Detection and analysis of circadian biomarkers for metabolic syndrome using wearable data and explainable artificial intelligence

Jeong-Kyun Kim, Sujeong Mun, Siwoo Lee

Submitted to: Journal of Medical Internet Research
on: November 27, 2024

Table of Contents

Detection and analysis of circadian biomarkers for metabolic syndrome using wearable data and explainable artificial intelligence

Jeong-Kyun Kim[1] PhD; Sujeong Mun[1] PhD, KMD; Siwoo Lee[2] PhD, KMD

[1]Korea Institute of Oriental Medicine Daejeon KR
[2]Korea Institute of Oriental Medicine ??????? KR

Corresponding Author:
Siwoo Lee PhD, KMD
Korea Institute of Oriental Medicine
1672 Yuseong-daero, Yuseong-gu, Daejeon, 34054, Republic of Korea
1002 ho
???????
KR

Abstract

Background: Digital biomarker detection using wearable devices is utilized as a solution for managing metabolic syndrome (MetS) in daily life.

Objective: This study aimed to detect digital biomarkers based on sleep and circadian rhythm using step counts and heart rate data obtained from wearable devices and to analyze important biomarkers for MetS risk groups.

Methods: Circadian rhythm markers based on heart rate and step counts were analyzed, including the newly proposed continuous wavelet circadian rhythm energy. The detected markers were analyzed for their contribution to MetS using SHapley Additive exPlanations, Explainable Boosting Machine, and Tabular Neural Network models.

Results: Analysis of sleep and circadian rhythm biomarkers using statistical analysis and artificial intelligence methods revealed that circadian rhythm markers were more important for MetS than sleep markers. Among circadian rhythm markers, heart rate-based markers were found to be more important than step counts. The continuous wavelet circadian energy proposed in this study showed the highest contribution to MetS in the artificial intelligence analysis results.

Conclusions: The risk of MetS can be continuously identified and monitored in daily life by utilizing circadian rhythm markers.

(JMIR Preprints 27/11/2024:69328)
DOI: https://doi.org/10.2196/preprints.69328

Original Manuscript

Original Paper

Detection and analysis of circadian biomarkers for metabolic syndrome using wearable data and explainable artificial intelligence

Abstract

Background: Digital biomarker detection using wearable devices is utilized as a solution for managing metabolic syndrome (MetS) in daily life.
Objective: This study aimed to detect digital biomarkers based on sleep and circadian rhythm using step counts and heart rate data obtained from wearable devices and to analyze important biomarkers for MetS risk groups.
Methods: Circadian rhythm markers based on heart rate and step counts were analyzed, including the newly proposed continuous wavelet circadian rhythm energy. The detected markers were analyzed for their contribution to MetS using SHapley Additive exPlanations, Explainable Boosting Machine, and Tabular Neural Network models.
Results: Analysis of sleep and circadian rhythm biomarkers using statistical analysis and artificial intelligence methods revealed that circadian rhythm markers were more important for MetS than sleep markers. Among circadian rhythm markers, heart rate-based markers were found to be more important than step counts. The continuous wavelet circadian energy proposed in this study showed the highest contribution to MetS in the artificial intelligence analysis results.
Conclusions: The risk of MetS can be continuously identified and monitored in daily life by utilizing circadian rhythm markers.

Keywords: metabolic syndrome; wearable device; digital biomarker; circadian rhythm; explainable artificial intelligence

Introduction

Metabolic syndrome (MetS) is a multifaceted disorder that includes various metabolic conditions, such as obesity, hypertension, and diabetes. These conditions are becoming increasingly prevalent worldwide, posing significant concerns with profound implications for individual health, societal well-being, and the economy. Metabolic diseases involve complex pathophysiological mechanisms [1,2]. Promoting healthy eating habits, integrating appropriate physical activity, and effectively managing stress can significantly reduce the risk of developing MetS [1,3].
Currently, health-management systems utilizing wearable devices are gaining significant attention [4]. These systems offer personalized healthcare by continuously monitoring and analyzing the health status of an individual in real-time. Wearable devices enable regular assessment of health-related indicators, eliminating the need for frequent hospital visits [2]. Achieving this requires the integration of various technologies, including semiconductors, artificial intelligence, and the Internet of Things [5]. Smartwatches and bands are among the most commonly used wearable devices in daily life. Smartwatches are equipped with diverse sensors such as optical heart rate monitors, electrocardiograms, and inertial sensors, enabling the collection of vital signs such as step count, heart rate, blood pressure, pulse, and oxygen saturation [5].
Wearable devices can continuously monitor an individual's vital signs in real-time. This involves the continuous tracking of crucial indicators related to MetS, such as heart rate, blood pressure, and activity levels, aiding in the real-time assessment of an individual's health status and the early

detection of anomalies [2,6]. The daily data generated through wearable devices is invaluable for MetS research. By analyzing these data, the factors influencing the onset and progression of MetS can be identified.

