ORIGINAL RESEARCH ARTICLE

Influence of decompensated heart failure on cardiac acoustic biomarkers: impact on early readmissions

Julia W. Erath[1] (iD), Piotr Wanczura[2], Jerzy Wranicz[3], Axel Linke[4], Ursula Rohrer[5] and Daniel Scherr[5]* (iD)

[1]Department of Cardiology, J. W. Goethe University, Frankfurt am Main, Germany; [2]Independent Public Health Care, The Ministry of Internal Affairs and Administration Hospital, Rzeszow, Poland; [3]Department of Electrocardiology, Medical University of Lodz, Lodz, Poland; [4]Heart Center, Technical University Dresden, Dresden, Germany; [5]Division of Cardiology, Medical University of Graz, Auenbruggerplatz 15, Graz, 8036, Austria

Abstract

Aims   Preventing hospitalization by detecting early evidence of heart failure (HF) decompensation in an outpatient setting can improve patient's quality of life and reduce costs of care. The purpose of this study was to assess the value of cardiac acoustic biomarkers (CABs), a combination of cardiohaemic vibrations synchronized with ECG signals, and heart rate (HR) for detecting HF decompensation during first 3 months after hospital discharge for HF.

Methods and results   Patients with an ejection fraction ≤35% (HFrEF) and hospitalized for decompensated HF were enrolled in a prospective observational study. All subjects wore a wearable cardioverter-defibrillator (ZOLL LifeVest®, Pittsburgh, PA, USA) that is capable of recording CABs and HR. The primary endpoint of the study was the first HF event, defined as HF readmission or HF emergency room visit. From June 2017 through August 2019, 671 patients with HFrEF were enrolled. Eighty-one patients (12.1%) had a total of 112 HF events. The algorithm detected HF events with a median of 32 days (interquartile range = 11-45) in advance of the first HF event. The algorithm had a sensitivity of 69%, specificity of 60%, positive predictive value of 19%, and a negative predictive value of 94%. Of note, the baseline (first 7 days post-enrolment) algorithm using CABs and HR was superior to New York Heart Association classification in detecting patients more likely to have HF decompensation (sensitivity and specificity of 61% and 68% vs. 46% and 55%, respectively).

Conclusions   This prospective international registry showed that an algorithm incorporating CABs and HR data detected HF events 30 days in advance of the event in patients with HFrEF during first 3 months after hospital discharge. Therefore, integrating CAB technology into clinical practice may prevent HF rehospitalizations.

Introduction

The risk of heart failure (HF) readmission persists well beyond the first 30 days after hospital discharge with HF readmission at a rate of 6–11% within 30 days and 7–18% within 90 days.[1–3] The reason for rehospitalization is usually symptoms associated with elevated ventricular filling pressures that lead to pulmonary and systemic venous congestion.[4] Increases in ventricular filling pressures typically precede the congestion symptoms by 3–4 weeks.[4,5] Remote monitoring of these pressure changes directly or its surrogate measures such as intrathoracic impedance, lung fluid levels, systolic time intervals, or the presence of abnormal heart sounds may help to

prevent hospitalization by detecting early evidence of HF decompensation.[6–8] To date, most clinical studies for HF management using medical devices have primarily focused on chronic HF (>3 months from the index hospitalization).[9] However, these chronic patients represent a lower risk group compared with the recent post-discharge patients with HF.[10,11] Hence, there is an unmet need for managing patients with HF during the immediate post-discharge period.

Concurrently recorded cardiohaemic vibrations and electrocardiograms (ECGs) can be algorithmically interpreted to provide information regarding systolic and diastolic time intervals and measures of abnormal cardiohaemic vibrations (e.g. third and fourth heart sounds). These systolic and

diastolic parameters are collectively described as cardiac acoustic biomarkers (CABs). Previous studies have shown the utility of CABs to identify HF exacerbations and for predicting post-discharge outcomes in patients with HF.[12–14]

The wearable cardioverter-defibrillator (WCD) is indicated for temporarily protecting patients who are at high risk of sudden cardiac death (SCD).[9,15–18] It is typically prescribed to recently discharged patient populations with a primary or secondary SCD prevention indication, with the majority being patients with HF without an indication for immediate implantable cardioverter-defibrillator (ICD) implantation.[19] In such patients the WCD not only protects patients from SCD but may also help identify subjects at risk for HF decompensation by incorporating a sensor to record CABs. Therefore, the purpose of this study was to prospectively assess the value of CABs and heart rate (HR) to detect HF decompensation in patients with an ejection fraction ≤35% (HFrEF) and fitted with the WCD during the first 3 months after hospital discharge.

