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ORIGINAL ARTICLES

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Implantable defibrillator-detected heart failure status predicts ventricular tachyarrhythmias

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Abstract

Introduction: The prediction of ventricular tachyarrhythmias among patients with implantable cardioverter defibrillators is difficult with available clinical tools. We sought to assess whether in patients with heart failure (HF) and reduced ejection

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fraction with defibrillators, physiological sensor-based HF status, as summarized by the HeartLogic index, could predict appropriate device therapies.

Methods: Five hundred and sixty-eight consecutive HF patients with defibrillators ($n = 158$, 28%) or cardiac resynchronization therapy-defibrillators ($n = 410$, 72%) were included in this prospective observational multicenter analysis. The association of both HeartLogic index and its physiological components with defibrillator shocks and overall appropriate therapies was assessed in regression and time-dependent Cox models.

Results: Over a follow-up of 25 (15–35) months, 122 (21%) patients received an appropriate device therapy (shock, $n = 74$, 13%), while the HeartLogic index crossed the threshold value (alert, HeartLogic ≥ 16) 1200 times (0.71 alerts/patient-year) in 370 (65%) subjects. The occurrence of ≥1 HeartLogic alert was significantly associated with both appropriate shocks (Hazard ratios [HR]: 2.44, 95% confidence interval [CI]: 1.49–3.97, $p = .003$), and any appropriate defibrillator therapies. In multivariable time-dependent Cox models, weekly IN-alert state was the strongest predictor of appropriate defibrillator shocks (HR: 2.94, 95% CI: 1.73–5.01, $p < .001$) and overall therapies. Compared with stable patients, patients with appropriate shocks had significantly higher values of HeartLogic index, third heart sound amplitude, and resting heart rate 30–60 days before device therapy.

Conclusion: The HeartLogic index is an independent dynamic predictor of appropriate defibrillator therapies. The combined index and its individual physiological components change before the arrhythmic event occurs.

KEYWORDS

cardiac resynchronization therapy, heart failure, ICD shock, implantable cardioverter-defibrillation, risk stratification, ventricular arrhythmias

1 | INTRODUCTION

Ventricular arrhythmias are very common and represent a major cause of mortality in patients with heart failure (HF).[1,2] Implantable cardioverter-defibrillator (ICD) therapy has proven to be associated with a reduction in all-cause mortality, and is currently recommended for the management of chronic HF.[1] However, the occurrence of ventricular tachycardia or fibrillation is associated with increased mortality and HF hospitalizations in ICD patients, despite effective termination of the arrhythmias.[3] Indeed, not only are ICD shocks a marker of deterioration, they may also independently contribute to adverse outcomes, and a direct causal relationship between shocks and HF progression and cardiac mortality has been hypothesized.[4,5]

Some modern ICDs are equipped with automated algorithms that provide detailed information on the HF condition daily. Such tools shed light on the reciprocal causal mechanisms of HF and ventricular arrhythmias and could help to identify predisposing factors. In the Multisensor Chronic Evaluation in Ambulatory Heart Failure Patients (MultiSENSE) study,[6] a novel algorithm for HF monitoring was implemented: the HeartLogic (Boston Scientific) index, which combines physiological data from multiple ICD-based sensors.[6] The index proved to be a sensitive and timely predictor of impending HF decompensation. In the present study, we sought to evaluate the association between HeartLogic index values and the incidence of appropriate ICD therapies in patients with HF and reduced ejection fraction, and to assess the performance of the index in detecting follow-up periods of significantly increased arrhythmic risk. Furthermore, we aimed to assess the relationship between physiological parameters and ventricular arrhythmias.

2 | METHODS

2.1 | Patient selection

The study was a prospective, nonrandomized, multicenter evaluation of patients who had received an ICD or cardiac resynchronization therapy ICD (CRT-D) implementing the HeartLogic™ diagnostic algorithm. Consecutive HF patients with reduced left ventricular ejection fraction (≤35% at the time of

implantation) who had received a device in accordance with standard indications,[1] and were enrolled in the LATITUDE (Boston Scientific) remote monitoring platform were included at 27 centers (full list of participating centers in Supporting Information: Data). All patients were followed up in accordance with the standard practice of the participating centers. Data on the clinical events that occurred during follow-up were collected at the study centers within the framework of a prospective registry (ClinicalTrials.gov identifier: NCT02275637). The study complied with the Declaration of Helsinki, all patients provided written informed consent for data storage and analysis, and institutional Review Boards approved the study protocol. The data underlying this article will be shared on reasonable request to the corresponding author.

