

Prediction of vasovagal syncope using artificial intelligence-enabled smartwatch photoplethysmography-derived heart rate variability

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Aims	Vasovagal syncope (VVS) can cause injury and impaired quality of life, and effective prevention requires timely warning before loss of consciousness. To evaluate whether smartwatch photoplethysmography (PPG)-derived heart rate variability (HRV) can predict VVS before symptom onset, and to identify an optimal observation window and lead time.
Methods and results	We prospectively enrolled 132 patients with suspected neurally mediated syncope who underwent head-up tilt (HUT) testing while wearing a wrist-worn Samsung Galaxy Watch 6 for continuous multiwavelength PPG acquisition (25 Hz). The HRV features ($n = 107$) were extracted. An Extra Trees classifier (600 trees) was trained using an 80/20 subject-level split and evaluated on a hold-out test set. Model performance was assessed using AUROC and threshold metrics, including specificity, at a fixed sensitivity of 0.90. Sixty-three participants were HUT-positive, and 69 were HUT-negative. The 5-min presyncope window achieved the highest discrimination (AUROC, 0.91; 95% CI 0.77–1.00). At 90% sensitivity, specificity was 0.64 (95% CI 0.40–0.85). Using a fixed 5-min window, early prediction remained robust at a 5-min lead time (AUROC 0.91; 95% CI 0.76–1.00; accuracy 84.6%; 95% CI 0.65–0.92). The most informative predictors included nonlinear complexity metrics (approximate entropy and composite multiscale entropy) and autonomic balance indices (normalized low-frequency, log-transformed high-frequency, and the cardiac vagal index).
Conclusion	Artificial intelligence-enabled analysis of smartwatch PPG-derived HRV can prospectively predict VVS during HUT using a short 5-min observation window while maintaining clinically meaningful performance at a 5-min lead time, supporting the feasibility of wearable, real-time warning systems.

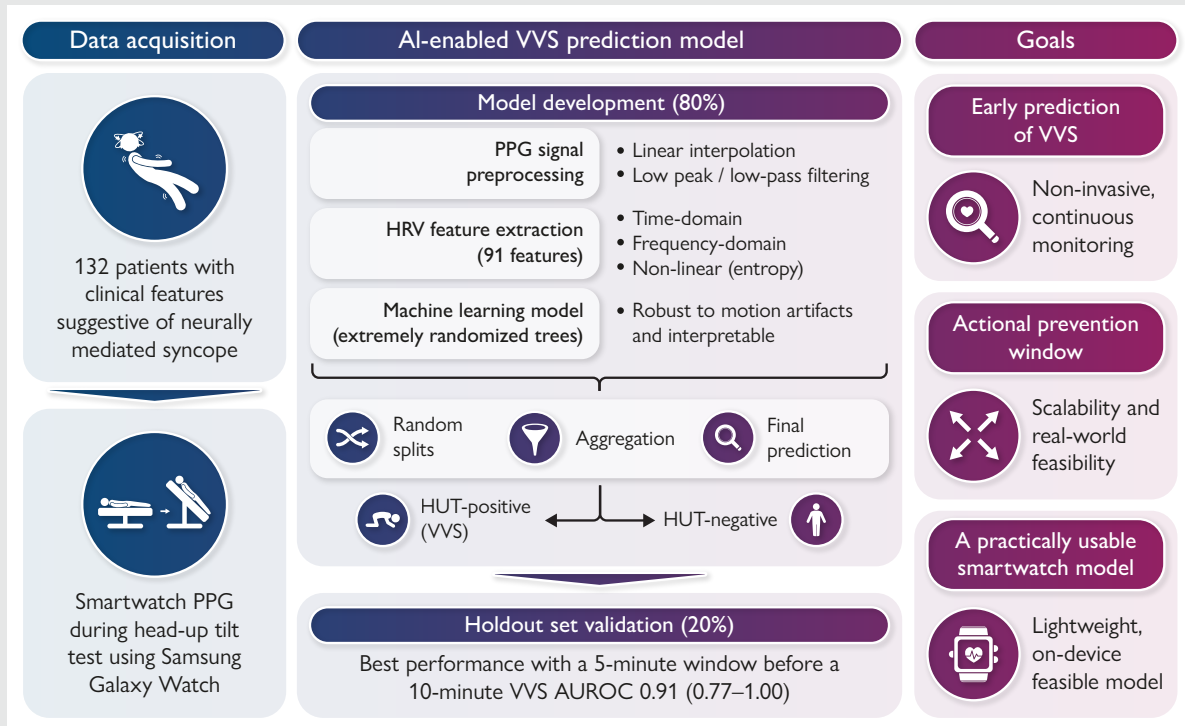
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Graphical Abstract



Keywords Vasovagal syncope • Photoplethysmography • Smartwatch • Heart rate variability • Prediction algorithm • Artificial intelligence

Introduction

Vasovagal syncope (VVS) is a subtype of neurally mediated reflex syncope characterized by transient loss of consciousness resulting from an abrupt decline in blood pressure and a concomitant decrease in heart rate.^{1,2} Although generally considered benign, VVS can substantially impair the quality of life and may even precipitate post-traumatic stress disorder.^{3,4} It also poses a significant risk of injury, including falls and intracranial haemorrhage, particularly in older adults without prodromal symptoms and individuals in safety-critical occupations.^{5,6} Despite the availability of non-pharmacological preventive strategies such as increased fluid and salt intake, physical counterpressure manoeuvres, and the use of compression stockings, the two-year recurrence rate approaches 50%, underscoring the need for early prediction and prevention before syncope occurs.^{1,2}

Although the pathophysiological mechanisms of VVS are not fully understood, it is thought to be characterized by autonomic dysregulation, an initial surge in sympathetic activity, followed by a vagally mediated increase in parasympathetic activity, and subsequent sympathetic withdrawal.⁷ This rapid autonomic dysregulation is reflected in short-term fluctuations of heart rate variability (HRV).^{8,9} Continuous, non-invasive tracking of HRV could therefore enable early warning of impending VVS, motivating the use of peripheral optical signals obtained from wearable sensors.^{10,11}

