ORIGINAL RESEARCH ARTICLE

Multiparameter diagnostic sensor measurements in heart failure patients presenting with SARS-CoV-2 infection

Roy S. Gardner[1]*, Robert C. Capodilupo[2], Rezwan Ahmed[3], Craig M. Stolen[3], Qi An[3], Viktoria Averina[3], Adrian F. Hernandez[4] and John P. Boehmer[5]

[1]*Golden Jubilee National Hospital, Clydebank, Glasgow, UK;* [2]*New England Heart and Vascular Institute, Catholic Medical Center, Manchester, NH, USA;* [3]*Boston Scientific, Arden Hills, MN, USA;* [4]*Duke University School of Medicine, Durham, NC, USA; and* [5]*Penn State Milton S Hershey Medical Center, Hershey, PA, USA*

Abstract

Aims Implantable device-based sensor measurements including heart sounds, markers of ventilation, and thoracic imped-ance have been shown to predict heart failure (HF) hospitalizations. We sought to assess how these parameters changed prior to COVID-19 (Cov-19) and how these compared with those presenting with decompensated HF or pneumonia.

Methods and results This retrospective analysis explores patterns of changes in daily measurements by implantable sensors in 10 patients with Cov-19 and compares these findings with those observed prior to HF ($n = 88$) and pneumonia ($n = 12$) hos-pitalizations from the MultiSENSE, PREEMPT-HF, and MANAGE-HF trials. The earliest sensor changes prior to Cov-19 were ob-served in respiratory rate (6 days) and temperature (5 days). There was a three-fold to four-fold greater increase in respiratory rate, rapid shallow breathing index, and night heart rate compared with those presenting with HF or pneumonia. Furthermore, activity levels fell more in those presenting with Cov-19, a change that was often sustained for some time. In contrast, there were no significant changes in 1st or 3rd heart sound (S_1 and S_3) amplitude in those presenting with Cov-19 or pneumonia compared with the known changes that occur in HF decompensation.

Conclusions Multi-sensor device diagnostics may provide early detection of Cov-19, distinguishable from worsening HF by an extreme and fast rise in respiratory rate along with no changes in S3.

Introduction

Heart failure (HF) is associated with severe symptoms, a high mortality rate, and frequent and recurrent hospitalization. Whilst treatment options have improved dramatically over the last three decades,[1–4] predicting and preventing HF decompensation remain a challenge. There has been growing interest in the use of device diagnostics in the management of HF patients. One such algorithm, HeartLogic, has been proven to provide a sensitive and early alert for impending cardiac decompensation.[5] This algorithm combines data from ICD or CRT-D based measurements of heart sounds, ventila-tion, impedance, heart rate, and activity.[5,6] As a potentially

useful new feature, these devices also have the ability to measure temperature in the pulse generator. As it is not calibrated to core body temperature, the device temperature trend is not currently displayed on the patient reports. How-ever, deviations in core body temperature could be reflected in the device's temperature measurements, and the prospect of an expansion of the device's diagnostic ability to detect other causes of acute dyspnoea (e.g. respiratory infection) is tantalizing.

A novel coronavirus, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was first identified in December 2019 and declared a pandemic 4 months later. The resulting stress on healthcare resources has created evolving models

of healthcare delivery with increased reliance on telehealth and telemonitoring.[7] Common symptoms of those with SARS-CoV-2 infection resulting in COVID-19 include cough and shortness of breath,[8] and as less than half of patients exhibit fever at the time of admission, the differentiation between decompensated heart failure and COVID-19 can be challenging. Whilst great hope has been placed on the rapidly developed vaccines for this condition,[9,10] the ability to differentiate between causes of acute breathlessness is of great interest.[11]

The aim of this analysis was to characterize the suite of HeartLogic sensor data, as well as the new device-based feature that can detect changes in pulse generator temperature, in ten patients leading up to a presentation with COVID-19 to assess how these differ from those with decompensated heart failure.

Methods

This retrospective study analyses device-derived HeartLogic data from 10 patients presenting with COVID-19 (six patients from PREEMPT-HF study, ClinicalTrials.gov Identifier: NCT03579641; three patients from MANAGE-HF study, ClinicalTrials.gov Identifier: NCT03237858; and one patient consented outside of a clinical study) and compares these with data obtained from 88 patients presenting with cardiac decompensation in the MultiSENSE study[5] (ClinicalTrials.gov Identifier: NCT01128166) and 12 patients with pneumonia events occurring prior to February 2020 in the MANAGE-HF study. All patients had heart failure and were implanted with a Boston Scientific Cardiac Resynchronization Therapy Defibrillator or Implantable Cardioverter Defibrillator that had HeartLogic. Full inclusion and exclusion criteria can be found with the trial registrations at ClinicalTrials.gov. These patients represent all COVID-19 patients reported in MANAGE-HF and PREEMPT as of 6 October 2020. The PREEMPT study is ongoing, and additional cases may be subsequently identified.

HeartLogic comprises a diverse suite of sensors designed to target different aspects of pathophysiology associated with common signs and symptoms of heart failure. These include accelerometer-measured first and third heart sounds (S_1 and S_3, respectively), impedance-based measures of ventilation including respiratory rate and rapid shallow breathing index (RSBI, the ratio of respiratory rate to relative tidal volume), intra-thoracic total impedance, night heart rate, and patient activity. A multisensor algorithm, HeartLogic, was developed to aggregate daily changes from these sensor values to create the composite HeartLogic index that predicts an individual's daily risk for worsening HF.[5] This algorithm and set of implanted sensors are available in current implantable cardioverter defibrillators and cardiac resynchronization

therapy defibrillators (CRT-D) manufactured by Boston Scientific, Marlborough, MA.