2.2 | Device characteristics

Commercially available ICD/CRT-Ds equipped with the HeartLogic™ diagnostic feature and standard transvenous leads were used in this study. The details of the HeartLogic algorithm have been reported previously.[6] Briefly, the algorithm combines data from multiple sensors: accelerometer-based first and third heart sounds, intrathoracic impedance, respiration rate, the ratio of respiration rate to tidal volume, night heart rate, and patient activity. Each day, the device calculates the degree of worsening in sensors from their moving baseline and computes a composite index. An alert is issued when the index crosses a programmable threshold (nominal value, ≥16), and when the index enters an alert state, the "exit-alert" threshold is automatically dropped to a recovery value (nominal value, 6). An example of daily trend data is provided in Figure 1.

2.3 | Study objectives

The primary objectives of the present study were to test the hypothesis of a possible association between the HeartLogic index and the incidence of appropriate therapies delivered by the ICD, and to evaluate the performance of the HeartLogic index in detecting time periods of significantly increased risk of ventricular arrhythmias. The episodes considered in the analysis were spontaneous ventricular tachyarrhythmias detected and treated by the implanted device and subsequently validated by the local investigators. The primary endpoint was the first appropriate ICD shock therapy, while the secondary endpoint was the first appropriate ICD therapy (a composite of appropriate antitachycardia pacing and shock) for ventricular tachycardia or ventricular fibrillation. As secondary objective, we exploratively assessed the relationship between physiological parameters and ventricular arrhythmias, by analyzing the HeartLogic index and individual sensor changes surrounding the ICD therapy.

2.4 | Important definitions

In the present study, IN-alert and OUT-of-alert periods were identified and defined as follows: IN-alert periods started when the HeartLogic index crossed the threshold (nominal value, 16) and ended at the time of the first ICD therapy or were censored when the index decreased to below the recovery threshold (nominal value, 6) or at the end of follow-up; OUT-of-alert periods started on the day of HeartLogic algorithm activation (at the end of the initialization period) or at the end of a previous IN-alert period and ended at the time of the first ICD therapy or were censored when the index rose above the threshold (or at the end of follow-up).

2.5 | Statistical analysis

Quantitative variables are reported as means and standard deviations if normally distributed, or medians with 25th–75th percentiles in the case of skewed distribution. Normality of distribution was tested by means of the nonparametric Kolmogorov–Smirnov test. Categorical data are expressed as percentages.

To test the primary hypothesis, the time to the first episode was analyzed by means of the Kaplan–Meier method; Cox proportional hazards models were used to determine the association between patients' baseline characteristics and the occurrence of the endpoints during the follow-up period, and to estimate the hazard ratios (HRs) and the 95% confidence intervals (CIs). The weekly IN- or OUT-of-alert state was also treated as a time-varying co-variate by means of time-dependent Cox models. All variables displaying statistical significance ($p < .05$) in univariable models were entered into the multivariable regression analysis. To evaluate the performance of the index in detecting follow-up periods of significantly increased arrhythmic risk, we compared the IN- and OUT-of-alert periods, in terms of time to the first ICD therapy, by means of the Andersen–Gill model, an extension of the Cox proportional hazards model that considers multiple evaluations in patients. Thus, a single patient contributes more than one piece of information depending on the number of individually observed events. The hazard is estimated by using the event times of every observed event, and recurrent events are assumed to be independent (i.e., the model assumes that the instantaneous risk to experience an event remains the same irrespective of the fact whether previous events occurred or not). The model was adjusted for those baseline variables that proved to be associated with the occurrence of therapies on univariable analysis.

To test the secondary hypothesis, the time course of HeartLogic index and sensor changes surrounding the ICD therapy was described by recording average values over the days before and after the first occurrence of therapy. For control purposes, averaged sensor data were calculated in patients who did not undergo ICD therapies during clinical follow-up. These trends were aligned on a random day during the observation period.[7] A 30-day baseline (−60 to −30 days) was