Methods

Participants

All subjects included in the current analyses were enrolled as part of an international, multicentre HEARIT-Registry study (ClinicalTrials.gov Identifier: NCT03203629). Patients hospitalized for a primary reason for HF (in the setting ischaemic and non-ischaemic cardiomyopathy) with left ventricular ejection fraction (LVEF) ≤35% and at risk for SCD were enrolled within 10 days after hospital discharge. Patients were anticipated to wear the WCD for at least 3 months and had to be at least 18 years old. Patients were excluded if they had an ICD, pacemaker, or cardiac resynchronization therapy device or were waiting for heart transplant. Other exclusion criteria were history of atrial fibrillation, current hospitalization for myocardial infarction, planned revascularization within 30 days of screening, pregnancy, or life expectancy <1 year. All patients provided written informed consent. Subjects were followed with structured weekly phone calls during the 3 month wear period to collect information regarding HF hospitalizations, HF related emergency room (ER) visits, HF symptoms, and survival status.

Wearable cardioverter-defibrillator and cardiac acoustic biomarkers description

Details of the WCD components and its functions have been described previously.[20] Briefly, the WCD monitoring electrodes are held in place circumferentially around the chest by tension from an elastic belt to provide two non-standard, orthogonal surface ECG leads; electrodes are paired front-to-back and side-to-side. One defibrillation electrode is placed in

a cardiac apical position, while the remaining two defibrillation electrodes are placed posteriorly on the upper thorax. The apical defibrillation electrode incorporates a three-axis accelerometer, located left of the xiphoid process over the fifth intercostal space, to measure the cardiohaemic vibrations. The automated algorithm of the WCD monitor uses the cardiohaemic vibrations and the timing information obtained from the simultaneous ECG signal analysis to calculate the following CABs (*Figure 1*)[21]:

1. Electromechanical activation time (EMAT): Measured from Q wave onset to the peak of the first heart sound (S1). EMAT reflects the time required by the ventricles to close the atrioventricular valves. Prolongation of EMAT reflects alterations in systolic function.
2. S3 strength (scaled between 0 and 10): Unitless measure of the third heart sound based on its intensity, frequency, and persistence. As a reference, S3 strength >5 generally indicates the presence of the third heart sound.[22]

The values for the aforementioned CABs and HR were calculated using 10 s recordings every 5 min and stored in the WCD monitor. These data were transmitted every 24 h to manufacturer's servers.

### Heart failure event detection algorithm

The algorithm was developed by combining the CAB parameters, EMAT and S3 strength, with HR to provide a daily binary risk classification (high vs. low) for HF events. HF events were defined as new HF hospitalization or a new HF related ER visit. The risk for an HF event was set to high if the combination of CABs and HR exceeded the upper decompensation threshold (*Figure 2*). Thereafter, the risk was maintained high until the combination of CABs and HR values fell below the lower recovery threshold. At this point, the risk for HF event was labelled as low (*Figure 2*). Signs and symptoms were not included in the HF detection algorithm because previous studies have shown that they have limited sensitivity and/or specificity for early detection of HF events.[4,11]

Per the study protocol, the algorithm for detecting HF events was developed using all the enrolled subjects who either had CABs and HR data prior to an HF event (HF-event subjects) or had complete CABs and HR data throughout WCD use (non-HF event subjects). Only night-time (12 AM–7 AM) median data were used to reduce the influence of activity on these recordings.

Data analysis

The primary endpoint of the study was the first HF event. A combined measure of sensitivity and specificity, defined by