Recently, there has been a significant increase in attention to the daily monitoring of sleep and circadian rhythms using wearable devices [7,8]. Sleep and circadian rhythm biomarkers derived from activity-based wearable devices are now applied in studies on various conditions, including obesity [7], depression [8,9], cognitive function [10], prematurity [11], and mortality [12]. Common sleep markers include sleep timing (sleep onset, sleep offset), sleep duration (total sleep time), mid-sleep time, and wake after sleep onset [7,8]. Circadian rhythm markers are assessed using both parametric methods, such as amplitude, acrophase, midline estimating statistic of rhythm (MESOR), and circadian quotient (CQ) via cosinor analysis [8,12], and non-parametric methods, such as interdaily stability (IS), intradaily variability (IV), and relative amplitude (RA) [9-11]. Given the periodic nature of circadian rhythms, energy-based methods have been proposed. For example, singular value decomposition (SVD) has been used to calculate energy values from activity data, suggesting potential markers for cognitive function [10]. Traditional methods for measuring signal energy, such as Fourier transform, discrete cosine transform, and wavelet analysis, have been employed in various biosignal analysis studies [13,14]. In this study, we propose a novel marker called continuous wavelet circadian rhythm energy (CCE) using continuous wavelet transform (CWT) for time-frequency analysis of heart rate as a circadian rhythm marker.

The majority of the previous studies detected everyday features obtained from wearable devices and analyzed the features limited to statistical techniques without incorporating artificial intelligence technology [9-12]. Explainable artificial intelligence (XAI) techniques that interpret predictive results are gaining attention in the analysis of biosignals and healthcare information [5,7]. Specifically, research on circadian rhythm analysis based on wearable devices in relation to MetS is still in its early stages. This area requires multifaceted analysis, including the development of circadian rhythm biomarkers specifically tailored for MetS and the application of XAI for data interpretation.

Therefore, in this study, we detected circadian rhythm markers based on step count and heart rate to develop a wearable-based circadian rhythm marker for MetS and analyzed circadian rhythm markers important for MetS through artificial intelligence technologies such as SHapley Additive exPlanations (SHAP), Explainable Boosting Machine (EBM) and Tabular neural Network models (TabNet).

Methods

Recruitment

The Korean Medicine Daejeon Citizen Cohort (KDCC) dataset was used to validate the proposed biomarker. The data from the KDCC, spanning from 2020 to 2023, encompassed demographic, lifestyle, clinical, and biochemical measurements collected from 2,000 participants. Daily data was obtained using Fitbit Versa or Inspire 2 wristbands (Fitbit, San Francisco, California, USA) [15].

Among the 2,000 participants, 500 participants who wore a Fitbit device continuously for 5 weekdays were used for the marker analysis. MetS was defined as meeting three or more of the following criteria based on the 5 criteria system:

- Waist circumference (≥90 cm for men, ≥85 cm for women)
- Systolic blood pressure (≥130 mmHg) or diastolic blood pressure (≥85 mmHg), or current use of antihypertensive medications
- Low HDL (high-density lipoprotein) cholesterol levels (<40 mg/dL in men and <50 mg/dL in women) or use of medication for lipid abnormalities

- Triglyceride level (≥150 mg/dL) or medication for lipid abnormalities
- Fasting blood glucose level (≥100 mg/dL) or medication for type 2 diabetes

Among 500 participants (158 males and 342 females), 88 participants (44 males and 44 females) met the criteria for MetS, and 184 participants (28 males and 156 females) did not meet any of the five criteria and were classified as non-MetS.
This study was approved by the Institutional Review Board (DJDSKH-17-BM-12) of Daejeon Korean Medicine Hospital of Daejeon University, and written informed consent was obtained from all participants.

Circadian Rhythm and Sleep Indicator

Wearable data included minute-level heart rate and step-count records collected from Fitbit devices. Additionally, the sleep duration records provided by Fitbit were collected. Notably, the minute-level heart rate records from the Fitbit devices occasionally had missing values, represented by zeros. Missing values were converted to the nearest heart rate.
The most commonly used indicators in sleep analysis are mid-sleep time (MST), total sleep time (TST), and wake after sleep onset (WASO) [7,8]. MST is used to determine phenotype, such as whether an individual is a morning or evening sleeper. Knowing MST and TST can reveal the amount of sleep and phenotype, but it does not provide information about sleep efficiency. Therefore, the ratio of total sleep time to total time spent in bed for sleep is used. However, it is difficult to estimate sleep efficiency with step count and heart rate data provided by Fitbit.
Cosinor analysis is frequently used to analyze circadian rhythms based on activity and heart rate. Cosinor analysis fits sine waves to time series using the least squares method [16]. It is often used in biological time series analysis and can be applied to time series with non-uniform intervals. Cosinor analysis expresses observed time series data as a cosine function, as shown in Equation 1. Y(t) is the observation at time t, M is the mean (MESOR), A is the amplitude, τ is the period, t is the time, and φ is the phase. MESOR is the middle value of periodic oscillations and represents the central tendency of the data. The amplitude is the amount of variation in the period and represents how much the data deviates from the mean. The phase is the location of the variation corresponding to a specific time in the period and can mean the time when the peak of the data occurs. Amplitude, acrophase, MESOR, and CQ (amplitude/MESOR) are used as cosinor-related indicators [8,9,12].