An internal feature of these devices is the ability to monitor temperature at the location of the pulse generator. It is used within the devices for component monitoring purposes, such as battery status and not intended to provide a measure of core body temperature. The use of this feature in this setting is investigational. However, this parameter has the additional potential to help differentiate heart failure from infectious causes of breathlessness, such as COVID-19.

A COVID-19 event is defined as a positive SARS-CoV-2 test result. A HF event is defined as a clinical event with a primary cause of HF and (i) with a calendar date change; or (ii) with IV decongestive medications, aquapheresis, or other parenteral therapy. Similarly, a pneumonia event is defined as a hospital admission with a primary cause of pneumonia. All COVID-19 events were reported by the investigators and by an independent event committee. All HF events collected from the MultiSENSE study, and all pneumonia events plus three COVID-19 events from MANAGE-HF were adjudicated by an independent event committee. The remaining COVID-19 events were reported by principal investigators of the PREEMPT-HF study and by a HF physician but not independently adjudicated.

Statistical analysis

The daily sensor trends surrounding the clinical events were extracted and aligned by the day of events to reflect the sensor changing pattern. All trends other than the temperature trend were updated daily using averages across multiple measurements within a day. The temperature trend was a daily trend of temperature measurement collected once every 21 h.

A qualitative analysis was performed to understand the consistency of sensor changes across all identified COVID-19 events. We defined a baseline window of 30 days starting 60 days before the admission or test date and a pre-event window of 3 days including the day of admission or test. The averaged sensor data were compared between the pre-event and baseline windows for all COVID-19 events. A sensor trend is defined as changing, that is, increasing or decreasing, leading to a specific COVID-19 event when the pre-event value differ by (greater than or equal to) 1 standard deviation from the baseline value of that event.

The sensor trends from individual patients may demonstrate different patterns due to various pathophysiological impacts and clinical manifestations of COVID-19. As a result, we evaluated the time course of sensor changes by averaging sensor data across all patients in a 181-day window starting 90 days before each event. This window covered both pre-event and post-event sensor changes. Standard

error of mean was calculated on each day to represent the between-patient variations.

Because these physiological sensors were originally chosen based on their ability to reflect changes due to the worsening of HF, we were also interested in comparing sensor change patterns between HF, COVID-19, and other related diseases, for example, pneumonia. We quantified the sensor changes by comparing the averaged pre-event window data to the averaged baseline data as percentage of changes. To maintain consistency in comparison across the three disease events, we defined a fixed baseline window of 30 days starting 60 days before the admission or test date and a pre-event window of 3 days including the day of admission or test. Note that the baseline window used for this comparison does not match HeartLogic algorithm's baseline definition,[5] which was optimized for the HF application and thus may underrepresent the individual HF-related sensor changes seen by HeartLogic. The sensor changing results from these three types of events were compared against each other to provide more insights between diseases. All comparisons of sensor changes between COVID-19 events vs. HF events and COVID-19 events vs. pneumonia events were evaluated using an independent *t*-test.

Baseline demographics were compared using ANOVA for normally distributed continuous measurements and a Kruskal–Wallis test for non-normally distributed continuous measurements. A Fisher's exact test was used to compare categorical characteristics.

All statistical analyses were performed using SAS v9.4 (SAS Institute, Cary, North Carolina) or R v3.6.0 (R Foundation for Statistical Computing, Vienna). An alpha level of 0.05 was used for statistical significance. The study was conducted in accordance with the ethical standards of the institutional and national research committees and with the 1964 Declaration of Helsinki and its later amendments.

Results

Device-derived sensor data were obtained from ten patients diagnosed with COVID-19, 12 patients admitted with pneumonia, and 88 patients presenting with HF decompensation. Five of the 10 COVID-19 patients were hospitalized on the day of diagnosis, two patients were hospitalized 2 days after diagnosis, one subject 49 days after diagnosis, one received care in a long-term care facility, and one was treated as an outpatient. The average length of stay was 8.4 ± 5.3 days. One patient died, 2 months after diagnosis, with worsening of functional class from COVID-19 as the immediate cause of death. Overall, there were no statistically significant differences in the baseline clinical and demographic data between the COVID-19, pneumonia, and HF decompensation

cohorts (*Table 1*), although the mean age of those with COVID-19 was numerically lower at 61 years, and all were male, compared with those presenting with HF (67 years and 77% male).

Sensor data findings

Table 2 summarizes the sensor data at baseline and pre-event for patients presenting with COVID-19, pneumonia, or HF decompensation. Significant differences were observed between these presentations in a number of these parameters (*Figure 1*), most notably respiratory rate, rapid shallow breathing index, night-time heart rate, and patient activity. Of these changes, respiratory rate appears to rise first preceding increases in temperature (*Figure 2*). Moreover, respiratory rate and night-time heart rate sensors consistently showed a significant increase prior to events for almost all COVID patients (*Figure 3*).

Markers of ventilation

Although respiratory rate was seen to increase in pneumonia, HF decompensation, and COVID-19, the latter presentation increased five times more, with a mean increase of 27% from baseline (*Figure 1*), sometimes persisting long after presentation (*Figure 2*). Rapid shallow breathing index (RSBI), the ratio of respiration rate to relative tidal volume, was also seen to increase more notably in those with COVID-19 with a mean increase of 42% at diagnosis.

Night-time heart rate

Night-time heart rate increased leading up to all presentations, but this increase was nearly four times greater in those with COVID-19 (*Figure 1*), with an increase from a mean of 68 b.p.m. at baseline to 78 b.p.m. pre-event.

Patient activity

A reduction in patient activity was observed in all acute presentations although the fall from baseline in those with COVID-19 was greater than those presenting with decompensated heart failure or pneumonia, with a mean pre-event 3-day average activity of 0.75 h per day. Recovery time was also notably prolonged (*Figure 2*) in the COVID-19 cohort.

