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CLINICAL RESEARCH

Combination of an implantable defibrillator multi-sensor heart failure index and an apnea index for the prediction of atrial high-rate events

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Aims

Patients with atrial fibrillation frequently experience sleep disorder breathing, and both conditions are highly prevalent in presence of heart failure (HF). We explored the association between the combination of an HF and a sleep apnoea (SA) index and the incidence of atrial high-rate events (AHRE) in patients with implantable defibrillators (ICDs).

Methods and results

Data were prospectively collected from 411 consecutive HF patients with ICD. The IN-alert HF state was measured by the multi-sensor HeartLogic Index (>16), and the ICD-measured Respiratory Disturbance Index (RDI) was computed to identify severe SA. The endpoints were as follows: daily AHRE burden of ≥5 min, ≥6 h, and ≥23 h. During a median follow-up of 26 months, the time IN-alert HF state was 13% of the total observation period. The RDI value was ≥30 episodes/h (severe SA) during 58% of the observation period. An AHRE burden of ≥5 min/day was documented in 139 (34%) patients, ≥6 h/day in 89 (22%) patients, and ≥23 h/day in 68 (17%) patients. The IN-alert HF state was independently associated with AHRE regardless of the daily burden threshold: hazard ratios from 2.17 for ≥5 min/day to 3.43 for ≥23 h/day ($P < 0.01$). An RDI ≥ 30 episodes/h was associated only with AHRE burden ≥5 min/day [hazard ratio 1.55 (95% confidence interval: 1.11–2.16), $P = 0.001$]. The combination of IN-alert HF state and RDI ≥ 30 episodes/h accounted for only 6% of the follow-up period and was associated with high rates of AHRE occurrence (from 28 events/100 patient-years for AHRE burden ≥5 min/day to 22 events/100 patient-years for AHRE burden ≥23 h/day).

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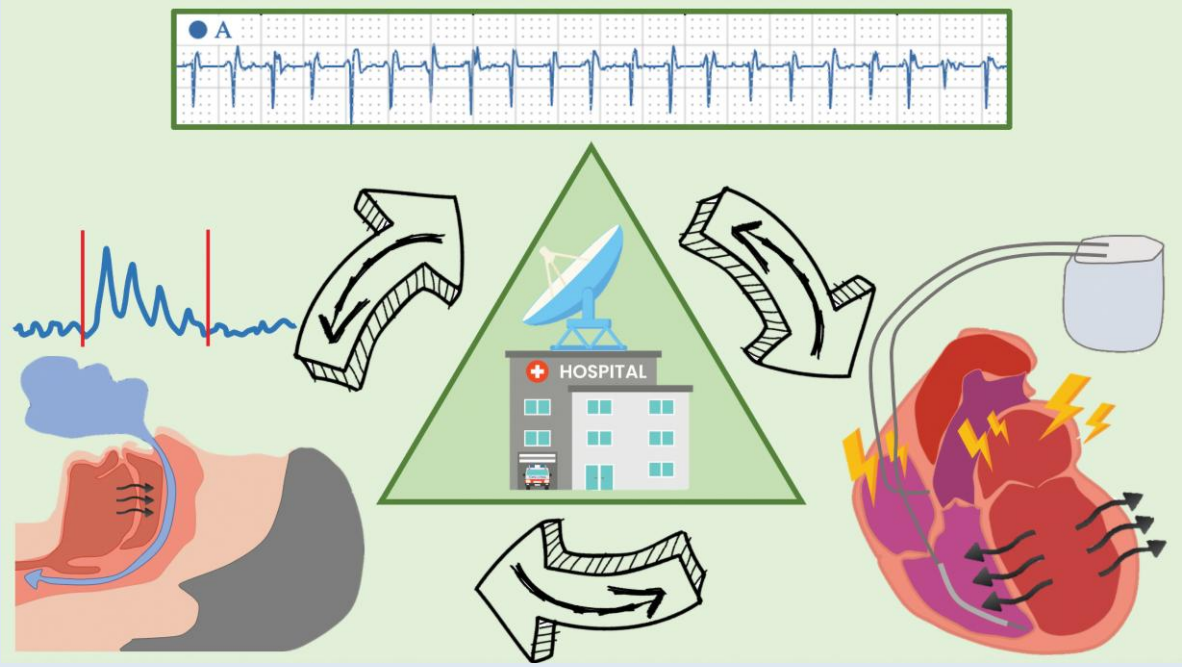
Conclusions In HF patients, the occurrence of AHRE is independently associated with the ICD-measured IN-alert HF state and RDI ≥ 30 episodes/h. The coexistence of these two conditions occurs rarely but is associated with a very high rate of AHRE occurrence.

