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ORIGINAL ARTICLE

Predicting acute decompensated heart failure using circadian markers from heart rate time series

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Abstract

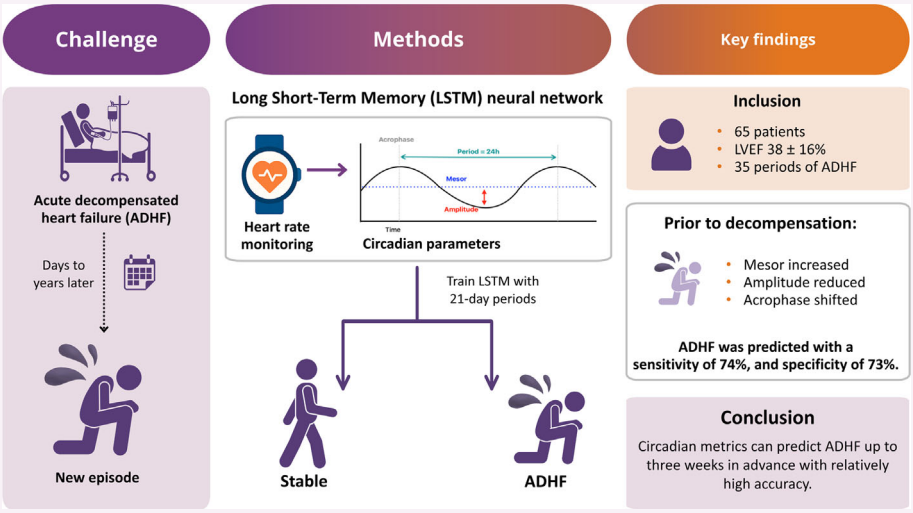
Aims Hospital admissions for acute decompensated heart failure (ADHF) are linked to high readmission rates, emphasizing the need for early intervention. Dysregulation of the circadian rhythm that regulates key physiological processes, such as heart rate (HR), blood pressure and sleep–wake cycles, may precede weight gain and clinical symptoms of worsening heart failure (HF) by weeks, providing a window for timely intervention. This study aims to develop a predictive algorithm for early and accurate ADHF detection.

Methods and results Sixty-five patients discharged after ADHF hospitalization monitored HR with a wrist-worn device for 6 months after reaching stable HF. Circadian parameters (mesor, amplitude and acrophase) were extracted via cosinor analysis and used to train a long short-term memory neural network. The algorithm analysed 21-day periods before an HF event, defined as unplanned outpatient visits for congestion episode, increased diuretics, ADHF hospitalization or sudden cardiac death. Circadian changes appeared in the 21 days preceding HF events, with elevated mesor (70.6 vs. 73.6 b.p.m.; $P < 0.001$), reduced amplitude (8.3 vs. 4.9 b.p.m.; $P = 0.046$) and acrophase shifts (11.3 vs. 12.2 h; $P = 0.706$). The classification algorithm showed 74% sensitivity, 73% specificity and a 74% AUC ($P < 0.001$). Amplitude was the strongest predictor, contributing 62% to the algorithm's feature importance.

Conclusions Circadian metrics from a wrist-worn device showed progressive alterations over the 3 weeks preceding ADHF, offering potential early detection of HF decompensation with moderate prediction performance. Future research should refine these metrics and results in larger, diverse populations, using various sensor types and explore early interventions.

Graphical Abstract

Circadian metrics—amplitude, mesor, and acrophase—derived from a wrist-worn heart rate monitor can predict acute decompensated heart failure (ADHF) up to 21 days before onset. In 65 post-ADHF patients, an LSTM model achieved 74% sensitivity, and 73% specificity trained on 21-day sequences. These findings support circadian rhythm analysis as a promising approach for early detection of cardiovascular deterioration. Future studies should refine these metrics in larger cohorts and enable timely intervention to improve outcomes.



Keywords Circadian rhythm; Heart failure; Machine learning; Wearables; Predictive modelling; Telemonitoring

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Introduction

Heart failure and telemonitoring strategies

Heart failure (HF) poses a significant global health burden, affecting over 64 million people worldwide.[1] Its prevalence is expected to increase further by approximately 46% between 2012 and 2030, primarily due to demographic growth, an aging population and advances in the diagnosis and management of cardiovascular diseases.[1] Once hospitalized for acute decompensated HF (ADHF), patients have a high risk on early readmission, with 30-day readmission rates reaching 22%.[2] These frequent hospitalizations contribute to the substantial socio-economic impact of HF, with estimated costs up to €25 000 per patient per year in Western countries.[1]

Non-invasive telemonitoring (TM), typically consisting of remote monitoring of vital signs and symptoms, has emerged as a valuable strategy for detecting early deterioration in patients with HF.[3] TM has the potential to prevent recurrent hospitalization due to ADHF, by enabling timely intervention through medication adjustments and self-management. However, a significant limitation of non-invasive TM is its primarily reliance on spot measurements, such as body weight or daily symptom reporting. These spot measurements methods typically detect changes only several days before hospitalization and are only limited sensitive to subtle changes. Consequently, their value in timely predicting impending HF events remains questionable.[4] Implantable cardiac devices involving invasive haemodynamic monitoring, on the other hand, offer the advantage of continuous monitoring of multiple parameters related to autonomic adaptation, pulmonary fluid accumulation, and physical activity.[5] While these devices offer possibilities to detect early signs of deterioration, recent meta-analyses have yielded mixed results regarding their impact on overall mortality and hospitalization rates.[6] Where invasive haemodynamic monitoring, which involves measuring the pulmonary artery pressure (e.g., CardioMEMS), was associated with markedly reduced hospitalizations[7], effects of monitoring with implantable devices (pacemaker and implantable cardiac defibrillator systems) are less clear.[8] However, while the use of invasive TM is promising in certain

patient populations, its invasive nature, associated risks and high costs limit its widespread use. This leaves a narrow window for effective clinical intervention, stressing the need for non-invasive alternatives.[4]

Circadian rhythm and heart failure progression

Circadian rhythms regulate key physiological processes such as heart rate (HR), blood pressure, and sleep–wake cycles.[9] Disruptions in these patterns, often linked to molecular clock dysregulation, may precede or exacerbate cardiac decompensation, making them potential early indicators of worsening HF. This dysregulation is bidirectional—external factors (e.g., irregular sleep, light exposure and stress) can impair the internal clock, contributing to myocardial injury, fibrosis and systolic dysfunction, while HF itself further disrupts circadian regulation.[9]

A promising avenue for non-invasive monitoring of circadianity is the use of wearable devices that track, for example, HR, skin temperature and actigraphy.[10] These devices provide continuous insights into circadian function and offer a practical, user-friendly solution for tracking circadian rhythm changes in a home setting.[10] By monitoring physiological parameters over time, they can detect subtle circadian disruptions that precede hospitalization due to ADHF, potentially several weeks before clinical symptoms manifest, facilitating timely intervention.