FIGURE 1 ECG (top trace) and cardiohaemic vibrations (bottom trace) recordings. Q represents the beginning of the Q wave with S1, S2, S3, and S4 representing the first, second, third, and fourth heart sound, respectively. EMAT is electromechanical activation time and S3 strength is a unitless measure based on intensity, frequency, and persistence of S3. S3 strength is scaled between 0 and 10.
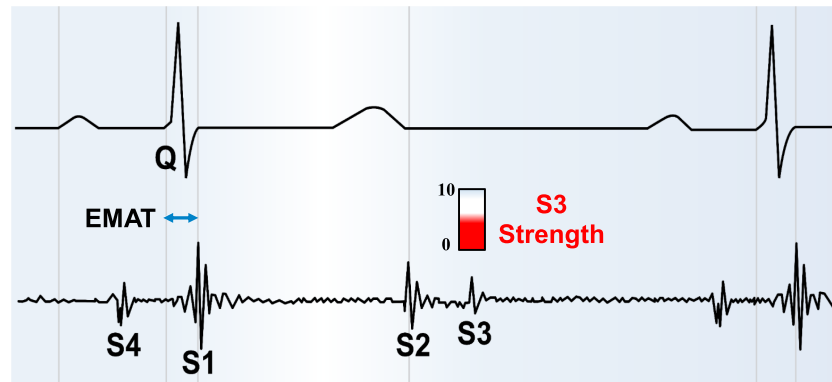
FIGURE 2 Example of the double threshold for the CAB parameter S3 strength and the fluctuation of the risk for an HF event. When the S3 value is below the upper threshold, the risk for HF event is set to low. The risk is set to high when S3 crosses the upper decompensation threshold and is maintained high until the S3 value crosses the lower recovery threshold. Note, as shown here, that subjects can have several high and low risks for an HF event during their WCD period.
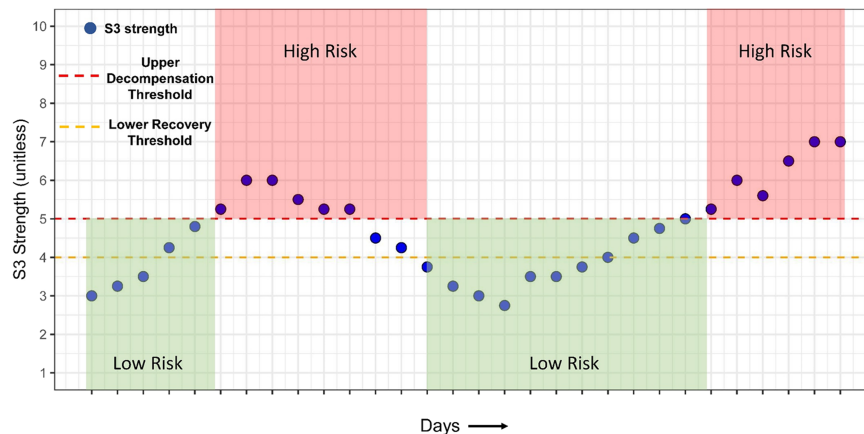
the Youden Index = sensitivity + specificity − 100,[23] was used to select the combination of CABs and HR that maximized the Youden Index value. This maximization was performed concurrently to also identify the optimal decompensation threshold value for each of the CAB parameters and HR in the algorithm. The recovery threshold was set lower than the decompensation threshold and was determined by accounting for intra-subject variability of CAB parameters and HR. Of note, sensitivity was defined as the percentage of subjects with an HF event who were determined as high risk at least once by the algorithm prior to the first HF event. Specificity was defined as the percentage of subjects without an HF event classified as low risk throughout the WCD wear period.

A time-dependent Cox model was used to analyse the association of high-risk and low-risk groups as determined by the CABs/HR algorithm with HF events. In the Cox model, the time-to-event was defined from the first day of WCD wear to the first HF event. Because subjects' daily risk for HF event as determined by the CABs/HR algorithm fluctuated during the WCD use (e.g. starting from high-risk and moving to low-risk and then back to high-risk; also see *Figure 2*), subjects were grouped based on these fluctuations. Then for each group, the relative risk of having an HF event was compared. Additionally, analysis was performed to determine if baseline (first 7 days of WCD wear post-enrolment) CABs and HR were associated with HF events independent of clinical history. Demographic and clinical data were presented as means ± SD and for skewed distributions as medians and interquartile range (IQR). These data were analysed using *t*-tests or Mann–Whitney *U*-tests for continuous variables and

χ^2 tests for categorical variables. All analyses were conducted using RStudio version 1.1.44 (RStudio Inc, Boston, MA). $P < 0.05$ was considered significant.

Results

Patient characteristics and follow-up

From June 2017 through August 2019, 671 patients with HFrEF (77% male) with a mean age of 61 ± 13 years were enrolled. Ischaemic and non-ischaemic patients were equally represented in the study (45% vs. 48%; $P = 0.35$), and 66% of the study patients had at least one hospitalization in the 3 months preceding the index HF hospitalization. The median number of days from the first HF diagnosis to study enrolment was 15 days (IQR = 6-328 days).

During a median follow-up of 85 days (IQR = 76-91 days), 81 patients (12%) had a total of 112 HF events, and four patients (0.6%) died during the study. None of the deceased patients had a WCD shock due to a shockable rhythm at end of life. Only one patient was wearing WCD at the time of death and had a documented asystole due to cardiogenic shock following dilative cardiomyopathy. The remaining three subjects had ischaemic heart disease, and one patient died due to end-of-life HF. For two patients, the exact mode of death remains unclear to the investigators.

Herat failure-related hospital readmission accounted for 99 (88%) of the 112 HF events with HF-related ER visits accounted for the remaining 12%. Regarding distribution of these HF events, 33 (41%) of the 81 patients with an HF event were readmitted within 30 days from study enrolment, 29 (36%) were readmitted between 30 and 60 days, and the remaining were readmitted beyond 60 days. The ejection fraction (EF) at WCD end of use for the HF event group was 30% ± 11% compared with 35% ± 10% for the non-HF event group ($P = 0.005$).

