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ORIGINAL RESEARCH ARTICLE

Multiparameter diagnostic sensor measurements during clinically stable periods and worsening heart failure in ambulatory patients

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Abstract

Aims This study aims to characterize the range of implantable device-based sensor values including heart sounds, markers of ventilation, thoracic impedance, activity, and heart rate for patients with heart failure (HF) when patients were deemed to be in clinically stable periods against the time course of acute decompensation and recovery from HF events.

Methods and results The MultiSENSE trial followed 900 patients implanted with a COGNIS CRT-D for up to 1 year. Chronic, ambulatory diagnostic sensor data were collected and evaluated during clinically stable periods (CSP: unchanged NYHA classification, no adverse events, and weight change $\leq$2.27 kg), and in the timeframe leading up to and following HF events (HF admissions or unscheduled visits with intravenous HF treatment). Physiologic sensor data from 1667 CSPs occurring in 676 patients were compared with those data leading up to and following 192 HF events in 106 patients. Overall, the mean age was 66.6 years, and the population were predominantly male (73%). Patients were primarily in NYHA II (67%), with a mean LVEF of 29.6% and median NT-proBNP of 754.5 pg/mL. Sensor values during CSP were poorer in patients who had HF events during the study period than those without HF events, including first heart sound (S1: 2.18 ± 0.84 mG vs. 2.62 ± 0.95 mG, P = 0.002), third heart sound (S3: 1.13 ± 0.36 mG vs. 0.91 ± 0.30 mG, $P < 0.001$), thoracic impedance (45.66 ± 8.78 Ohm vs. 50.33 ± 8.43 Ohm, $P < 0.001$), respiratory rate (19.09 ± 3.10 br/min vs. 17.66 ± 2.39 br/min, P = 0.002), night time heart rate (73.39 ± 8.36 b.p.m. vs. 69.56 ± 8.09 b.p.m., P = 0.001), patient activity (1.69 ± 1.84 h vs. 2.56 ± 2.20 h, P = 0.006), and HeartLogic index (11.07 ± 12.14 vs. 5.31 ± 5.13, P = 0.001). Sensor parameters measured worsening status leading up to HF events with recovery of values following treatment.

Conclusions Device-based physiologic sensors not only revealed progressive worsening leading up to HF events but also differentiated patients at increased risk of HF events when presumed to be clinically stable.

Keywords Heart failure; CRT; Prognostication; Ambulatory monitoring; Decompensation

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Introduction

The assessment of patients with heart failure (HF) has changed with the availability of modern technology. Whilst the bedside evaluation of clinical signs and symptoms of heart failure define the heart failure syndrome, the ability to utilize technology to better quantitate and trend these parameters may represent an important opportunity for the management of patients with chronic heart failure. However, predicting (and thereby potentially averting) HF decompensation has always been a challenge. Whilst our treatment options have improved, heart failure hospitalization still

accounts for the largest proportion of HF healthcare expenditure.[1] It is time to revisit evaluation of physiological signs in the assessment of HF patients.

The key clinical findings in patients with cardiac decompensation were described 60 years ago when Thomas W. Mattingly recognized that the gallop rhythm of a third heart sound (S3) could precede 'the frank development of congestive failure'.[2] He also noted that the first heart sound was 'often noticeably decreased'. Other important signs—increased respiratory rate,[3] reduced tidal volume,[4,5] reduced patient activity,[6,7] as well as the most common finding of fluid retention[8]—have also been well documented.

The aim of this analysis was to go back to a bedside approach of assessing HF patients, but via modern technology permitting daily trending of multiple pathophysiologic changes of cardiac decompensation. We will present temporal changes in these parameters leading to, and in recovery from, an HF event and provide a library of sensor ranges during clinically stable periods.

Methods

The MultiSENSE study has been previously published (ClinicalTrials.gov Identifier: NCT01128166).[9] In brief, MultiSENSE is an international, multicentre, non-randomized study designed to develop and evaluate a multi-sensor based algorithm for the early detection of worsening heart failure. To be enrolled, patients were required to be implanted with an existing COGNIS™ cardiac resynchronization therapy defibrillator (CRT-D) (Boston Scientific, Marlborough, MA). Following enrolment, patient demographics and clinical status were collected, and the patient's CRT-D had custom research firmware installed on the device converting it to a Sensor Research Device. Scheduled follow-ups occurred every 3 months if the patient had remote monitoring, otherwise patient follow-up occurred every 6–8 weeks to allow for sensor data download. Patients were followed for up to 12 months, at the end of which their device was reconverted to the market approved COGNIS firmware. All patients provided written informed consent. 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.