Leveraging machine learning models and time-series data for early prediction

Advanced machine learning (ML) models, such as long short-term memory (LSTM) artificial neural networks,[11] offer a promising approach for analysing time-series data from wearable devices.[12] By training these models on HR-related circadian parameters such as the amplitude (the difference between the peak and mean HR),[13] acrophase (a measure of the peak HR values recurring in each cycle)[13] and mesor (a rhythm-adjusted mean),[13] extracted through 24 h cosinor analysis over the 21 days preceding ADHF, we test the possibility to identify patterns that precede acute deterioration. LSTM networks are particularly suited for this task because they can capture long-term dependencies in sequential data,[12] making them potentially ideal for detecting subtle shifts in baseline physiological features weeks before an event occurs. While traditional statistical analyses of average mesor, amplitude and acrophase can identify group-level differences, they do not account for how these parameters evolve over time. LSTM models, by contrast, enable learning from the sequential dependencies and temporal fluctuations in these rhythms, which may provide additional predictive power for detecting early signs of decompensation.

Objectives of the study

This study aims to improve the prediction of ADHF by utilizing changes in circadianity detected through wearable devices. By applying cosinor analysis to quantify circadian rhythm parameters, such as mesor, amplitude and acrophase, and using artificial neural networks on time-series data from the 3 weeks preceding ADHF, we aim to predict its onset in advance. The ultimate goal is to provide a non-invasive, continuous monitoring solution that enables timely intervention, potentially reducing hospitalizations and improving patient outcomes.

Methods

Study population

Eligible participants were patients hospitalized for ADHF, irrespective of HF type (reduced, mildly reduced, or preserved ejection fraction) (see *Appendix A* for detailed inclusion and exclusion criteria). Screening for eligibility occurred during the hospital stay by two of the cardiac researchers (M.v.L. and I.D.L.). The researcher provided detailed study information to eligible patients, and informed consent was obtained prior to hospital discharge. The study conforms with the principles outlined in the Declaration of Helsinki. A detailed description of the study protocol can be found in van Leunen et al. (2023),[14] Netherlands Trial Registry (NTR) NL9619. The primary trial outcomes will follow upon completion of the ongoing long-term follow-up.

Study protocol

Upon hospital discharge, all patients were enrolled in the Remote Patient Monitoring (RPM) programme as part of standard care. The programme involves daily monitoring of vital parameters (blood pressure, HR and weight) and symptoms a digital platform (Mibida, Eindhoven, The Netherlands), which generates alerts for values outside the expected range. Alerts are reviewed by a specialized HF nurse, who contacts patients as needed to address potential decompensation early. Participants in this study were additionally provided with a Philips Health Band (PHB), a CE-marked wrist-worn device for continuous HR monitoring (details in *Appendix B*). They were instructed to wear the PHB continuously throughout the study period, except during showering, swimming, or charging. The PHB has been validated for HR assessment in patients with HF, demonstrating good accuracy during rest and low-intensity household activities, and moderate responsiveness to changes in cycling load and walking speed.[15] Given that HR data were averaged at hourly resolution for circadian modelling, potential motion artefacts during brief

activity periods were minimized, making the PHB suitable for use in this context.

Local investigator (M.v.L.) regularly reviewed medical records to categorize key events into predefined groups:

1. HF events: Increase in loop diuretic dose at the outpatient clinic, hospital readmission for ADHF, outpatient visit for congestion episode or death due to HF.
2. Clinically stable: Time intervals without any events following clinical compensation.

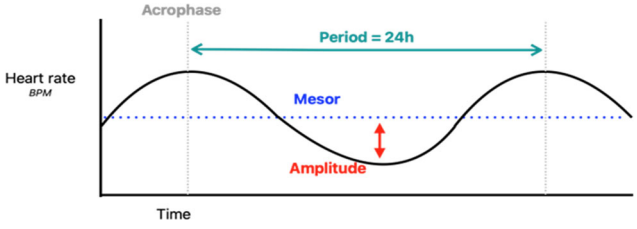
Data periods related to changes in medicine therapy, and hospitalization were excluded since they might influence the circadian rhythm (see *Appendix C* for a detailed description of these excluded time series).[9] The study ended 6 months after randomization (performed after reaching stable HF and optimal medical therapy), regardless of the recurrence of ADHF.

Data analysis

Data preprocessing and analysis were conducted, using an in-house MATLAB algorithm (version R2023b). Patients' baseline characteristics analysis was performed using SPSS (version 29.0).

To analyse circadian rhythms, a generalized linear model with a gamma distribution (GZLM-gamma) was used for cosinor fitting, following the approach by Doyle et al. (2022).[13] The cosinor fitting was applied to 24-h HR data to extract the mesor (a circadian rhythm-adjusted HR mean), amplitude (the difference between the peak and the mean HR value within a cycle) and acrophase (a measure of the timing at which the peak of the heart rate circadian rhythm occurs in the cycle) (*Figure 1*).[13] For further details on preprocessing and cosinor implementation, see *Appendix D*. These extracted circadian features formed the basis for sequence generation and subsequent classification.

Figure 1 Definition of circadian rhythm characteristics on cosinor fitted HR data of an HF patient. The mesor is a circadian rhythm-adjusted mean; the amplitude is the difference between the peak and the mean value within a cycle; the acrophase is a measure of the timing at which the peak of the heart rate circadian rhythm occurs in the cycle.