During the WCD use, 28% of the patients reported dyspnoea, 26% reported fatigue, 10% reported oedema, and 27% reported of other signs and symptoms (increased heart rate, persistent coughing/wheezing, nausea, etc.). Comparing the HF and non-HF event groups, 63% vs. 23% reported dyspnoea ($P < 0.01$), 51% vs. 21% reported fatigue ($P < 0.01$), 25% vs. 8% oedema ($P < 0.01$), and 62% vs. 23% reported other signs/symptoms correlated with symptomatic decompensated HF ($P < 0.01$).

Wearable cardioverter-defibrillator device data were used to determine the average wear time per day and the total number of days the WCD was worn. The median average wear time for the two groups (HF event vs. non-HF event) were 23.6 h (IQR: 16-24) and 23.5 h (IQR: 20-24), respectively. The median total days worn for the two groups (HF event vs. no non-HF event) were 71 days (IQR: 31-89) and

84 days (IQR: 46). Because WCD use was comparable between the two groups, there was no bias regarding CABs data availability.

### Algorithm performance for detecting heart failure events

Seventy-four out of 81 subjects with an HF event had CABs and HR recorded prior to the first HF event, and 552 out the 590 subjects with no HF event had CABs and HR data throughout their WCD use. Thus, only 7% (45 of 671) of the patients had missing data mostly due to not wearing the WCD. The CABs/HR algorithm with the Youden Index = 29% had the best performance with a sensitivity of 69%, specificity of 60%, positive predictive value (PPV) of 19%, and a negative predictive value (NPV) of 94%. For this algorithm the decompensation thresholds for EMAT, HR, and S3 strength were 120 ms, 75 b.p.m., and 4.5, respectively, with the recovery thresholds set to 110 ms, 65 b.p.m., and 3.5. During the WCD wear period, of the 271 patients who were determined to be at high risk for HF event by the algorithm, 51 patients (19%) had at least one HF event. In comparison, of the 355 patients who were determined to be at low risk, 23 patients (6%) had at least one HF event (*Figure 3*; hazard ratio = 2.92, 95% confidence interval (CI) [1.78–4.77]; $P < 0.001$).

Patients had varying relative risk (RR) for an HF event when they were grouped based on the daily fluctuations of the algorithm determined HF risk (*Figure 4*). Subjects determined to be high risk ($N = 50$) throughout the WCD wear period were 3.51 times more likely to have an HF event (RR = 3.51, 95% CI [2.04–6.04]; $P < 0.001$). A comparable relative risk elevation for an HF event was observed for patients ($N = 44$) who were initially in the low-risk category but later transitioned to and remained in the high-risk category (RR = 3.48, 95% CI [1.94–6.26]; $P < 0.001$). In contrast, patients who started at high risk and then transitioned to remain at low risk ($N = 28$) or had more than one change to their risk classification ($N = 149$) during the wear period had no significant ($P = 0.31$ and $P = 0.64$, respectively) increase in their relative risk for HF event (*Figure 4*). For patients ($N = 355$) who remained below the decompensation threshold throughout (low risk) actually had a relative risk reduction of 48% (RR = 0.52, 95% CI [0.37–0.73]; $P < 0.001$) of having an HF event.

Time to early detection of heart failure event

The median time from start of the first high-risk classification by the algorithm to an HF event was 32 days (IQR = 11-45), and the median time from the start of the last high-risk classification to an HF event was 27 days (IQR = 11-45).
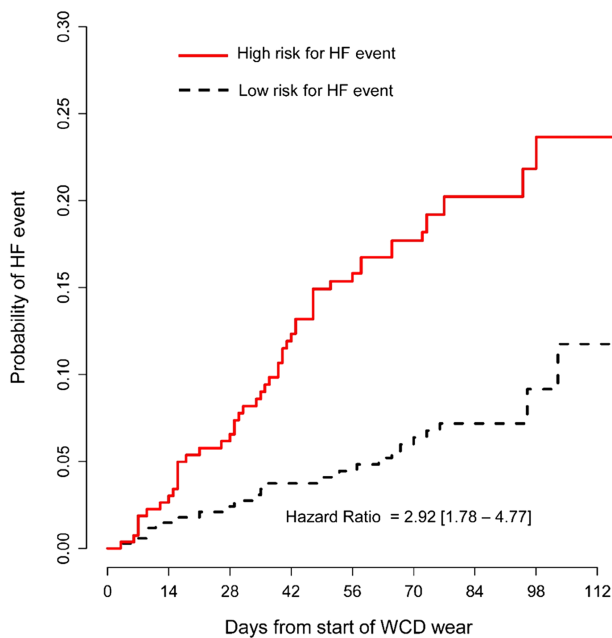
Furthermore, of the 51 patients who were classified as high-risk for an HF event, 57% were identified by the algorithm at least 4 weeks before their HF event; 63% were identified at least 3 weeks before the HF event; 69% were identified at least 2 weeks prior to the HF event; and a cumulative total of 90% were identified at least 3 days before the HF event.