Clinical trial registration URL: http://clinicaltrials.gov/Identifier: NCT02275637.

Graphical Abstract



Keywords Sleep apnoea • Heart failure • Implantable defibrillator • Atrial fibrillation • Risk stratification

What's new?

- Implantable cardioverter defibrillator/cardiac resynchronization therapy with defibrillator detected IN-alert heart failure state is independently associated with the occurrence of atrial high-rate events, regardless of their duration.
- High Respiratory Disturbance Index is mainly associated with shorter atrial high-rate events.
- When IN-alert HF state and High Respiratory Disturbance Index occur at the same time, the risk of AHRE is higher.

Introduction

Atrial fibrillation (AF) and sleep-disordered breathing (SDB), which include obstructive sleep apnoea (SA) and central SA (CSA), are two highly prevalent clinical conditions[1] with a common milieu and shared risk factors. Obstructive SA (OSA) is characterized by episodes of partial or total obstruction of the upper airway during sleep and is strongly associated with obesity.[1] Central SA is rarer than OSA and is characterized by the absence of respiratory movements, and its aetiology is not completely understood. Despite different mechanisms, OSA and CSA can coexist in the same patient.[2] The relation between AF and SDB is complex and only partially explained. Obstructive SA and CSA increase blood pressure, blood carbon dioxide levels, venous return, sympathetic activity of the autonomic ganglia on the epicardial surface of the heart and cause an inflammatory systemic response.[3] Sleep-disordered breathing leads to acute and chronic structural (left atrium dilatation, increase in atrial fibrosis, and atrial connexin down-regulation) and electrical remodelling (reduced atrial refractory period) of the atria with higher risk of AF vulnerability and recurrence.[4] Pacemakers, implantable cardioverter defibrillators (ICDs), and cardiac resynchronization therapy (CRT) devices with atrial leads allow monitoring of atrial high-rate events (AHRE). Atrial high-rate events are an expression of subclinical AF with an increased risk of stroke and systemic embolism in relation to episode duration.[5] Some modern pacemakers and ICDs are also equipped with automated algorithms for the detection advanced SA, by means of continuous measurement of thoracic impedance,[6] and algorithms that combine data from multiple sensors for the assessment of the heart failure (HF) condition.[7] Making use of such devices, we investigated the relationship between the occurrence of AHRE and the values of an HF and a Respiratory Disturbance Index (RDI) in patients with HF and systolic dysfunction.

Methods

Patient selection

The study was a prospective, non-randomized multi-centre evaluation of patients receiving an ICD or CRT with defibrillator (CRT-D) endowed

with the HeartLogic™ algorithm and the ApneaScan™ diagnostic feature. 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[8] were enrolled in the LATITUDE (Boston Scientific) remote monitoring platform were enrolled at 27 study centres (full list of participating centres in Supplementary material online, *Material* section) and followed up in accordance with the standard practice of the participating centres. Clinical data were collected at the study centres within the framework of a prospective registry. The Institutional Review Boards approved the study, and all patients provided written informed consent for data storage and analysis. This general project including this analysis was registered on ClinicalTrials.gov (identifier: NCT02275637).

Device characteristics

Commercially available ICD/CRT-Ds and transvenous leads were used in this study. Devices were equipped with the HeartLogic™ algorithm[7] that 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). When the index enters into an alert state, the 'exit-alert' threshold is automatically dropped to a recovery value (nominal value 6). In the validation study, the algorithm predicted impending worsening HF events with a sensitivity of 70% and an unexplained alert rate of 1.47 per patient-year at the nominal threshold.[7] Moreover, the rate of HF events was 10-fold higher while IN- than OUT-of-alert state. Devices were also equipped with the ApneaScan™ diagnostic feature, which continuously measures thoracic impedance changes in order to count respiration.[6] At night, the algorithm automatically detects apnoea/hypopnoea events by counting the inter-breath time intervals that exceed a minimum baseline value. The algorithm defines an apnoea episode as two consecutive deep breaths with an interval of >10 s between breaths and a hypopnoea episode as an interval >10 s between deep breaths, which additionally contains consecutive small breaths. The total number of apnoea and hypopnoea events is stored, and the RDI is calculated by dividing the number of events by the programmed sleep duration. The RDI was shown to accurately identify severe SA, with 87% sensitivity and 56% specificity.[6]

Association between device diagnostic parameters and atrial high-rate events occurrence