Time series labelling and grouping

Daily values of circadian parameters mesor, amplitude and acrophase were used to construct 21-day sequences for each patient. Each time series was labelled based on the clinical condition it represented: either 'clinically stable' or preceding 'HF event' (i.e., 21 days leading up to ADHF).

Statistical analysis of mesor, amplitude and acrophase in isolation

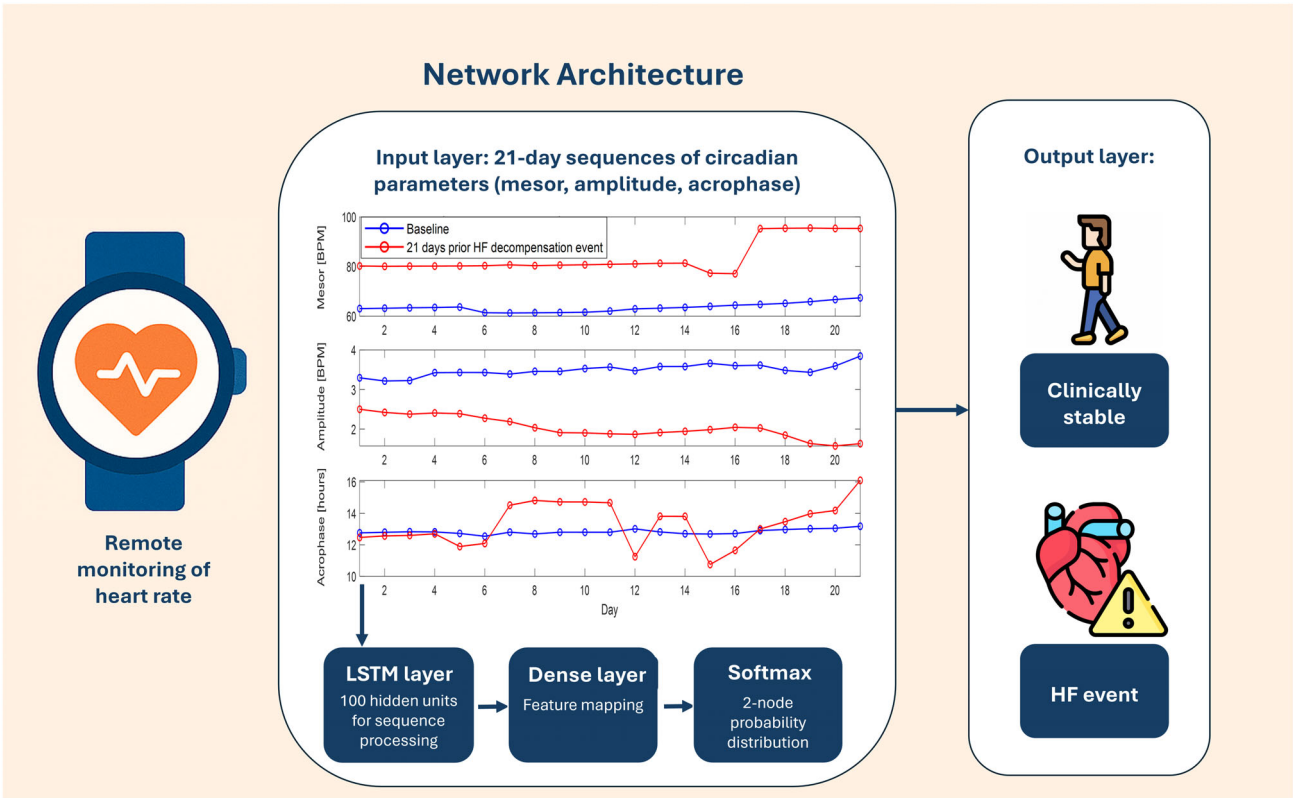
To evaluate whether circadian rhythm features differed between HF event and clinically stable periods, we applied linear mixed-effects models to the mean values of mesor, amplitude and acrophase across each 21-day sequence. Each model included the circadian parameter as the dependent variable, condition (HF event vs. clinically stable) as a fixed effect, and a random intercept for each patient to account for repeated measures. This approach controls for the non-independence of sequences originating from the same individual. A P-value < 0.05 was considered statistically significant.

ML model for predicting HF events

To derive a global measure that captures the dynamics of circadian rhythms and could potentially enhance clinical decision-making, we employed artificial neural networks, specifically a LSTM model, to classify 21-day circadian sequences. The input layer processed the time series of mesor, amplitude and acrophase, which were fed into an LSTM layer with 100 hidden units. This was followed by a fully connected dense layer and a SoftMax activation function with two output nodes, yielding class probabilities for HF event versus clinically stable states. Although binary classification can also be achieved using a sigmoid output unit, we used SoftMax for its compatibility with multiclass extensions and interpretability in probability space (*Figure 2*).

To ensure generalizability and prevent data leakage, model evaluation was performed using a leave-one-patient-out cross-validation (LOOCV) procedure. In each fold, one patient's data was held out as the test set, while the model was trained on all remaining patients. This process was repeated until each patient had been used once as the test subject. To mitigate class imbalance during training, we applied random undersampling of clinically stable sequences and oversampling of HF event sequences within each training fold, while the test fold remained untouched to reflect real-world distributions. Performance metrics were calculated by aggregating predictions across all test folds (i.e., all patients) and included sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), F1

Figure 2 The LSTM network architecture for the classification algorithm trained on 21-day sequences of mesor, amplitude and acrophase. The LSTM network architecture for the classification algorithm trained on 21-day sequences of mesor, amplitude, and acrophase. The 21-day sequences, obtained through remote monitoring of circadian rhythm parameters, are fed into the LSTM network. This network comprises an LSTM layer with 100 hidden units. The output is passed through a dense layer followed by a softmax activation layer with two outputs, providing class probabilities for HF event and clinically stable states.



score, receiver operating characteristics with area under the curve (ROC-AUC) and area under the precision–recall curve (AUPRC).