Table 1 Baseline demographic data in patients who presented with COVID-19, decompensated heart failure, and pneumonia events

Characteristic	Measurement	COVID-19 (N = 10)	HF (N = 88)	Pneumonia (N = 12)	P-value*
Age (years)	Mean ± SD	61.3 ± 10.5	67.2 ± 11.0	68.5 ± 14.1	0.26
Male sex	Male [N/total N (%)]	10/10 (100.0%)	68/88 (77.3%)	9/12 (75.0%)	0.28
NYHA class	N (%)				
	I	2 (22.2%)	4 (4.5%)	0 (0.0%)	
	II	3 (33.3%)	42 (47.7%)	6 (66.7%)	
	III	5 (50.0%)	40 (45.5%)	3 (33.3%)	
	Unknown	0 (0.0%)	2 (2.3%)	0 (0.0%)	
LV ejection fraction (%)	Mean ± SD	31.6 ± 12.9	27.2 ± 11.6	28.9 ± 7.1	0.47
Body mass index (kg/m²)	Mean ± SD	29.6 ± 7.8	30.1 ± 6.7	29.8 ± 6.4	0.96
Systolic blood pressure (mmHg)	Mean ± SD	121.4 ± 15.8	119.6 ± 18.7	117.4 ± 18.0	0.88
Resting heart rate (b.p.m.)	Mean ± SD	79.0 ± 12.9	72.9 ± 11.8	74.5 ± 10.9	0.56
Resting respiratory rate (br/min)	Mean ± SD	17.0 ± 1.2	18.9 ± 9.6	18.1 ± 4.1	0.90
History of atrial fibrillation	N/total N (%)	4/10 (40.0%)	46/88 (52.3%)	3/12 (25.0%)	0.19
Previous myocardial infarction	N/total N (%)	4/10 (40.0%)	45/88 (51.1%)	7/12 (58.3%)	0.73
Previous CABG	N/total N (%)	3/10 (30.0%)	33/88 (37.5%)	3/12 (25.0%)	0.71
Renal dysfunction	N/total N (%)	5/10 (50.0%)	48/88 (54.5%)	1/12 (8.3%)	0.008
Diabetes	N/total N (%)	6/10 (60.0%)	49/88 (55.7%)	6/12 (50.0%)	0.88
Serum creatinine (mg/dL)	Mean ± SD	1.2 ± 0.3	1.7 ± 1.3	1.2 ± 0.5	0.27
NT-proBNP (pg/mL)	Median (Q1, Q3)	884.0 (517.0, 1314.0)	1979.0 (1000.0, 4504.0)	1633.5 (578.0, 5441.0)	0.28†
Concomitant medications	Anti-coagulants	8/10 (80.0%)	83/88 (94.3%)	11/12 (91.7%)	0.13
	ACE-I/ARB/ARNI	7/10 (70.0%)	53/88 (60.2%)	10/12 (83.3%)	0.31
	Beta-blockers	10/10 (100.0%)	76/88 (86.4%)	12/12 (100.0%)	0.37
	Aldosterone antagonists	5/10 (50.0%)	38/88 (43.2%)	5/12 (41.7%)	0.94
	Diuretics	9/10 (90.0%)	78/88 (88.6%)	11/12 (91.7%)	1.00

*P-values were calculated using ANOVA for continuous measures and a Fisher's exact test for categorical measures.
†P-value for NT-proBNP was calculated using Kruskal–Wallis test.

ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; br, breath; CABG, coronary artery bypass graft; HF, heart failure; LV, left ventricular; N, number; SD, standard deviation; Q1/Q3, first and third quartile.

Table 2 Average sensor values at baseline (30-day average) and pre-event (3-day average) in 10 patients with COVID-19, 12 patients with Pneumonia, and 88 patients with decompensated heart failure events

Device sensors	COVID-19					Pneumonia				
	N	Baseline, mean ± SD	Pre-event, mean ± SD	Changes, mean ± SD	Paired t-test	N	Baseline, mean ± SD	Pre-event mean ± SD	Changes mean ± SD	Paired t-test
Respiratory rate (median, br/min)	10	17.19 ± 2.2	21.88 ± 3.84	4.7 ± 2.86	**<0.001**	12	16.76 ± 3.97	17.76 ± 4.24	1.00 ± 2.46	0.19
RSBI (br/min/Ohm)	10	15.12 ± 3.87	21.42 ± 6.54	6.3 ± 6.44	**0.01**	12	13.07 ± 5.96	14.47 ± 5.72	1.40 ± 3.02	0.14
Night heart rate (b.p.m.)	10	67.81 ± 11.14	77.5 ± 14.6	9.69 ± 5.85	**<0.001**	12	76.26 ± 8.71	79.64 ± 11.14	3.38 ± 6.33	0.09
Thoracic impedance (Ohm)	10	47.46 ± 9.66	50.08 ± 11.66	2.62 ± 2.64	**0.01**	12	47.63 ± 10.81	48.00 ± 10.12	0.37 ± 3.15	0.69
Temperature (F)	10	94.74 ± 1.59	97.04 ± 2.1	2.3 ± 2.0	**0.006**	12	95.00 ± 1.65	95.87 ± 0.55	0.59 ± 1.02	0.07
Activity (h)	10	1.41 ± 0.88	0.75 ± 0.54	−0.66 ± 0.68	**0.01**	12	0.99 ± 0.84	0.70 ± 0.53	−0.29 ± 0.52	0.08
Heart sounds S_1 (mG)	10	2.05 ± 1.31	2.28 ± 1.68	0.22 ± 0.42	0.12	12	2.73 ± 1.16	2.65 ± 1.07	−0.08 ± 0.45	0.56
Heart sounds S_3 (mG)	10	0.81 ± 0.17	0.84 ± 0.3	0.03 ± 0.19	0.69	12	1.04 ± 0.39	1.19 ± 0.63	0.16 ± 0.35	0.15
HeartLogic index	10	7.08 ± 9.28	8.75 ± 11.62	1.66 ± 9.12	0.58	12	14.32 ± 13.87	16.74 ± 15.36	2.42 ± 7.31	0.28