The objective of the study was to investigate the association between the HeartLogic Index values and the RDI values calculated by the ICD and the incidence of AHRE during the post-enrolment follow-up period. Current guidelines for the diagnosis and management of AF consider AHRE to be an expression of subclinical AF.[9] The incidence and duration of AHRE were derived from device data, which comprise the total time spent by the patient in AHRE on each day of the follow-up period. As recommended, AHRE were visually inspected by a local expert electrophysiologist for excluding artefacts or other causes of inappropriate detection.[9] In the present study, patients were considered to have experienced AHRE episodes as surrogate of AF episodes if the device detected a cumulative daily duration ≥5 min, ≥6 h, ≥23 h, in agreement with previous studies.[5]

Statistical analysis

Descriptive statistics are reported as means ± SD for normally distributed continuous variables 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. Analysis of the time to the first episode was made 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) of an episode. The weekly value of IN- or OUT-of-alert state and the weekly RDI value were also treated as time-varying covariates in time-dependent Cox models. All variables displaying statistical significance (P value < 0.05) were entered into a multivariate regression analysis. The model was adjusted for those baseline variables that proved to be associated with the occurrence of endpoints on univariate analysis. HeartLogic IN-alert periods started when the index crossed the threshold and ended at the time of the first AHRE episode or were censored when the index decreased to below the recovery threshold (or at the end of follow-up). OUT-of-alert periods started on the day of HeartLogic 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 AHRE episode or were censored when the index rose above the threshold (or at the end of follow-up). Weekly average RDI values were considered, as calculated by the algorithm during the entire follow-up period. Measures were stratified according to an RDI value ≥or <30 episodes/h.[6] A P value < 0.05 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, Vienna, Austria), with 'survival' package for Cox regression analysis.

Table 1 Demographics and baseline clinical parameters

	Total (N = 411)
Age, years	69 ± 10
Male, *n* (%)	317 (77)
Body mass index, kg/m^2	26 ± 4
Ischaemic heart disease, *n* (%)	193 (47)
NYHA class	19 (5)
I, *n* (%)	250 (61)
II, *n* (%)	134 (33)
III, *n* (%)	8 (2)
IV, *n* (%)	
LV ejection fraction, %	32 ± 8
History of atrial fibrillation, *n* (%)	136 (33)
Secondary prevention, *n* (%)	49 (12)
CRT device, *n* (%)	297 (72)
Diabetes, *n* (%)	113 (27)
Chronic kidney disease, *n* (%)	107 (26)
Pulmonary disease, *n* (%)	70 (17)
Hypertension, *n* (%)	223 (54)
β-Blocker use, *n* (%)	377 (92)
Diuretic use, *n* (%)	367 (89)
Anti-arrhythmic use, *n* (%)	86 (21)
ACE inhibitor, ARB or ARNI use, *n* (%)	386 (94)
Maximum RDI, episodes/h	54 ± 14

ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blockers; ARNI, angiotensin receptor-neprilysin inhibitor; CRT, cardiac resynchronization therapy; LV, left ventricular; NYHA, New York Heart Association; RDI, respiratory disturbance index.

Results

Study population

From December 2017 to June 2021, 411 patients received an ICD or CRT-D. They were enrolled in the remote monitoring platform and the HF algorithm was activated. *Table 1* shows the baseline clinical variables of all patients in analysis.

Follow-up

The median follow-up was 26 months (25th–75th percentile: 16–35). During the observation period, an AHRE burden of ≥5 min/day was