Device-based sensors and the HeartLogic heart failure index

The diverse set of implanted sensors was chosen to target different aspects of HF pathophysiology associated with common signs and symptoms of heart failure. These sensors include accelerometer measured first and third heart sounds (S1 and S3, respectively), impedance-based measures of ventilation including rate and rapid shallow breathing index (RSBI, the ratio of respiration rate to relative tidal volume), thoracic impedance, heart rate, and patient activity. Measures of these sensor values were recorded continuously within the device and aggregated into trends of daily values (value statistic depending on the sensor, such as average or median and whole day or periodic such as night-time). A multisensor algorithm, HeartLogic, was designed to aggregate daily changes from these daily sensor values weighted based on an individual's daily risk for worsening HF to create the composite HeartLogic index which was prospectively validated on an independent test set.[9]

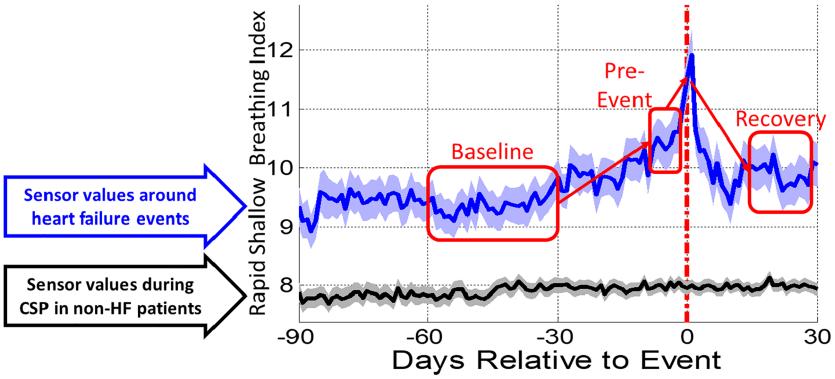
Heart failure events

An independent clinical events committee reviewed all-cause death, hospitalizations, and outpatient visits and adjudicated these as primary cause heart failure events if the patients had signs or symptoms of decompensated heart failure and received augmented heart failure therapy whilst admitted or received unscheduled intravenous decongestive therapy as an outpatient. Some of these HF events were unavailable for evaluating HeartLogic, because they either occurred early after conversion before a sensor baseline could be established or occurred with missing sensor data due primarily to non-compliance with study data collection visits. Such HF events were screened out of the HeartLogic analysis dataset based on pre-defined sensor data availability rules.[9] The remaining HF events were termed usable HF events. Treating clinicians and the clinical events committee were blinded to the unique sensor data and HeartLogic Index calculated within the study.

Sensor changes preceding and following heart failure events

The time course of sensor changes surrounding a heart failure event were evaluated in four different time points of the patient decompensation and recovery as shown with a representative sensor trend in *Figure 1*. First, a patient's 30-day moving baseline was compared with a 7-day pre-event decompensated state measured the day before the event. Second, sensor changes on the Event Day hospitalization/augmented therapy were compared with the same 7-day pre-event data. Third, patient recovery was evaluated by comparing sensor values from the Event Day to a 2-week average occurring 2 weeks post-event. Finally, the sensor values during the recovery period were compared back to the patient's baseline values. To avoid being confounded by missing sensor data, this analysis was limited to usable HF events.

Figure 1 Visual diagram of analysis windows. Temporal location of the baseline (−60 to −30 days), pre-event (−8 to −1 days), and recovery (+14 to +28 days) windows relative to the day of the heart failure event (Day 0). Sensor trends during clinically stable periods are aligned by the last day in CSP for each patient (Day +30). Successive periods in a patient meeting the definitions of clinical stability were concatenated to yield continuous trends spanning up to 120 days.



Clinically stable periods

HF status was assessed by in-office physical assessment at patient follow-up visits. Patients were deemed to be clinically stable between successive follow-up visits if all the following conditions were satisfied:

- unchanged NYHA classification;
- weight change ≤2.27 kg (5 lbs);
- no adverse events were reported between or at the two flanking visits.

Averaged sensor data from clinically stable periods (CSP) were calculated in two patient populations; those who did not have an HF event during the clinical follow-up representing the most clinically stable population and those who did have an HF event within the follow-up. These values were tabulated and compared between the two populations.

