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Fewer Worsening Heart Failure Events With HeartLogic on top of Standard Care: a Propensity-Matched Cohort Analysis

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ABSTRACT

Background: The implantable cardiac defibrillator-based HeartLogic algorithm aims to detect impending fluid retention in patients with heart failure (HF). Studies show that HeartLogic is safe to integrate into clinical practice. The current study investigates whether HeartLogic provides clinical benefit on top of standard care and device telemonitoring in patients with HF.

Methods: A multicenter, retrospective, propensity-matched cohort analysis was performed in patients with HF and implantable cardiac defibrillators, and it compared HeartLogic to conventional telemonitoring. The primary endpoint was the number of worsening HF events. Hospitalizations and ambulatory visits due to HF were also evaluated.

Results: Propensity score matching yielded 127 pairs (median age 68 years, 80% male). Worsening HF events occurred more frequently in the control group (2; IQR 0−4) compared to the HeartLogic group (1; IQR 0−3; $P = 0.004$). The number of HF hospitalization days was higher in controls than in the HeartLogic group (8; IQR 5−12 vs 5; IQR 2−7; $P = 0.023$), and ambulatory visits for diuretic escalation were more frequent in the control group than in the HeartLogic group (2; IQR 0−3 vs 1; IQR 0−2; $P = 0.0001$).

Conclusion: Integrating the HeartLogic algorithm in a well-equipped HF care path on top of standard care is associated with fewer worsening HF events and shorter duration of fluid retention-related hospitalizations. (*J Cardiac Fail 2023;29:1522−1530*)

Key Words: chronic heart failure, ICD, remote monitoring, heart failure hospitalization.

Heart failure (HF) is a common cause of unplanned hospital admissions, a phenomenon that is caused predominantly by fluid retention. These admissions are associated with significant morbidity and mortality rates and impair quality of life.[1−3] Timely detection of fluid retention is 1 of the major challenges in HF management because patient-reported symptoms and signs of fluid retention occur relatively late and are rather poor markers of the clinical status of patients with HF.[4,5] Timely detection of impeding fluid retention is crucial in ambulatory-treatment escalation and prevention of HF-related admissions.

According to the current European Society of Cardiologists (ESC) guidelines, an implantable cardiac defibrillator (ICD) is recommended in patients with HF and reduced ejection fraction to decrease the risk of sudden arrhythmic death.[1] Apart from detecting and treating arrhythmias, ICDs have the capability to sense and store various cardiac and noncardiac parameters, including heart rate variability, thoracic impedance and physical activity. These data are collected continuously and automatically, so ICDs can be used for telemonitoring with almost no effort on the part of patients.[2]

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The relatively novel multisensory ICD-based algorithm HeartLogic (Boston Scientific, Marlborough, MA, USA) aims to detect fluid retention at an early stage by using the capability of available sensors within the ICD.[3] The algorithm collects data about the following sensors: heart sounds (S1, S3 and their ratio), respiration rate and variation, thoracic impedance, nightly heart rate, and physical activity. These sensor data are automatically integrated into a single index value.[4]

The MultiSENSE (Multisensor Chronic Evaluation in Ambulatory Heart Failure Patients) trial was the first observational study in which the algorithm data were reviewed after a hospitalization due to HF had occurred.[3] An increase in the HeartLogic index above the nominal threshold of 16 could predict an episode of fluid retention with a sensitivity of 70%. These episodes could be predicted up to a median of 34 days prior to admission.[3] Since then, several studies have demonstrated that patients with alerts were at increased risk of fluid retention compared to patients without alerts.[5–9] Recently, the results of the phase-I MANAGE-HF (Multiple cArdiac seNsors for mAnaGEment of Heart Failure) trial showed a safe integration of the algorithm into clinical care and improvement in HF management.[10] In addition, the height of the alert has been shown to correlate with the severity of fluid retention.[11] A relatively small study (n = 68) with a pre/post design demonstrated that HeartLogic may help to prevent hospitalizations due to HF.[12] However, robust evidence showing that the HeartLogic algorithm provides clinical benefit on top of standard care is still absent. Results of the MANAGE-HF trial are expected, at the earliest, in 2024.

Therefore, we investigated a cohort of patients with HF and with an ICD, either with or without the HeartLogic algorithm, on top of conventional device telemonitoring. We performed propensity score matching and compared worsening HF events, HF hospitalizations and ambulatory HF visits in which diuretic therapy was intensified in both groups.

Methods

Patient Population, Data Sources

For this multicenter, retrospective cohort-sampling study, patients were recruited from 4 European HF centers. Patients were eligible for inclusion if they had HF, as defined in the European Society of Cardiology Guidelines, an ICD with device telemonitoring, and at least 1-year of follow-up.[1] Patients were excluded if they had incomplete baseline and/or matching variables and if they died during the first year of follow-up. Distribution of mortality and cause of death are presented in Supplementary Table S1. The study was conducted in accordance with the declaration of Helsinki, applicable local law, and the European directive for data protection. The 4 local institutional ethical committees approved the study. A study flowchart is depicted in Fig. 1.