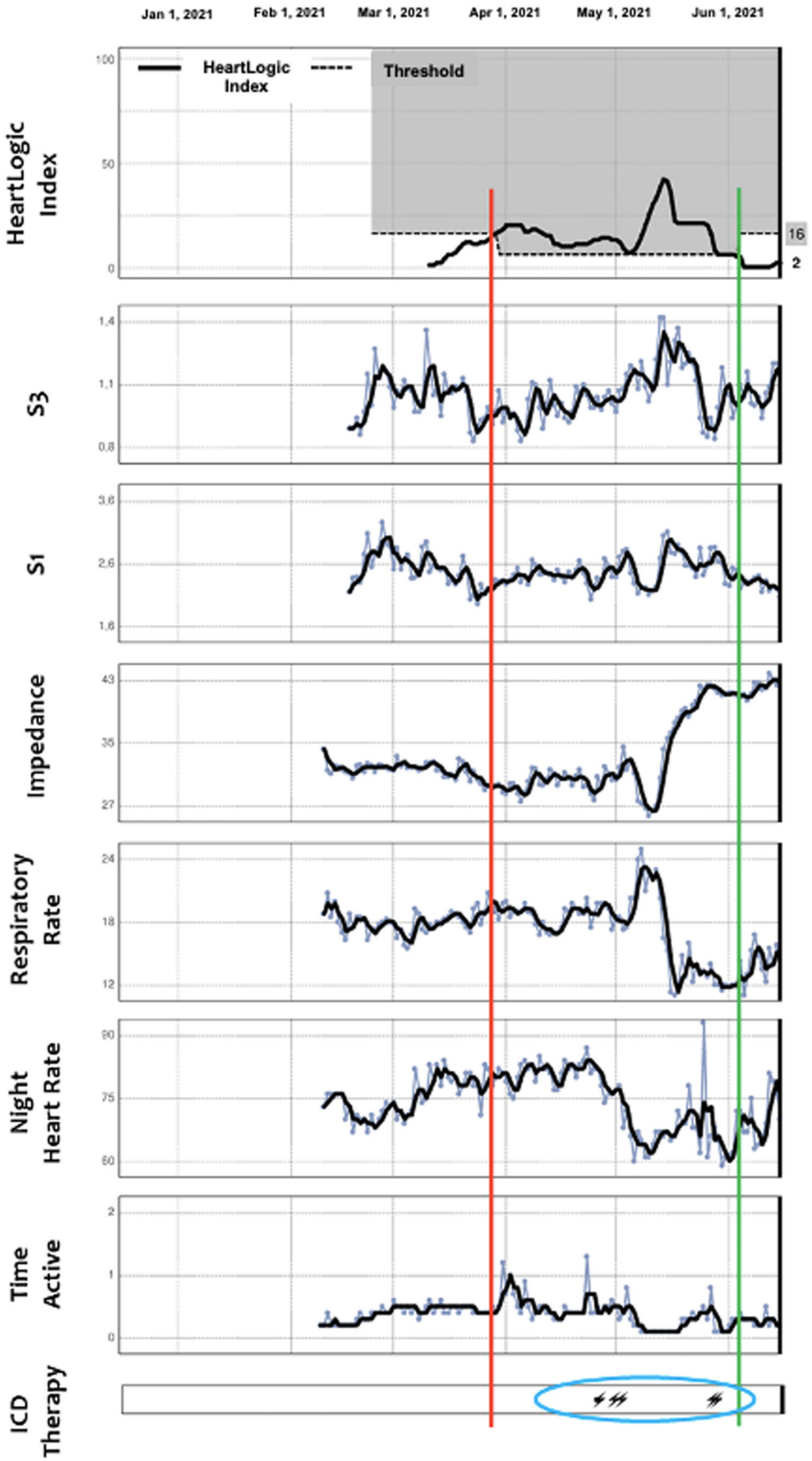

FIGURE 1 (See caption on next page)

compared with the state on the day of the ICD therapy.[8] Sensor data were compared between different temporal periods by means of a paired *t* test. A *p* value <.05 was considered significant for all tests. All statistical analyses were performed by means of R: a language and environment for statistical computing (R Foundation for Statistical Computing).

3 | RESULTS

3.1 | Study population

From December 2017 to June 2021, HeartLogic was activated in 568 patients who had received an ICD or CRT-D. Table 1 shows the baseline clinical variables of all patients in the present analysis. All patients received a device programmed to two detection zones (details of device programming are also in Table 1).

3.2 | Follow-up

The median follow-up was 25 months (25th–75th percentile: 15–35 months), that is, a total of 1159 patient-years. During the observation period, 36 patients died. One or more appropriate ICD shocks were documented in 74 (13%) patients. An appropriate ICD therapy (antitachycardia pacing or shock) for ventricular tachycardia or ventricular fibrillation was delivered in 122 (21%) patients (Figure 1). The HeartLogic index crossed the threshold value 1200 times (0.71 alerts/patient-year) in 370 patients.

3.3 | Association between HeartLogic index and endpoint occurrence

Supporting Information: Figure S1 shows the Kaplan–Meier analysis of time from implantation to the first episode of appropriate ICD shock or any appropriate ICD therapy for ventricular tachycardia or ventricular fibrillation, while Supporting Information: Table S1 shows characteristics of patients at baseline according to the occurrence of ICD shocks during follow-up. The occurrence of at least one HeartLogic alert was significantly associated with both appropriate ICD shocks (HR: 2.44, 95% CI: 1.49–3.97, $p = .003$), and all

TABLE 1 Baseline clinical parameters of the study population and device programming.