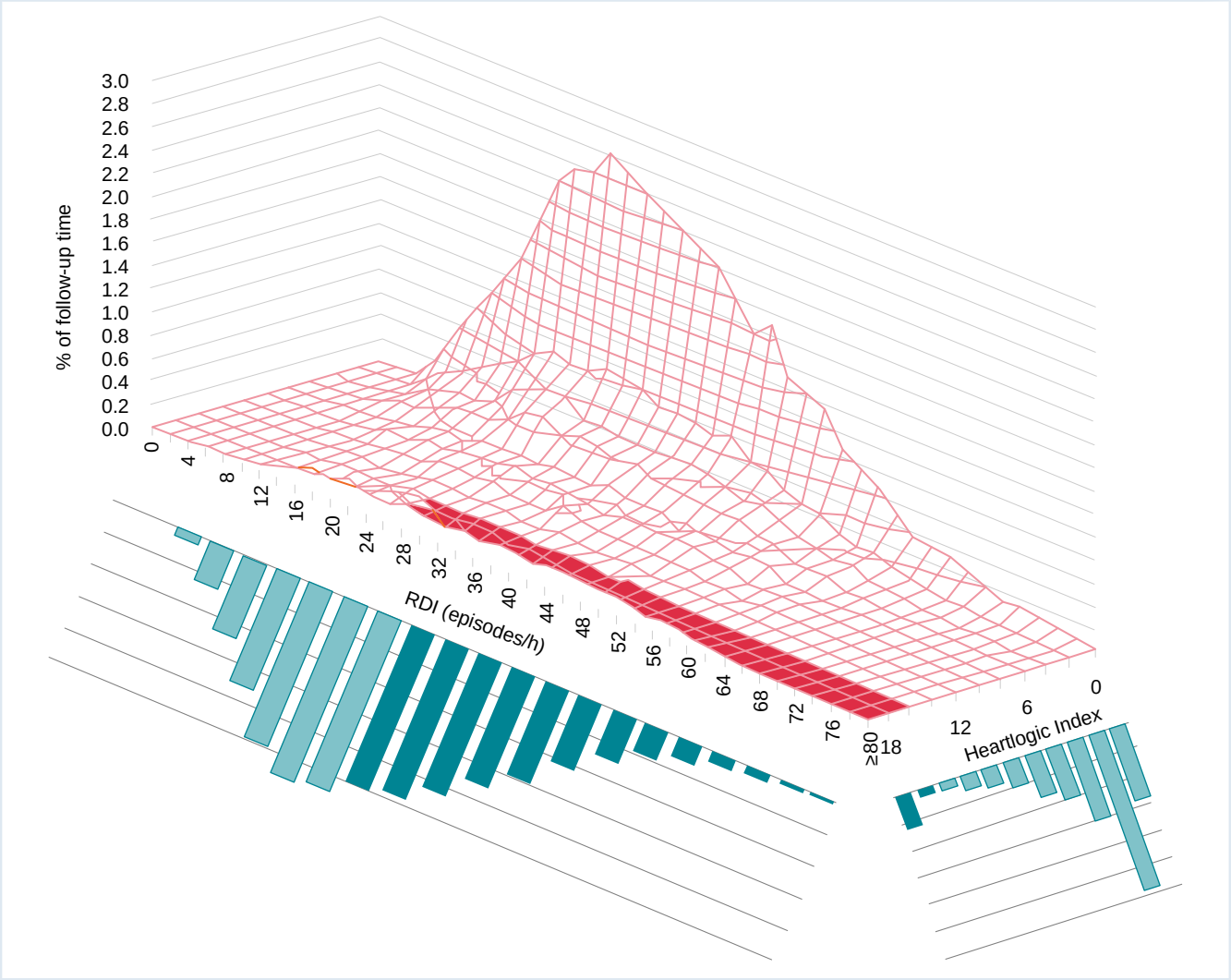


Figure 1 Combined distribution of weekly HeartLogic values and RDI values. The red area identifies the combination of HF alert (HeartLogic Index >16) and severe SA (RDI ≥30 episodes/h) conditions and accounts for only 6% of the follow-up period. HF, heart failure; RDI, Respiratory Disturbance Index.

documented in 139 (34%) patients, ≥6 h/day in 89 (22%) patients, and ≥23 h/day in 68 (17%) patients. During follow-up, the HF index crossed the threshold value 869 times (1.00 alerts/patient-year) in 268 patients. Overall, the time IN the alert state was 110 years (13% of the total observation period). The median time IN the alert state was 7% (25th–75th percentile: 0–20%). The ICD-detected RDI values recorded in all patients during the entire follow-up period were stored on the remote monitoring platform. The overall median of the weekly RDI was 33 episodes/h (25th–75th percentile: 24–45), and the maximum value on a patient basis was 54 ± 14 episodes/h. Overall, the RDI value was ≥30 episodes/h during 58% of the total observation period. The combined distribution of weekly HF index values and RDI values during the follow-up period is reported in *Figure 1*.

Association between implantable defibrillator-measured indexes and atrial fibrillation occurrence

The results of the regression analysis of baseline variables associated with AHRE occurrence, according to various thresholds of daily AHRE burden, are shown in *Table 2*. On using a time-dependent Cox model, the weekly IN-alert state was independently associated with the AHRE occurrence, regardless of the daily AHRE burden threshold, while the continuously measured weekly mean RDI ≥ 30 episodes/h was associated with AHRE burden ≥5 min/day, but not with longer AHRE burden values. These associations were confirmed after correction for age, pulmonary disease, chronic kidney disease, and history of AF (*Table 3*), as well as repeating the analysis in the subgroup of 275 patients without a history of AF at baseline.