$$Y(t) = M + A\cos\left(\frac{2\pi t}{\tau} + \varphi\right) \quad (1)$$

Non-parametric indicators used in circadian rhythm studies related to daily activity include RM, IV, and IS, which evaluate the stability and variability of individual activity patterns and circadian rhythms [8-10]. RM is an index that evaluates the variability of activity in circadian rhythms and is calculated by the difference in activity between the maximum and minimum activity times as shown in Equation 2. M10 means the average activity during the 10 h with the highest activity during the day, and L5 means the average activity during the 5 h with the lowest activity during the day. The higher the RM, the greater the difference in activity between day and night, indicating a more distinct circadian rhythm.
IV is an index that evaluates the variability of activity patterns between consecutive days, as shown in Equation 3. N is the total number of measured time data, Y_t is the activity at time t, and $\bar{Y}$ is the average activity over all times. The numerator of Equation 3 is the sum of the squares of the activity changes between consecutive time periods. The larger the change in activity between time periods during the day, the larger the IV value. The denominator is the total change in activity by time, which

expresses the variability for the average activity during the day.

IS is an index that evaluates the consistency of activity patterns during the day. It indicates how regular and consistent the activity patterns are maintained by the time zone of the day. In Equation 4, N is the total number of measured time data, S is the number of data per day, and $\acute{x}_h$ is the hourly average. The numerator is the variability of the time zone average with respect to the overall average, and the larger the deviation of the activity amount of the time zone, the larger the IS value.

$$RM = \frac{M10 - L5}{M10 + L5} \tag{2}$$

$$IV = \frac{\sum_{t=2}^{N} (Y_t - Y_{t-1})^2}{(N-1)\sum_{t=1}^{N} (Y_t - \acute{Y})^2} \tag{3}$$

$$IS = \frac{N\sum_{h=1}^{S} (\acute{x}_h - \acute{x})^2}{S\sum_{i=1}^{N} (x_i - \acute{x})^2} \tag{4}$$

Dimension reduction technology is being utilized as a method of analyzing biosignals, which is a method of converting high-dimensional data into low-dimensional data to easily visualize or analyze the data [17,18]. Dimension reduction is mainly used to reduce computational costs, remove noise, and express data more concisely while preserving the features of the data. Principle component analysis, linear discriminant analysis, and SVD are used as dimension reduction methods. In a study that applied dimension reduction technology to circadian rhythm, circadian activity rhythm energy (CARE) was proposed to detect the energy of sub-signals with a cycle of less than 24 h through singular spectrum analysis based on SVD to analyze the circadian rhythm of cognitive function. CARE showed a higher correlation coefficient than RM for melatonin amplitude [10].

The activity and heart rate obtained from wearable devices have a 24-h periodicity. Wavelet transform (WT) is used as a method to analyze signals that have time periodicity [19]. WT is a powerful tool that can analyze signals in the time and frequency domains simultaneously. WT analyzes frequency information in each time interval by decomposing them into wavelets of various sizes. CWT calculates wavelet changes for all times. Morlet wavelet is a sinusoidal waveform that is attenuated by a Gaussian curve, which is very advantageous in detecting the temporal changes of specific frequency components, allows for high-resolution frequency analysis, and captures continuous and periodic signal components well [14,20]. The CWT for a signal x(t) is obtained by computing the inner product with the Morlet wavelet. In Equations 5 and 6, $W_x(\cdot)$ is the CWT coefficient of a given signal x(t), a is a scale factor that controls the frequency variation. A smaller a corresponds to a higher frequency component, and a larger a corresponds to a lower frequency component. b is a shift parameter that controls the variation in time, and the signal is analyzed along the time axis as b changes. ψ^* is the complex combination of the Morlet wavelet, t is time, and x(t) represents the signal to be analyzed. $\psi(t)$ is the Morlet wavelet function, ω_0 is the center frequency, and i is the imaginary unit. The magnitude (energy) of the CWT coefficients $W_x(\cdot)$ represents how strongly the signal x(t) exists at a given scale a and time b. This energy is used to generate a spectrograph, which is a map that shows the intensity of the signal in the time-frequency plane. The center frequency means that the Morlet wavelet is optimized for analyzing signals in a specific frequency band. To obtain circadian rhythm markers for the acquired 5-day heart rate and step count

per min, spectrographs were obtained for each signal, and then the total energy of the center frequency was derived as a marker by adding up all the energy over time for each center frequency. The proposed CWT-based circadian rhythm energy is called CCE.

$$\psi(t)=\pi^{\frac{-1}{4}}\cdot e^{i\omega_0 t}\cdot e^{\frac{-t^2}{2}} \quad (5)$$

$$W_x(a,b)=\frac{1}{\sqrt{a}}\int_{-\infty}^{\infty} x(t)\cdot\psi^{\iota}\left(\frac{t-b}{a}\right)dt \quad (6)$$