Use of HeartLogic: Protocol for Follow-up

All patients were followed via scheduled outpatient clinic visits every 6 months for a device check-up and a review by the cardiologist (standard care). Extra visits were scheduled, if deemed necessary by the treating cardiologist. Patients were treated and followed-up in accordance with the ESC guidelines.[1,13] All patients were on device telemonitoring. In the HeartLogic group, patients were continuously followed-up according to a standardized protocol, which is described below. HeartLogic was, therefore, an additional service for patients and did not replace regular care.[14]

HeartLogic Index and Monitoring Protocol

The HeartLogic index is the result of a complex algorithm of which the formula is unknown to its users. Data are collected continuously from 5 sensors embedded in the ICD: heart sounds (S1, S3 and their ratio), intrathoracic impedance, respiratory rate, night heart rate, and physical activity.[3] The algorithm generates an index based on alterations in the 5 above-mentioned sensors. The number of sensors in which an alteration is measured and/or the rapidity of the change measured determines the level of the HeartLogic index. A high HeartLogic index (standard set at $\geq$ 16) indicates impending decompensation. A low HeartLogic index ($<$ 16) indicates a stable clinical status. The HeartLogic index is automatically transmitted to the hospital via the telemonitoring system (Latitude, Boston Scientific, Marlborough, MA, USA), which sends the HeartLogic index to the Latitude platform. If the threshold of 16 is surpassed, an alert signal is given off by the system.

Remote monitoring data were reviewed daily by a trained ICD technician and/or HF nurse. In case of an alert, the HeartLogic report was transferred to the HF caregiver. Within 72 hours, the patient was contacted by phone, and the following parameters were structurally evaluated: worsening HF symptoms or signs, body weight, blood pressure, and heart rhythm. In case of 2 or more symptoms or signs of HF (as defined by the ESC guidelines) on top of the elevated HeartLogic index, the alert was considered true-positive. All patients with a true-positive alert received lifestyle advice, and further therapeutic action was determined in line with the severity of the patients' symptoms and fluid status, in line with the ESC guidelines and at the discretion of the HF