To assess the significance of our results, we conducted a 1000 permutation test by shuffling the training data labels and evaluating whether the real classification performance metrics fall outside the 95th percentile of the permutation distribution ($P < 0.05$).[17] Moreover, to assess the impact of each individual time point on classification performance, we conducted an additional analysis by progressively excluding days leading up to a HF event during LSTM model training. As above, this analysis was assessed using the LOOCV procedure.

Feature importance analysis

We assessed feature contributions using permutation importance on the test dataset. Values for mesor, amplitude and acrophase were randomly permuted, and the drop in model accuracy was recorded as the feature's importance score. Scores were normalized to percentages, ranking each feature by its impact on distinguishing HF events from clinically stable periods.

Results

Data inclusion

Out of the 86 patients initially enrolled in the study, data from 65 patients were suitable for model training, with a median age of 76 (11), and LVEF 38 ± 16%. Twenty-one patients (24%) were excluded because of insufficient data (see *Appendix F* for details). Consequently, we had a total of 426 time series collected in 65 patients, each consisting of 21 consecutive days, labelled as either clinically stable or HF events, with a ratio of 391:35, respectively. The 35 HF events were collected in 24 different patients: 17 patients with one event, four patients with two events, two with three events, and one with four events, respectively. Among the 24 patients who experienced an HF event, 22 also had at least one clinically stable period. Patients who experienced HF events were significantly more likely to be older (>75 years), and to have either preserved ejection fraction (HFpEF). In addition, comorbidities such as chronic kidney disease (CKD) and atrial fibrillation (AF) were more prevalent among patients with HF events compared to those who remained clinically stable.

Baseline characteristics of patients participated in this study are represented in *Table 1*.

Statistical analysis of mesor, amplitude and acrophase in isolation: Clinically stable versus HF event

Prior to an HF event, the mesor increased significantly (70.6 vs. 73.6 b.p.m.; $P < 0.001$), the amplitude reduced (8.3 to 4.9 b.p.m.; $P = 0.045$), and the acrophase shifted (11.3 to 12.2 h; $P = 0.706$) as compared to clinical stability. *Figure 3* illustrates the mesor, amplitude and acrophase of a patient during clinically stable time series (blue curve) and 21 days prior to ADHF (red curve), and the mean distributions of the timeseries.

Artificial neural networks to predict ADHF: Algorithm performance

By combining mesor, amplitude and acrophase, and exploring the 21 days window, we trained and tested an LSTM neural network. The algorithm achieved sensitivity of 74%, successfully detecting true HF events, and a specificity of 73%, accurately identifying clinically stable periods. Moreover, the results demonstrated a high NPV of 97%, effectively minimizing missed detections. However, the PPV was 20%, reflecting a considerable number of false alarms due to the class imbalance between clinically stable periods and HF events (ratio of 391:35). The ROC analysis yielded an AUC of 74% ($P < 0.001$), confirming the algorithm's ability to distinguish between HF events and clinically stable periods. The precision–recall analysis resulted in an AUPRC of 21%, compared with a baseline of 8.2%. Although this reflects the impact of class imbalance on PPV, it nevertheless indicates that the algorithm substantially outperformed random classification (*Figure 4*).

The algorithm's classification performance remained stable despite the progressive removal of days prior to ADHF (*Table 2*). Sensitivity consistently ranged between 72% and 93%, and specificity remained within 31%–73%, indicating that predictive patterns were not solely restricted to the days immediately preceding the event. The AUC remained above 62%, suggesting that relevant circadian changes were present across different phases of the pre-event period. Exclusions beyond 12 days were not performed, as further shortening the time series would compromise the LSTM model's ability to effectively learn temporal dependencies.

Feature importance for algorithm predictions

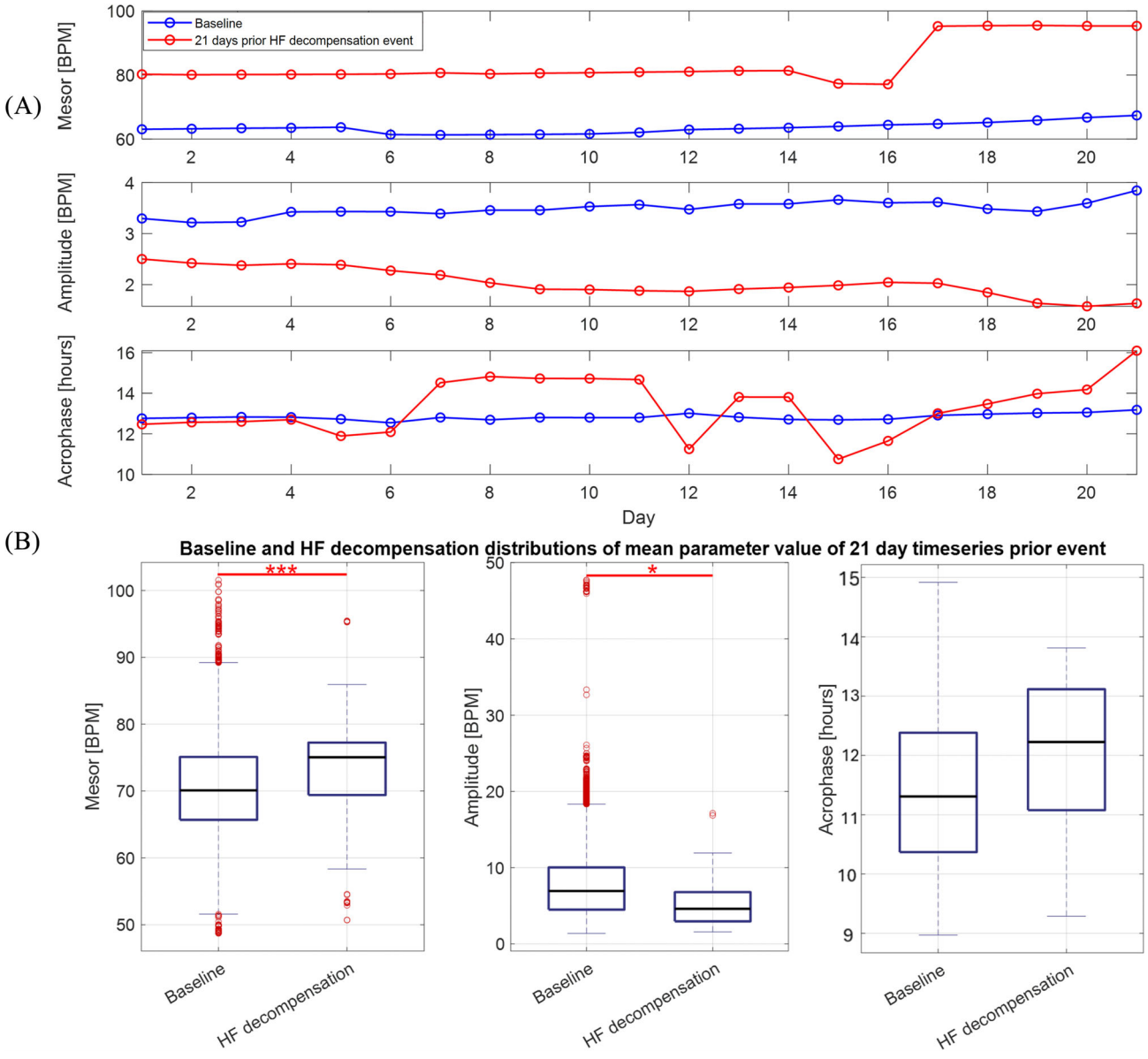
Relative feature contributions showed that the amplitude (62%) was the most critical predictor, followed by mesor (19%) and acrophase (19%), as represented in *Figure 4*. This underscores the dominant role of the amplitude in distinguishing HF events from clinically stable periods.