Feature Selection and XAI

XAI is a methodology used to interpret the results of machine learning models. XAI enabled us to analyze the contribution of the features to the model outcomes. The local interpretable model-agnostic explanation (LIME) and SHAP are commonly used XAI algorithms, particularly for analyzing tabular data. As LIME often focuses on local explanations, it may not effectively explain the global behavior of the models. SHAP is a model-agnostic post hoc algorithm that is gaining attention. SHAP offers special implementations of tree-based models and provides more accurate and efficient explanations [21]. A tree-based model was used to identify MetS. Thus, SHAP was used to analyze the important features. SHAP provides insight into the contribution of each feature to the model outcomes, considering both the positive and negative impacts of wearable-based daily life features on the identification of MetS. XGBoost was used as the SHAP learning model, and the resulting SHAP values were as follows [5]:

$$\varnothing_i(v)=\sum_{S\epsilon N\setminus\{i\}}\frac{|S|!\left(n-|S|-1\right)!}{n!}\left(v\left(S\cup\{i\}\right)-v(S)\right) \quad (7)$$

XGBoost is a boosting model for decision trees that enhances the performance of gradient-boosting machines in terms of their speed. Boosting models iteratively update the parameters of previous classifiers to create a more powerful classifier, thereby increasing the accuracy and reducing the gradient of the loss function [5].

EBM is an interpretable structure of the model itself, unlike SHAP, which explains how each feature contributes to the prediction [22]. EBM is based on a generalized additive model (GAM), and GAM models the relationship between features and target variables as a sum of functions for each feature [23]. EBM can visualize how each feature contributes to the prediction so that users can easily understand the influence of individual features on the results. Equation 8 represents GAM, where β_0 is a constant term, and $f_i(x_i)$ is a function learned for each feature, indicating how each feature contributes to the prediction. g is a link function that adjusts GAM to various settings, such as regression or classification. EBM learns each function $f_i(x_i)$ of GAM using boosting techniques. Boosting is a method of sequentially learning multiple weak models and correcting errors made by previous models, as shown in equation 9. $h_m(x_i)$ is the m-th weak model, α_m is the weight of the m-th weak model, and M represents the boosting step. EBM including GAM and boosting techniques, is shown in Equation 10, and EBM can automatically detect pairwise interactions between each feature that are important for prediction and include them in the model, as shown in Equation 11.

$$g(E[y])=\beta_0+f_1(x_1)+f_2(x_2)+f_3(x_3)+\cdots+f_n(x_n) \quad (8)$$

$$f_i(x_i) = \sum_{m=1}^{M} \alpha_m h_m(x_i) \quad (9)$$

$$g(E[y]) = \beta_0 + \sum_{i=1}^{n} \sum_{m=1}^{M} \alpha_m h_m(x_i) \quad (10)$$

$$g(E[y]) = \beta_0 + \sum f_i(x_i) + \sum f_{ij}(x_i, x_j) \quad (11)$$

In addition to EBM and XGBoost, TabNet, a deep learning architecture designed for tabular data, was used. TabNet leverages a novel attention mechanism that automatically selects relevant features and effectively learns their interactions [24]. TabNet is particularly well-suited for analyzing complex datasets because it handles missing values and displays the most influential features for prediction, providing interpretability. In TabNet, the method to automatically evaluate the importance of each feature to the model is related to the attention mechanism and Gated Linear Units (GLU). To evaluate the importance of each feature in a given input X, the attention weights W_a are calculated as in Equation 12. Z is the input value of the current layer, A is the learnable weight, and the Softmax function normalizes the weights so that the sum of the weights becomes 1. Consequently, A becomes a probability vector indicating the importance of each feature. TabNet performs prediction through features selected from each layer, and the set of selected features is defined as in Equation 13. GLU is used in the process of performing prediction using selected features. GLU can emphasize or suppress input features through non-linear transformation, as shown in Equation 14. W_g is a weight matrix, b is a bias, and σ is a sigmoid activation function, which provides a ratio representing the importance of each feature. The output computed through the attention weights and GLU of each layer evaluates the importance of each feature to the final prediction.

$$A = Softmax(Z \cdot W_a) \quad (12)$$

$$X_{selected} = A \cdot X \quad (13)$$

$$GLU(x) = x \cdot \sigma(W_g x + b_g) \quad (14)$$

The XGBoost parameters used were booster = gbtree and objective = binary logistic. The other parameters were set to the default values in Python (v3.10.9), Numpy (v1.23.5), and scikit-learn (v1.2.2). EBM was implemented using the interpret library version 0.6.4, and TabNet was implemented using pytorch-tabnet version 4.1.0 with max_epochs=1000 and batch_size=32.

Results

Associations of Sleep and Circadian Rhythm Indicators with MetS

Based on heart rate, step count, and sleep data obtained from wearable devices, bio-digital markers of circadian rhythm for MetS were detected and the significance of the markers was analyzed. For the analysis, continuous wearable data for 5 days during the week of 88 MetS and 184 non-MetS obtained from smart bands on the wrist were used. Demographic and clinical information used to determine MetS are shown in Table 1. The age of the MetS group was 48.94 years, which was 4 years older than that of non-MetS group. The average body mass index of MetS was 27.9. systolic blood pressure, diastolic blood pressure, triglyceride, high-density lipoprotein, and glucose used to determine MetS all showed statistically significant results ($p < 0.001$). The p-value was obtained

using an independent t-test.