Table 2 (continued)

Device sensors	Heart failure					COVID vs. pneumonia t-test	COVID vs. HF t-test
	N	Baseline mean ± SD	Pre-event mean ± SD	Changes mean ± SD	Paired t-test		
Respiratory rate (median, br/min)	85	19.12 ± 3.02	20.15 ± 3.35	1.03 ± 1.92	**<0.001**	**0.005**	**0.003**
RSBI (br/min/Ohm)	88	9.61 ± 3.17	11.26 ± 4.00	1.66 ± 2.08	**<0.001**	**0.05**	**0.05**
Night heart rate (b.p.m.)	87	73.94 ± 9.38	77.35 ± 10.42	3.41 ± 6.59	**<0.001**	**0.02**	**0.008**
Thoracic impedance (Ohm)	86	45.51 ± 9.38	42.82 ± 9.55	−2.69 ± 3.38	**<0.001**	**0.08**	**<0.001**
Temperature (F)	87	96.24 ± 1.30	96.24 ± 1.52	−0.01 ± 0.98	0.95	**0.03**	**0.005**
Activity (h)	88	1.41 ± 1.51	0.90 ± 1.23	−0.51 ± 0.91	**<0.001**	0.17	0.53
Heart sounds S_1 (mG)	87	2.13 ± 0.77	1.98 ± 0.71	−0.15 ± 0.38	**<0.001**	0.12	**0.02**
Heart sounds S_3 (mG)	85	1.22 ± 0.39	1.34 ± 0.45	0.12 ± 0.27	**<0.001**	0.28	0.18
HeartLogic index	84	11.77 ± 10.28	23.81 ± 17.02	12.04 ± 15.98	**<0.001**	0.83	**0.007**

Figure 1 Mean relative change in sensor data between baseline and prior to COVID-19, pneumonia, and heart failure events. Pre-event sensor changes were calculated based on a fixed baseline (60 to 30 day prior to the event) for all three disease events.
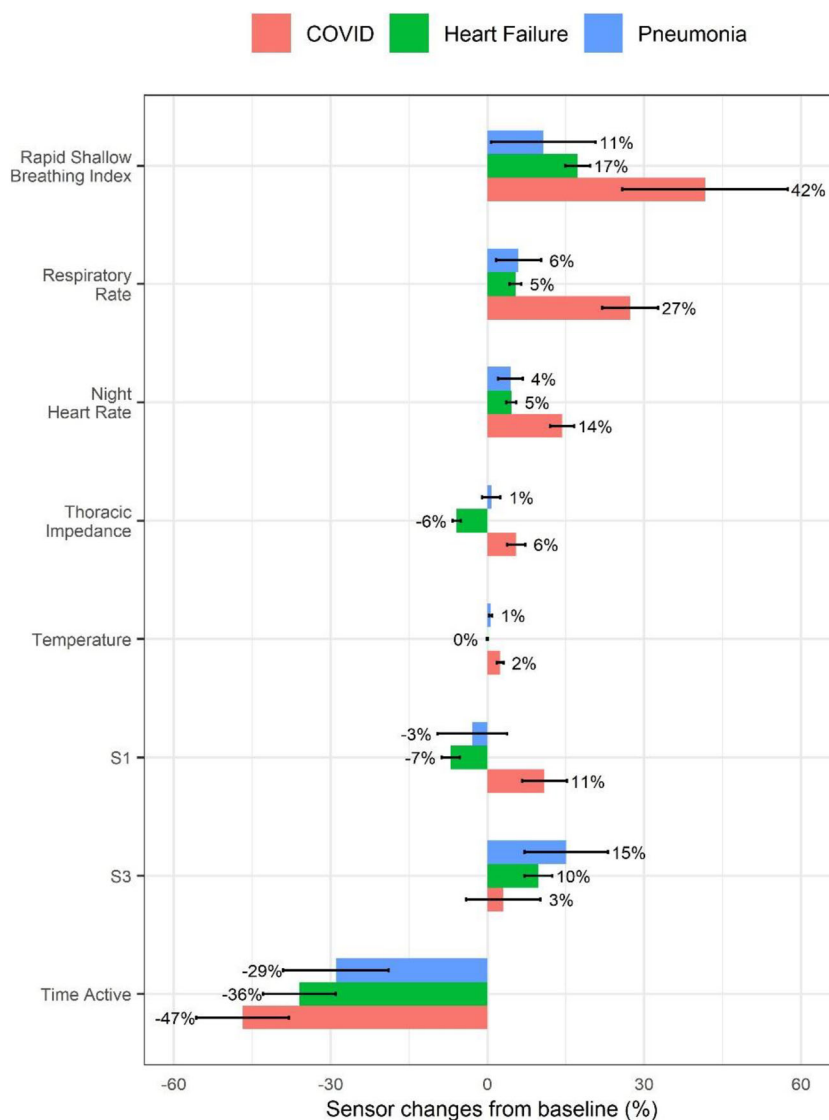
Heart sounds

As previously shown, there was a significant decrease in S_1 and increase in S_3 in those presenting with decompensated heart failure (both $P < 0.001$). However, no significant changes were seen in the amplitude of either heart sound in those presenting with COVID-19.

Thoracic impedance

In contrast to the reduction in thoracic impedance seen in patients with decompensated HF, there was a small—albeit variable—increase (mean 2.6 ± 2.6 ohms) in thoracic impedance leading up to diagnosis with COVID-19 ($P < 0.001$). There was no significant change in thoracic impedance in those with pneumonia.