Parameter	Total, *n* = 568
Male gender, *n* (%)	453 (80)
Age, years	69 ± 10
Ischemic etiology, *n* (%)	285 (50)
NYHA class	
Class I, *n* (%)	36 (6)
Class II, *n* (%)	351 (62)
Class III, *n* (%)	171 (30)
Class IV, *n* (%)	10 (2)
LV ejection fraction, %	32 ± 9
AF history, *n* (%)	196 (35)
Diabetes, *n* (%)	167 (29)
COPD, *n* (%)	89 (16)
Chronic kidney disease, *n* (%)	153 (27)
Hypertension, *n* (%)	334 (59)
β-Blocker use, *n* (%)	520 (92)
ACE-inhibitor, ARB or ARNI use, *n* (%)	536 (94)
Diuretic use, *n* (%)	506 (89)
Antiarrhythmic use, *n* (%)	116 (20)
Ivabradine use, *n* (%)	37 (7)
CRT device, *n* (%)	410 (72)
Primary prevention, *n* (%)	500 (88)
VT/VF detection zone 1	
Cut-off ≥ 170 bpm	494 (87%)
Delay before therapy ≥ 5 s	528 (93%)
VT/VF detection zone 2	
Cut-off ≥ 200 bpm	530 (93%)
Delay before therapy ≤ 2.5 s	483 (85%)

Abbreviations: ACE, angiotensin-converting enzyme; AF, atrial fibrillation; ARB, angiotensin II receptor blockers; ARNI, angiotensin receptor-neprilysin inhibitor; COPD, chronic obstructive pulmonary disease; CRT, cardiac resynchronization therapy; LV, left ventricular; NYHA, New York Heart Association; VF, ventricular fibrillation; VT, ventricular tachycardia.

FIGURE 1 Example of daily trend data. The HeartLogic algorithm combines data from multiple sensors. The sensor trends are combined into a composite index, which is updated daily. An alert is issued when the index crosses a programmable threshold (nominal value, 16). When the index enters an alert state (gray area), the threshold is automatically set to a recovery value, which is less than the programmed threshold, to ensure full normalization of values before exiting the alert state. In the example, HeartLogic index crossed the 16 threshold on March 29th (red line). Starting from April 25th, ventricular tachycardia events were recorded, and antitachycardia pacing therapies and shocks were delivered (blue circle). The arrhythmic episodes recurred during the IN-alert period, which ended on June 4th (green line). ICD, implantable cardioverter-defibrillator.

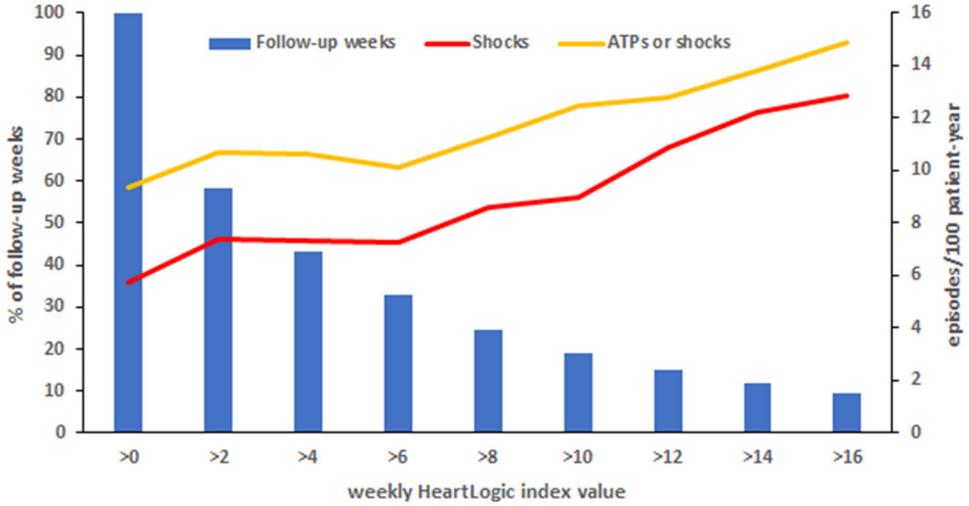

FIGURE 2 Rates of shocks and overall appropriate therapies according to weekly HeartLogic index values. The blue bars represent the cumulative distribution of weekly HeartLogic index values, while the red and orange curves represent the rates of shocks and shocks or antitachycardia pacing according to weekly HeartLogic index value, respectively.

appropriate ICD therapies (ATPs plus shocks, HR: 1.95, 95% CI: 1.37–2.85, $p = .003$). Overall, the time in the IN-alert state was 151 years (13% of the total observation period). A HeartLogic index ≥ 16 was more frequently measured during the weeks in which the device delivered appropriate shocks (22%, $p = .002$) or any appropriate therapies for ventricular tachycardia or ventricular fibrillation (15%, $p = .048$) than in the remaining weeks (10%). Conversely, the rate of both shocks and shocks or ATPs increased with greater weekly HeartLogic Index values, as depicted in Figure 2.