Event rates were calculated according to the HF alert status (IN vs. OUT) and to the weekly RDI value (≥ vs. <30 episodes/h). Event rates were also calculated for the combination of HF alert and RDI conditions (*Figure 2*). Low RDI values (<30 episodes/h) or OUT of HF alert comprised the largest proportion of follow-up duration (94%) and had low AHRE occurrence rates. During IN-alert periods, if high RDI values were also recorded (6% of follow-up), the risk of events was much higher, with rates ranging from 28 per 100 patient-years for AHRE burden ≥5 min/day to 22 per 100 patient-years for AHRE burden ≥23 h/day.

Table 2 Univariate analysis of baseline variables associated with AHRE occurrence

	AHRE burden of ≥5 min			AHRE burden of ≥6 h			AHRE burden of ≥23 h		
	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P
Age	1.02	1.00–1.03	0.047	1.03	1.01–1.06	0.004	1.03	1.00–1.05	0.039
Male gender	0.67	0.46–1.02	0.058	0.72	0.45–1.16	0.180	0.77	0.44–1.32	0.341
Body mass index	1.00	0.96–1.05	0.916	0.98	0.93–1.05	0.613	1.00	0.94–1.07	0.951
NYHA class	1.07	0.81–1.42	0.617	1.21	0.86–1.71	0.272	1.08	0.73–1.61	0.700
Ischaemic heart disease	1.28	0.92–1.78	0.147	1.29	0.85–1.96	0.293	1.27	0.79–2.04	0.325
Ejection fraction	0.99	0.98–1.02	0.834	1.01	0.98–1.03	0.669	1.00	0.97–1.03	0.895
History of AF	1.98	1.42–2.76	<0.001	4.04	2.63–6.20	<0.001	4.81	2.90–7.98	<0.001
Hypertension	0.76	0.55–1.06	0.110	0.90	0.59–1.36	0.609	1.02	0.64–1.65	0.924
Pulmonary disease	1.51	1.01–2.24	0.045	2.20	1.40–3.47	<0.001	2.30	1.38–3.85	0.002
Diabetes	0.82	0.56–1.19	0.300	0.80	0.49–1.29	0.358	0.89	0.52–1.52	0.666
Chronic kidney disease	1.34	1.01–1.92	0.048	2.26	1.48–3.44	<0.001	2.15	1.33–3.48	0.002
CRT device	1.35	0.90–2.03	0.153	1.76	0.98–3.06	0.053	1.84	0.97–3.50	0.064
≥1 HeartLogic alert	1.56	1.06–2.30	0.023	2.93	1.63–5.26	<0.001	3.23	1.60–6.48	0.001
Maximum RDI	1.01	0.99–1.02	0.537	1.00	0.99–1.02	0.577	1.01	0.99–1.03	0.294
Weekly IN-alert state[a]	2.48	1.58–3.90	<0.001	3.14	1.85–5.34	<0.001	4.60	2.56–8.24	<0.001
RDI ≥30 episodes/h[a]	1.52	1.09–2.11	0.013	1.23	0.82–1.85	0.310	1.21	0.75–1.95	0.440

AF, atrial fibrillation; AHRE, atrial high-rate events; CI, confidence interval; HR, hazard ratio; NYHA, New York Heart Association; for other abbreviations, see *Table 1*.
[a]Time-dependent Cox model.