Temperature

Although this new feature is currently commercially inaccessible, we observed a 2.3% increase in temperature in those presenting with COVID-19 from a median of 35.29 degrees Celsius (range 33.13–37.15°C) (95.53 degrees Fahrenheit, range 91.63–98.87) 7 days prior diagnosis to 36.38°C (range 35.12–38.05°C), (97.49°F, range 95.23–100.49°F) 3 days prior to diagnosis, and a median of 36.23° C

Figure 2 (A) Mean sensor trends leading up COVID-19 diagnosis (day 0). Solid line denotes mean sensor value with surrounding shading representing SEM. Blue dashed line, baseline; green line, earliest rise. (B) Comparison of mean sensor changes trends leading to a COVID-19 diagnosis (day 0), a decompensated heart failure event (day 0), or hospitalization for pneumonia (day 0). Solid line denotes mean percent change from baseline, with surrounding shading representing SEM. Dashed lines denote earliest rise from baseline. Red = COVID-19, green = heart failure, blue = pneumonia.
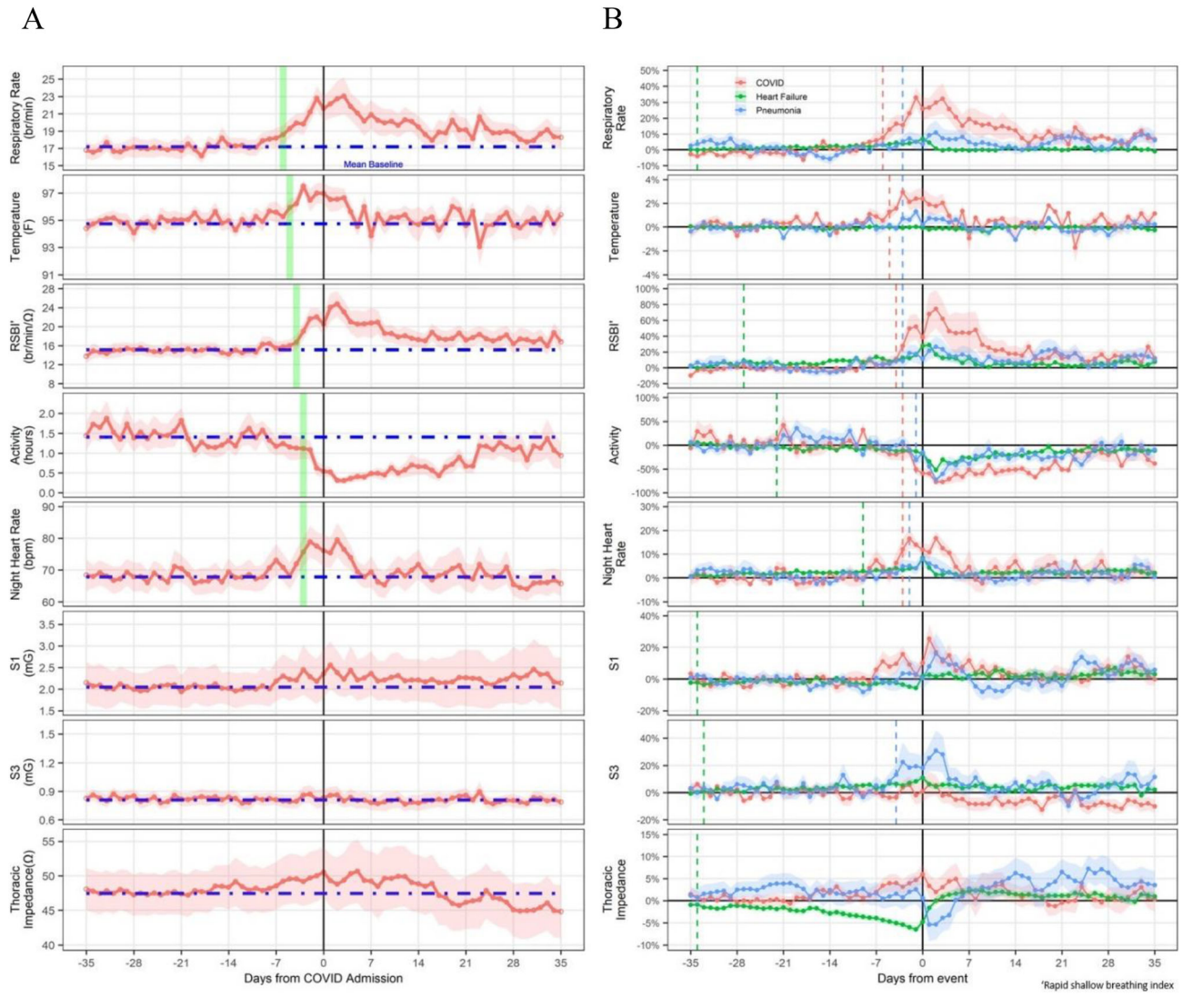
(range 34.03–38.54°C) (97.22°F, range 93.25–101.37°F) at the time of the SARS-CoV-2 test (*Figure 1*).

HeartLogic

As expected, there was a significant two-fold increase in HeartLogic index in those presenting with decompensated heart failure (*P* < 0.001; *Table 1*). This contrasts with both infective presentations where there was no significant increase in HeartLogic leading up to COVID-19 or pneumonia events. However, the average HeartLogic index was observed to increase *after* diagnosis with COVID-19, demonstrating the

specificity of the algorithm for heart failure and suggesting that COVID-19 exacerbates the heart failure syndrome.

Discussion

In this paper, we have demonstrated the ability of an implanted device to characterize the pathophysiologic changes of COVID-19. Furthermore, we have shown how these changes can be differentiated from those already described in cardiac decompensation.