Photoplethysmography (PPG) is an optical technique that measures the pulsatile blood volume signal generated when arterial pressure waves propagate through the peripheral vasculature. The resulting waveform encodes rich information about cardiac activity, overall cardiovascular status, and interactions between the parasympathetic and sympathetic nervous systems, enabling estimation of oxygen saturation, heart rate and HRV, blood pressure, and cardiac output.¹² Because it is low-cost and non-invasive, PPG has been widely used as an ambulatory diagnostic and monitoring tool in wearable devices, such as smartwatches. However, despite the widespread availability of smartwatch PPG sensors capable of continuous HRV tracking, no study has prospectively evaluated whether PPG-derived HRV can predict VVS. Therefore, the objectives of this study were to evaluate whether PPG-derived HRV can predict VVS before symptom onset and to determine the optimal window duration, earliest feasible lead time, and most informative wavelength channel.

Methods

Study population

We prospectively enrolled 132 patients with clinical features suggestive of neurally mediated syncope between March 2023 and July 2025 and performed head-up tilt testing (HUT) as part of a standardized evaluation protocol. All participants underwent baseline

medical evaluations in accordance with the European Society of Cardiology guidelines.¹ Patients were excluded if they had contraindications to HUT (e.g. significant carotid/cerebrovascular stenosis, unstable or significant coronary artery disease, obstructive hypertrophic cardiomyopathy, severe valvular stenosis, severe anaemia, or other clinically unstable conditions), if syncope was attributed to an alternative aetiology (e.g. arrhythmic, structural cardiopulmonary, or neurological causes), or if they were pregnant or unable to provide informed consent. Medications with potential autonomic effects, such as beta-blockers, were withheld for at least five half-lives before HUT. During HUT, each participant wore a wrist-worn Samsung Galaxy Watch 6® (Samsung Electronics Co., Ltd., Suwon, Republic of Korea) to enable continuous PPG acquisition. This study was approved by the Institutional Review Board of the Chung-Ang University Gwangmyeong Hospital (IRB No. 2207-015-019) and complied with the principles of the Declaration of Helsinki.

Head-up tilt test

HUT testing was performed in a quiet, distraction-free laboratory following the Italian protocol.^{1,13} An electrically actuated tilt table with a footplate was used. After 20 min of supine rest with continuous blood pressure and electrocardiographic monitoring, the participants were tilted to 60° for 20 min. If syncope did not occur, 300 µg of sublingual nitroglycerin spray was administered, and the 60° tilt was maintained for an additional 20 min unless syncope developed during this provocation phase. The test was considered complete when syncope occurred, prompting immediate return to the supine position, or when the provocation phase ended without symptoms. Haemodynamic responses were classified according to the VASIS criteria.¹⁴ Based on the HUT results, participants were categorized as HUT-positive, defined as those who developed syncope during testing, or HUT-negative, defined as those without syncope.

Data acquisition and signal preprocessing

During HUT, continuous PPG signals were recorded at a sampling rate of 25 Hz using a wrist-worn Samsung Galaxy Watch 6 equipped with a multi-wavelength optical sensor. The device provides infrared and green reflective channels, as well as motion compensation channels, and each wavelength was analysed independently. Given the susceptibility of PPG signals to motion artefacts and signal dropout, a standardized preprocessing and quality control pipeline was used to ensure signal integrity. This process included artefact correction, low-pass filtering, and rigorous peak detection to exclude unreliable segments. Peak detection and HRV feature extraction were performed using NeuroKit2 (version 0.2.12), a validated open-source toolbox for physiological signal processing.¹⁵ Systolic peaks were identified using an Elgendi-based approach.¹⁶ The PPG signal was first cleaned using a second-order Butterworth band-pass filter (0.5–8 Hz) to suppress baseline drift and high-frequency noise. Candidate beats were detected using moving-average-based adaptive thresholding with a minimum inter-peak distance of 0.3 s to reduce spurious detections. Detailed procedures for signal acquisition and preprocessing are provided in [Supplementary material online, Method S1](#).

HRV feature extraction

Heart rate variability (HRV) analysis was performed on preprocessed PPG signals in accordance with established guidelines. The extracted features included the time, frequency, and nonlinear-domain metrics. For data segmentation, PPG segments from the 10-minute interval immediately preceding syncope were analysed for the HUT-positive group, whereas a physiologically stable 10-min segment from the pre-provocation phase was selected for the HUT-negative group. Inter-beat intervals (IBIs) were computed from valid signal segments, followed by spectral analysis and normalisation.

IBIs were calculated as successive differences between detected peak times and expressed in milliseconds. For each subject, the

power spectrum was computed using the complete IBI series available within the selected analysis window. Segments containing fewer than 10 detected peaks were excluded to avoid unstable HRV estimates.

Frequency-domain HRV features were derived using Welch's periodogram method for power spectral density (PSD) estimation.¹⁷ The unevenly sampled IBI series was interpolated to a uniformly sampled time series at 100 Hz prior to spectral analysis, following the NeuroKit2 default workflow.¹⁸ No explicit detrending beyond constant-mean removal was applied before PSD estimation.

In total, 107 HRV features were extracted, and their full list is provided in the [Supplementary material online, Table S1](#). Specific extraction methodologies are detailed in [Supplementary material online, Method S2](#).

Modelling strategy and configuration

To evaluate the clinical feasibility of VVS detection using wearable PPG signals, we selected the Extra Trees classifier as the representative model. This model was chosen because it is robust to noise and offers a relatively high degree of interpretability, both of which are important when analysing physiological data obtained from ambulatory wearable devices.^{19–21} In addition, its ensemble structure is well-suited for handling a large number of correlated HRV features relative to the available sample size, reducing the risk of overfitting in high-dimensional settings. We used a standard Extra Trees configuration with 600 trees and default splitting rules. Among the available PPG channels, the infrared channel was selected for model development because it showed the most stable and discriminative performance in the preliminary analyses (see [Supplementary material online, Table S2](#)).