Table 1 Baseline characteristics of patients with (at least one) and without HF events

	HF event ($n = 24$)	No HF event ($n = 41$)	All ($n = 65$)	*P*-value
Baseline characteristics				
Age, years (IQR)	77 (7)	73 (13)	76 (11)	0.08
Age, <75 years	6 (25.0%)	22 (53.7%)	28 (43.1%)	**0.024**
Sex, male (%)	18 (75.0%)	25 (61.0%)	45 (67.2%)	0.25
BMI	27.4 ± 5.8	28.1 ± 5.6	27.9 ± 5.6	0.63
LVEF, %	47.9 ± 14.9	32.9 ± 13.6	38.4 ± 15.7	**<0.001**
HFpEF	15 (62.5%)	8 (19.5%)	22 (34.4%)	**<0.001**
HFmrEF	1 (4.2%)	4 (9.8%)	5 (7.8%)	0.65
HFrEF	8 (33.3%)	29 (70.7%)	37 (57.8%)	**0.005**
HF aetiology				
Ischaemic	3 (12.5%)	7 (17.1%)	10 (15.4%)	0.62
Arrhythmia	6 (25.0%)	13 (31.7%)	19 (29.2%)	0.57
Dilated	0	4 (9.8%)	4 (6.2%)	0.29
Other[a]	15 (62.5%)	17 (41.5%)	32 (49.2%)	0.10
Comorbidities				
Hypertension	14 (58.3%)	26 (63.4%)	40 (61.5%)	0.68
Stroke	4 (16.7%)	7 (17.1%)	11 (16.9%)	1.00
Diabetes mellitus	4 (16.7%)	10 (24.4%)	14 (21.5%)	0.47
Chronic kidney disease	14 (58.3%)	12 (29.3%)	26 (40.0%)	**0.021**
Hyperlidaemia	8 (33.3%)	11 (26.8%)	19 (29.2%)	0.59
Myocardial infarction	6 (25.0%)	6 (14.6%)	12 (18.5%)	0.34
Coronary revascularization	6 (25.0%)	5 (12.2%)	11 (16.9%)	0.30
Atrial fibrillation	21 (87.5%)	20 (48.8%)	41 (63.1%)	**0.002**

N (%), means ± SD or median (IQR).
HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; IQR, interquartile range; LVEF, left ventricular ejection fraction.
[a]Toxic damage (1.5%), infiltration (1.5%), immune-mediated and inflammatory (6.2%), hypertension (7.7%), acquired valve defect (7.7%) and idiopathic (23.1%).

Figure 3 Mesor, amplitude and acrophase during clinically stable period and 21 days prior to ADHF. (A) A typical illustration of the mesor, amplitude and acrophase during a clinically stable period and 21 days prior to ADHF. (B) Distributions of means on the 21-day timeseries of mesor, amplitude and acrophase at a clinically stable period versus ADHF. ADHF, acute decompensated heart failure; b.p.m., beats per minute.