Table 1. Demographic and clinical characteristics of MetS and non-MetS groups

	Non-MetS	MetS	p-value
Sex, n (%)			
Male	28(38.9)	44(61.1)	
Female	156(78.0)	44(22.0)	
Age	44.04±6.48	48.94±6.92	<0.001
BMI	21.70±2.08	27.90±2.94	<0.001
Waist			
Male	81.82±5.28	96.98±7.41	<0.001
Female	75.88±5.11	90.45±8.04	<0.001
SBP	110.32±8.98	130.68±15.42	<0.001
DBP	67.97±8.80	83.07±11.31	<0.001
Triglyceride	78.29±26.62	210.01±102.54	<0.001
HDL	68.17±14.21	46.40±11.35	<0.001
LDL	123.02±33.19	124.13±35.95	0.741
Total_Cholesterol	204.94±35.05	200.51±42.11	0.454
Glucose	82.97±6.52	99.89±20.84	<0.001

BMI: Body Mass Index, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, HDL: High Density Lipoprotein, LDL: Low Density Lipoprotein

Twenty-six indicators were identified as sleep and circadian rhythm markers. The sleep-related indicators consist of four measures: the mean and standard deviation of MST and TST. MESOR, amplitude, acrophase, and CQ for both step count and heart rate, derived from cosinor analysis, make up eight indicators. Ten indicators, including L5, M10, RA, IS, and IV for step count and heart rate, were calculated as non-parametric indicators. Additionally, one indicator was based on dimension reduction proposed in a previous study, and three indicators using CCE based on heart rate were introduced in this study.

The statistical significance of MetS in the results obtained by analyzing the energy of the CWT based on the central frequency of the circadian rhythm for step count and heart rate, in order to detect MetS markers related to the CCE proposed in this study, is shown in Figure 1. The CCE value for step count showed the lowest *p*-value at a central frequency of 70 min, but it did not reach a value below 0.001. However, heart rate exhibited statistical significance below 0.001 at central frequencies of 70 min and 1000 min. Therefore, the total CCE value was obtained for the central frequencies between 69 and 80 min (mid-frequency) and between 900 and 1100 min (low-frequency). Additionally, the ratio of the two central frequency ranges (mid_low ratio) was calculated as a single indicator. The energy of heart rate according to the central frequency reaches its highest at the 1440-min circadian cycle and also shows high energy in the 700-min range (Figure 2). In the central frequency range of 69 – 80 min, the energy of MetS is lower than that of non-MetS, while in the 900 – 1100-min range, the energy of MetS is higher.

Figure 1. Statistical Significance of Step Count and Heart Rate CWT Based on Central Frequency in MetS

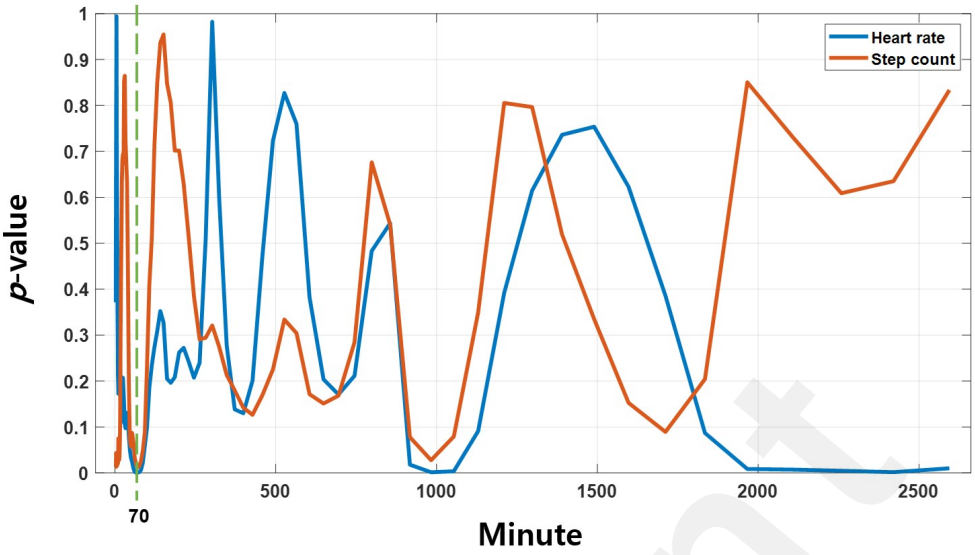
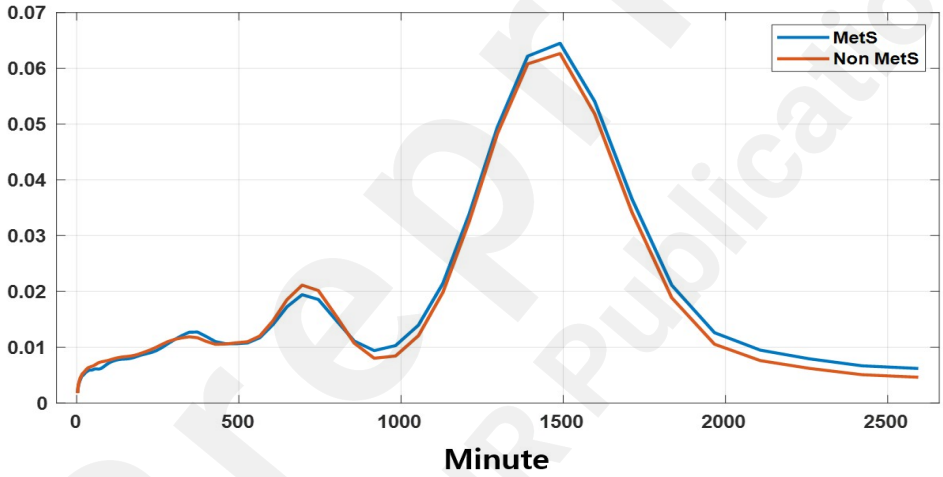