The dataset was randomly divided into a training set comprising 80% of the data and a hold-out test set comprising the remaining 20%. All splits were performed strictly at the subject level, and no data from the same individual appeared in either the training or test sets, ensuring the absence of subject-level data leakage even when multiple windows were analysed. The model was trained using the training set, and its performance was evaluated only on the holdout test set to ensure generalisability and prevent data leakage. Performance was assessed using the area under the receiver operating characteristic curve (AUROC), accuracy, sensitivity, specificity, and the F1-score.

To characterize the temporal dynamics of VVS-related autonomic changes, HRV features were compared across different observation window lengths. All window duration analyses were anchored to the 5-min presyncope interval, within which windows of 5, 10, 15, and 20 min were evaluated. Once the window-duration analysis determined the most informative interval, the same window length was held constant for subsequent offset analyses, in which the window was shifted to lead times of 5, 10, 15, and 20 min before syncope onset. Together, these analyses enabled a systematic assessment of the influence of the observation duration and prediction horizon on discriminative performance.

Statistical analysis

Continuous variables are summarized as mean values with their corresponding standard deviations, whereas categorical variables are expressed as counts and percentages. The principal metric used to assess model performance was AUROC. Sensitivity was calculated as the proportion of true positives relative to all individuals with the condition, and specificity was calculated as the proportion of true negatives among all individuals without the condition. Additionally, to evaluate model performance at a clinically meaningful decision threshold, we fixed the sensitivity at 90% for each model. For each model, the probability-score cutoff corresponding to 0.90 sensitivity was determined using the training set and applied unchanged to the held-out test set, and the corresponding specificity was then reported.²²

To better understand which variables contributed the most to the classifier and provide interpretability of the model's behaviour, we incorporated two analytic perspectives. First, we derived feature

importance rankings based on the decrease in aggregated impurity across the 600 decision trees comprising the Extra Trees ensemble, focusing on the 20 most influential features. Second, we generated SHAP (Shapley Additive ExPlanations) visualisations to illustrate how increases or decreases in individual feature values shift the output of the model. In the SHAP summary plot, red markers denote higher feature values and blue markers denote lower values; points on the negative SHAP axis indicate a suppressive effect on the predicted risk, whereas points on the positive axis reflect an amplifying effect.

All statistical analyses were performed using Python (version 3.7.0) and R (version 4.2.2).

Results

Baseline characteristics

A total of 132 patients were included in the analysis: 63 (47.7%) in the HUT-positive group and 69 (52.3%) in the HUT-negative group. The baseline characteristics are summarized in [Table 1](#). No statistically significant differences were observed between the two groups regarding age (49.6 ± 19.0 vs. 49.6 ± 19.1 years, $P = 0.989$), sex (44.4% vs. 56.5% male, $P = 0.140$), baseline heart rate (66.0 vs. 68.3 bpm, $P = 0.218$), systolic blood pressure (123.9 vs. 129.0 mmHg, $P = 0.106$), or diastolic blood pressure (75.0 vs. 76.5 mmHg, $P = 0.526$).

HUT test characteristics

Among the 63 HUT-positive participants, 16 developed syncope during the passive phase and 47 during the nitroglycerin provocation phase. The overall mean time from HUT initiation to syncope was 42.77 ± 11.25 min. The mean time to syncope during the passive phase was 25.06 ± 7.62 min, whereas syncope during the nitroglycerin provocation phase occurred at a mean time of 48.81 ± 2.32 min.

Prediction performance by window duration

The relationship between the observation window length and the delineation of autonomic patterns associated with VVS is summarized in [Table 2](#) and [Figure 1](#). The 5-min interval provided the clearest separation between HUT-positive and HUT-negative responses, yielding the highest discrimination (AUROC 0.91, 95% CI 0.77–1.00). As the observation window extended, this discriminatory capacity progressively diminished. These findings suggest that acute autonomic perturbations preceding VVS are most prominently captured within short time intervals, whereas longer windows may obscure these transient physiological signals due to increased baseline variability. This indicates that longer windows may attenuate the transient presyncopal autonomic signals by incorporating greater baseline variability.

When sensitivity was fixed at 0.90 to evaluate threshold-based clinical performance, the 5- and 10-min windows demonstrated the highest corresponding specificity (0.64, 95% CI 0.40–0.85 for both windows), whereas longer windows showed noticeably reduced specificity ([Table 3](#)). This sensitivity-focused operating point was used to minimize missed syncopal events.

Early prediction performance (offset analysis)

Based on the window-duration analysis, which identified the 5-min interval as providing the strongest discriminatory capability, early prediction analyses were conducted using a fixed 5-min window ([Table 4](#) and [Figure 2](#)). This window was systematically shifted to lead times of 5, 10, 15, and 20 min before syncope onset to evaluate prediction feasibility at progressively earlier

stages. As expected, the discriminatory performance was the highest when the window was positioned close to the syncopal event. The model maintained robust accuracy at the 5-min offset, achieving an AUROC of 0.91 (95% CI 0.76–1.00) and an accuracy of 84.6% (95% CI 0.65–0.92), indicating that the device provides a clinically meaningful therapeutic window for preventive intervention. Performance naturally diminished at earlier offsets, such as beyond 10 min prior to onset.

Feature importance and physiological interpretation

Several interpretative analyses were performed to clarify the physiological factors contributing to model predictions. The feature importance analysis ([Figure 3](#)) demonstrated that nonlinear complexity metrics, such as approximate entropy (HRV_ApEn) and composite multiscale entropy (HRV_CMSEn), were the most discriminative features. Autonomic indices reflecting sympathovagal balance, including normalized low frequency (HRV_LFn), log-transformed high frequency (HRV_LnHF), and the cardiac vagal index (HRV_CVI), also played substantial roles in the decision-making process of the model.