Figure 3 Patient-specific sensor changes between baseline and the period prior to COVID-19 events. Each row displays a specific COVID-19 patient's sensor change status. A patient's sensor increase or decrease is determined when the sensor difference at pre-event is greater than or equal to 1 standard deviation of their own baseline.
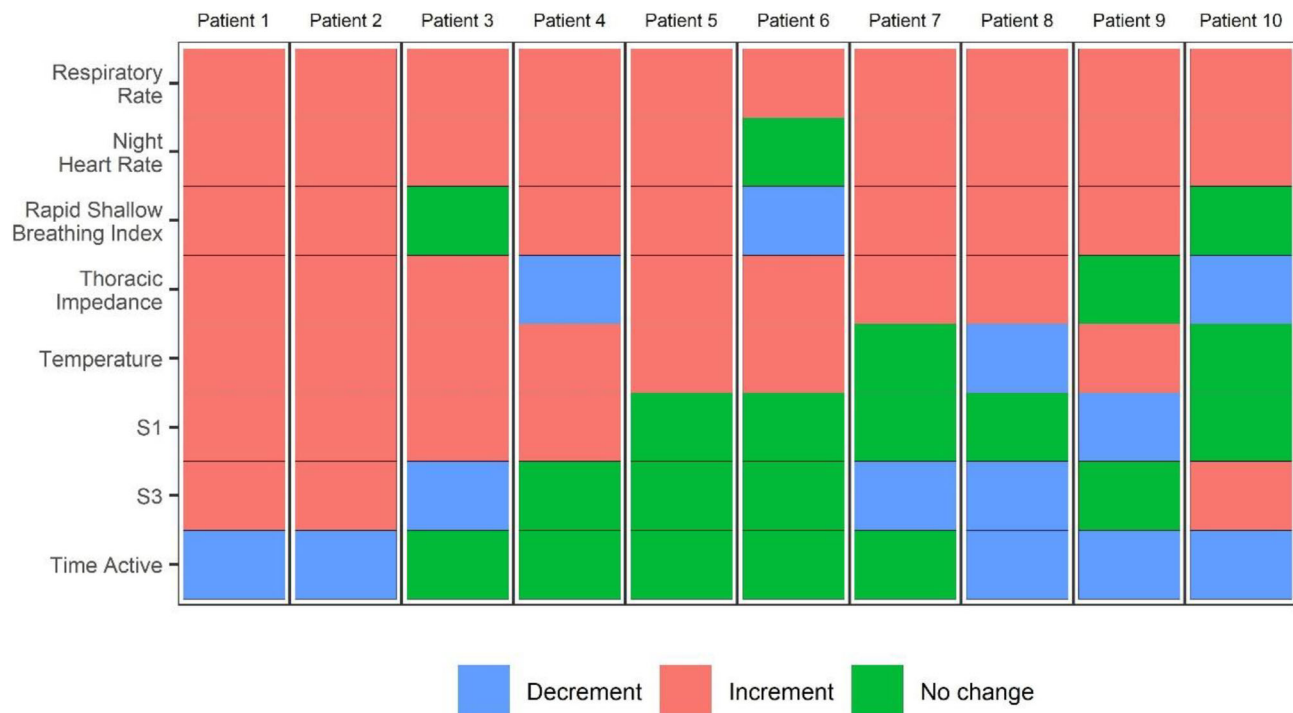
These innovative, physiologically relevant sensors were designed to monitor common signs associated with worsening HF, including heart sounds,[12,13] markers of ventilation, and patient activity, together with traditional device-based parameters such as thoracic impedance and heart rate. As such, they have the potential to enable the bedside approach of assessing HF patients, but in an automatic and continuous fashion in ambulatory patients. Moreover, these parameters have been shown to change predictably leading up to a HF event, and a multisensory algorithm (HeartLogic) has been shown to detect 70% of HF events with a median of 34 days advance notice.[5] Additionally, the risk of having a HF event was 10-fold higher in those with a HeartLogic alert than those who were outside an alert.[6]

Given the pandemic declared due to COVID-19, healthcare resources have been stretched worldwide. As such, the use of remote monitoring technology has never been so sought after.[7] In the UK, HF represents the leading cause of acute hospital admission in those over 65 years of age. However, decompensated heart failure and COVID-19 share common symptoms including cough and shortness of breath,[8] and less than half of patients with COVID-19 exhibit fever at the time of admission. Subsequently, in clinical practice, differentiating between decompensated heart failure and COVID-19 can be challenging.

Unlike in decompensated heart failure where the first heart sound diminishes and the third heart sound becomes more prominent,[12] there were no such changes seen in patients with COVID-19. However, enhanced by the acute nature of COVID-19 infection (compared with the more insidious onset of cardiac decompensation), there were pronounced changes in the other device-based parameters, most notably markers of ventilation and patient activity.

Respiratory distress is common in HF with 89% of patients hospitalized for HF in the ADHERE registry reporting the presence of dyspnoea.[14] Whilst we confirmed that respiratory rates rise prior to a heart failure decompensation, there was a consistent and dramatic (on average five-fold larger) increase in respiratory rate (mean of 27%, 4.7 br/min vs. 5%, 1.03 br/min) in patients presenting with COVID-19. Furthermore, rapid shallow breathing index—which synergistically combines the progressive increase in respiratory rate and decrease in tidal volume to yield a single combined index of emerging respiratory distress—increased on average more than four times more than that following an admission with cardiac decompensation. Additionally, the magnitude of respiratory changes in patients presenting with COVID-19 was also much larger than those presenting with pneumonia, suggesting a much more severe disease.

A modest increase in thoracic impedance was seen in those presenting with COVID-19 and contrasts with the fall seen in those with HF decompensation. This is also different from patients presenting with pneumonia, where there was no significant change in this parameter. In several patients following COVID-19 diagnosis, a further rise in impedance was seen, possibly reflecting volume loading that frequently occurs in the septic patient.