Influence of clinical variables on heart failure events

At the time of enrolment, BMI and weight of the HF event group were significantly lower than the non-HF event group ($P < 0.05$; *Table 1*). The HF event group had significantly ($P < 0.05$) greater percentage of co-morbidities such as previous history of HF, chronic kidney disease, and New York Heart Association (NYHA) IV classification (*Table 1*). Although the enrolment EF was statistically lower for the HF event group ($P = 0.04$), this difference between the two groups was less than 5% (*Table 1*). Additionally, there were no differences in the prescription rates of HF medications between the two groups (*Table 1*).

Using the enrolment clinical variables, analyses were performed to evaluate whether these clinical variables affected performance of CABs and HR data in detecting HF events. To do so, we first developed a baseline (first 7 days of post-enrolment wear) CABs and HR algorithm to detect HF events. The baseline algorithm with the best Youden Index (=29%) had a sensitivity of 61% and specificity of 68%. In contrast, enrolment NYHA Class had a sensitivity of 46% and specificity of 55% (Youden Index = 1%) and history of HF had a sensitivity of 65% and specificity of 51% (Youden Index = 16%). All other clinical history variables had poor sensitivity and/or specificity (<40%). Furthermore, combining the baseline CABs/HR data with enrolment NYHA and history of HF had almost no additional benefit (the algorithm with

FIGURE 4 Forest plot of the relative risk for an HF event between the HF and non-HF event groups during the entire WCD wear period. The fluctuations in the risk classification are based on fluctuations the risk (e.g. from high to low, and back to high) for an HF event as determined by the CABs/HR algorithm. Categories 'Always High' and 'Always Low' represent the category where the determined risk is always high and low, respectively. The category 'High to Low' represents the risk being high initially and becoming low for the reminder of the WCD wear period. Similarly, the category 'Low to High' represents the risk being low initially and becoming high. The category 'Several Highs and Lows' represents more than one change to the risk classification. Also shown are the point estimate of the relative risk and the 95% confidence interval along with the *P*-values.
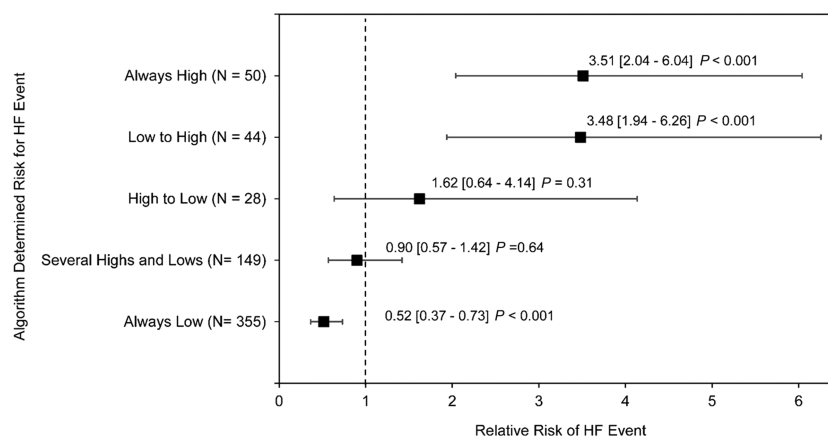
Table 1 Patient baseline characteristics at study enrolment