The SHAP summary plot ([Figure 4](#)) further illustrates the direction and magnitude of the contribution of each feature and reveals several distinct physiological patterns. First, both HRV_ApEn and HRV_CMSEn showed negative associations with syncope risk. Lower entropy values, indicative of a more rigid and periodic heart rate pattern, were linked to a higher likelihood of VVS. Second, HRV_LFn, a marker of sympathetic modulation, also exhibited a negative association, reflecting the withdrawal of sympathetic tone before syncopal events. Finally, a divergence emerged between the linear and nonlinear parasympathetic markers; while HRV_LnHF displayed a negative association, the nonlinear index HRV_CVI demonstrated a strong positive association. This pattern suggests that, even when the overall parasympathetic spectral power is reduced, acute vagal surges may still occur and be effectively captured by the model.

Discussion

The present study provides prospective evidence that HRV features derived from smartwatch PPG can discriminate impending VVS during the HUT test. Among 132 participants with comparable baseline characteristics, an artificial intelligence (AI)-enabled machine learning approach using PPG-derived HRV demonstrated strong discriminatory performance, with optimal results obtained when features were extracted from a short pre-syncope observation window. Specifically, the 5-minute window achieved the highest AUROC of 0.911. These findings suggest that abrupt and transient autonomic perturbations immediately preceding VVS can be captured non-invasively using smartwatch-based PPG signals.

Blood volume redistribution and venous pooling leading to central hypovolaemia are central mechanisms in VVS and have motivated both non-pharmacological and pharmacological preventive strategies. Common non-pharmacological approaches, such as increased fluid and salt intake and physical counter-pressure manoeuvres, are widely recommended but have shown inconsistent effectiveness. Even targeted interventions, such as thigh-length compression stockings, have failed to reduce VVS recurrence.²³ Pharmacological therapies, including fludrocortisone and midodrine, have likewise demonstrated limited benefit in randomized trials, with no consistent reduction in

Table 1 Baseline characteristics of the study population

	Total (n = 132)	HUT-positive (n = 63)	HUT-negative (n = 69)	P-value
Age, years	49.6 ± 18.9	49.6 ± 19.0	49.6 ± 19.1	0.989
Male (%)	67 (50.8%)	28 (44.4%)	39 (56.5%)	0.140
Heart Rate (BPM)	67.2 ± 10.9	66.0 ± 10.8	68.3 ± 10.9	0.218
SBP (mmHg)	126.6 ± 18.2	123.9 ± 14.6	129.0 ± 17.5	0.106
DBP (mmHg)	75.8 ± 13.1	75.0 ± 11.4	76.5 ± 14.6	0.526

HUT, head-up tilt testing; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 2 Diagnostic performance across different observation windows (cutoff = 0.5)

Window	AUROC (95% CI)	Accuracy (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	F1-score (95% CI)
5 min	0.91 (0.77–1.00)	0.81 (0.65–0.92)	0.75 (0.50–1.00)	0.86 (0.64–1.00)	0.78 (0.53–0.93)
10 min	0.88 (0.70–1.00)	0.85 (0.69–0.96)	0.75 (0.50–1.00)	0.93 (0.75–1.00)	0.82 (0.60–0.96)
15 min	0.83 (0.66–0.97)	0.81 (0.65–0.92)	0.66 (0.38–0.92)	0.93 (0.75–1.00)	0.76 (0.50–0.93)
20 min	0.81 (0.62–0.96)	0.74 (0.56–0.89)	0.69 (0.40–0.92)	0.79 (0.56–1.00)	0.72 (0.46–0.89)

Performance metrics were calculated using the hold-out test set. All observation windows were anchored to the 10-minute presyncope interval in the HUT-positive group, and time-matched physiologically stable intervals were used for the HUT-negative group.
AUROC, area under the receiver operating characteristic curve; HUT, head-up tilt; min, minutes.