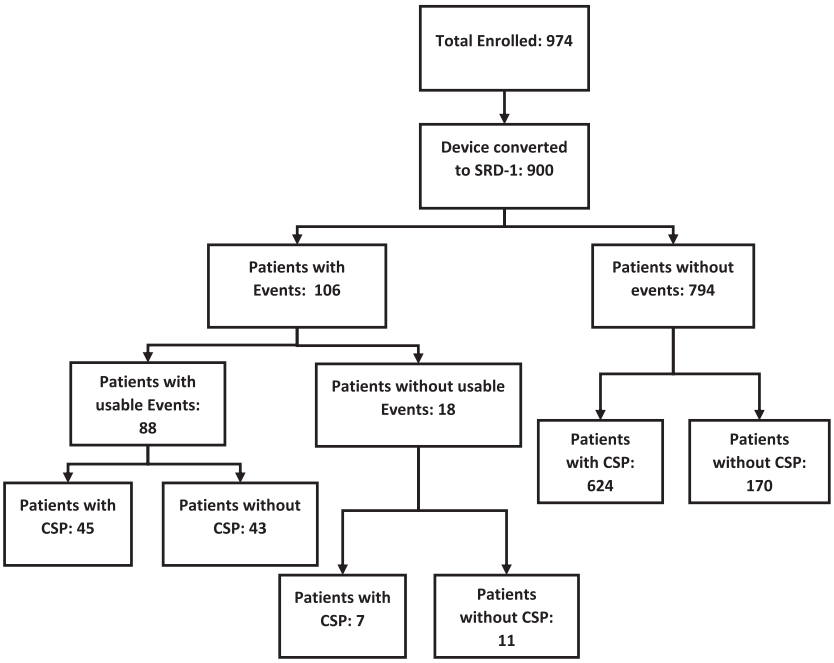
Statistical analysis

Baseline characteristics were compared between patients with an HF event and patients without an HF event. For continuous variables, an independent *t*-test was used for normally distributed variables or a Wilcoxon rank-sum test for non-normally distributed variables. A χ^2 test was used for categorical variables. Sensor data for CSP in patients without an HF event were compared with CSP in patients with an HF event using an independent *t*-test. Sensor data in only patients with an HF event were compared between different temporal periods using a paired *t*-test. Due to correlation of repeated measurements, sensor data were also compared between different temporal periods using a mixed model with a random intercept for patient heterogeneity and a fixed effect for temporal period (stable period in non-HF event patients, stable period in HF event patients, baseline period in HF event patients, pre-HF event period, HF event period, and recovery period in HF event patients). The effect of btemporal period on sensor measurement was adjusted for baseline characteristics: gender, age, NT-proBNP, NYHA class (III/IV vs. I/II), LVEF, renal dysfunction, history of cardiac ischaemia, and history of atrial fibrillation. An unstructured covariance matrix was used to account for correlation among repeated measurements. An alpha of 0.05 was used and pairwise comparisons of modelled means between temporal periods were Bonferroni corrected. All statistical analyses were performed using SAS v9.4.

Results

Nine hundred and seventy-four patients were enrolled at 93 centres (75 North America/13 Europe/5 Asia) between July 2010 and October 2013 of which 900 patients underwent device conversion for the collection of sensor data (*Figure 2*). *Table 1* compares baseline clinical and demographic data between the 106 patients with an HF event during the course of the study against those without an event. Overall, the mean age was 66.6 years, and the population were predominantly male (73%). Patients were primarily in NYHA II (67%), with a mean LVEF of 29.6% and median NT-proBNP of 754.5 pg/mL (1st and 3rd quartile 257.5, 1786.5). Patients with HF events tended to have worsened NYHA status, lower LVEF, lower systolic blood pressure, and higher resting heart rates at baseline. These patients also had a greater prevalence of history of myocardial infarction, atrial arrhythmia, renal disease, and diabetes. Baseline NT-proBNP concentrations were also significantly higher in those who experienced an HF event.

Figure 2 Patient flow chart. A breakdown of all enrolled patients based on whether they did or did not have at least one clinically stable period (CSP), and whether they did or did not have a heart failure event.



Excluding HF events based on pre-defined sensor availability rules (see methods), 146 usable HF events occurred in 88 patients over follow-up. There were 1667 stable periods in 676 patients, the average duration of CSP was 60 ± 22 days. A total of 45 patients had both clinically stable periods and at least one usable HF event, whereas 52 patients had both clinical stable periods and at least one HF event. A total of 624 patients had CSP but no HF events (*Figure 2*).

Sensor data findings

Table 2 summarizes the sensor data during clinically stable periods, comparing the values in patients who had a HF event within the study to those who did not have any HF events. The population of patients in CSP without HF events may be representative of sensor values typical of chronically stable HF patients. Significant differences existed across all sensor values and the composite index between patients with versus without HF events within the study even during these stable timeframes.