Figure 2. Comparison of Heart Rate Energy at Central Frequencies in MetS and Non-MetS



In Tables 2 and 3, the means, standard deviations, and statistical significance of 26 indicators for MetS and non-MetS can be observed. Statistical significance was assessed using parametric testing (independent t-test) and non-parametric testing (Wilcoxon rank sum test) [25].

Sleep-related indicators did not show statistical significance for MetS ($p < 0.05$). For the Cosinor and non-parametric methods, step count showed statistical significance with CQ (MetS was 0.04 larger, $p = 0.043$), L5 (MetS was 0.031 larger, $p < 0.001$), RA (MetS was 0.012 smaller, $p < 0.001$), and IS (MetS was 0.067 smaller, $p < 0.001$). Heart rate showed statistical significance with MESOR (MetS increased by 3.14, $p < 0.001$), L5 (MetS increased by 4.36, $p < 0.001$), M10 (MetS increased by 2.67, $p = 0.012$), RA (MetS decreased by 0.018, $p < 0.001$), IS (MetS decreased by 0.054, $p = 0.002$), and IV (MetS decreased by 0.04, $p = 0.04$). The CARE method based on step count did not show statistical significance for MetS. In this study, the proposed indicators CCE showed statistical significance in mid-frequency (MetS decreased by 0.005, $p < 0.001$), low-frequency (MetS increased by 0.005, $p = 0.003$), and mid_low ratio (MetS decreased by 0.382, $p < 0.001$).

Table 2. Comparison of sleep, cosinor, and non-parametric indicator values in MetS and non-MetS

Indicator		**Non-MetS**	**MetS**	**t-test (*p*)**	**Wilcoxon(*p*)**
Sleep					

MST	Mean	207.55 (36.36)	207.08 (28.06)	0.916	0.660
	STD	39.76 (24.48)	45.00 (35.50)	0.157	0.198
TST	Mean	414.92 (72.72)	410.70 (57.33)	0.634	0.464
	STD	79.50 (48.96)	84.00 (44.81)	0.468	0.249
Cosinor					
MESOR	SC	7.41 (3.66)	6.47 (2.46)	0.028	0.104
	HR	71.98 (6.44)	75.12 (7.26)	<0.001	<0.001
Amplitude	SC	1.86 (1.23)	1.90 (1.16)	0.824	0.663
	HR	3.56 (2.16)	4.00 (2.59)	0.143	0.365
Acrophase	SC	-4.25 (1.49)	-4.20 (1.56)	0.804	0.959
	HR	-4.30 (1.55)	-3.92 (1.88)	0.084	0.231
CQ	SC	0.26 (0.14)	0.30 (0.16)	0.037	0.043
	HR	0.050 (0.03)	0.054 (0.037)	0.329	0.872
Nonparametric					
L5	SC	0.172 (0.307)	0.203 (0.239)	0.411	<0.001
	HR	61.60 (6.43)	65.96 (7.25)	<0.001	<0.001
M10	SC	12.80 (6.42)	11.02 (4.39)	0.020	0.071
	HR	83.51 (7.24)	86.18 (7.68)	0.006	0.012
RA	SC	0.973 (0.043)	0.961 (0.043)	0.024	<0.001
	HR	0.152 (0.04)	0.134 (0.03)	<0.001	<0.001
IS	SC	0.507 (0.165)	0.440 (0.129)	<0.001	<0.001
	HR	0.684 (0.142)	0.630 (0.130)	0.003	0.002
IV	SC	1.246 (0.311)	1.249 (0.274)	0.934	0.912
	HR	0.535 (0.157)	0.495 (0.156)	0.049	0.040

SC: step count, HR: heart rate, STD: standard deviation

Table 3. Comparison of dimension reduction and frequency analysis values in MetS and non-MetS

Indicator		**Non-MetS**	**MetS**	**t-test *(p)***	**Wilcoxon *(p)***
SSA_CARE	SC	0.066 (0.040)	0.061 (0.030)	0.373	0.697
CCE					
Mid-Frequency	HR	0.029 (0.010)	0.024 (0.008)	<0.001	<0.001
Low-Frequency	HR	0.029 (0.013)	0.034 (0.015)	0.003	0.003
Mid_Low Ratio	HR	1.247 (0.859)	0.865 (0.466)	<0.001	<0.001