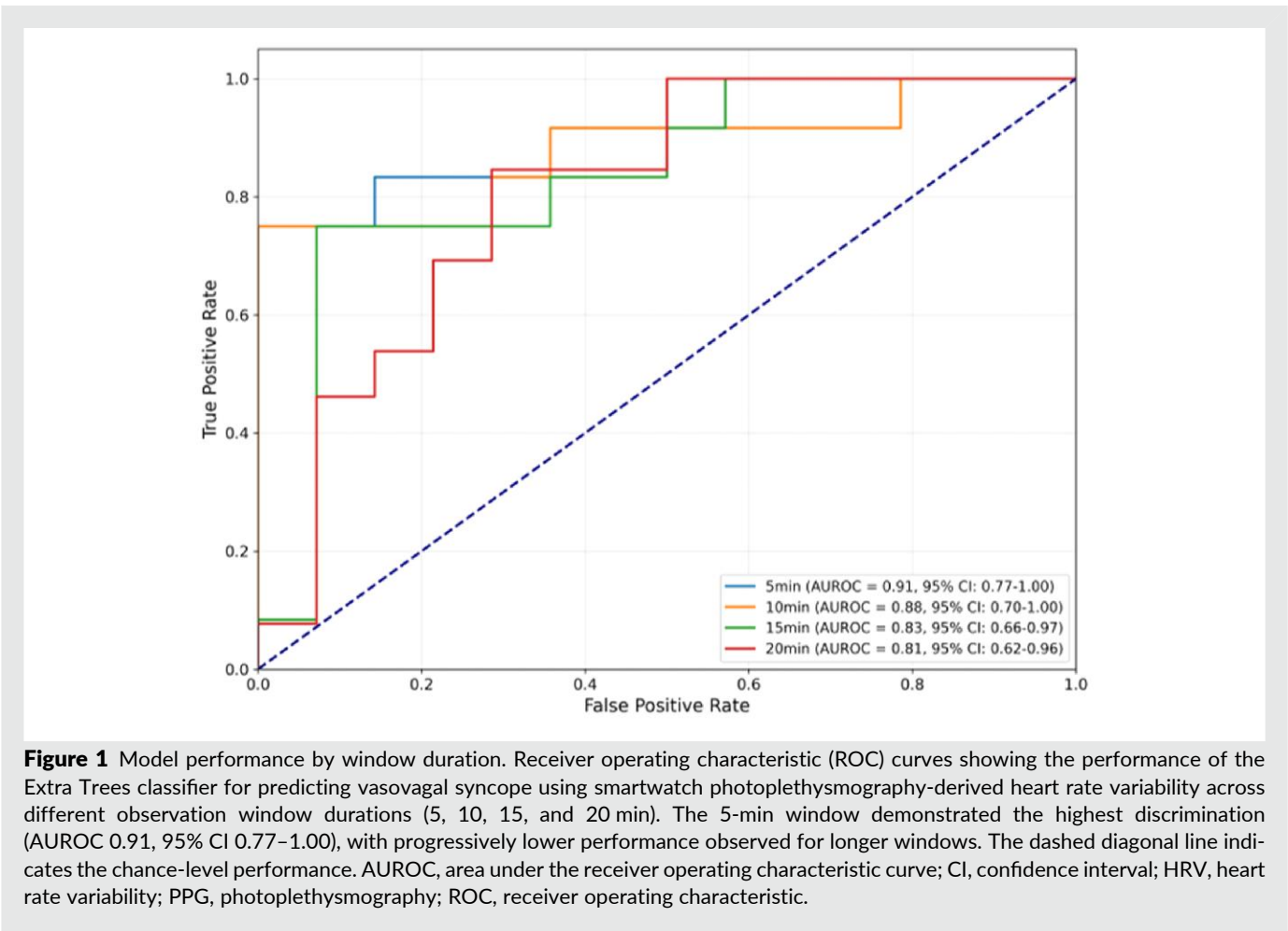


Table 3 Diagnostic performance across different observation windows

Window	AUROC	Accuracy	Sensitivity	Specificity	Cutoff (at sensitivity =0.9)
5 min	0.91	0.77	0.90	0.64	0.37
10 min	0.88	0.73	0.90	0.64	0.31
15 min	0.83	0.69	0.90	0.50	0.13
20 min	0.81	0.70	0.90	0.50	0.19

Performance metrics were calculated using the hold-out test set. All observation windows were anchored to the 10-minute presyncope interval in the HUT-positive group, and time-matched physiologically stable intervals were used for the HUT-negative group. AUROC, area under the receiver operating characteristic curve; HUT, head-up tilt; min, minutes.

Table 4 Diagnostic performance across different offset intervals before syncope onset

Offset	AUROC (95% CI)	Accuracy (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	F1-score
5 min	0.91 (0.76–1.00)	0.81 (0.65–0.92)	0.75 (0.50–1.00)	0.86 (0.64–1.00)	0.78 (0.54–0.93)
10 min	0.81 (0.59–0.98)	0.84 (0.69–0.96)	0.67 (0.39–0.92)	1.00 (1.00–1.00)	0.80 (0.57–0.95)
15 min	0.79 (0.56–0.96)	0.77 (0.62–0.92)	0.58 (0.30–0.87)	0.93 (0.77–1.00)	0.70 (0.42–0.90)
20 min	0.81 (0.62–0.97)	0.81 (0.65–0.92)	0.84 (0.62–1.00)	0.77 (0.53–1.00)	0.81 (0.63–0.94)

Performance metrics were calculated using the hold-out test set. For offset analyses, the observation window was fixed at the optimal duration identified in the window-length evaluation and was shifted to lead times of 5, 10, 15, and 20 min prior to syncope onset in the HUT-positive group. AUROC, area under the receiver operating characteristic curve; HUT, head-up tilt; min, minutes.