Predictably, patient activity fell in all sets of patients prior to hospitalization, although this effect was more pronounced in those presenting with COVID-19. The long-lasting effect of COVID-19 on several patient's activity levels following diagnosis most likely represents the prolonged recovery time experienced by many of those suffering from this viral illness.

Although not commercially accessible currently, the changes in body temperature identified by these implanted devices are very interesting and potentially open future possibilities for this technology. Differentiating between an infective presentation and decompensation episode would be very valuable in clinical practice. In this observational series, temperature was seen to rise by a median of 0.9°C (1.7°F) between a week prior to diagnosis, and on presentation, although the peak was 3 days prior to diagnosis, possibly reflecting the use of anti-pyretics (e.g. paracetamol [acetaminophen]) thereafter.

Overall, COVID-19 events were preceded by a unique pattern of sensor trends that were readily distinguishable from that of worsening HF or pneumonia, and that differed in individual contribution, magnitude, and onset of change (*Figures 1* and *2*).

To ensure prevention of COVID-19 in ambulatory HF patients, the European Society of Cardiology (ESC) has encouraged the use of remote monitoring with implantable device data and a transition to virtual patient contact to assess the need for urgent care and to avoid face-to-face encounters when possible.[15] A robust framework for remote monitoring and telemedicine services were not well implemented prior to the COVID-19 pandemic, and new strategies are needed to optimize remote care.[15–17] Egolum *et al*. have reviewed a remote monitoring approach with HeartLogic during the COVID-19 global pandemic and presented two cases where HeartLogic allowed for appropriate remote triage of patients for expediated admission or managed care at home.[18] Numerous individual case studies with HeartLogic capable devices and SARS-CoV-2 infections have also suggested that individual sensors may help identify patients who are COVID-19 positive, even before patients themselves report symptoms.[19–22] The sensor changes reported in these individual cases are consistent with the quantitative trends that we report here, including increasing respiratory rate and impedance.

The findings, presented here, suggest that alerts derived from a combination of sensors including that of respiratory rate, RSBI, night-time heart rate and temperature, together with HeartLogic, could enable ambulatory patient monitoring and early triage for potential exposure to SARS-CoV-2 and heart failure exacerbation. Furthermore, the dramatic sensor changes leading up to a COVID-19 diagnosis (*Table 2*, *Figure 1*, and *Figure 2*) could encourage early isolation and evaluation for COVID-19 using more conventional approaches for diagnosing COVID-19 (e.g. chest X-ray, CT, O_2 saturation, and SAR-CoV-2 PCR). In the future, applications may allow automated remote monitoring for SAR-CoV-2 infection in heart failure patients with implantable devices.

However, the findings need to be replicated in a larger prospective study. This would enable comparison of the sensor trends to conventional COVID-19 and heart failure diagnostic techniques, including pulse oximetry, radiological investigations, and remote evaluation of JVP, which were not systematically collected or evaluated in this study.

This case series has demonstrated that several device-based features could have helped differentiate between an acute presentation with COVID-19 and cardiac decompensation. In the future, it is tantalizing to think that this technology could become more universally available, where all HF patients had device diagnostics via an injectable cardiac monitor rather than this luxury being reserved for the relative minority who receive an ICD or CRT. However, ultimately, the utility of device diagnostics requires sensible people looking at meaningful data to ensure that appropriate decisions are made.

Conclusion

This observational study has illustrated the merits of device diagnostics in differentiating between acute presentations with COVID-19 and cardiac decompensation, with COVID-19 distinguishable by an extreme and fast rise in respiratory rate along with no changes in S_3. Furthermore, the novel ability of HF devices to detect changes in temperature extend the potential utility of remote monitoring in the future.

Acknowledgements

Conflict of interest

R.S.G. is a consultant for Abbott, Astra Zeneca, Boehringer Ingelheim, Boston Scientific, Novartis, Servier, and Vifor. J.P.

References

1. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, Falk V, González-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GMC, Ruilope LM, Ruschitzka F, Rutten FH, van der Meer P, ESC Scientific Document Group. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 2016; **37**: 2129–2200.

2. McMurray JJ, Packer M, Desai AS, Gong J, Lefkowitz MP, Rizkala AR, Rouleau JL, Shi VC, Solomon SD, Swedberg K, Zile MR. Angiotensin-neprilysin inhibition versus enalapril in heart failure. *N Engl J Med* 2014; **371**: 993–1004.

3. McMurray JJV, Solomon SD, Inzucchi SE, Køber L, Kosiborod MN, Martinez FA, Ponikowski P, Sabatine MS, Anand IS, Bělohlávek J, Böhm M, Chiang C-E, Chopra VK, de Boer RA, Desai AS, Diez M, Drozdz J, Dukát A, Ge J, Howlett JG, Katova T, Kitakaze M, Ljungman CEA, Merkely B, Nicolau JC, O'Meara E, Petrie MC, Vinh PN, Schou M, Tereshchenko S, Verma S, Held C, DeMets DL, Docherty KF, Jhund PS, Bengtsson O, Sjöstrand M, Langkilde A-M. Dapagliflozin in patients with heart failure and reduced ejection fraction. *N Engl J Med* 2019; **381**: 1995–2008.

4. Packer M, Anker SD, Butler J, Filippatos G, Pocock SJ, Carson P, Januzzi J, Verma S, Tsutsui H, Brueckmann M, Jamal W, Kimura K, Schnee J, Zeller C, Cotton D, Bocchi E, Böhm M, Choi DJ, Chopra V, Chuquiure E, Giannetti N, Janssens S, Zhang J, Gonzalez Juanatey JR, Kaul S, Brunner-la Rocca HP, Merkely B, Nicholls SJ, Perrone S, Pina I, Ponikowski P, Sattar N, Senni M, Seronde MF, Spinar J, Squire I, Taddei S, Wanner C, Zannad F. Cardiovascular and renal outcomes with empagliflozin in heart failure. *N Engl J Med* 2020; **383**: 1413–1424.