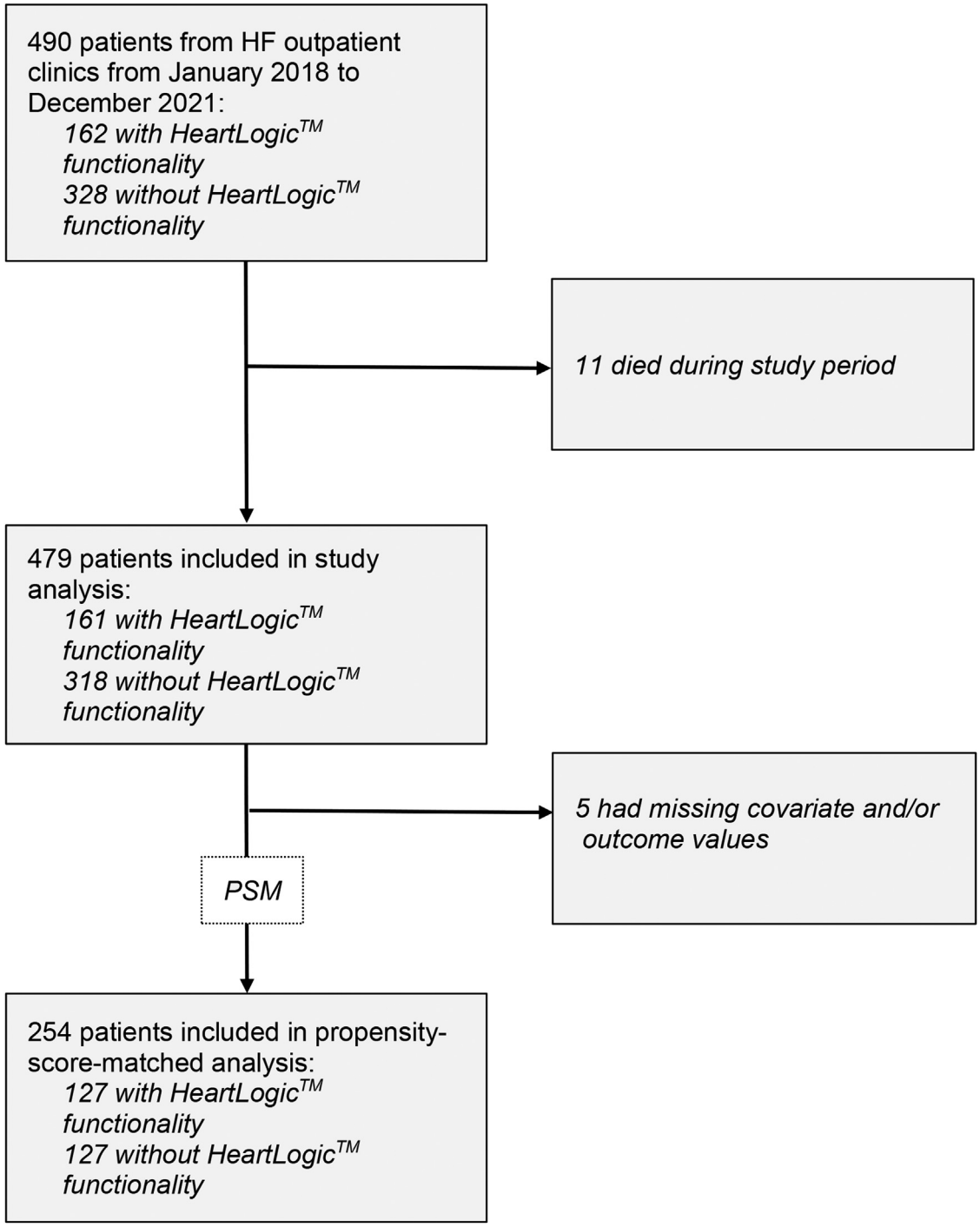

Fig. 1. Study flowchart, patient selection. HF, heart failure; FU, follow-up; PSM, propensity score matching.

cardiologist.[13] Medication adjustment was performed according to a standardized dosage-escalation scheme. The first step was to double the cumulative daily dose of oral loop-diuretic for the duration of 3 days (either furosemide or bumetanide). A digital follow-up was scheduled after 72 hours to evaluate the effect. If there were no more symptoms and/or signs of HF, diuretics dosage was lowered to the initial dosage. If symptoms and/or signs persisted, the increased dosage of diuretics was continued or further increased, or the patient was scaled-up to intravenous treatment at the day clinic (depending on the initial response and the severity of congestion). After each pharmacological adjustment, the patient was contacted after 72 hours for evaluation, and all patients were reevaluated by means of a phone call after 2 weeks.

Alternatively, in case of fewer than 2 symptoms or signs of HF, a new remote evaluation in 2 weeks was planned. This remote evaluation, again, consisted of

a medical history, a rhythm assessment and an evaluation of body weight, blood pressure and the level of the HeartLogic index. In case of the development of 2 or more signs and symptoms on top of a persistent HeartLogic alert, the alert was considered true-positive, and treatment was escalated, as described above. After 3 consecutive remote evaluations (at 2, 6 and 10 weeks after the initial alert) with consistently fewer than 2 symptoms or signs of HF at each evaluation, an ongoing alert was disregarded and classified as false-positive.

Data Collection and Endpoints

Demographic data, risk factors, comorbidities, technical examinations, and laboratory tests were obtained through retrospective chart review by trained nurses and physicians. Clinical data were collected from the electronic medical records of all participating centers. HeartLogic data were collected from the LATITUDE Device Support (Boston Scientific) website from the moment that calibration was completed (nominally 45 days, specific for the HeartLogic feature).

The primary endpoint of this study was the number of worsening HF events. A worsening HF event was defined as a composite of a hospital admission for decompensated HF and an unplanned ambulatory (digital or physical) HF visit, during which lifestyle advice was given, and/or the diuretic therapy was escalated because of congestion. Secondary outcome parameters were the number of HF hospitalizations and their durations. In addition, the number of ambulatory HF-care visits in which lifestyle advice was given and diuretic therapy was intensified were evaluated.

Of note, an HF admission was defined in accordance with the 2017 cardiovascular and stroke endpoints definitions for clinical trials[14] as an "unscheduled hospital admission for a primary diagnosis of HF with a length of stay that either exceeds 24 hours or crosses a calendar day." At presentation, at least 2 typical signs and 2 typical symptoms of HF had to be present.[13] Patients had to receive intravenous diuretics as part of their treatment during hospitalization.[14] Elective hospitalization for ICD implantations and hospitalizations during the calibration period were not considered, because no HeartLogic alerts could have been generated during this "blind" period.

Propensity Score-Based Matching

Propensity score-based matching (PSM) was performed as described peviously.[15] Briefly, the treatment was defined as the HeartLogic algorithm's being switched on during the follow-up period. In the overall sample, continuous variables and categorical variables were compared between treatment groups using the standard Student *t* test and the χ^2 test, respectively. Absolute mean differences were used (and reported) to compare baseline characteristics between the 2 groups.

Estimation of the Propensity Score

An initial propensity score model was estimated using the variables described in Table 1. To estimate the propensity score, a logistic regression model was used, in which treatment status was regressed according to the baseline characteristics.

Matching on the Propensity Score

Treated and untreated participants were matched on the propensity score in a 1:1 matching without replacement. In the data set, there were more untreated participants (no HeartLogic feature) than treated participants (HeartLogic feature switched on). Participants were matched on the propensity score by using a caliper of width equal to 0.2 of the standard deviation of the logit of the estimated propensity score.