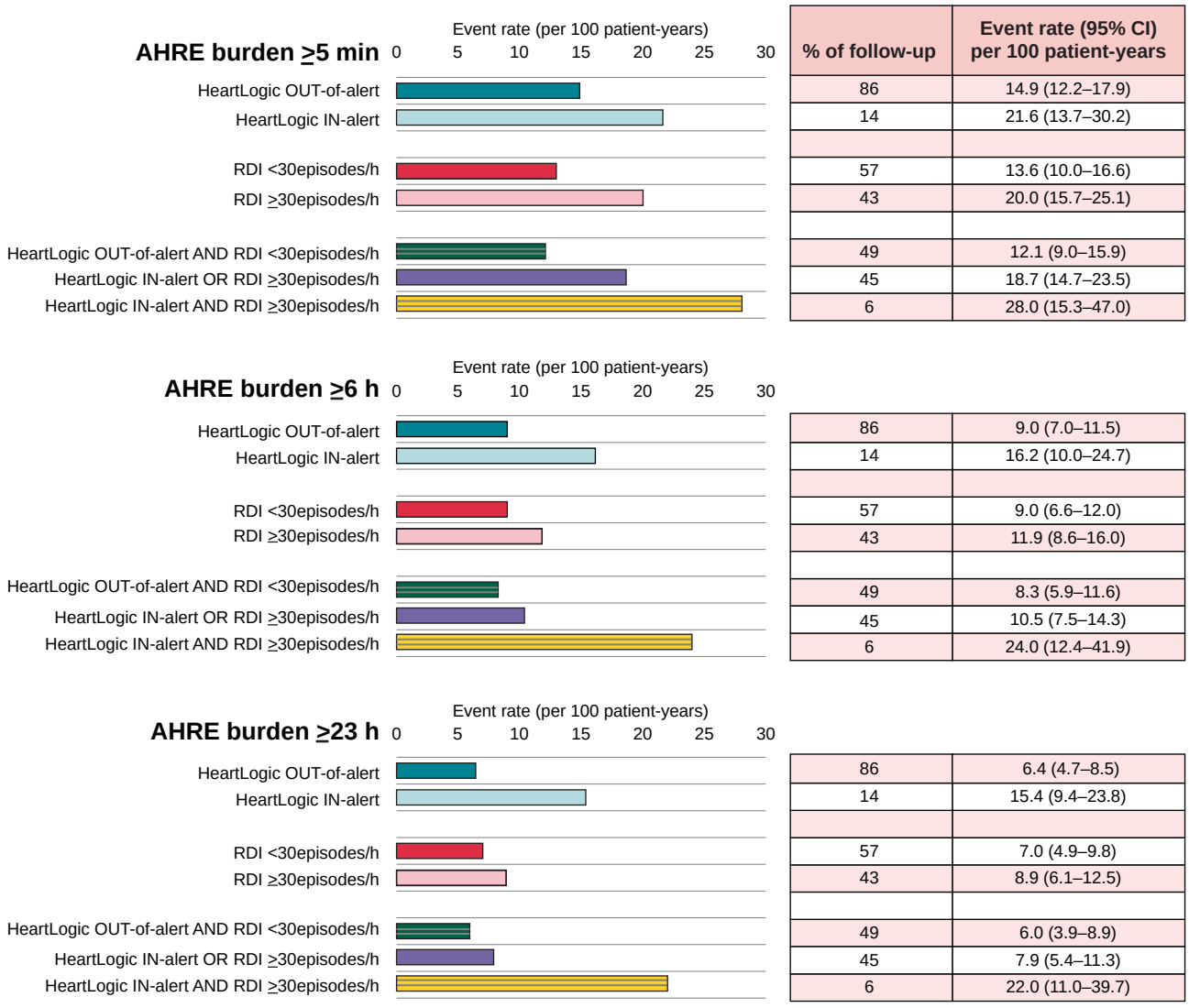
Table 3 Results of the time-dependent Cox model

	AHRE burden of ≥5 min			AHRE burden of ≥6 h			AHRE burden of ≥23 h		
All patients (*N* = 411)	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P
Age	1.00	0.98–1.02	0.835	1.00	1.98–1.03	0.809	0.99	0.97–1.02	0.518
History of AF	1.52	1.07–2.16	0.020	2.81	1.74–4.55	<0.001	3.53	1.94–6.43	<0.001
Pulmonary disease	1.34	0.91–1.99	0.139	1.59	1.01–2.49	0.045	1.66	0.98–2.83	0.061
Chronic kidney disease	1.08	0.77–1.53	0.646	1.57	1.06–2.31	0.023	1.41	0.88–2.24	0.150
HeartLogic IN-alert state	2.17	1.36–3.46	0.001	2.33	1.34–4.06	0.003	3.43	1.85–6.37	<0.001
RDI ≥30 episodes/h	1.55	1.11–2.16	0.011	1.28	0.85–1.94	0.238	1.28	0.79–2.06	0.316
Patients without a history of AF at baseline (*n* = 275)									
Age	1.01	0.99–1.04	0.358	1.03	1.00–1.07	0.067	1.04	1.00–1.09	0.037
Pulmonary disease	1.21	0.66–2.21	0.530	1.75	0.83–3.70	0.139	2.34	1.03–5.33	0.043
Chronic kidney disease	0.94	0.54–1.62	0.824	1.27	0.62–2.63	0.517	1.34	0.55–3.26	0.525
HeartLogic IN-alert state	3.92	2.18–7.04	<0.001	5.89	2.76–12.59	<0.001	14.01	5.49–35.79	<0.001
RDI ≥30 episodes/h	1.53	1.05–2.52	0.028	0.95	0.47–1.91	0.875	1.18	0.49–2.83	0.712

For abbreviations, see *Tables 1* and *2*.