Additionally, all sensors detected additional progressive worsening in the timeline leading up to an HF event. *Table 3* presents baseline, pre-event, day of event, and recovery sensor values in patients with HF events. As compared with the baseline period, pre-event sensor data were significantly lower for S1 amplitude, thoracic impedance and activity, and significantly higher for S3 amplitude, ratio of S3 to S1 amplitude, respiratory rate, RSBI, and heart rate. A further sharp worsening occurred on the day of event in the S3 amplitude, respiratory rate, RSBI, and heart rate. During the recovery period, all of the sensors with the exception of the S1 amplitude significantly improved and most sensors recovered to their baseline values. This pattern also occurred with the HeartLogic Index. These sensor trends are shown in *Figure 3*, which compares the CSP values of non-event patients (black lines) with a 120-day peri-event window (blue lines). As can be seen in the panels of *Figure 3*, the *S1* amplitude, S3 by S1 ratio, and thoracic impedance sensor values have already begun recovering on Day 0, this is likely due to the daily averaging of sensor data and rapid recovery following interventions administered on the day of the event. After adjusting for patient demographics and baseline clinical characteristics, the progressive worsening of sensor values leading up to a heart failure event followed by improvement during recovery largely remained significant, as shown in *Figure 4*.

Discussion

In this paper, we have characterized the ability of novel physiologic sensor data derived from implanted devices to reflect the pathophysiologic changes of cardiac decompensation. These innovative, physiologically relevant sensors are designed to monitor common signs associated with

Table 1 Baseline demographic data in patients who had and those who did not have a heart failure event during the study

Characteristic	Measurement	With HF event (N = 106)	No HF event (N = 794)	P-value*
Age (years)	Mean ± SD	67.4 ± 10.5	66.5 ± 10.5	0.38
Male sex	Male	85 (80)	569 (72)	0.06
NYHA class				<**0.001**
	I	5 (5)	38 (5)	
	II	53 (50)	552 (70)	
	III	46 (43)	195 (25)	
	IV	0 (0)	4 (1)	
	Unknown	2 (2)	5 (1)	
LV ejection fraction (%)	Mean ± SD	26.6 ± 10.9	30.0 ± 11.4	**0.004**
Body mass index (kg/m^2)	Mean ± SD	30.4 ± 6.7	30.5 ± 6.8	0.87
Systolic blood pressure (mmHg)	Mean ± SD	119 ± 18	124 ± 19	**0.02**
Resting heart rate (b.p.m.)	Mean ± SD	73 ± 11	70 ± 9	**0.004**
Resting respiratory rate (br/min)	Mean ± SD	19 ± 9	18 ± 6	0.10
History of cardiac ischaemia	N (%)	70 (66)	387 (49)	<**0.001**
History of dilated cardiomyopathy	N (%)	55 (52)	478 (60)	0.10
History of valvular disease	N (%)	35 (33)	234 (29)	0.45
History of valve surgery	N (%)	12 (11)	66 (8)	0.30
History of atrial fibrillation or atrial flutter	N (%)	57 (54)	249 (31)	<**0.001**
Previous myocardial infarction	N (%)	57 (54)	297 (37)	**0.005**
Previous CABG	N (%)	41 (39)	217 (27)	0.02
Renal dysfunction	N (%)	57 (54)	169 (21)	<**0.001**
Sodium (mEq/L)	Mean ± SD	139 ± 3	139 ± 3	0.79
Potassium (mEq/L)	Mean ± SD	4.4 ± 0.5	4.4 ± 0.5	0.45
Total haemoglobin (g/dL)	Mean ± SD	12.8 ± 1.8	13.2 ± 1.8	**0.03**
BUN (mg/dL)	Mean ± SD	30.3 ± 18.6	23.4 ± 11.5	<**0.001**
Serum creatinine (mg/dL)	Mean ± SD	1.6 ± 1.2	1.3 ± 0.8	<**0.001**
NT-proBNP (pg/mL)	Median (Q1, Q3)	1979 (1022, 4356)	652 (230, 1538)	<**0.001**†
Concomitant medications	Anti-platelets	73 (69)	530 (67)	0.66
	Anti-coagulants	44 (42)	268 (34)	0.12
	ACE-inhibitors/ARBs	68 (64)	680 (86)	<**0.001**
	Beta-blockers	93 (88)	746 (94)	**0.02**
	Mineralocorticoid receptor antagonists	41 (39)	319 (40)	0.77
	Diuretics	92 (87)	602 (76)	**0.01**
	Vasodilators	35 (33)	172 (22)	**0.009**
	Cardiac glycosides	32 (30)	199 (25)	0.26
	Amiodarone	30 (28)	113 (14)	<**0.001**

ACE: angiotensin converting enzyme; ARB: angiotensin II receptor blockers; br: breath; CABG: coronary artery bypass graft; HF: heart failure; LV: left ventricular; N: number; SD: standard deviation; Q1/Q3: first and third quartiles.
*P-values were calculated using a Student's T-test for continuous measures and a Chi-squared test for categorical measures.
†P-value for NT-proBNP was calculated using Wilcoxon rank-sum test.

