to presentation and 4 days prior to symptom onset in at least one patient (Patient 1) (Table 2). The mean heart rate trends were available on CIED interrogation for three patients and each patient had an increase in heart rate in the days leading up to his hospitalization. It is important to highlight that the changes identified by CIED interrogation began prior to reported symptom onset for each patient, though the exact number of days varied between each patient. After discharge, each derangement returned to normal, further suggesting that they were COVID-19-mediated. The time course here emphasizes that objective

Table 2 **Physiologic changes identified through remote device interrogation**

Patient	Prior to reported symptoms			After discharge		
	Respiratory rate	Activity level	Heart rate variability	Respiratory rate	Activity level	Heart rate variability
1	↑	↓	↓	↓	↔	↑
2	↑	↓	↓	↓	↑	↑
3	↑	↓	NA	↔	↑	NA
4	NA	↓	↔	NA	↑	↑

NA, not available; ↑, trend increased; ↓, trend decreased; ↔, trend steady.

data, which can be collected via remote interrogations, begin to deviate from the norm prior to subjective complaints (*Figure 1*).

In those with infectious illness, it is well documented and often observed that activity level and HR may have a pathologically inverse relationship.[8,9] Similarly, HRV, determined via different proprietary CIED algorithms, can be influenced by a person's autonomic nervous system, thermoregulation, or endocrine system.[10,11] Heart rate variability has been demonstrated to decline in patients with systemic illness and is collected by CIEDs in an effort to predict acute heart failure exacerbations.[1,7–12] Rising respiratory rate and decreasing activity level are also signs of a person's deteriorating well-being.[8,9] Interestingly, individuals with COVID-19 are more likely to have shallow and rapid breathing.[13] Patient 3's 'missing' respiratory data from the CIED may be due to shallow or irregular breathing. Other possibilities include noise detection by the minute ventilation sensor, or reduction in the amplitude of the respiratory impedance signal; however, in this case, shallow or irregular breathing is most likely.[6]

It should be noted that each patient here had CIED parameter derangements despite having relatively mild disease courses with no intensive care admissions, intubations, or mortality. Patient 4, who had

elevated inflammatory markers, is the only patient without a change in HRV, though Patients 1 and 2 had reduced HRV despite normal CRP. These data call into question the sensitivity and specificity of HRV in identifying COVID-19 infection, but this warrants further study, including whether these obtained measures from CIEDs can be used alone or in conjunction to predict outcomes of COVID-19.

We also demonstrate the plausibility of using data from remote interrogations as a means of contract tracing. Currently, individuals who are unknowingly exposed to COVID-19 may be contacted by a committee or agency to inform them of the exposure and instructed to quarantine and/or complete viral testing.[7] Responses to questions regarding the onset of symptoms may be influenced by subjectivity and difficulty with recall. The cases presented here suggest that implantable device data may have added value in contact tracing, by identifying a period of infection objectively, even prior to the onset of reported symptoms.

Cardiac implantable electronic device interrogation as a means to assess SARS-CoV-2 transmissibility warrants more investigation, as it presumes that changes in activity level, heart and respiratory rate, and HRV correspond with not just infection, but a sufficient viral load to transmit. Furthermore, this small case series draws no conclusions about the

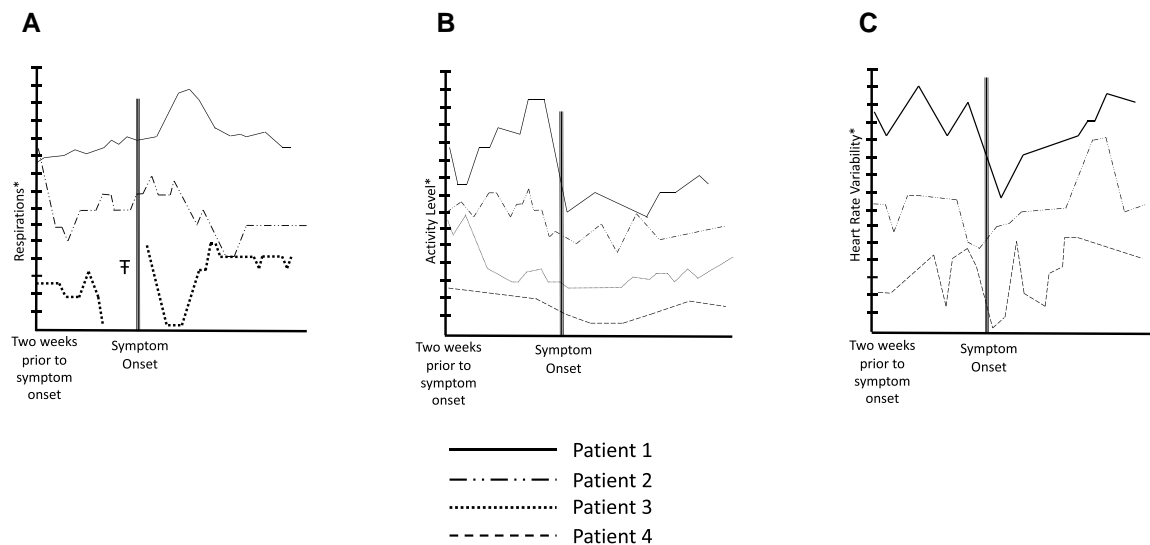Physiologic Trends Relative to COVID-19 Symptom Onset

Figure 1 Each tracing represents a running 3-day average of the parameter. (*A*) Respiratory rate, (*B*) activity level, and (*C*) heart rate variability. *The curves are offset on the vertical axis for interpretability. The vertical axis represents incremental units of measure, but not absolute values, and therefore is not numerically labelled. Full tracings for each parameter are available in Supplementary material online. ‡Respiratory rate data are unavailable in the time preceding symptoms for Patient 4. Per device manufacturer, the most common source of respirometer malfunction is shallow breathing.[6]

association of CIED findings with biomarker values or COVID severity, which has previously been well examined.[2] As this is a case series, we did not investigate the association of CIED data with outcomes.

As SARS-CoV-2 variants continue to affect many regions around the world, contact tracing remains crucial in keeping communities safe. Contact tracing currently largely depends on patient-reported data subject to various forms of bias. This case series of four patients with CIEDs who were hospitalized for COVID-19 illustrates that objective, quantifiable physiologic changes occurred prior to patient-reported symptom onset. These findings suggest CIED interrogations may enhance current contact tracing efforts.

Lead author biography

Dr Matthew S. Delfiner is a Fellow in Cardiovascular Medicine at the Lewis Katz School of Medicine at Temple University Hospital. He has a particular interest in haemodynamics, echocardiography, and medical education.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

Data availability

A statement that full tracings are available in the supplementary data is provided. There is no other data used in the case series.

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