Statistical Reporting of Data

Descriptive data are reported as mean ± SD for normally distributed continuous variables or by median with interquartile range (IQR) in the case of non-normally distributed variables, unless mentioned otherwise. Normality testing was performed by using the Kolmogorov-Smirnov and the Shapiro-Wilk tests. After a matching McNemar test, a Wilcoxon signed rank test or a Pratt test (the latter in case of excessive 0s) was used to assess the statistical significance of differences between the matched cohorts. A *P* value lower than 0.05 was considered statistically significant. Statistical analysis was performed by means of GraphPad Prism 9.0 (GraphPad Software, San Diego, CA, USA) and R (R Core Team, 2021).

Results

Patient Population

Retrospective cohort sampling was performed between January 2018 and December 2021. In total, 490 patients were deemed eligible for inclusion. Eleven patients died during follow-up; they were excluded from analysis. Accordingly, the final study population comprised 479 patients: 318 in the control group (without HeartLogic) and 161 in the HeartLogic group. Because baseline variables and/or follow-up parameters were missing in 5 patients, they were also excluded. Table 1 displays the baseline characteristics of the unmatched and the

Table 1. Baseline characteristics before and after propensity matching

Baseline Characteristics	Before Matching			After Matching		
	Non-HL (n = 318)	HL (n = 161)	SMD	Non-HL (n = 127)	HL (n = 127)	SMD
Age, median, IQR	67.0 [59.3, 74.0]	68.0 [58.3, 75.0]	0.028	68.0 [60.5, 75.0]	68.0 [58.5, 75.5]	0.007
Male, %	173 (77.9)	123 (79.9)	0.019	101 (79.5)	102 (80.3)	0.008
Ischemic etiology, %	117 (52.7)	71 (46.1)	0.067	62 (48.8)	58 (45.7)	0.032
eGFR, mL/min/1.73m^2, median, IQR	64 [44, 81]	66 [45, 82]	0.055	66 [47, 84]	68 [50, 85]	0.012
LVEF, %, median, IQR	33 [26, 42]	35 [27, 42]	0.026	34 [28, 41]	35 [27, 45]	0.034
LVEDd, mm, median, IQR	60 [53, 66]	60 [55, 65]	0.014	58 [52, 66]	59 [55, 65]	0.008
NYHA class III or IV, %	67 (30.2)	47 (30.5)	0.003	39 (30.7)	38 (29.9)	0.008
Mitral regurgitation, %						
Mild	144 (64.9)	110 (71.4)	0.066	94 (74.0)	88 (69.3)	0.047
Moderate	64 (28.8)	28 (18.2)	0.107	23 (18.1)	28 (22.0)	0.039
Severe	14 (6.3)	16 (10.4)	0.041	10 (7.9)	11 (8.7)	0.008
Diabetes, %	63 (28.4)	25 (16.2)	0.121	28 (22.0)	25 (19.7)	0.024
No CRT function (only ICD), %	124 (55.9)	52 (33.8)	0.221	52 (40.9)	52 (40.9)	0.000
Year of study, %						
2018	80 (36.0)	48 (31.2)	0.049	45 (35.4)	40 (31.5)	0.039
2019	82 (36.9)	59 (38.3)	0.014	52 (40.9)	49 (38.6)	0.024
2020	60 (27.0)	47 (30.5)	0.035	30 (23.6)	38 (29.9)	0.063

CRT, cardiac resynchronization therapy; eGFR, estimated glomerular filtration rate; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; LVEDd, left ventricular end-diastolic diameter; NYHA, New York Heart Association.

matched populations. Before matching, the characteristics of the control group differed significantly from those of the HeartLogic group: diabetes was more prevalent in the control group, and that group comprised fewer carriers of cardiac resynchronization therapy defibrillators. In addition, control patients were more frequently included in 2018−2019 vs HeartLogic patients than in 2019−2020. Propensity score matching yielded 127 matched pairs with highly similar baseline characteristics (Table 1) (Fig. 2a, b). All patients were followed-up for 365 days. Accordingly, total follow-up duration consisted of 254 patient-years. The median age was 68 years, and 80% of patients were male. The etiology of HF was ischemic in 49% of the control patients and in 46% of the HeartLogic patients, and the median ejection fraction, according to echocardiographical measurement, was 34% and 35%, respectively.

HeartLogic Alerts in the Unmatched HeartLogic Group

The unmatched HeartLogic group comprised 161 patients, and during follow-up, 66 (41%) of these patients had 1 or more HeartLogic alerts. In total, 130 alerts occurred in these patients. Of all patients with an alert, 26 patients (39%) had only 1 HeartLogic alert, 23 patients had 2 alerts (35%), and 17 patients had 3 or more alerts (26%). The average number of alerts per patient-year was 0.8, with a mean duration of alert of 36 ± 9 days. The number of false-positive alerts was 33 (25%), the number of true-positive alerts was 97 (75%). There were 12 events of worsening HF that were not detected by HeartLogic. The