Table 2 Average sensor values during clinically stable periods in patients with (N = 52) and without (n = 624) HF events

	Patients without any heart failure events		Patients with a heart failure event during the study		
Daily Trends	Mean ± SD	N	Mean ± SD	N	P-value*
S1 amplitude (mG)	2.62 ± 0.95	622	2.18 ± 0.84	52	0.002
S3 amplitude (mG)	0.91 ± 0.30	622	1.13 ± 0.36	52	<0.001
S3 by S1 ratio	0.41 ± 0.21	622	0.62 ± 0.31	52	<0.001
Thoracic impedance (Ohm)	50.33 ± 8.43	622	45.66 ± 8.78	52	<0.001
Respiratory rate (median, br/min)	17.66 ± 2.39	623	19.09 ± 3.10	52	0.002
Daytime RSBI (br/min/Ohm)	8.04 ± 2.46	622	9.78 ± 3.04	52	<0.001
Night heart rate (b.p.m.)	69.56 ± 8.09	621	73.39 ± 8.36	52	0.001
Activity (h)	2.56 ± 2.20	622	1.69 ± 1.84	52	0.006
HeartLogic Index	5.31 ± 5.13	621	11.07 ± 12.14	52	0.001

RSBI: Rapid Shallow Breathing Index; S1, S3: 1st, 3rd heart sound; SD: standard deviation; Day: 6 am to 12 am; Night: 12 am to 6 am.
*P-value calculated using independent t-test.

worsening HF, including heart sounds, 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.

Table 3 Average sensor values during heart failure events and recovery

Daily trends	*N*	Baseline Mean ± SD	Pre-Event Mean ± SD	Pre-Event *P-value against baseline	Day of Event Mean ± SD	Day of Event *P-value against pre-event	Recovery Mean ± SD	Recovery *P-value against day of event	Recovery *P-value against baseline
S1 amplitude (mG)	80	2.16 ± 0.77	2.02 ± 0.73	**<0.001**	2.08 ± 0.71	0.056	2.14 ± 0.77	0.38	0.63
S3 amplitude (mG)	77	1.24 ± 0.39	1.34 ± 0.42	**<0.001**	1.41 ± 0.52	**0.014**	1.27 ± 0.43	**<0.001**	0.35
S3 by S1 ratio	77	0.66 ± 0.32	0.77 ± 0.36	**<0.001**	0.75 ± 0.32	0.18	0.68 ± 0.33	**0.009**	0.52
Thoracic impedance (Ohm)	80	45.09 ± 8.93	42.74 ± 9.15	**<0.001**	42.85 ± 9.31	0.64	45.66 ± 9.23	**<0.001**	0.16
Respiratory rate (median, br/min)	78	19.26 ± 2.98	19.97 ± 3.20	**<0.001**	20.49 ± 3.45	**0.002**	19.39 ± 3.15	**<0.001**	0.45
Daytime RSBI (br/min/Ohm)	83	9.71 ± 3.18	10.90 ± 3.89	**<0.001**	11.60 ± 4.35	**0.020**	9.93 ± 3.35	**<0.001**	0.30
Night heart rate (b.p.m.)	80	73.99 ± 9.47	76.64 ± 10.5	**<0.001**	79.37 ± 11.70	**0.001**	75.67 ± 10.16	**<0.001**	**0.033**
Activity (h)	83	1.44 ± 1.54	1.15 ± 1.38	**<0.001**	0.76 ± 1.06	**<0.001**	1.15 ± 1.63	**0.002**	**0.005**
HeartLogic Index	79	12.13 ± 10.46	22.87 ± 16.36	**<0.001**	25.15 ± 17.69	**<0.001**	14.39 ± 15.22	**<0.001**	0.19

Matched sensor data in patients with usable HF events during (1) 30-day average baseline calculated 30 days prior to HF event, (2) 7 day average pre-event calculated 1 day prior to the HF event, (3) daily average on the day of the HF event, and (4) 14-day average recovery period beginning 14 days post HF event. Statistical comparison (paired *t*-test) is also reported between sensor data from baseline and pre-event; between pre-event and day of the event; and between recovery period and on the day of event. Statistical comparison is limited to patients that had sensor data in each of the four epochs (indicated by column *N*). However, the results are robust even if extended to include all pairs available for any given paired analysis.

HF: heart failure; RSBI: Rapid Shallow Breathing Index; S1, S3: 1st, 3rd heart sound. Daytime: 6 am to 12 am; Night = 12 am to 6 am.

*P-values computed using a paired *t*-test.

Our results show that these sensor measurements are significantly different not only progressively leading up to HF events but also across clinically stable periods in patients with and without HF events. Importantly, each sensor begins to change approximately 30 days or more in advance of an HF event, consistent with the findings that a multisensory algorithm using these diagnostics, HeartLogic, was shown to detect 70% of HF events with a median of 34 days advance notice.[9] Additionally, those within a HeartLogic alert state were 10 times more likely to experience an HF event than when outside an alert.[10] Once an alert occurs the clinician is provided with individual sensor trends and daily data via remote monitoring. The mean population sensor trends shown in *Table 3* may provide a contextual reference for clinicians as they respond to an alert.