	HF event, *n* = 81	*n*	Non-HF event, *n* = 590	*n*	*P*-value
Age, years	61 ± 14	81	60 ± 13	590	0.66
Male, *n* (%)	58 (72%)	81	456 (77%)	590	0.26
Diagnosis, *n* (%)					
ICM	39 (48%)	81	264 (45%)	590	0.56
NICM	36 (44%)	81	285 (48%)	590	0.51
Mix	4 (5%)	81	33 (6%)	590	0.81
Unknown	2 (2%)	81	8 (1%)	590	0.44
BMI, kg/m^2	27 ± 5	81	29 ± 6	590	0.006[*]
Height, cm	173 ± 9	81	173 ± 10	590	0.92
Weight, kg	80 ± 18	81	87 ± 21	590	0.03[*]
Blood pressure, mmHg					
Systolic	118 ± 15	81	121 ± 16	588	0.15
Diastolic	74 ± 9	81	75 ± 11	588	0.51
HR, b.p.m.	78 ± 16	81	75 ± 15	588	0.09
Hospitalizations 3 months prior to enrolment, *n* (%)					
0	25 (31%)	81	200 (34%)	586	0.59
1	43 (53%)	81	291 (49%)	586	0.53
2	11 (14%)	81	86 (15%)	586	0.81
3	2 (2%)	81	9 (2%)	586	0.53
NYHA class at enrolment, *n* (%)					
I	9 (11%)	81	44 (7%)	590	0.25
II	43 (53%)	81	342 (58%)	590	0.40
III	19 (23%)	81	150 (25%)	590	0.70
IV	4 (5%)	81	9 (2%)	590	0.04[*]
Unknown	6 (7%)	81	45 (8%)	590	0.94
Enrolment EF, %	24 ± 7	81	26 ± 7	590	0.04[*]
History, *n* (%)					
HF	54 (67%)	81	288 (49%)	590	0.003[*]
Hypertension	57 (70%)	81	408 (69%)	590	0.82
Diabetes	30 (37%)	81	185 (31%)	590	0.30
COPD	12 (15%)	81	56 (9%)	590	0.14
Sleep apnoea	5 (6%)	81	31 (5%)	590	0.73
CKD	18 (22%)	81	78 (13%)	590	0.03[*]
SCA	4 (5%)	81	27 (5%)	590	0.88
MI	35 (43%)	81	219 (37%)	590	0.29
HF medication prescription at enrolment					
Beta-blockers	73 (90.1%)	81	553 (94.2%)	587	0.24
Diuretics	64 (79%)	81	494 (84.2%)	587	0.31
ACEi/ARBs/ARNi	68 (84%)	81	521 (88.8%)	587	0.28

ACEi, angiotensin converting enzyme inhibitors; ARBs, angiotensin receptor blockers; ARNi, angiotensin receptor neprilysin inhibitor; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; EOU, WCD end of use; HF, heart failure; HR, heart rate; ICM, ischaemic cardiomyopathy; MI, myocardial infarction; NICM, non-ischaemic cardiomyopathy; SCA, sudden cardiac arrest.
[*]*P* < 0.05.
Demographic and baseline clinical characteristics. Continuous variables are shown as mean ± standard deviation.

the best Youden Index of 28% had a sensitivity of 55% and specificity of 73%).

Discussion

This prospective international, multicentre registry, using CABs and HR values in patients with HFrEF during the early phase after hospital discharge, was able to identify patients likely to decompensate an average of 30 days in advance of their symptomatic HF presentation. In comparison, detailed analysis using only variables from the clinical history had a lower performance for identifying future HF events. Of note, the baseline (first 7 days post-enrolment) algorithm using CABs and HR was superior to NYHA classification in detecting

patients more likely to have HF decompensation. Importantly, the addition of clinical history information to the CAB/HR algorithm did not improve the algorithm performance.

This study is also the first to report HF event rates in patients with HFrEF who were prescribed to wear the WCD for at least 3 months post-discharge. The patient-based HF event rate during this "vulnerable phase" after hospitalization for HF was 12% during the WCD wear period, comparable with the 90 day HF event rate of 7–18% reported in the literature.[24–26]

The CABs and HR algorithm identified patients likely to have an HF events with a sensitivity of 69%, specificity of 60%, PPV of 19%, and a NPV of 94% indicating that patients with low risk for HF decompensation had no HF event during the study period. On the contrary, high-risk patients had an

almost threefold increase in the risk for an HF event. In comparison, the SENSE-HF study (501 patients with chronic low EF receiving ICDs or CRT-Ds), which evaluated measurements of thoracic impedance, reported an overall sensitivity for detection of HF hospitalization of 21% and a PPV of 5% during the first 6 months post-implant.[27] The HeartLogic algorithm used in some ICDs and CRT-Ds incorporates HR, thoracic impedance, respiration rate, activity, and heart sounds to detect HF decompensation. In a recently published retrospective case series of 58 patients, the median time from the high-risk alert to hospitalization was 38 days (IQR = 15-61 days),[28] similar to that reported in this study. Each of the high-risk alerts of the HeartLogic algorithm had contributions from changes in S1 and/or S3 amplitudes providing additional evidence that CABs are useful in early detection of an impending HF event. The authors concluded that this algorithm might be able to detect clinical worsening in patients with HF early before a critical clinical deterioration.[28]

When comparing patients with HF events versus patients without HF events, our results show that patients with HF events had a significantly lower EF at the end of WCD use compared with patients without HF events (31 ± 10% vs. 35% ± 10%; *P* = 0.005), and patients with HF events more often reported symptoms related to decompensated HF (*P* < 0.001). In our CABs and HR algorithm, we used a dual threshold strategy to stratify patients into low-risk and high-risk group categories for an HF event. Patients who were classified into the low-risk category had an NPV of 94% with a relative risk reduction of 48% of having an HF event.