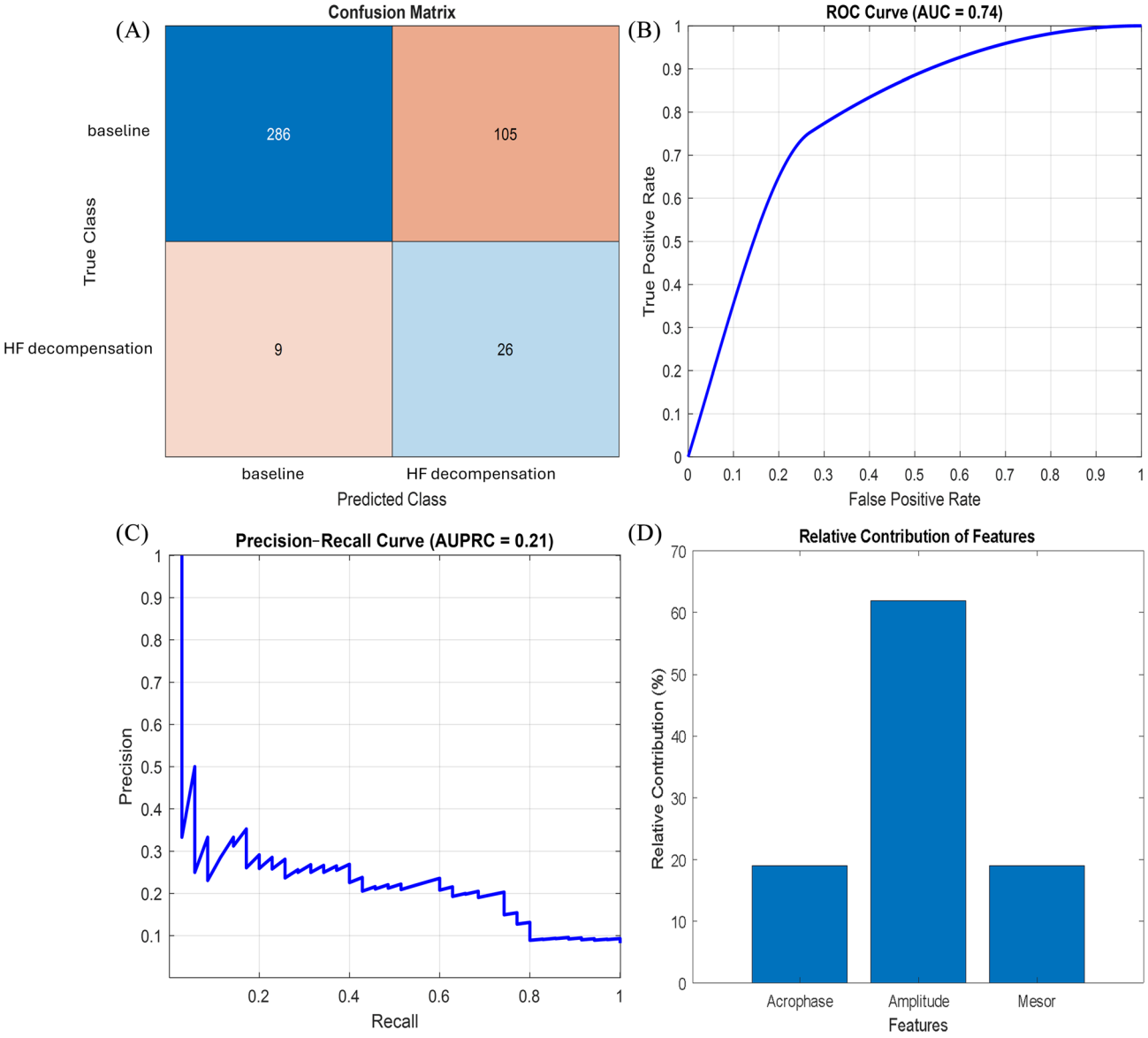
Discussion

Summary of the findings

This study demonstrated that HR-based circadian rhythm metrics amplitude, mesor, and acrophase exhibit measurable shifts in the final 3 weeks preceding ADHF and contain predictive information for decompensation. Temporal exclusion analysis showed that predictive patterns remained detectable even when using only data from 12 to 21 days prior to clinical deterioration, suggesting that circadian changes emerge well before overt clinical worsening.

The ML algorithm, trained on data from a wrist-worn device in a real-life setting, enabled earlier detection compared to standard non-invasive RPM, which typically identifies changes only a few days before hospitalization and has limited sensitivity to subtle variations.[4] The algorithm demonstrated moderate but clinically meaningful performance, achieving good sensitivity, specificity, NPV and high AUC, effectively distinguishing HF events from clinically

Figure 4 Algorithm performance and relative feature contributions. (A) Confusion matrix illustrating classification performance of the algorithm on the test data. (B) ROC analysis with AUC of 74%, supporting the model's ability to discriminate between HF events and clinically stable periods. (C) Precision–recall analysis yielding an AUPRC of 21%, compared with a baseline of 8.2%, indicating substantial improvement over random classification despite class imbalance. (D) Relative feature contributions show that the circadian parameters contributed to predicting HF events versus clinically stable periods with highest importance for the amplitude 62%, followed by the mesor 19% and the acrophase 19%.



stable periods. A higher tolerance for false alarms was accepted in the algorithm as avoiding missed detections was prioritized, given the high clinical risk associated with undetected HF deterioration, potentially hospitalization or death. Despite the class imbalance, precision–recall analysis confirmed that the algorithm's performance was substantially better than random classification. These results highlight that, while false positives remain a challenge, the model meaningfully identifies early signatures of decompensation. Future studies could mitigate false positives and potentially enhance the algorithm's performance by incorporating additional HF event data and broader physiological markers.

Results in context

The LINK-HF multicentre study was among the first to demonstrate the utility of a personalized ML algorithm for detecting ADHF, achieving a median prediction window 6 to 8 days

Table 2 Impact of removing days prior to ADHF on model performance

Removed days prior HF event	Sensitivity	Specificity	PPV	NPV	F1 score	AUC
0 (1st to 21st day prior ADHF)	**74%**	**73%**	**20%**	**97%**	**31%**	**74%**
1 (2nd to 21st day prior ADHF)	86%	66%	21%	98%	34%	76%
2 (3rd to 21st day prior ADHF)	81%	55%	20%	96%	32%	68%
3 (4th to 21st day prior ADHF)	82%	68%	27%	96%	41%	75%
4 (5th to 21st day prior ADHF)	80%	50%	20%	94%	30%	64%
5 (6th to 21st day prior ADHF)	79%	59%	24%	94%	37%	69%
6 (7th to 21st day prior ADHF)	70%	56%	24%	94%	36%	68%
7 (8th to 21st day prior ADHF)	93%	31%	21%	96%	34%	62%
8 (9th to 21st day prior ADHF)	89%	41%	20%	96%	33%	65%
9 (10th to 21st day prior ADHF)	72%	67%	30%	92%	42%	70%
10 (11th to 21st day prior ADHF)	83%	50%	27%	93%	40%	66%
11 (12th to 21st day prior ADHF)	75%	60%	32%	91%	45%	68%

ADHF, acute decompensated heart failure; AUC, area under the curve; NPV, negative predictive value; PPV, positive predictive value.

before hospitalization.[18] The study used data from a wearable patch sensor (Vital Connect, San Jose, CA) with incorporated metrics such as ECG waveforms, heart rate variability (HRV), respiratory rate, activity, posture and arrhythmia burden, yielding a sensitivity of 76%, specificity of 85% and an AUC of 89%.