Discussion

In the present study, we found that the occurrence of AHRE is independently associated with the value of two indexes automatically measured by ICD algorithms, the HeartLogic Index, a measure of patient's HF status, and the RDI, an indicator of SDB severity. Indeed, we reported higher incidence of AHRE in periods when the multi-sensor HF algorithm was IN the alert state and when the ApneaScan™ diagnostic feature was detecting severe SA (RDI ≥ 30 episodes/h). The detection of IN-alert state seemed to predispose to the onset of short-term AHRE (cumulative daily duration of episodes ≥5 min) as well as more sustained events (≥23 h). Conversely, the occurrence of RDI ≥ 30 episodes/h appeared associated more with short-term AHRE. The present analysis also provided evidence on the use of both ICD indexes for a dynamic AF risk stratification. Indeed, the



	% of follow-up	Event rate (95% CI) per 100 patient-years
AHRE burden ≥5 min		
HeartLogic OUT-of-alert	86	14.9 (12.2–17.9)
HeartLogic IN-alert	14	21.6 (13.7–30.2)
RDI <30episodes/h	57	13.6 (10.0–16.6)
RDI ≥30episodes/h	43	20.0 (15.7–25.1)
HeartLogic OUT-of-alert AND RDI <30episodes/h	49	12.1 (9.0–15.9)
HeartLogic IN-alert OR RDI ≥30episodes/h	45	18.7 (14.7–23.5)
HeartLogic IN-alert AND RDI ≥30episodes/h	6	28.0 (15.3–47.0)
AHRE burden ≥6 h		
HeartLogic OUT-of-alert	86	9.0 (7.0–11.5)
HeartLogic IN-alert	14	16.2 (10.0–24.7)
RDI <30episodes/h	57	9.0 (6.6–12.0)
RDI ≥30episodes/h	43	11.9 (8.6–16.0)
HeartLogic OUT-of-alert AND RDI <30episodes/h	49	8.3 (5.9–11.6)
HeartLogic IN-alert OR RDI ≥30episodes/h	45	10.5 (7.5–14.3)
HeartLogic IN-alert AND RDI ≥30episodes/h	6	24.0 (12.4–41.9)
AHRE burden ≥23 h		
HeartLogic OUT-of-alert	86	6.4 (4.7–8.5)
HeartLogic IN-alert	14	15.4 (9.4–23.8)
RDI <30episodes/h	57	7.0 (4.9–9.8)
RDI ≥30episodes/h	43	8.9 (6.1–12.5)
HeartLogic OUT-of-alert AND RDI <30episodes/h	49	6.0 (3.9–8.9)
HeartLogic IN-alert OR RDI ≥30episodes/h	45	7.9 (5.4–11.3)
HeartLogic IN-alert AND RDI ≥30episodes/h	6	22.0 (11.0–39.7)

Figure 2 Event rates for HeartLogic alert status (light yellow shading for OUT-of-alert, dark yellow shading for IN-alert) and RDI value (light blue shading for <30 episodes/h and dark blue shading for ≥30 episodes/h) individually and in combination. AHRE, atrial high-rate events; RDI, Respiratory Disturbance Index.

verification of both alert conditions identified a very low proportion of follow-up duration characterized by a very high AHRE occurrence rate.

In HF patients, AF is a common comorbidity and is associated with a worse prognosis. Indeed, HF was the strongest independent risk factor for new-onset AF in the Framingham Heart Study.[10] Heart failure is known to predispose patients to AF via numerous mechanisms such as elevated atrial pressure, altered myocardial conduction, maladaptive gene expression, and structural remodelling.[11] Modern ICD algorithms for HF monitoring are based on the combination of multiple physiological variables and allow accurate continuous, automatic HF diagnosis. They have been proposed as predictors of impending HF decompensation that can trigger timely interventions and identify periods of increased risk of HF. Indeed, the HeartLogic Index and alert algorithm were shown to provide a sensitive and timely predictor of impending HF decompensation and a measure of the risk of an HF event independent of baseline clinical variables.[7] These algorithms can shed light on the dynamic nature of the association between HF and AF and possibly on their reciprocal causal mechanisms.[12] The automated ICD algorithms allow to investigate also other factors that have been implicated for predisposing patients with HF to AF, such as the SA.[4] Although the multisensor HF algorithm itself makes use of impedance-based measures of the respiration rate and the tidal volume, additional and independent information is provided by the RDI index that quantifies the extent and frequency of nocturnal apnoea and hypopnoea events. The RDI was demonstrated to accurately identify severe SA and demonstrated good agreement with apnoea–hypopnoea index values measured by ambulatory polygraphy.[6] The RDI was also shown to predict the occurrence of AHRE in HF patients with ICDs and in pacemaker recipients.[13] Our results extend previous findings by demonstrating that the continuously measured weekly RDI values allow dynamic stratification for AHRE risk during follow-up, unlike the maximum RDI value calculated during the entire follow-up period. In agreement with pervious results obtained in pacemaker patients,[14] we observed a considerable variability in ICD-detected SA. This suggests the superiority of the