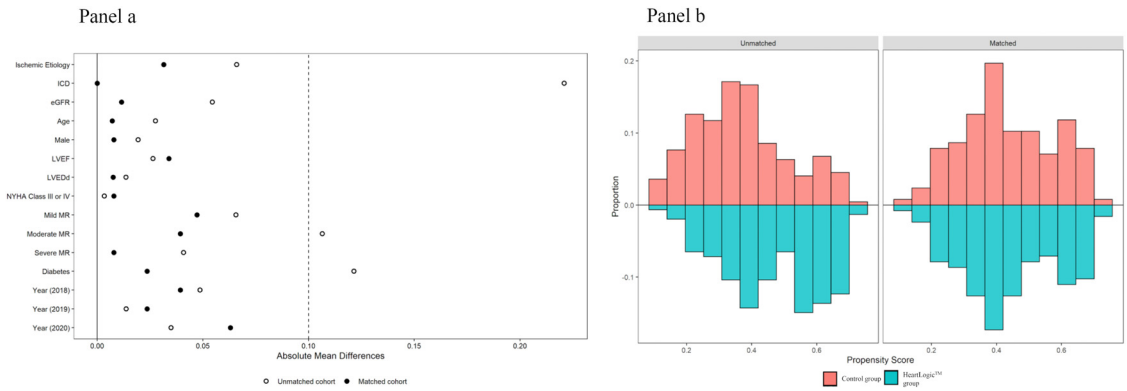

Fig. 2. a, Absolute mean differences (AMDs) of baseline variables used for matching, before (°) and after (•) propensity score matching (PSM). After matching, all AMDs are smaller than 0.10. b, visual output of PSM of distribution balance. Left, both groups before PSM; right, both groups after PSM.

unexplained alert rate (UAR) was 0.2 per patient-year; the true positive alert rate was 0.6 per patient-year. UAR was defined as the number of alerts that could not be explained by worsening HF per patient-year. The true-positive alert rate was defined as the number of alerts caused by worsening HF per patient-year. Of the 130 alerts, only 5% were addressed exclusively by lifestyle reinforcement or modifications (without pharmacological escalation). In most of the alerts (74%), doubling of the cumulative daily dose of oral diuretic treatment was sufficient to recompensate the patient. In 86% of these alerts, doubling the diuretic dosage for 3 days was enough, whereas in 14%, continuation for more than 3 days was necessary. For some (3%) alerts, an additional single dose of intravenous diuretics was required. Only 4% of patients with a HeartLogic alert were admitted to the hospital for intravenous therapy. In the remaining alerts, other oral pharmacological therapy for HF (eg, sacubitril/valsartan) was initiated or escalated, or an electrical cardioversion was performed due to atrial arrythmia.

Worsening HF Events After Matching

In the control group, the median number of worsening HF events was 2 (IQR 0–4). As shown in Fig. 3, this was significantly higher than the median of 1 (IQR 0–3) worsening HF event that was observed in the HeartLogic group ($P = 0.004$). The number of patients experiencing at least 1 worsening HF event was 85 (67%) in the control group and 77 (60%) in the HeartLogic group. Of note, the cumulative number of worsening HF events was 331 in the control group and 206 in the HeartLogic group. A hospitalization due to HF occurred in 17 (13%) control patients and in 8 (6%) HeartLogic patients. There was a nonsignificant trend toward a lower number of HF hospitalizations in the HeartLogic group ($P = 0.096$) (Table 2). In those hospitalized, the number of HF hospitalization days was significantly higher in the control group, with 8 (IQR 5–12) hospitalization days compared to 5 (IQR 2–7) days in the HeartLogic group ($P = 0.025$) (Fig. 4). Intensifying diuretic therapy in the ambulatory setting was required in 83 (65%) control patients and in 76 (60%) HeartLogic patients. There was a significantly higher number of ambulatory visits for intensifying diuretics in the control group (2; IQR 0–3) compared to 1 (IQR 0–2) in the HeartLogic group ($P = 0.0001$) (Table 2). The number of contacts per episode of fluid retention was, on average, 3.0 contacts in the control group and 3.6 contacts per episode of fluid retention in the HeartLogic group ($P = 0.498$).

Discussion

The main finding of this multicenter propensity cohort-matching study is that patients with an activated HeartLogic feature on their ICD have significantly less worsening HF events compared to patients on standard care alone. Furthermore, there was a significantly lower number of hospitalization days in patients in the HeartLogic group and a trend toward a lower number of hospitalizations due to HF. Notably, the number of ambulatory visits was significantly lower in patients with the HeartLogic feature on their ICDs.