Our study extended the prediction window to 21 days. Despite differences in prediction windows and feature sets, our approach achieved comparable predictive performance, with a sensitivity of 74%, specificity of 73% and an AUC of 74%. Notably, our metrics were slightly lower, but we used the LOOCV method to obtain a robust estimate of the effect. These findings demonstrate that extended time series data can support early detection of ADHF with accuracy comparable to that of more immediate prediction algorithms. While our approach does not directly outperform existing multi-parameter models, it offers a novel and complementary avenue by leveraging circadian HR dynamics derived from a single non-invasive wearable.

The SELENE-HF multicenter study further underscores the diversity of approaches for HF prediction. Their threshold-based algorithm, derived from implanted defibrillator data, predicted hospitalizations up to 42 days in advance.[19] Although this approach achieved earlier predictions, it had a lower sensitivity (66%) compared to our study (74%) and relied on invasive monitoring. Importantly, SELENE-HF demonstrated that HR-related metrics, such as 24 h HR (25% contribution), resting HR (20%) and HRV (13%), were the most predictive features for early detection of HF events, confirming the predictive value of HR-related parameters in this context.

Potential mechanisms of our findings

Circadian parameters demonstrated significant importance in the early prediction of ADHF. The HR changes within a 24 h cycle (amplitude), the most influential feature, declined prior to ADHF indicating diminished autonomic oscillations and heightened sympathetic dominance. Reduced amplitude is associated with suprachiasmatic nucleus (SCN) dysfunction, altered melatonin and cortisol levels, and a loss of nocturnal autonomic recovery.[20,21,22] This aligns with the absence of nocturnal blood pressure dips seen in most HF patients.[22,23] Interventions targeting circadian regulation, such as melatonin supplementation and morning cortisol mitigation, may help restore autonomic balance. These findings support incorporating amplitude into predictive algorithms to identify high-risk periods for proactive intervention.

Mesor, representing the average 24 h HR, emerged as another important predictor. An elevated mesor, observed before decompensation, reflects increased resting HR and reduced cardiac efficiency, hallmark signs of HF progression.[24] Elevated resting HR has been linked to worsening myocardial strain, reduced ejection fraction, and increased HF risk.[25] These findings position mesor as a critical marker for early detection of ADHF, emphasizing its role in identifying heightened physiological strain and impending cardiac dysfunction.

Acrophase represents the timing of peak HR within a circadian cycle. Shifts in acrophase timing were detected up to 3 weeks before HF events, suggesting disrupted circadian regulation. The SCN coordinates cardiac and autonomic functions via timing of neurohumoral signals like cortisol and melatonin.[9,21] Dysregulation in these rhythms is linked to adverse outcomes, including increased morning cardiovascular events and disrupted diurnal hormone patterns in HF.[20,22] Our findings highlight acrophase as an early marker of autonomic dysregulation, suggesting potential for chronotherapy and other interventions targeting circadian misalignment.

Future perspectives

Integrating circadian parameters into wearable monitoring systems could enable proactive management by alerting patients and clinicians to early signs of decompensation. However, wrist-worn sensors may not be suitable for all HF patients. For some, alternative solutions such as implantable devices, sensor-embedded patches or fabric-integrated systems may be more appropriate for continuous 24 h HR

monitoring.[26] Tailoring monitoring strategies to meet individual patient needs and preferences are essential for improving adherence.

Multimodal systems that integrate diverse physiological metrics offer promising solutions, as ADHF is often preceded by various physiological changes, such as shifts in filling pressure, autonomic function and fluid accumulation. In this study, we applied changes in circadian rhythm related to autonomic alterations. Other modalities provide complementary insights: kino- and seismography, measure changes in kinetic energy and chest vibrations generated by the heart muscle resulting from elevated filling pressures, respectively, while intrathoracic impedance-based methods quantify variations in pulmonary fluid status.[27] Speech analysis, enabling remote detection of phonation changes caused by fluid overload and increased filling pressure, shows promise as an assessment tool.[28] For instance, the Zoll HFMS patch-like device incorporates ECG electrodes, a radiofrequency sensor, and an accelerometer, enabling the simultaneous assessment of cardiac electrical activity, lung fluid status and physical activity.[29] Future research should focus on developing personalized, user-friendly sensors and rigorously evaluating their effectiveness across diverse patient populations and HF stages. Simultaneously, the combined predictive value of circadian heart rate parameters (mesor, amplitude and acrophase) and HRV should be evaluated further to improve the accuracy of heart failure deterioration prediction.

Strengths and limitations

A notable strength of this study was its focus on non-invasive, wearable monitoring of circadian markers in real-world settings, enhancing its clinical applicability. By applying cosinor modelling and averaging HR values to an hourly resolution, we visualized a clear periodic pattern without being overly sensitive to moment-to-moment variations, such as noise due to motion artefacts or poor sensor placement.

However, there were some limitations to our study. Firstly, circadian patterns can vary due to environmental or behavioural factors. Secondly, our dataset was unbalanced, with fewer HF events compared with clinically stable periods. While significant differences in age, HF phenotype (HFrEF), CKD and AF were observed between patients with and without HF events (*Table 1*), the relatively small number of HF events limited our ability to investigate whether these factors influenced HR circadian dynamics or model performance. Notably, both AF and CKD have previously been associated with disturbances in cardiac autonomic regulation, closely related to circadian rhythm, including reduced HRV, blunted diurnal HR fluctuations and elevated cardiovascular risk.[30,31] In particular, atrial fibrillation may attenuate circadian variation in ventricular rate due to irregular AV nodal conduction,[30] whereas CKD-related hyperphosphatemia has been linked to impaired HRV and increased blood pressure variability.[31]

Moreover, a significant portion of patient data was excluded from the final algorithm training. Twenty-four percent of the initial participants (21/86) data was lost, primarily due to non-wear periods related to anxiety, forgetfulness or patient behaviour. Moreover, we excluded time sequences potentially influenced by medication adjustments, hospitalization or emergency room visits to ensure clean and consistent input sequences for training the LSTM model on well-defined stable versus decompensated periods (see *Appendix C*). While data imputation methods could offer a future solution for recovering partial sequences, we opted not to apply them at this early modelling stage, as imputation within these small, fragmented time windows could introduce potential bias and compromise the temporal integrity needed for stable LSTM training.