5. Boehmer JP, Hariharan R, Devecchi FG, Smith AL, Molon G, Capucci A, An Q, Averina V, Stolen CM, Thakur PH, Thompson JA, Wariar R, Zhang Y, Singh JP. A multisensor algorithm predicts heart failure events in patients with implanted devices: results from the MultiSENSE study. *JACC Heart Fail* 2017; **5**: 216–225.

6. Gardner RS, Singh JP, Stancak B, Nair DG, Cao M, Schulze C, Thakur PH, An Q, Wehrenberg S, Hammill EF, Zhang Y, Boehmer JP. HeartLogic multisensor algorithm identifies patients during periods of significantly increased risk of heart failure events: results from the MultiSENSE study. *Circ Heart Fail* 2018; **11**: e004669.

7. Abraham WT, Fiuzat M, Psotka MA, O'Connor CM. Heart failure collaboratory statement on remote monitoring and social distancing in the landscape of COVID-19. *JACC Heart Fail* 2020; **8**: 692–694.

8. Guan W-j, Ni Z-y, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui DSC, Du B, Li LJ, Zeng G, Yuen KY, Chen RC, Tang CL, Wang T, Chen PY, Xiang J, Li SY, Wang JL, Liang ZJ, Peng YX, Wei L, Liu Y, Hu YH, Peng P, Wang JM, Liu JY, Chen Z, Li G, Zheng ZJ, Qiu SQ, Luo J, Ye CJ, Zhu SY, Zhong NS, China Medical Treatment Expert Group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020; **382**: 1708–1720.

9. Mahase E. Covid-19: UK approves Pfizer and BioNTech vaccine with rollout due to start next week. *BMJ* 2020; **371**: m4714.

10. Tanne JH. Covid-19: FDA panel votes to approve Pfizer BioNTech vaccine. *BMJ* 2020; **371**: m4799.

11. Cleland JG, Clark RA, Pellicori P, Inglis SC. Caring for people with heart failure and many other medical problems through and beyond the COVID-19 pandemic; the advantages of universal-access to home telemonitoring. *Eur J Heart Fail* 2020; **22**: 995–998.

12. Thakur PH, An Q, Swanson L, Zhang Y, Gardner RS. Haemodynamic monitoring of cardiac status using heart sounds from an implanted cardiac device. *ESC Heart Fail* 2017; **4**: 605–613.

13. Cao M, Gardner RS, Hariharan R, Nair DG, Schulze C, An Q, Thakur PH, Kwan B, Zhang Y, Boehmer JP. Ambulatory monitoring of heart sounds via an implanted device is superior to auscultation for prediction of heart failure events. *J Card Fail* 2020; **26**: 151–159.

14. Yancy CW, Lopatin M, Stevenson LW, de Marco T, Fonarow GC, ADHERE Scientific Advisory Committee and Investigators. Clinical presentation, management, and in-hospital outcomes of patients admitted with acute decompensated heart failure with preserved systolic function: a report from the Acute Decompensated Heart Failure National Registry (ADHERE) Database. *J Am Coll Cardiol* 2006; **47**: 76–84.

15. Zhang Y, Coats AJS, Zheng Z, Adamo M, Ambrosio G, Anker SD, Butler J, Xu D, Mao J, Khan MS, Bai L, Mebazaa A, Ponikowski P, Tang Q, Ruschitzka F, Seferovic P, Tschöpe C, Zhang S, Gao C, Zhou S, Senni M, Zhang J, Metra M. Management of Heart Failure Patients with COVID-19. A joint position paper of the Chinese Heart Failure Association & National Heart Failure Committee and the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail* 2020; **22**: 941–956.

16. Charman SJ, Velicki L, Okwose NC, Harwood A, McGregor G, Ristic A, Banerjee P, Seferovic PM, MacGowan GA, Jakovljevic DG. Insights into heart failure hospitalizations, management, and services during and beyond COVID-19. *ESC Heart Fail* 2021; **8**: 175–182.

17. Salzano A, D'Assante R, Stagnaro FM, Valente V, Crisci G, Giardino F, Arcopinto M, Bossone E, Marra AM, Cittadini A. Heart failure management during the COVID-19 outbreak in Italy: a telemedicine experience from a heart failure university tertiary referral centre. *Eur J Heart Fail* 2020; **22**: 1048–1050.

18. Egolum UO, Parikh K, Lekavich C, Wosik J, Frazier-Mills C, Fudim M. Applications of the Multisensor HeartLogic Heart Failure Monitoring Algorithm During the COVID-19 Global Pandemic. *JACC Case Rep* 2020; **2**: 2265–2269.

19. Heggermont W, Nguyen PAH, Lau CW, Tournoy K. A steep increase in the HeartLogic index predicts COVID-19 disease in an advanced heart failure patient. *Case Rep Cardiol* 2020; **2020**: 8896152.

20. Bontempi L, Cerini M, Salghetti F, Fabbricatore D, Nozza C, Campari M, Valsecchi S, Curnis A. Use of a novel implantable cardioverter-defibrillator multisensor algorithm for heart failure monitoring in a COVID-19 patient: a case report. *Clin Case Rep* 2021; **9**: 1178–1182.

21. Yapejian AR, Fudim M. Novel findings of respiratory rate increases using the multisensor HeartLogic heart failure monitoring algorithm in COVID-19-positive patients: a case series. *Eur Heart J Case Rep* 2021; **5**: ytab067.

22. Shumway JL, Stolen CM, Ahmed R, Plumer M, Capodilupo RC. Case reports of implantable cardiac device physiologic sensor changes in subjects with coronavirus disease-2019 infection. *J Card Fail* 2021; **27**: 373–378.