The results of the regression analysis of variables associated with appropriate ICD shock occurrence are shown in Table 2. In a time-dependent Cox model, the weekly IN-alert state was independently associated with appropriate ICD shocks (HR: 2.94, 95% CI: 1.73–5.01, $p < .001$), after correction for age, secondary prevention, and use of CRT. The weekly IN-alert state was also associated with appropriate antitachycardia pacing or shocks (HR: 1.72, 95% CI: 1.08–2.73, $p = .022$). Figure 3 shows the Kaplan–Meier plot of the time to the first appropriate ICD shock and the time to the first appropriate antitachycardia pacing or shock, in the IN- and OUT-of-alert states. Comparison of the episode rates in the IN-alert state with those in the OUT-of-alert state yielded HRs of 2.18 (95% CI: 1.06–4.48, $p = .001$) for appropriate ICD shock, and 1.81 (95% CI: 1.03–3.16, $p = .003$) for appropriate antitachycardia pacing or shock, in models adjusted for those baseline clinical variables that had proved to be associated with the occurrence of episodes on univariable analysis (Table 2).

3.4 | Sensor data findings

The trends in the average HeartLogic index and sensor values surrounding the first appropriate ICD shock episode are reported in Figure 4, while main study findings are resumed in the Graphical Abstract. Average sensor data from clinically stable periods (from patients who did not have ICD therapies during follow-up) are reported for comparison. Compared with the baseline period (average calculated 30 days before the shock, i.e., −60 to −30 days), the HeartLogic index value was significantly higher on the day of the ICD shock, as were the S3 amplitude and the night heart rate. Intrathoracic impedance and patient activity were significantly lower. In the control group of clinically stable periods, no changes in the combined index or sensor values were noted. The comparison of baseline periods between patients who underwent appropriate ICD shocks and those who did not showed significantly higher values of the combined index, S3 amplitude, and respiratory rate in the trends preceding the shock than in the control group.

4 | DISCUSSION

In the present study, we found an association between HeartLogic index values continuously measured by the ICD and the occurrence of appropriate shocks and any appropriate ICD therapies delivered during a follow-up of more than 2 years in patients with HF and reduced ejection fraction. Moreover, the HeartLogic index and its physiological parameters proved to be sensitive markers of increased risk of ventricular arrhythmias, showing significant changes several weeks before appropriate device therapy.

The adverse myocardial changes that occur as HF progresses can lead to the development of an electrophysiologic substrate that fosters ventricular arrhythmias.[9] As a consequence, patients with severe HF are at increased risk of arrhythmias, which in turn promote further maladaptive remodeling and lead to clinical deterioration.[10] As of today, several tools have been proposed to identify periods of increased risk of ventricular arrhythmias among patients with HF, including ECG, Holter monitoring,

TABLE 2 Univariable and multivariable analysis of baseline variables associated with the occurrence of shock.

	Univariable analysis			Multivariable analysis[a]		
	HR	95% CI	*p*	HR	95% CI	*p*
Age	0.98	0.97–0.99	.026	0.98	0.96–0.99	.041
Male gender	0.99	0.56–1.77	.977	–	–	–
Ischemic heart disease	0.88	0.56–1.39	.580	–	–	–
NYHA class	1.23	0.84–1.79	.284	–	–	–
Ejection fraction	0.99	0.97–1.02	.754	–	–	–
History of atrial fibrillation	1.18	0.74–1.88	.481	–	–	–
Secondary prevention	2.17	1.25–3.76	.006	2.06	1.23–3.44	.006
CRT device	0.58	0.36–0.93	.023	0.61	0.38–0.98	.042
Diabetes	0.80	0.48–1.35	.414	–	–	–
Chronic kidney disease	1.03	0.62–1.71	.915	–	–	–
Pulmonary disease	1.60	0.92–2.78	.095	–	–	–
Hypertension	0.67	0.42–1.05	.083	–	–	–
β-Blocker use	0.66	0.33–1.32	.242	–	–	–
Diuretic use	0.69	0.35–1.33	.269	–	–	–
Antiarrhythmic use	1.50	0.90–2.47	.119	–	–	–
ACE-inhibitor, ARB, or ARNI use	0.87	0.35–2.16	.772	–	–	–
Weekly IN-alert state[a]	2.82	1.68–4.72	<.001	2.94	1.73–5.01	<.001
≥1 HeartLogic alert	2.44	1.32–4.51	.005			
Percentage time in alert	5.80	1.59–21.21	.008			
Mean HeartLogic index	1.09	1.05–1.13	<.001			

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blockers; ARNI, angiotensin receptor-neprilysin inhibitor; CI, confidence interval; CRT, cardiac resynchronization therapy; HR, hazard ratio; NYHA, New York Heart Association.