To date, only one previous study has reported using CABs data to manage HF in an outpatient setting.[14] In that single-blinded, randomized study of 225 patients with acute HF, HF medications were uptitrated using periodically assessed CAB parameters with the goal to reduce CABs below pre-specified thresholds. They found a 30% reduction in HF rehospitalization or cardiovascular mortality in 1 year in the treatment group compared with the control group which had symptom-only titration of medications.[14]

The results from this study support the potential utility of using CABs and HR to identify 'at-risk' patients and adjust their individual treatment plans during the vulnerable post-discharge phase, with a goal of reducing early HF readmission. Furthermore, changes or trends in the CABs-based and HR-based risks for an HF event during the WCD use support the importance and need for continuous monitoring to track HF health status trajectory. Integrating CAB technology in clinical practice may prevent HF rehospitalizations early and efficiently.

Limitations of the study

This is a prospective registry study hence all potential limitations of such a design apply to this analysis. The interventional collective has not been compared with a control group. Further we did not reassess echocardiographic parameters with a core lab. In this study, the algorithm for early HF detection was developed on the entire data set with no separate validation. Thus, the CAB/HR algorithm requires validation in a prospective randomized trial. Future analysis could apply this algorithm to commercial WCD populations as a validation set.

Conclusions

This prospective international multicentre registry suggests that the use of cardiac acoustic biomarkers in patients with HF with reduced LVEF and fitted with a WCD may provide early detection of patients with an increased probability of a decompensated HF event after hospital discharge. Cardiac acoustic biomarkers were superior to NYHA classification in identifying the 'at-risk' population.

Acknowledgements

Conflict of interest

J.W.E. reports receiving consultant fees, travel support, and lecture fees from ZOLL Medical; travel grants from Bayer Vital, St. Jude Medical/Abbott, and Novartis; and lecture fees from Servier and Bayer and was a fellow of the Boston Scientific heart rhythm fellowship program. D.S. reports travel support and lecture fees from ZOLL Medical. All other authors report no conflict of interest.

Funding

References

1. Ambrosy AP, Pang PS, Khan S, Konstam MA, Fonarow GC, Traver B, Maggioni AP, Cook T, Swedberg K, Burnett JC, Grinfeld L, Udelson JE, Zannad F, Gheorghiade M. On behalf of the EVEREST trial investigators Clinical course and predictive value of congestion during hospitalization in patients admitted for worsening signs and symptoms of heart failure with reduced ejection fraction: findings from the EVEREST trial. *Eur Heart J* 2013; **34**: 835–843.

2. Ross JS, Chen J, Lin Z, Bueno H, Curtis JP, Keenan PS, Normand SLT, Schreiner G, Spertus JA, Vidán MT, Wang Y, Wang Y, Krumholz HM. Recent national trends in readmission rates after heart failure hospitalization. *Circ Heart Fail* 2010; **3**: 97–103.

3. Saito M, Negishi K, Marwick TH. Meta-analysis of risks for short-term readmission in patients with heart failure. *J Cardiol* 2016; **117**: 626–632.

4. Zile MR, Bennett TD, St. John Sutton M, Cho YK, Adamson PB, Aaron MF, Aranda JM Jr, Abraham WT, Smart FW, Stevenson LW, Kueffer FJ, Bourge RC. Transition from chronic compensated to acute decompensated heart failure: pathophysiological insights obtained from continuous monitoring of intracardiac pressures. *Circulation* 2008; **118**: 1433–1441.

5. Ritzema J, Troughton R, Melton I, Crozier I, Doughty R, Krum H, Walton A, Adamson P, Kar S, Shah PK, Richards M, Eigler NL, Whiting JS, Haas GJ, Heywood JT, Frampton CM, Abraham WT. Physician-directed patient self-management of left atrial pressure in advanced chronic heart failure. *Circulation* 2010; **121**: 1086–1095.

6. Bhimaraj A. Remote monitoring of heart failure patients. *Methodist Debakey Cardiovasc J* 2013; **9**: 26–31.

7. Abraham WT, Stough WG, Pina IL, Linde C, Borer JS, De Ferrari GM, Mehran R, Stein KM, Vincent A, Yadav JS, Anker SD. Trials of implantable monitoring devices in heart failure: which design is optimal? *Nat Rev Cardiol* 2014; **11**: 576–585.

8. Sung S-H, Yu W-C, Cheng H-M, Chang Y-P, Chen C-H. Use of acoustic cardiography to guide outpatient therapy of patients with acute heart failure syndrome. *J Am Coll Cardiol* 2014; **63**: A541.

9. Klein HU, Meltendorf U, Reek S, Smid JA, Kuss S, Cygankiewicz I, Jons C, Szymkiewicz S, Buhtz F, Wollbrueck A, Zareba W. Bridging a temporary high risk of sudden arrhythmic death. Experience with the wearable cardioverter defibrillator (WCD). *Pacing Clin Electrophysiol* 2010; **33**: 353–367.