continuous monitoring vs. a single overnight sleep study that may result in the misclassification of severe SA and is also hypothesized by other authors.[15]

Sleep-disordered breathing is common in patients with HF and AF. In particular, CSA is highly prevalent in HF patients, while OSA is more common in patients with AF. In both conditions, SDB increases sympathetic activity with higher morbidity and mortality.[2] In this analysis, high RDI values were mainly associated with shorter AHRE episodes, while IN-alert HF state seemed associated with AHRE events, regardless of their duration. Heart failure is a condition in which persistent elevation of left atrial pressure causes pathological genes expression leading to anatomical and electrical myocardial remodelling. Left ventricular dysfunction also causes a neurohormonal response that promotes initiation and persistence of AF.[11] Moreover, HF and AF have a chronic bidirectional relation that leads to a progressive increase in AF burden with longer time in decompensated HF status associated with longer AF episodes. By contrast, SA causes predominantly acute modifications of haemodynamic: high negative intrathoracic pressure, acute increase of venous return, deoxygenation, and reoxygenation alternans.[2] These changes during the apnoea episodes cause acute atrial stretch with increased risk of AF paroxysm during obstructive events.[16] Long-term exposure to SDB causes also chronic changes, such as structural and electrical atrial remodelling, that are important in sustaining AF,[17] but this mechanism appears to be less important.

In the present study, we also explored the combined value of the two ICD indexes of HF alert and SA severity for the dynamic AHRE risk stratification. For about 94% of the follow-up period, our patients were in OUT-of-alert state or were not experiencing severe SA (weekly average RDI < 30 episodes/h). In these conditions, AHRE events were very infrequent. By contrast, when both alert conditions were verified (only 6% of the follow-up period), the risk of AHRE was much higher. This potentially allows care to be redirected from patients in their low-risk periods to more vulnerable patients in their high-risk periods. Possible actions could be early HF therapeutic interventions, i.e. diuretics for congestion relief and reduction of sympathetic drive, ACE inhibitors[9] or optimal CRT,[18] or therapies for SDB.[19,20] Observational studies suggested that treatment with continuous positive airway pressure has a positive impact on AF recurrences after electrical cardioversion and improves catheter ablation outcomes.[21]

Limitations

The limitations of our study should be acknowledged. First, its observational design may have introduced an inherent bias. Second, device-detected AHRE are a surrogate of subclinical—and not clinical—AF, which has different clinical implications and potentially different degrees of progression along with time.[22] Third, we included patients with history of AF, introducing a possible selection bias not fully corrected by means of the statistical adjustment. However, the analysis repeated in the subgroup of patients without a history of AF at baseline confirmed the results. Fourth, our results were obtained in a selected population of ICD patients and may not be generalizable to the overall HF population. Fifth, we have not performed conventional polysomnography to confirm diagnosis of SA, and the algorithm for SDB detection does not distinguish between obstructive and CSA. Finally, although the HeartLogic proved to be a sensitive predictor of impending HF decompensation, we have not confirmed diagnosis of acute HF.

Conclusions

In HF patients with reduced ejection fraction, the occurrence of AHRE was independently associated with the ICD-measured IN-alert HF state and high RDI values. The coexistence of these two conditions occurred rarely but was associated with a very high rate of AHRE. These findings suggest that ICD indexes of HF status and SA severity may integrate the clinical assessment of individual patients and facilitate the stratification of AF risk resulting in improved decision-making.

Supplementary material

Supplementary material is available at *Europace* online.

Conflict of interest: M. Campari and S. Valsecchi are employees of Boston Scientific, Inc. G. Boriani reports receiving small speaker's fees from Bayer, Boston, Janssen, and Sanofi. No other conflicts of interest exist.

Data availability

The experimental data used to support the findings of this study are available from the corresponding author upon reasonable request.

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