[a]Time-dependent Cox model.

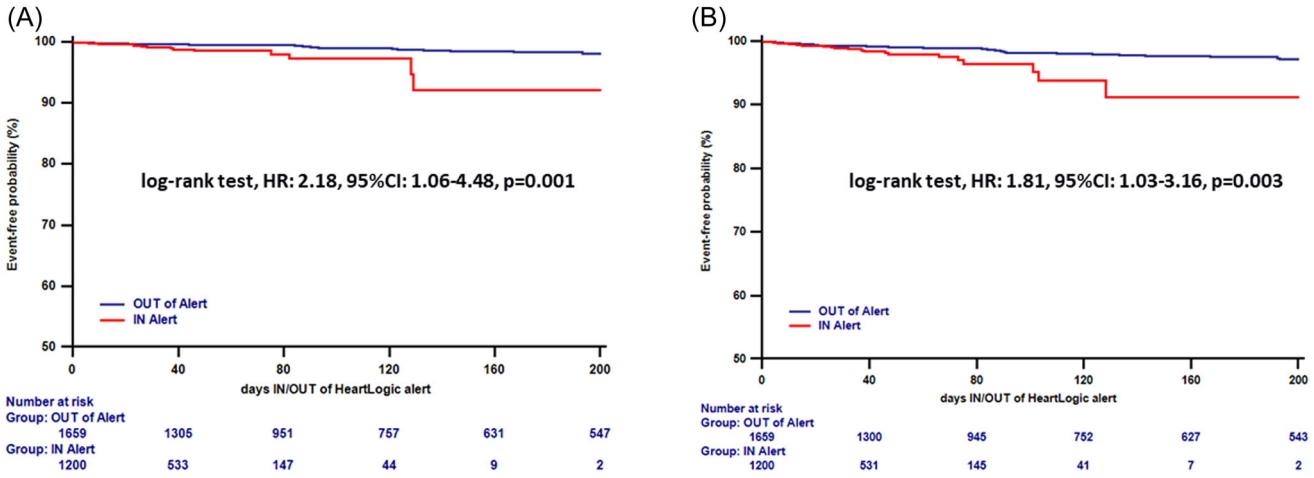

FIGURE 3 Time course of appropriate implantable cardioverter-defibrillator (ICD) shocks and overall appropriate therapies in the IN- and OUT-of-alert states. (A) Kaplan–Meier plot of the time to the first appropriate ICD shock in the IN- and OUT-of-alert states. (B) Kaplan–Meier plot of the time to the first appropriate antitachycardia pacing or shock in the IN- and OUT-of-alert states. CI, confidence interval; HR, hazard ratio.