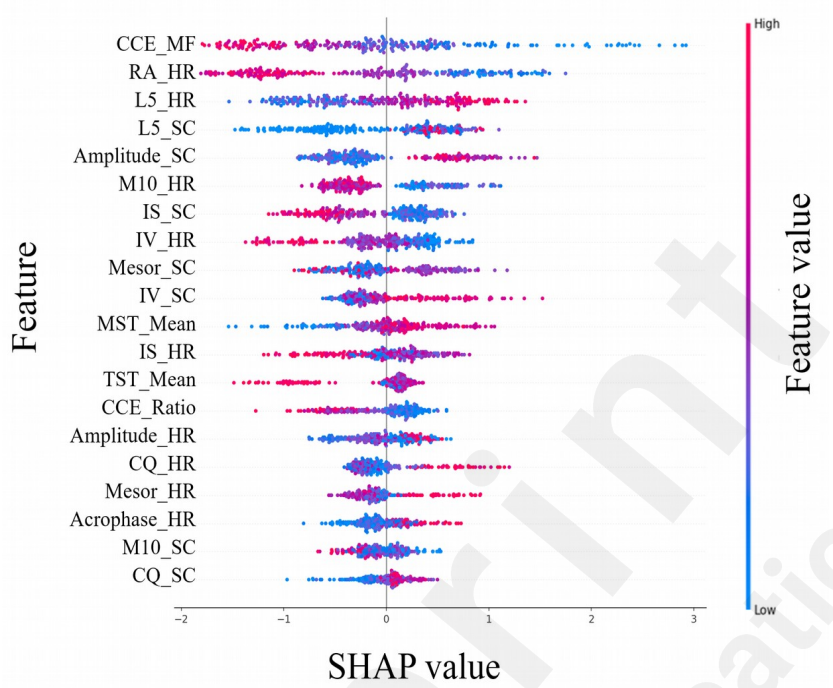
SC: step count, HR: heart rate

XAI-Based Importance Analysis of Sleep and Circadian Rhythm Indicators for MetS

An importance analysis was conducted on the 26 detected sleep and circadian rhythm indicators using SHAP (with XGBoost), EBM, and TabNet. Figure 3 presents the SHAP plot, where the color gradient from red to blue reflects the value of each indicator, with higher values appearing in red. The x-axis represents the contribution direction: positive values indicate a higher contribution to

predicting MetS, while negative values correspond to a higher contribution to non-MetS. Indicators positioned higher on the y-axis are considered more important.

Figure 3. Important Indicators Identified by SHAP for MetS



Figures 4 and 5 display the importance values of indicators using EBM and TabNet, respectively. Among the three models, the mid-frequency of CCE (CCE_MF), proposed in this study, exhibited the highest importance for identifying MetS-related circadian rhythm patterns. Additionally, relative amplitude of heart rate (RA_HR) consistently ranked among the top three indicators across all three methods. These findings highlight the critical role of both CCE_MF and RA_HR in distinguishing between MetS and non-MetS groups.

Figure 4. Important Indicators Identified by EBM for MetS

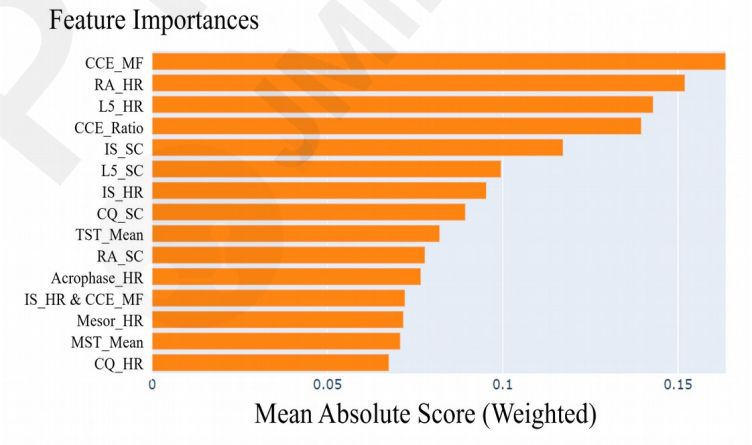
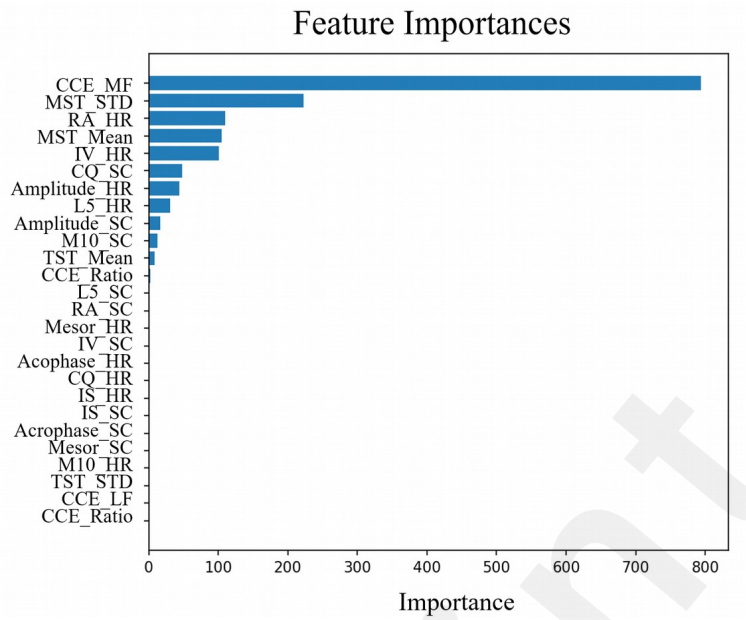