Early detection of impending worsening HF is a key issue in HF management, and it aims to create a

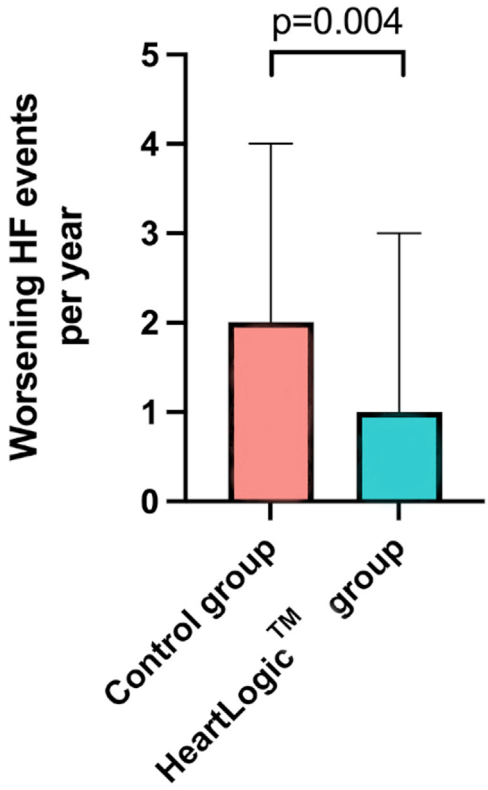

Fig. 3. Number of worsening heart failure events (a composite of a hospital admission for decompensated heart failure and an unplanned ambulatory heart failure visits) per year in the control group (2; IQR 0–4) compared to the HeartLogic group (1; IQR 0–3; $P = 0.004$).

Table 2. Clinical outcome data

Outcomes	Control (n = 127)	HeartLogic (n = 127)	*P* value
Worsening Heart Failure			
Worsening HF episodes (median [IQR])	2 (0–4)	1 (0–3)	0.004
Hospitalization due to Heart Failure			
Number of HF hospitalization (median [IQR])	0 (0–0)	0 (0–0)	0.096
Hospitalization days in those hospitalized (median [IQR])	8 (5–12)	5 (2–7)	0.023
Ambulatory Care			
Number of ambulatory visits (median [IQR])	2 (0–3)	1 (0–2)	0.0001

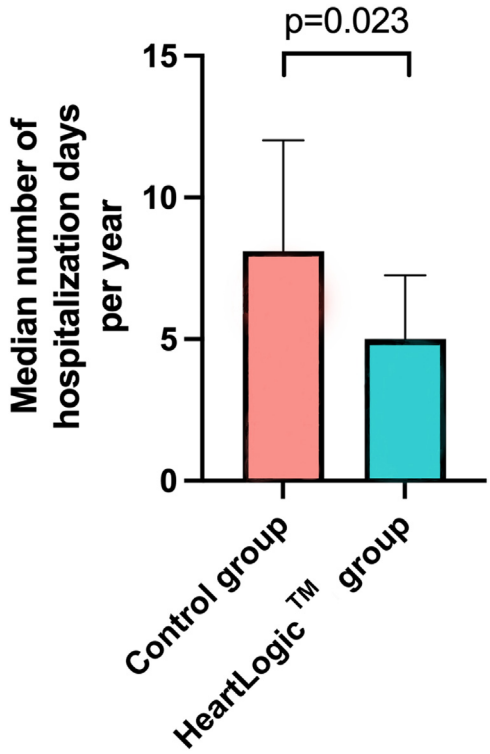

Fig. 4. Median number of hospitalizations days in those hospitalized, in the control group (8; IQR 5−12) compared to the HeartLogicTM group (5; IQR 2−7); $P = 0.023$.

time window for medical interventions.[16] Fluid retention-related signs and symptoms typically appear in a late stage of decompensated HF.[17] Frequently used measurements, such as an increase in body weight or symptoms such as dyspnea, are not robust enough to detect changes in clinical HF status in a timely manner, in part, because they occur very late in the decompensation episode. Patients typically contact their physicians with signs and symptoms of congestion 2 days before hospitalization, whereas the HeartLogic algorithm is able to detect signs of fluid detection with a median of 34 days in advance.[3] The HeartLogic algorithm is a multisensory index that is incorporated in ICDs and aims to detect impending worsening HF.[3] Current literature reports demonstrate that HeartLogic can detect impending fluid retention with a sensitivity between 70% and 90% and a specificity between 86% and 89%.[3,6,11,12,18] Few patients with impending fluid retention are not recognized by the algorithm, as demonstrated by the high negative predictive values of 99%−91%, as reported in the MultiSENSE trial and in a study from Feijen et al., respectively.[3,11] Therefore, patients out of alert are safe while monitored, and health care resources can be directed to patients that are in highest need; this makes HeartLogic a very good tool for risk stratification. Furthermore, the average alert rate was 0.8 alerts per patient-year in this patient cohort, which is comparable to the 0.76−1.76 alerts per patient-year found in previous studies.[6,10−12,18,19] Numerous studies have demonstrated that the overall unexplained alert rate is low, namely 0.16−1.47 per patient-year, which is in line with the UAR of 0.2 per patient-year in the current cohort.[3,6,10−12,18] Therefore, using HeartLogic does not result in substantial increase in daily workload, and its implementation could potentially even reduce the logistical burden of robust management of patients with HF.