Furthermore, the HF events included were heterogeneous, ranging from outpatient assessments to hospitalizations and sudden cardiac death. Due to the limited number of events, subgroup analyses by HF event type could not be performed.

As a result, our findings should be interpreted as preliminary, and further studies with larger, more balanced cohorts are needed to validate these results, assess generalizability beyond our patient population, and explore whether specific circadian changes differ across patient subgroups (e.g., comorbidities, age, sex and HF phenotype), HF event severity or stages of decompensation.

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V.v.E., M.v.L., and H.K. contributed to the concept and design of the study. M.v.L. and I.D.L. contributed to the acquisition of data. V.v.E. and M.v.L. drafted the manuscript. M.v.L. labelled the data and analysed the patient characteristics. V.v.E. analysed the PHB data and made the artificial neural network. All authors critically revised the manuscript. All gave final approval and agreed to be accountable for all aspects of the work ensuring integrity and accuracy.

Conflict of interest

The authors declare no conflict of interest.

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Appendix A: Detailed description of the inclusion and exclusion criteria

Inclusion criteria:

- Aged $\geq$ 18 years
- Diagnosed with congestive heart failure
- Hospitalised primarily for ADHF at the time of inclusion
- Sufficient digital literacy or caretaker with digital literacy
- Able to speak and read the Dutch language

Exclusion criteria:

- Unable to understand the purpose and procedures of the study
- Unable to walk a distance of 4 m independently (walking aids are allowed)
- Cardiac rehabilitation programme followed in the previous 12 months
- No internet connection
- Untreated life-threatening cardiac arrhythmias
- Early phase after acute coronary syndrome (latest 3 months)
- Uncontrolled hypertension
- Advanced atrioventricular block
- Severe aortic stenosis
- Upcoming major (cardiac) surgery in 3 months

Appendix B: Monitoring device Philips Health Band

The PHB is a CE-marked medical class IIa wrist-worn device used for continuous monitoring of physiological and movement parameters. The device includes a photoplethysmography (PPG) sensor, an altimeter, and a tri-axial accelerometer. HR was recorded through the PPG sensor at a sampling frequency of one data point per minute. The PHB transmitted data to the Philips Actigraphy Server System (PASS) via Bluetooth. The PASS, consisting of a mobile phone app and a Philips Health Suite data platform, allowed authorized clinicians and participants to view the data. The PHB was maintained with the latest firmware updates throughout the study.

Appendix C: Excluded timeseries

Control events (Type 1): Adjustments in HF disease-modifying agents including sacubitril/valsartan, beta-blockers, mineralocorticoid receptor antagonists (MRAs), and sodium-glucose cotransporter 2 inhibitors (SGLT2-i) (either increasing or reducing dose).

Control events (Type 2): hospitalization for non-HF reasons, or non-HF-related emergency room visits.

Appendix D: Data preprocessing and cosinor modelling

Data marked as 'off-wrist' by the PHB's algorithms were excluded from the analysis. Additionally, data points showing an HR of 0 b.p.m. were removed to eliminate artefacts. To capture the 24 h cycle, the HR data were averaged to an hourly resolution. Using this strategy, a clear periodic pattern could be visualized without being overly sensitive to moment-to-moment variations like noise and small fluctuations due to e.g. motion artefacts or bad sensor placement.[16]

The GZLM-gamma cosinor model was applied using the equation[13]:

$$Y(\tau) = M + \beta 1 * cos\left(2\pi\frac{\tau}{24}\right) + \beta 2 * sin\left(2\pi\frac{\tau}{24}\right)$$

with

$$\beta 1 = \mathrm{A} * \cos(\phi)$$

and

$$\beta 2 = \mathrm{A} * \sin(\phi)$$

In this equation, $Y(\tau)$ represents the modelled HR at time τ over the 24 h period. M is the mesor representing the rhythm-adjusted mean of the HR. The acrophase ϕ reveals the timing of the overall high HR values recurring in each cycle, and A represents the curve amplitude which is a measure of half the extent of predictable HR variation within a cycle.[13] 21-day sequences of these cosinor-derived parameters (mesor, amplitude and acrophase) were subsequently used as inputs for model training.

Appendix E: Model training

A recurrent neural network architecture was implemented using an LSTM network to account for temporal dependencies in the extracted circadian HR features. Model training was performed using a LOOCV approach, where in each fold the data from one participant were held out as test data, and the remaining participants were used for training.

The following training parameters were applied for each LOOCV iteration:

- Optimizer: Adam
- Max Epochs: 100
- Mini-Batch Size: 32
- Initial Learning Rate: 0.01
- Gradient Threshold: 1.0
- Validation frequency: every 5 iterations

Training loss, validation accuracy, and model convergence were continuously monitored to prevent overfitting. The LOOCV procedure ensured that model performance was evaluated independently for each individual, enhancing generalizability despite the relatively small sample size.

The core steps of data preprocessing, feature extraction, and model training are fully detailed in *Appendices D* and *E*. All analyses were conducted using a custom in-house MATLAB pipeline.

Due to privacy regulations and institutional data protection policies, the raw patient data cannot be shared outside the secured hospital environment. Since the algorithms rely on protected clinical datasets for input, full executable code cannot be made openly available. However, we are committed to supporting reproducibility: interested researchers are welcome to contact the authors for technical clarification, pseudocode or methodological details, provided that appropriate data governance agreements are in place.

Appendix F: Detailed subdivision of reasons for exclusion of patient's data

The exclusion of 21 (24%) patients' data was due to insufficient data days. A subdivision of reasons for this exclusion was because of

- Experiencing discomfort wearing or not wanting to wear the wrist-worn device (n = 6),
- Personal circumstances (n = 7),
- Occurrence of an adverse event during the 21-day window making it no longer possible to cleanly label it as clinically stable or HF event (n = 8).