Device measured heart sounds are an innovative approach to the ambulatory assessment of heart failure patients. The third heart sound (S3), caused by rapid deceleration of the blood against a stiff ventricle during early diastolic filling, is regarded as an ominous finding on cardiac examination, with very high specificity for heart failure.[11–13] However, there is great variability in a clinician's ability to identify this sign,[14,15] with the S3 often being below the audible frequency range. A separate analysis of the MultiSENSE study showed that device measured S3 was better able to predict heart failure decompensations than auscultation.[16] In the present analysis, the third heart sound has a significantly higher magnitude in patients experiencing an HF event, and crescendos on the day of admission.

The first heart sound (S1) is caused by the closure of the atrioventricular valves, and thus, its amplitude is driven by the pressure gradient across the AV valve driving the valves to close. The S1 amplitude has been known to correlate with myocardial contractility.[17] A depressed S1 leading up to worsening heart failure may arise from depressed myocardial contractility due to progressive loss of contractile function, a reduced pressure gradient across the AV valve due to elevated filling pressures, or both. In a recent pre-clinical study using this device, ischaemia-induced reductions in cardiac contractility (as measured by dp/dtmax) were mirrored by a reduction in S1.[18] We found that stable patients had a louder S1, and that this diminishes in those experiencing an HF event then recovers post-treatment. Interestingly, S1 appears to be one of the earliest reflectors of recovery along with thoracic impedance, as they already begin to change direction on the day of the HF event. We postulate the S1 recovery may be attributable to an improvement in contractile status due to reduction in the overwhelming of the Frank–Starling mechanism as an immediate response to the decongestive therapies that are typical frontline response to decompensated heart failure or is a reflection of a rapid decrease in filling pressure.

Respiratory distress is common in HF with 89% of patients hospitalized for HF in the ADHERE registry reporting the presence of dyspnoea.[8,19] Higher respiratory rates are known to be

Figure 3 Temporal profile of sensor trends. Average values in patients surrounding a HF event (blue) and during clinically stable periods in patients without any HF event (black). Data are displayed as mean ± SEM. The shaded regions represent the SEM. RSBI = rapid shallow breathing index, S1/S3 = first/third heart sound.