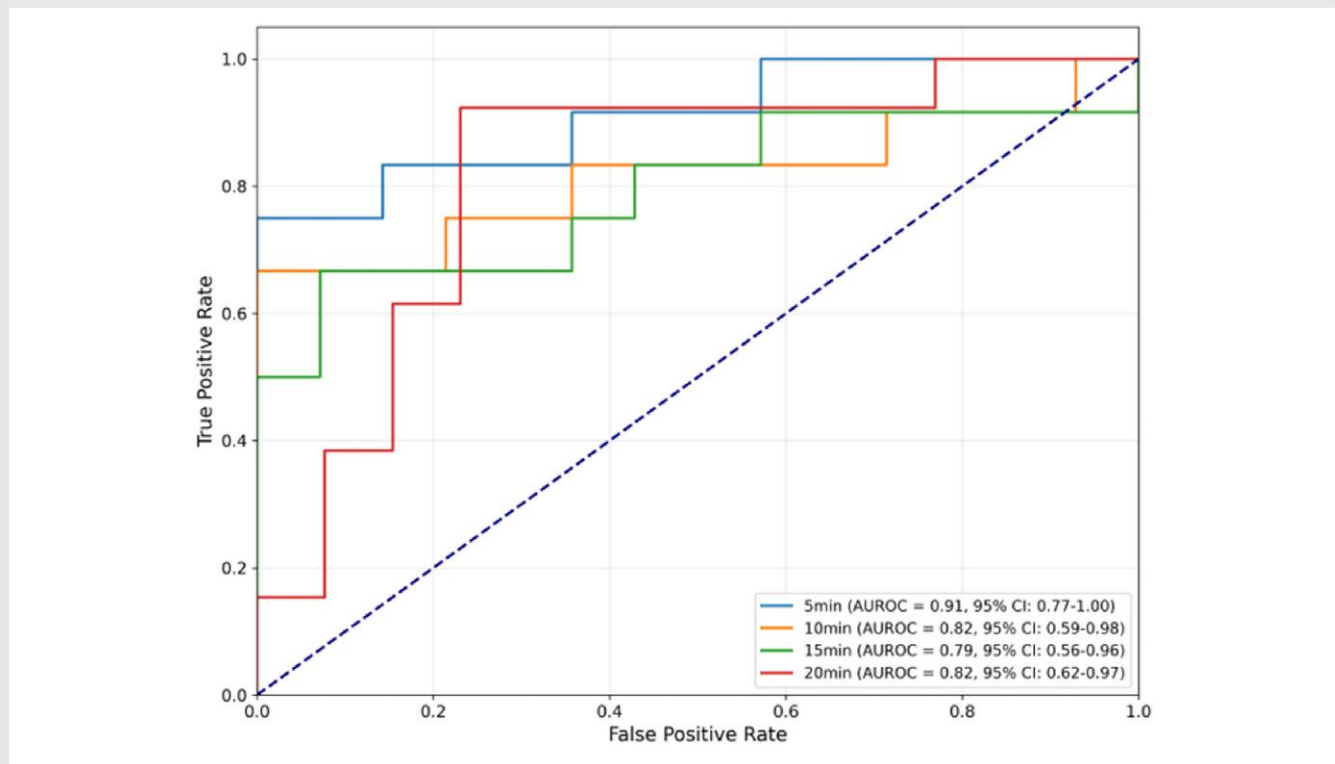


Figure 2 Model performance by offset. Receiver operating characteristic (ROC) curves showing the performance of the Extra Trees classifier in predicting vasovagal syncope at different lead times before syncope onset using a fixed 5-minute observation window. Discriminative performance was highest when the window was positioned closest to the event (5-min offset; AUROC 0.91, 95% CI 0.77–1.00) and declined progressively at earlier offsets. The dashed diagonal line indicates the chance-level performance. AUROC, area under the receiver operating characteristic curve; CI, confidence interval; ROC, receiver operating characteristic.

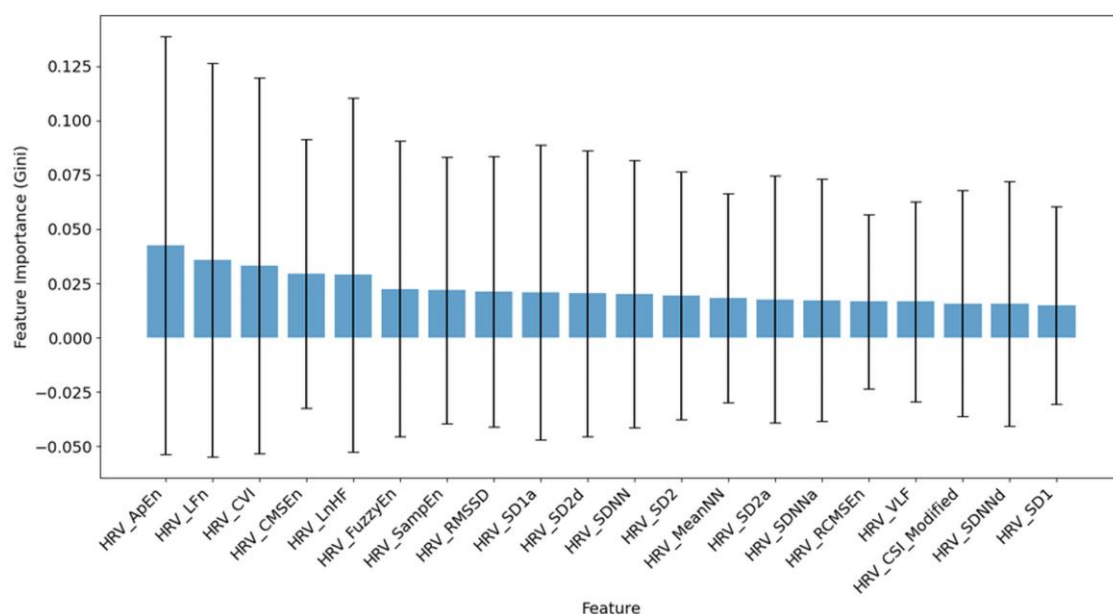


Figure 3 Top 20 feature importance across 600 trees in the extra trees (extremely randomized trees) model. Bar plot showing the 20 most important heart rate variability features contributing to the Extra Trees classifier for vasovagal syncope prediction. Feature importance was calculated as the mean decrease in Gini impurity across 600 trees, with error bars indicating standard deviation. Nonlinear complexity measures (e.g. Approximate Entropy and Composite Multiscale Entropy) and autonomic balance indices (e.g. normalized low-frequency power and Cardiac Vagal Index) are among the most influential features. Definitions of all HRV features and abbreviations are provided in the [Supplementary material online, Table S1](#).

syncope recurrence and concerns regarding tolerability and adherence.^{19,24} As a result, despite multiple available interventions, the two-year recurrence rate of VVS remains as high as 50%. This persistent disease burden underscores the need for approaches that enable the early identification of impending VVS episodes, rather than relying solely on reactive or partially effective preventive therapies.

From a clinical translation standpoint, a key goal of any warning system is to provide sufficient lead time for preventive action. In offset analyses using a fixed 5-min window, discrimination was the highest when the window was positioned close to the syncopal event, and performance decreased at earlier lead times. Notably, the model maintained robust performance at a 5-min lead time (AUROC 0.911; accuracy 84.6%), indicating a potentially meaningful 'therapeutic window during which patients could adopt countermeasures (e.g. physical counter-pressure manoeuvres, sitting or lying down, and hydration)' to avert syncope and reduce fall-related injuries. This feature is particularly valuable for older adults with minimal prodromal symptoms and for individuals in safety-critical occupations. In addition, when sensitivity was fixed at 0.90, the model retained a specificity of 0.64 for the 5-min window, representing a clinically acceptable and deployable operating point that prioritizes safety while limiting excessive false alerts.²⁵ However, in real-world clinical deployment, the key question may not be how early syncope can be predicted, but whether imminent syncope within a very short time horizon, such as within the next minute, can be reliably distinguished. In the present study, we focused on identifying a clinically actionable therapeutic window that allows patients to implement preventive countermeasures. The robust performance observed at a 5-minute lead time aligns

with this practical objective. Future studies using larger datasets should further evaluate ultra-short horizon prediction within individuals to refine real-time warning strategies. The relatively small number of cases in the non-nitroglycerin and nitroglycerin phases ($n = 16$ and $n = 47$, respectively) limited our ability to perform a robust subgroup analysis. As such, the impact of protocol phase-specific effects could not be definitively assessed and warrants further investigation in larger cohorts.