The algorithm has been thoroughly investigated for safe implementation, and alert-based follow-up has been shown to be more efficient than scheduled follow-up.[6,10,18−20] Early clinical action seems to be more effective in preventing a worsening HF event than a wait-and-see strategy after an alert.[10,19,20] However, to date, no data concerning optimal timing of clinical action or standardized treatment protocols are available. Current ongoing, large randomized clinicals trials, such as the PREEMPT-HF (Precision Event Monitoring for Patients With Heart Failure Using HeartLogic) (NCT03579641) and the MANAGE-HF (NCT03237858) phase II trial aim to evaluate the effects of HeartLogic on mortality and HF hospitalizations.

Furthermore, to date, evidence of clinical benefits of the HeartLogic algorithm is scarce. So far, only 1 study in our study's group demonstrated in a pre- and postactivation design showing that the number of hospitalizations was significantly reduced in patients after HeartLogic activation.[12] However, no data evaluating the HeartLogic feature on top of standard care is currently available. This study demonstrates for the first time that HeartLogic-driven care is associated with a lower number of worsening HF events as compared to standard care by means of telemonitoring cardiac implantable electronic devices.

In addition, there was a trend toward a lower number of hospitalizations due to decompensated HF. These results are in line with the previously mentioned study by our group, although now evaluated in a multicenter, prospective propensity-matched setting. The overall number of hospitalizations in this preselected cohort was low. Intrinsic in the nature of the propensity-matched cohort, patients that passed away during follow-up were excluded from analysis. These patients were likely to have been more severely affected, and that might possibly explain the relatively low number of hospitalizations seen in the current study.

Even though in some cases, hospitalization was inevitable, the number of hospitalization days was significantly lower in patients in the HeartLogic group. Patients with a HeartLogic alert were treated with lifestyle advice reinforcement and a stepwise escalation of the diuretic regimen. This suggests

that these patients were not as severely decompensated as the control patients who were on regular telemonitoring. Even though outpatient treatment regimens could not prevent hospitalization in all cases, HeartLogic-driven action might have facilitated a quicker recompensation. Another explanation is that HeartLogic patients might have been admitted at an earlier stage of (sub-)clinical deterioration. These patients are strictly followed-up and monitored, so deterioration of clinical status is notified at an earlier stage, which empowers timely clinical action.

Clinical Perspectives and Implementation

Several aspects are crucial for successful implementation of HeartLogic-driven care in clinical practice. First, a structured and standardized workflow is needed, and responsibilities should be clearly divided within the team of device technicians, device cardiologists, HF nurses, and HF cardiologists. Moreover, effective and timely communication among the team members is essential.

The algorithm alerts with a median of 34 days before a hospitalization, so alert handling time should be short enough to enable treatment adjustments.[3] Therefore, regular check-ups of the alert status must be performed by dedicated team members. Device technicians are already heavily involved in home monitoring and are logical team members to review the alert status. Several timeframes to review the index were suggested in previous research, ranging from every day to every 2 weeks.[4,11,12,19,21] After a device check-up, the alert should be transferred within 72 hours to the treating physician or HF nurse. Afterwards, a contact to review clinical HF status is needed. Several protocols for alert handling are proposed, and these protocols all suggest reevaluating the clinical status at a set timeframe.[4,11,12,19,21] However, standardized alert management protocols are not yet available. The mentioned PREEMPT-HF and MANAGE-HF trials should direct us toward novel protocols for standardized action. With a low overall alert rate of 0.8−1.7 alerts per patient-year and an even lower unexplained alert rate (0.2−1.5 per patient year), the logistical burden of frequently checking and handling alerts remains largely acceptable. Furthermore, alert-based follow-up was safe, and the algorithm has a high negative predictive value. This allows the shifting of resources to patients who are in the greatest need of care.

Strengths, Limitations and Future Research

The current multicenter propensity-matched study is, to the best of our knowledge, the first study to compare HeartLogic with standard telemonitoring in a real-world population. However, some limitations in the results of this study should be noted. First, this was a retrospective, propensity-matched cohort study; therefore, residual unmeasured confounders may still be present. Second, this is a preselected cohort of relatively stable patients with HF and, in line with the study design, patients who died during follow-up were excluded, which might explain the relatively low number of hospitalizations. Consequently, it remains to be investigated whether HeartLogic is effective in patients with advanced HF. Last, the use of HeartLogic was not blinded for patients or for health care practitioners. The results of a randomized controlled trial are, therefore, eagerly awaited. Nevertheless, our data are in line with earlier, smaller studies and with the results of the phase-I MANAGE-HF trial.

Conclusion

Integrating the HeartLogic algorithm in a well-equipped HF care path on top of standard care is associated with clinical benefits characterized by less worsening HF events and shorter fluid retention-related hospitalizations.

Lay Summary

Early detection of fluid retention is essential to prevent hospitalizations due to decompensated heart failure. The novel multisensory HeartLogic algorithm is able to detect impending fluid retention. However, robust evidence showing that HeartLogic provides clinical benefit on top of standard care is absent. The current study demonstrates that activation of the HeartLogic algorithm on top of standard care is associated with fewer worsening heart failure events and shorter durations of fluid-related hospitalizations.