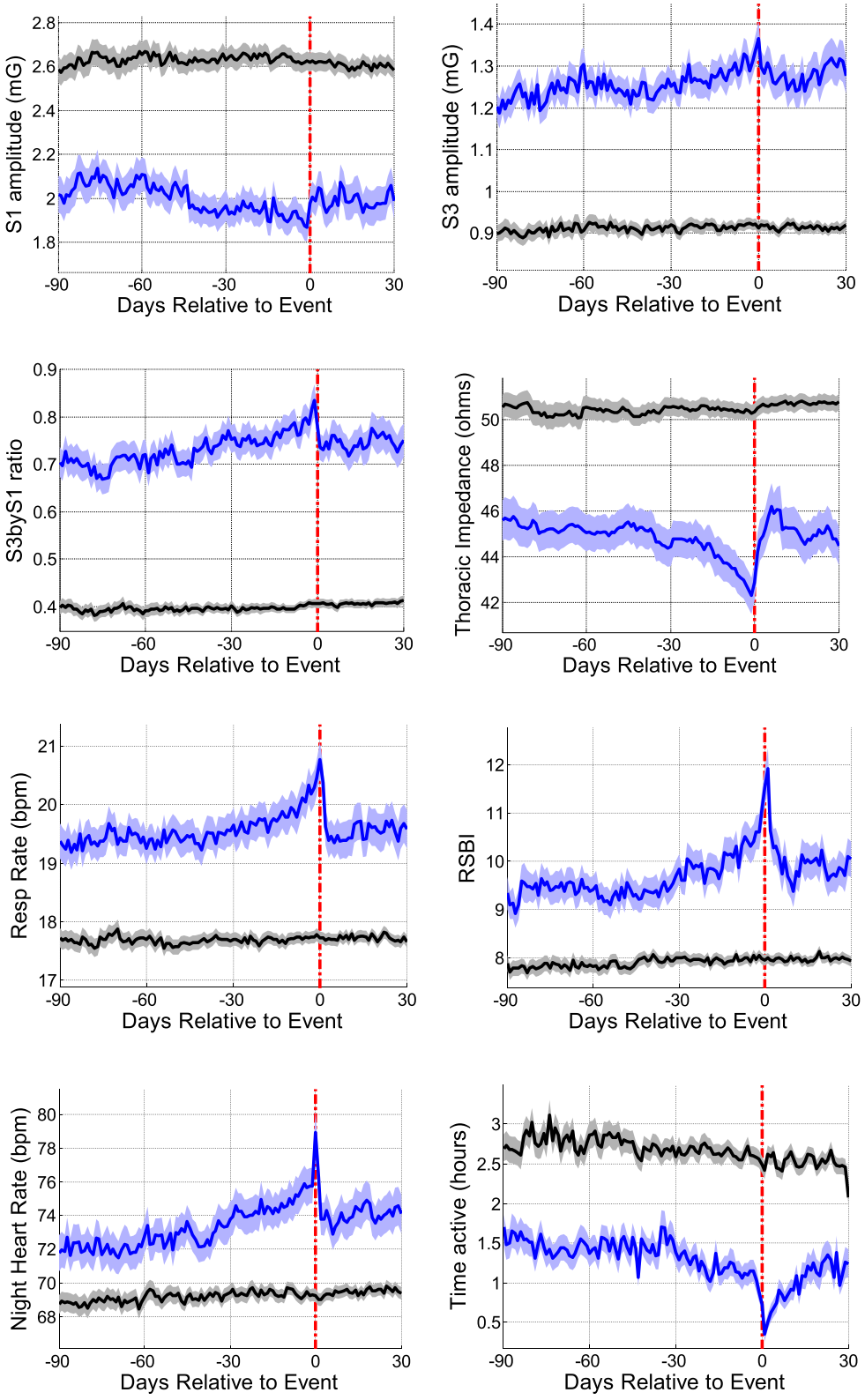


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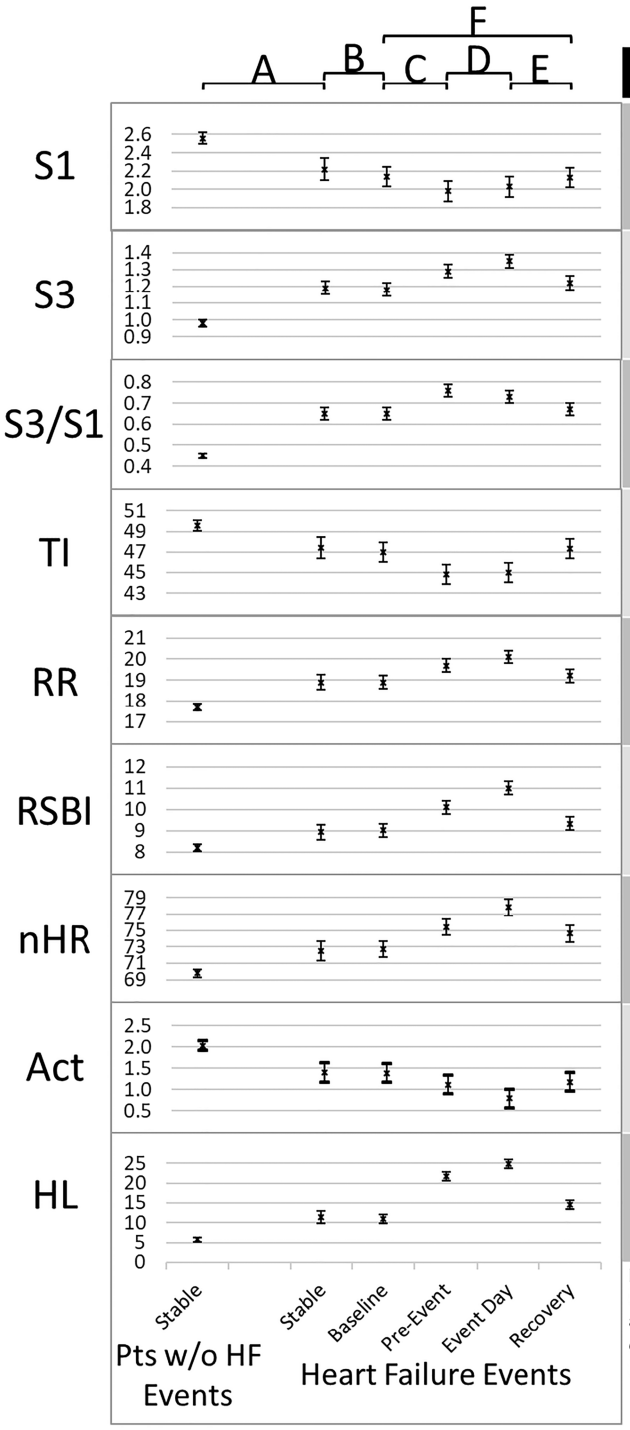
Figure 4 Sensor value changes during HF events. Data displayed as mean (*x*) with standard error after adjustments. Statistical analysis comparing: (A) CSP values between patients without HF events and patients with HF events, (B) CSP values to baseline values, (C) worsening HF from baseline to pre-event, (D) pre-event to event day, (E) response to therapy from event day to recovery, and (F) recovery to baseline. Act = duration of activity, CSP = clinically stable periods, HF = heart failure, HL = HeartLogic index, nHR = night time heart rate, RR = respiration rate, RSBI = rapid shallow breathing index, S1/S3 = first/third heart sound, TI = thoracic impedance.