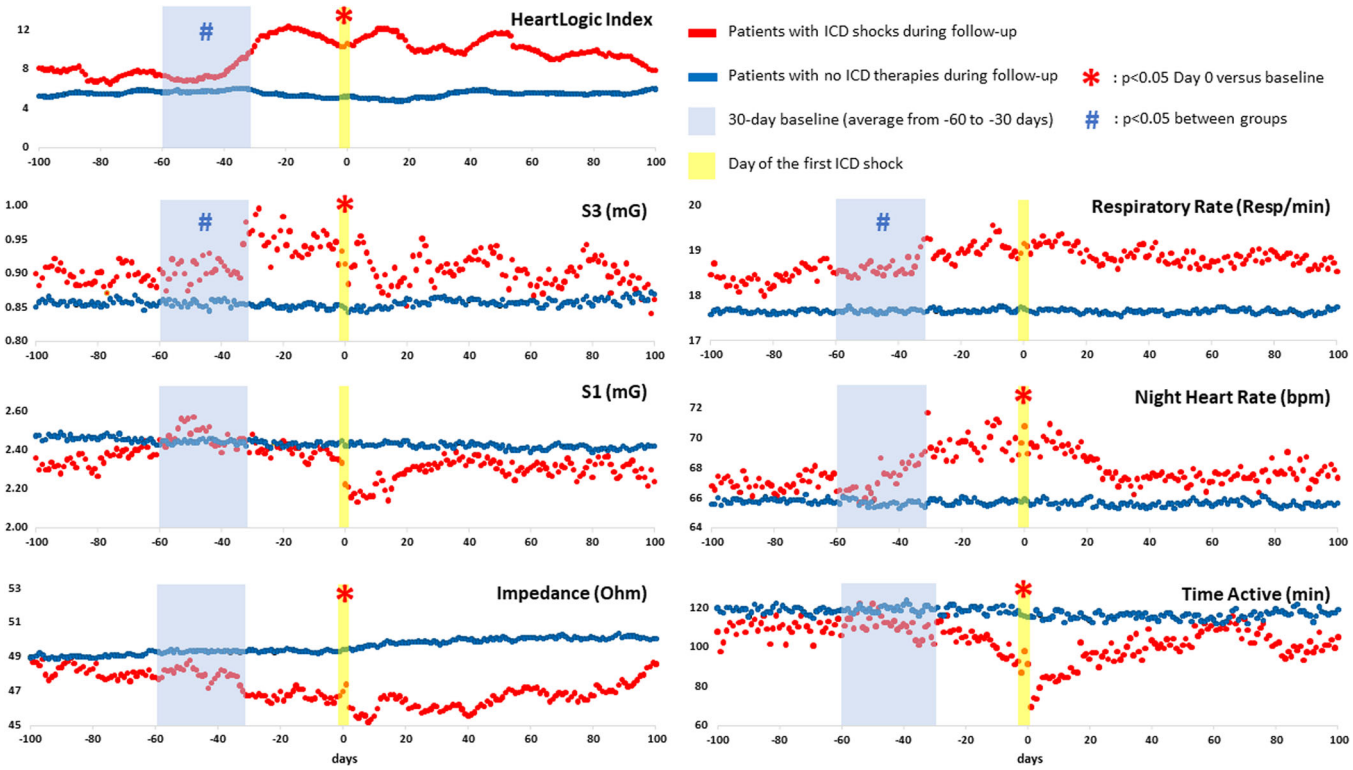

FIGURE 4 Average temporal trends of HeartLogic index and individual sensor values surrounding the first appropriate implantable cardioverter-defibrillator (ICD) shock. In the figure, the overall HeartLogic index, accelerometer-based third (S3) and first (S1) heart sounds, intrathoracic impedance, respiration rate, night heart rate, and patient activity are displayed. Red trends: average values surrounding the first appropriate ICD shock (Day 0 is the day of the first ICD shock). Blue trends: average sensor data from clinically stable periods from patients who did not have ICD therapies during follow-up (aligned on a random day during the observation period). *$p < .05$ for the comparison between Day 0 and 30-day baseline (average from −60 to −30 days) among patients who experienced ICD shocks during follow-up; #$p < .05$ for the comparison between baseline values of the two groups (patient with vs. without ICD shocks during follow-up). Note that the HeartLogic index, S3 heart sound amplitude, night heart rate, intrathoracic impedance, and patient activity are significantly different in patients receiving shocks on the day of the ICD shock, compared with the 30-day baseline; furthermore, the HeartLogic index, S3 amplitude, and respiratory rate are significantly different among patients receiving ICD shock compared with stable patients 30–60 days before the shock.

electrophysiology study, echocardiography,[11] and, more recently, cardiac magnetic resonance imaging,[12] but none of these allows a continuous day-to-day risk assessment.[1,12] Furthermore, even left ventricular ejection fraction, which currently represents the main parameter to select patients for ICD implantation,[1] suffers from significant intra- and interobserver variability, and is also sensitive to the imaging method used for its measurement.[13] It is therefore reasonable to think that dynamic tools for assessing the progression of HF may improve risk stratification.

Modern algorithms for HF monitoring are based on the combination of multiple physiological variables, and allow accurate, continuous, and automatic HF assessment.[6] They have been proposed as predictors of impending HF decompensation that can trigger timely interventions,[14] and can identify time intervals when patients are at significantly increased risk of worsening HF.[14] Such tools may also enable the association between HF status and the occurrence of ventricular arrhythmias to be analyzed.

In our work, patients who experienced ICD-diagnosed HF events were those at the greatest risk of receiving ICD therapies. Specifically, after correction for baseline confounders, we observed a three fold higher risk of appropriate ICD shocks during IN-alert state weeks, a condition that accounted for approximately 13% of the follow-up time. We also found a similar association between IN-alert state and any appropriate ICD therapy (antitachycardia pacing or shock).

The finding of a shorter time to ICD therapy after a HeartLogic alert suggests the possibility to implement targeted therapeutic strategies. These therapies might be directed to preventing further worsening of HF, such as diuretics for congestion relief, which might in turn reduce sympathetic drive, or other standard HF agents.[9,15] Indeed, some guideline-recommended HF therapies (β-blockers, renin/angiotensin/aldosterone system inhibitors) as well amiodarone are known to reduce the need for ICD therapies.[1,16] Sacubitril–Valsartan, an angiotensin receptor-neprilysin inhibitor reduces both sudden and HF worsening-related death,[17,18] and, in an observational study of ICD patients, reduced appropriate ICD shocks in comparison with angiotensin inhibition alone.[19] In addition, the selective sodium-dependent glucose transporter 2 inhibitor empagliflozin and the soluble guanylate cyclase stimulator vericiguat have been shown to reduce HF events[20,21]; they might therefore be