Disclosures

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.cardfail.2023.04.012.

References

1. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Bohm M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J 2021;42:3599–726.
2. Hindricks G, Taborsky M, Glikson M, Heinrich U, Schumacher B, Katz A, et al. Implant-based multiparameter telemonitoring of patients with heart failure (IN-TIME): a randomised controlled trial. Lancet 2014;384:583–90.
3. Boehmer JP, Hariharan R, Devecchi FG, Smith AL, Molon G, Capucci A, et al. A multisensor algorithm predicts heart failure events in patients with implanted devices: results from the MultiSENSE study. J Am Coll Cardiol 2017;5:216–25.
4. Feijen M, Egorova AD, Beeres S, Treskes RW. Early detection of fluid retention in patients with advanced heart failure: a review of a novel multisensory algorithm, HeartLogic(TM). Sensors (Basel) 2021;4:1361.
5. Calo L, Capucci A, Santini L, Pecora D, Favale S, Petracci B, et al. ICD-measured heart sounds and their correlation with echocardiographic indexes of systolic and diastolic function. J Interv Card Electrophysiol 2020;58:95–101.
6. Capucci A, Santini L, Favale S, Pecora D, Petracci B, Calo L, et al. Preliminary experience with the multisensor HeartLogic algorithm for heart failure monitoring: a retrospective case series report. ESC Heart Fail 2019;6:308–18.
7. de Juan Baguda J, Gavira Gomez JJ, Pachon Iglesias M, Cozar Leon R, Escolar Perez V, Gonzalez Fernandez O, et al. Remote heart failure management using the HeartLogic algorithm: RE-HEART registry. Rev Esp Cardiol (Engl ed.) 2022;75:709–16.
8. Gardner RS, Singh JP, Stancak B, Nair DG, Cao M, Schulze C, et al. HeartLogic multisensor algorithm identifies patients during periods of significantly increased risk of heart failure events results from the MultiSENSE study. Circ Heart Fail 2018;8:e000029.
9. Gardner RS, Thakur P, Hammill EF, Nair DG, Eldadah Z, Stancak B, et al. Multiparameter diagnostic sensor measurements during clinically stable periods and worsening heart failure in ambulatory patients. ESC Heart Fail 2021;8:1571–81.
10. Hernandez AF, Albert NM, Allen LA, Ahmed R, Averina V, Boehmer JP, et al. Multiple cArdiac seNsors for mAnaGEment of Heart Failure (MANAGE-HF): phase I evaluation of the integration and safety of the HeartLogic multisensor algorithm in patients with heart failure. J Card Fail 2022;28:1245–54.
11. Feijen M, Egorova AD, Treskes RW, Mertens BJA, Jukema JW, Schalij MJ, et al. Performance of a HeartLogic(TM)-based care path in the management of a real-world chronic heart failure population. Front Cardiovasc Med 2022;9:883873.
12. Treskes RW, Beles M, Caputo ML, Cordon A, Biundo E, Maes E, et al. Clinical and economic impact of HeartLogic(TM) compared with standard care in heart failure patients. ESC Heart Fail 2021;8:1541–51.
13. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, et al. 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;37:2129–200.
14. Hicks KA, Mahaffey KW, Mehran R, Nissen SE, Wiviott SD, Dunn B, et al. 2017 cardiovascular and stroke endpoint definitions for clinical trials. Circulation 2018;137:961–72.
15. Lunceford JK, Davidian M. Stratification and weighting via the propensity score in estimation of causal treatment effects: a comparative study. Stat Med 2004;23:2937–60.
16. Abraham WT, Perl L. Implantable hemodynamic monitoring for heart failure patients. J Am Coll Cardiol 2017;70:389–98.
17. Adamson PB. Pathophysiology of the transition from chronic compensated and acute decompensated heart failure: new insights from continuous monitoring devices. Curr Heart Fail Rep 2009;6:287–92.
18. Santini L, D'Onofrio A, Dello Russo A, Calo L, Pecora D, Favale S, et al. Prospective evaluation of the multisensor HeartLogic algorithm for heart failure monitoring. Clin Cardiol 2020;43:691–7.
19. Calo L, Bianchi V, Ferraioli D, Santini L, Dello Russo A, Carriere C, et al. Multiparametric implantable cardioverter-defibrillator algorithm for heart failure risk stratification and management: an analysis in clinical practice. Circ Heart Fail 2021;14:e008134.
20. Guerra F, D'Onofrio A, De Ruvo E, Manzo M, Santini L, Giubilato G, et al. Decongestive treatment adjustments in heart failure patients remotely monitored with a multiparametric implantable defibrillators algorithm. Clin Cardiol 2022;45:670–8.
21. Heggermont WA, Van Bockstal K. Heartlogic(TM): ready for prime time? Expert Rev Med Devices 2022;19:107–11.