	A	B	C	D	E	F
S1	.059	1.00	.037	1.00	.85	1.00
S3	<.001	1.00	.009	.32	<.001	1.00
S3/S1	<.001	1.00	<.001	1.00	.13	1.00
TI	.36	1.00	<.001	1.00	<.001	1.00
RR	.015	1.00	.003	.20	<.001	1.00
RSBI	.57	1.00	<.001	.008	<.001	1.00
nHR	.22	1.00	.016	.039	.002	.26
Act	.11	1.00	.16	.044	.009	.64
HL	.002	1.00	<.001	.19	<.001	.13

p-values were adjusted for Bonferroni correction
Random Intercept model – adjusted for gender, age, NT-proBNP, LVEF, NYHA (III/IV vs. I/II), History of AF, History of Cardiac Ischemia, Renal Dysfunction

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associated with an adverse outcome in this population, and device-measured respiratory rate trends have previously been shown to help identify patients at risk of worsening heart failure.[3] However, respiratory distress is often characterized by not only rapid but also shallow breathing with an elevated respiratory rate and a reduced tidal volume.[4,5] Rapid shallow breathing index (RSBI) synergistically combines the progressive increase in respiratory rate and decrease in tidal volume to yield a single combined index of emerging respiratory distress. On top of the progressive changes leading up to an HF event, respiratory parameters show a significant and sharp rise on the day of the event as compared with preceding 7 days, consistent with the clinical experience that it is ultimately the respiratory distress that drives patients to seek urgent care.

Congestion is also common in HF with the ADHERE registry reporting 75% of the hospitalized patients showing signs of congestion.[8] Whilst patients can be trained to self-adjust their diuretic dose based on monitoring of symptoms/signs of congestion and daily weight measurements, this is not an exact science.[20] It is for that reason that several devices have been designed to monitor haemodynamics in the hope that they can predict the transition from the compensated to decompensated HF state.[21,22] Direct measurements of intracardiac pressures by a dedicated sensor found RV systolic pressures begin to rise approximately one-month before a heart failure event,[23] similar to the timeframe found in this analysis. In particular, the use of daily pulmonary artery pressure measurements via a CardioMEMS device saw a 39% reduction in heart failure related hospitalization.[21] However, clearly this requires the implantation of an additional costly device and so it is tantalizing to consider that meaningful data could be obtained from widely used cardiac devices such as ICDs, CRT, or even injectable cardiac monitors.

As a surrogate for congestion, intrathoracic impedance held significant promise, as it has been shown to inversely correlate with pulmonary capillary wedge pressure and thoracic fluid content.[24,25] As predicted, thoracic impedance was lower in those experiencing an HF event compared with those without and was seen to fall prior to such an event. This was mirrored by an increase in S3, another device-detected marker of congestion.

Other parameters such as patient activity and night heart rate also appear useful. Patient activity is not only an indicator of general well-being but has been shown to be prognostic and indicative of future risk of HF hospitalizations.[26,27] Night heart rate is a simple surrogate of resting heart rate and can provide insights into autonomic tone and the state of autonomic dysfunction or imbalance that characterizes HF. Moreover, a lower resting heart rate in sinus rhythm is associated with a better outcome in patients with HF.[28]

Historically, there has been a degree of scepticism in the cardiology community about device-based alerts for worsening heart failure following the 79% increase in hospitalization seen in the DOT-HF study with single-sensor thoracic impedance monitoring.[29] Multi-parameter approaches such as Heart Failure Risk Status (HFRS) have been attempted to overcome the limitations of thoracic impedance as a single sensor.[30] HFRS combines intra-thoracic impedance, activity, and night heart rate, with the additional measures including heart rate variability, atrial arrhythmias, and ventricular pacing percentage. However, the high risk notification triggered by this diagnostic is still dominated by thoracic impedance, with 89% of the high risk evaluations driven by thoracic impedance.[31] In contrast, HeartLogic combines thoracic impedance, activity and night heart rate, with sensors that are physiologically relevant to heart failure such as heart sounds and respiration. A recent study showed that in a real-world experience heart sounds was the primary driver of HeartLogic alerts followed by respiration, suggesting that these alerts may be more relevant and specific to heart failure.[29] Because it combines multiple physiologic parameters that target different aspects of HF pathophysiology, HeartLogic is a gestalt that provides a holistic picture of the patient's status. Further evidence is required to ensure that action upon such an alert leads to improved patient outcomes, and this is the subject of the ongoing MANAGE-HF study (NCT03237858).

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Conflict of interest

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