10. Chun S, Tu JV, Wijeysundera HC, Austin PC, Wang X, Levy D, Lee DS. Lifetime analysis of hospitalizations and survival of patients newly admitted with heart failure. *Circ Heart Fail* 2012; **5**: 414–421.

11. Desai AS, Stevenson LW. Rehospitalization for heart failure: predict or prevent? *Circulation* 2012; **126**: 501–506.

12. Chang CC, Sung SH, Yu WC, Cheng HM, Chen CH. Night-time electromechanical activation time, pulsatile hemodynamics, and discharge outcomes in patients with acute heart failure. *ESC Hear Fail* 2015; **2**: 184–193.

13. Collins SP, Lindsell CJ, Peacock WF, Hedger VD, Storrow AB. The effect of treatment on the presence of abnormal heart sounds in emergency department patients with heart failure. *Am J Emerg Med* 2006; **24**: 25–32.

14. Sung S, Huang C, Cheng H, Huang WM, Yu WC, Chen CH. Effect of acoustic cardiography-guided management on one-year outcomes in patients with acute heart failure. *J Card Fail* 2020; **26**: 142–150.

15. Zishiri ET. The role of the wearable cardioverter-defibrillator in contemporary clinical practice. *J Innov Card Rhythm Manag* 2011; **2**: 307–316.

16. Feldman AM, Klein H, Tchou P, Murali S, Hall WJ, Mancini D, Boehmer J, Harvey M, Heilman MS, Szymkiewicz SJ, Moss AJ. Use of a wearable defibrillator in terminating tachyarrhythmias in patients at high risk for sudden death: results of the WEARIT/BIROAD. *Pacing Clin Electrophysiol* 2004; **27**: 4–9.

17. Reek S, Geller JC, Meltendorf U, Wollbrueck A, Szymkiewicz SJ, Klein HU. Clinical efficacy of a wearable defibrillator in acutely terminating episodes of ventricular fibrillation using biphasic shocks. *Pacing Clin Electrophysiol* 2003; **26**: 2016–2022.

18. Epstein AE, Haines D, Bianco N, Szymkiewicz S. Wearable cardioverter-defibrillator use in patients perceived to be at high risk early post MI. *J Am Coll Cardiol* 2013; **62**: 2000–2007.

19. Priori S, Blomstrom-Lundqvist C, Mazzanti A, Blom N, Borggrefe M, Camm J, Elliott PM, Fitzsimons D, Hatala R, Hindricks G. 2015 ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). *Eur Heart J* 2015; **36**: 2793–2867.

20. Adler A, Halkin A, Viskin S. Wearable cardioverter-defibrillators. *Circulation* 2013; **127**: 854–860.

21. Burkhoff D, Bailey G, Gimbel JR. Characterization of cardiac acoustic biomarkers in patients with heart failure. *Ann Noninvasive Electrocardiol* 2020; **25**: e12717.

22. Wang S, Lam Y, Liu M, Fang F, Wang J, Shang Q, Sun JP, Sanderson JE, Yu CM. Acoustic cardiography helps to identify heart failure and its phenotypes. *Int J Cardiol* 2013; **167**: 681–686.

23. Youden WJ. Index for rating diagnostic tests. *Cancer* 1950; **3**: 32–35.

24. Schjodt I, Larsen P, Johnsen SP, Stromberg A, Logstrup BB. Risk factors for readmission to hospital in adult patients with heart failure and reduced ejection fraction: a systematic review protocol. *JBI Database Syst Rev Implement Rep* 2017; **15**: 1561–1574.

25. Arora S, Patel P, Lahewala S, Patel N. Etiologies, trends, and predictors of 30-day readmission in patients with heart failure. *Am J Cardiol* 2017; **119**: 760–769.

26. Dharmarajan K, Lin Z, Ross JS, Horwitz LI, Barreto-Filho JA, Kim N, Bernheim SM, Suter LG, Drye EE. Diagnoses and timing of 30-day readmissions after hospitalization for heart failure, acute myocardial infarction, or pneumonia. *JAMA* 2013; **309**: 355–363.

27. Conraads VM, Tavazzi L, Santini M, Oliva F, Gerritse B, Yu CM, Cowie MR. Sensitivity and positive predictive value of implantable intrathoracic impedance monitoring as a predictor of heart failure hospitalizations: the SENSE-HF trial. *Eur Heart J* 2011; **32**: 2266–2273.

28. Capucci A, Santini L, Favale S, Pecora D, Petracci B, Calò L, Molon G, Cipolletta L, Bianchi V, Schirripa V, Santobuono VE, la Greca C, Campari M, Valsecchi S, Ammirati F, D'Onofrio A. Preliminary experience with the multisensor HeartLogic algorithm for heart failure monitoring: a retrospective case series report. *ESC Hear Fail* 2019; **6**: 308–318.