To facilitate interpretability and align predictions with a plausible physiology, we examined feature importance and SHAP explanations. Unlike ECG-derived HRV, PPG-derived pulse interval variability reflects not only cardiac autonomic modulation but also peripheral vascular influences, including pulse transit time and vasomotor tone.²⁶ Therefore, PPG-based indices should be interpreted as composite signals integrating both cardiac and vascular dynamics rather than as direct surrogates of cardiac autonomic activity. VVS is characterized by autonomic instability, progressing from an initial surge in sympathetic activity to a vagally mediated increase in parasympathetic tone, followed by relative sympathetic withdrawal.⁷ HRV analysis is a well-established method for assessing dynamic changes in autonomic modulation of cardiovascular function and has been combined with HUT testing to elucidate the mechanisms of syncope development and to predict HUT outcomes. In previous studies, the reported association with syncope varied substantially depending on the HRV parameters employed. In a previous study, an algorithm based on spectral analysis of heart rate and systolic blood pressure variability achieved a sensitivity of 95% and a specificity of 93% for predicting VVS in 1150 patients undergoing HUT, with an average prediction time of 128 ± 206 s and a median of 59 s.¹¹ In addition, our group predicted VVS using ECG-derived HRV alone,

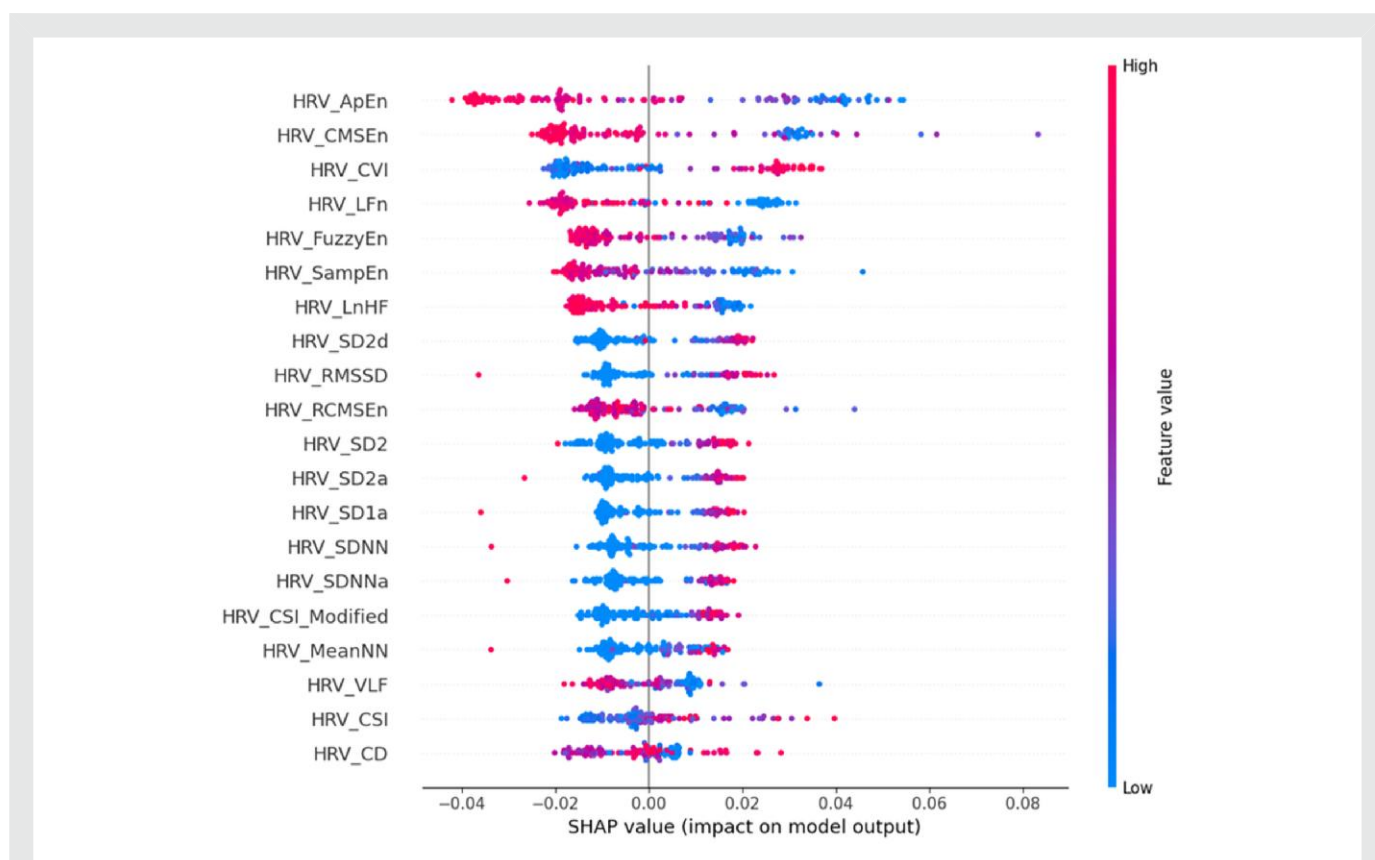


Figure 4 Shapley additive ExPlanations (SHAP) summary of the model. The red points (feature value) in the negative SHAP value indicate a negative correlation, and those in the positive SHAP values indicate a positive correlation. The blue points do the opposite. SHAP summary plot illustrating the global contribution of heart rate variability features to the Extra Trees model for vasovagal syncope prediction. Each point represents an individual observation, with the x-axis indicating the SHAP value (impact on the model output). Red points denote higher feature values, and blue points denote lower feature values. Positive SHAP values indicate an increased predicted risk of syncope, while negative SHAP values indicate decreased predicted risk. Feature definitions and abbreviations are listed in [Supplementary material online, Table S1](#). HRV, heart rate variability.