expected to prevent ventricular arrhythmias via reverse remodeling. Under-prescription of guideline-recommended drugs, as well as low adherence and persistence by HF patients, are unfortunately common and frequently represent a triggering cause of HF decompensation.[1] Remote monitoring could provide reliable and real-time physiological data assisting clinicians in the optimization of medical therapy under these circumstances. Device reprogramming to optimize CRT is another potentially effective post-alert action. Indeed, the percentage of biventricular pacing has been associated not only with the outcome,[22] but also with the extent of reverse remodeling,[23] which in turn is associated with the burden of ventricular arrhythmic events in patients treated with CRT.[24] Accordingly, it has recently been shown that the odds of optimal biventricular pacing are lower in the HeartLogic IN-alert state than in the OUT-of-alert state.[25]

Our analysis of pre-event trends allowed us to investigate the mechanisms that triggered the arrhythmias, and which ideally could facilitate the identification of targeted interventions. We noted changes in both the combined index and individual sensors about one month before the onset of the arrhythmic event. Specifically, we observed an increase in the third heart sound amplitude and a decrease in thoracic impedance suggestive of elevated left ventricular filling pressure,[26] and more severe congestion,[27] possibly resulting in greater myocardial stretch. In turn, myocardial stretch may induce membrane depolarization and facilitate ventricular ectopy, which may act as a trigger of ventricular tachycardia or fibrillation.[28] Consistent with a pre-eminent role of myocardial stretch, Rodio and colleagues recently showed that significant drops in ICD-measured thoracic impedance (a marker of lung congestion and impending HF hospitalization) are associated with malignant ventricular arrhythmias in ICD patients,[29] possibly suggesting that our findings with HeartLogic may be extrapolated to other device-based congestion metrics. Furthermore, a higher resting heart rate is reported to be indicative of a potentially proarrhythmic elevated sympathetic tone.[30] Finally, in patients with ICD shocks, we recorded elevated values of third heart sound amplitude and respiratory rate even months before the events, these variables probably being sensitive to the worse baseline functional status and systolic function.[31]

As a corollary, our results allow us to speculate on the well-known pathophysiologic link between ICD shocks and increased mortality in HF patients.[4,5] In fact, the finding that ICD shocks are more likely to be observed in periods of worsened HF status (i.e., with higher HeartLogic index) and are preceded by changes in physiological parameters suggests that ICD shocks are more markers of a worse clinical status, than direct triggers of a deadly patient trajectory, thereby being indirectly associated with higher risk of mortality.

4.1 | Limitations

Some limitations of our study should be acknowledged. First, its observational design may have introduced an inherent bias. However, the large number of patients enrolled, and the long follow-up time clearly strengthen our observations. Second, the lack of a central review and adjudication of endpoints may have introduced a bias. Third, rate-detection settings and ICD programming were left to the discretion of the implanting physicians, according to their knowledge of the individual patient's arrhythmia history, and different individual rate settings may have affected the frequency of ICD therapy, which could have influenced our analysis. However, both detection cut-offs and delays to therapy were generally in line with modern device programming, as reported in Table 1. Fourth, for the sake of immediate clinical applicability of our findings, we only tested the index value of 16, which is the nominal threshold of the algorithm. Although this value was shown to maximize the accuracy of HF prediction in the development phase of the algorithm,[6] we may not exclude the possibility that a different threshold value may allow a better performance in the prediction of ventricular arrhythmias. Fifth, although the algorithm showed high sensitivity, the overall positive predictive value for the prediction of appropriate ICD therapies was suboptimal, similar to what was previously reported regarding its predictive role for HF events.[6] However, we demonstrated that the system facilitates the identification of subjects at high clinical and arrhythmic risk in their highest risk periods, potentially allowing a more rational use of available resources, which may translate into significant economic savings, as recently demonstrated in a study in which activation of the algorithm led to reduced rate of HF hospitalizations.[32]

5 | CONCLUSIONS

In the present study, patients who experienced ICD-diagnosed periods of worsening HF status were more likely to receive appropriate ICD therapies. During HeartLogic IN-alert state weeks, a condition that accounted for approximately 13% of the follow-up time, we observed a three fold higher risk of ICD shocks. Changes in both the HeartLogic index and individual physiological parameters (third heart sound amplitude, thoracic impedance, night heart rate) preceded device therapies by approximately one month.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author, Paolo Compagnucci.

ETHICS STATEMENT

The study complied with the Declaration of Helsinki, all patients provided written informed consent for data storage and analysis, and institutional Review Boards approved the study protocol.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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