yielding an AUC of 0.801 and could predict syncope events approximately 3 min before their occurrence.¹⁰ Notably, these prior approaches primarily focused on short-term haemodynamic or electrophysiological changes immediately preceding syncope. Although most previous studies were ECG-based or described haemodynamic changes during HUT retrospectively, to the best of our knowledge, the present study is the first to prospectively predict VVS using PPG-derived HRV. This emphasis on short-term autonomic dynamics is aligned with earlier investigations that analysed time-variant HRV changes in the minutes immediately preceding tilt-induced syncope. Prior studies have demonstrated that transient and abrupt autonomic shifts occurring shortly before syncope can provide meaningful predictive information, and subsequent work conducted under tightly controlled experimental conditions has similarly underscored the importance of focusing on the presyncopal phase to capture rapid autonomic perturbations.^{27,28} The present study extends these observations by demonstrating that such short-term autonomic dynamics can be prospectively captured using wearable PPG signals in a clinically relevant cohort.

Importantly, our interpretability analyses highlighted that nonlinear complexity metrics (e.g. approximate entropy and composite multiscale entropy) were among the most discriminative predictors, and lower entropy values were associated with a

higher VVS risk. This pattern is consistent with a loss of dynamic complexity and a more rigid, periodic heart rhythm pattern preceding syncope, reflecting reduced autonomic adaptability during impending reflex decompensation.²⁹ Autonomic balance indices (e.g. normalized LF and parasympathetic markers) also contributed substantially, supporting the concept that sympathetic withdrawal and altered parasympathetic dynamics occur near the event. The divergence between linear spectral markers and nonlinear vagal indices observed in the SHAP patterns suggests that brief nonstationary vagal surges or complex autonomic transitions are better captured by nonlinear HRV measures than by conventional power spectra alone. These findings suggest that the loss of autonomic complexity, rather than absolute spectral power alone, may be a key presyncopal signature that is detectable by wearable sensors. Notably, nonlinear HRV features may be more robust to sampling-rate limitations inherent to wearable PPG acquisition than conventional spectral indices, which rely on precise inter-beat interval timing.

Taken together, these findings support the feasibility of translating PPG-derived HRV into a real-time, safety-oriented warning system for VVS in daily life settings. By providing timely alerts, such a system can enable patients to adopt immediate countermeasures, such as physical counterpressure manoeuvres, postural adjustment, or hydration, to reduce syncope-related falls and

injuries. To be practical for smartwatch-based deployment, the model must operate within short rolling windows (5–10 min), while remaining computationally lightweight to preserve battery life. Robust signal quality assessment and artefact-resistant pre-processing are essential for ensuring reliability under ambulatory conditions. Consistent with these requirements, we evaluated model performance at a clinically meaningful operating point by fixing sensitivity at 0.90 and reporting the corresponding specificity. Although this safety-prioritized setting minimizes missed events, the resulting moderate specificity highlights the importance of personalized alert thresholds and complementary strategies, such as signal quality gating or multimodal integration with accelerometry, posture, or haemodynamic surrogates, to enhance precision without compromising safety. Therefore, future studies should focus on validating lightweight on-device implementations that combine personalisation and multimodal sensing to enable reliable real-world deployment. Collectively, these findings add to the growing body of research supporting the clinical translation of AI-enabled smartwatch sensing from signal detection to actionable workflows in routine care.³⁰ Recent advances in AI have also expanded the role of data-driven approaches in syncope care, including natural language processing for automated case identification, machine learning models for risk stratification, and large language models for diagnostic decision support.^{31–33} Together, these developments suggest that wearable-based physiological monitoring may form one component of a broader AI-enabled ecosystem for early recognition and management of syncope.

The present study had several limitations. First, although participants were prospectively enrolled and data were acquired under a standardized protocol, the modelling analysis was performed retrospectively on a relatively limited sample size at a single centre using a single wearable device. Therefore, multicentre, multi-device external validation is warranted. Second, although HUT is the gold standard for diagnosing VVS, it is a standardized laboratory-based provocation test and may not fully replicate spontaneous real-world events. Because syncope during HUT can occur across a spectrum of autonomic susceptibility, physiological patterns observed in longer observation windows before syncope may reflect generalized orthostatic adaptation or test-related autonomic modulation rather than a specific pathological presyncopal signature. Therefore, our findings should be primarily interpreted in the context of short-term prediction immediately preceding syncope. Third, PPG data acquisition can be constrained by motion, posture changes, and cutaneous optical properties, which may act as confounders. Therefore, additional sensitivity analyses addressing class imbalance and the potential for data leakage, as well as rigorous temporally separated validation, may be necessary. Fourth, the machine learning models developed herein did not undergo external validation. Future studies should evaluate their performance using larger, independent test datasets to ensure robustness. Finally, whether real-time alerts based on PPG-derived HRV reduce syncope recurrence or injury risk remains to be tested in pragmatic intervention trials.

Conclusion

This study demonstrated that an AI-enabled analysis of smartwatch PPG-derived HRV can prospectively predict VVS during HUT, with optimal discrimination achieved using a short 5-min observation window and clinically meaningful performance maintained at a 5-min lead time. Nonlinear HRV features that capture autonomic complexity emerged as key predictors, providing physiologically plausible insights into presyncopal

autonomic instability. Taken together, these findings support the feasibility of clinically actionable, wearable, and real-time warning systems to enable timely countermeasures and potentially reduce the burden of recurrent VVS, pending external validation and real-world effectiveness studies.

Supplementary material

Supplementary material is available at *European Heart Journal – Digital Health*.

Author contributions

Hak Seung Lee (Formal analysis, Writing—original draft, Writing—review & editing [equal]), Junho Song (Formal analysis, Methodology [lead], Writing—original draft [equal]), Moonki Jung (Data curation [supporting]), Yong-Yeon Jo (Formal analysis [equal]), Joon-Myoung Kwon (Project administration, Supervision [equal]), and Jun Hwan Cho (Conceptualisation, Data curation, Project administration [lead], Writing—original draft, Writing—review & editing [equal])

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Data availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

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