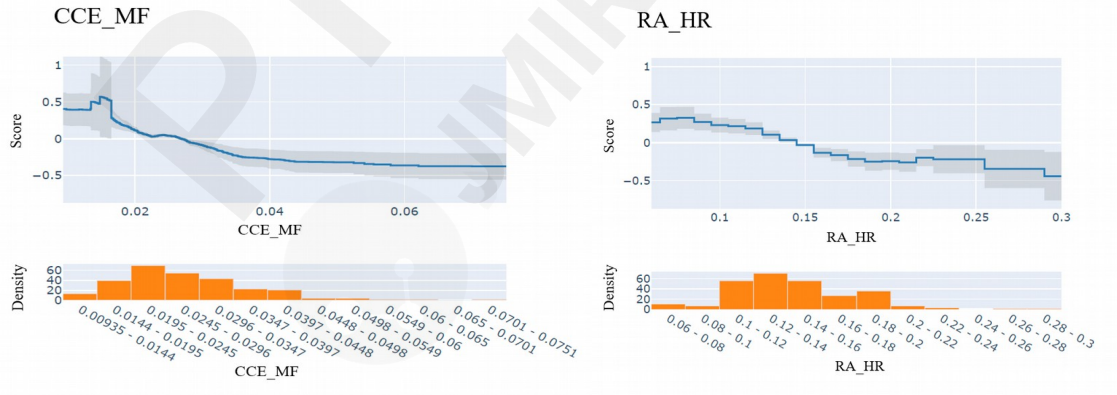
Figure 5. Important Indicators Identified by TabNet for MetS



Apart from CCE_MF and RA_HR, differences in importance rankings were observed between the tree-based models (SHAP and EBM) and the deep learning-based TabNet. In the SHAP plot, both CCE_MF and RA_HR showed a higher contribution to MetS as their values decreased. Figure 6 further visualizes the changes in scores based on CCE_MF and RA_HR using EBM. The average value of CCE_MF was 0.029 for the MetS group and 0.034 for the non-MetS group, with most data points concentrated in the range of 0.0195 – 0.0245. A lower CCE_MF value was associated with a higher contribution to MetS, while non-MetS data were distributed over a broader range from 0.03 to 0.08.

Similarly, RA_HR values were distributed between 0.1 and 0.2, with a significant shift observed in the EBM plot. When RA_HR exceeded 0.15, its contribution to non-MetS increased, while values above 0.25 were associated with a substantial reduction in the probability of MetS.

Figure 6. Score Changes for CCE_MF and RA_HR Identified by EBM for MetS



The top 10 indicators identified by each model varied as follows:

- SHAP: CCE_MF, RA_HR, L5_HR, L5_SC, Amplitude_SC, M10_HR, IS_SC, IV_HR, MESOR_SC, IV_SC
- EBM: CCE_MF, RA_HR, L5_HR, CEE_Ratio, IS_SC, L5_SC, IS_HR, CQ_SC, TST_Mean, RA_SC

- TabNet: CCE_MF, MST_STD, RA_HR, MST_Mean, IV_HR, CQ_SC, Amplitude_HR, L5_HR, Amplitude_SC, M10_SC

Among the top 10 indicators, SHAP identified 5 HR-related and 5 SC-related indicators. EBM included 5 HR-related, 4 SC-related, and 1 sleep-related indicator, while TabNet identified 5 HR-related, 3 SC-related, and 2 sleep-related indicators. Across all three methods, HR-related indicators showed a high contribution to MetS. Notably, CCE_MF, RA_HR, and L5_HR consistently appeared as key contributors across all models.
Lastly, the comparison between the statistical methods and the XAI-based importance analysis revealed that sleep-related indicators, which did not achieve statistical significance, emerged among the top 10 indicators in the XAI-based analysis. These findings underscore the value of explainable AI methods in uncovering hidden patterns that may be missed by traditional statistical approaches.

Discussion

Currently, studies analyzing circadian rhythm digital markers related to MetS are still in their early stages. Previous research has primarily focused on individual factors such as physical activity levels and sleep patterns, but in-depth analysis of circadian rhythm markers for metabolic diseases using wearable devices has rarely been conducted [26-28]. This study aimed to identify and analyze circadian rhythm indicators related to MetS using data from wearable devices.
In addition to existing circadian rhythm indicators, recent studies are proposing new indicators tailored to each target disease area. Table 4 shows studies focused on wearable-based sleep and circadian rhythm analysis. For instance, Cui proposed CARE as a circadian rhythm marker for cognitive function, comparing it with existing indicators like RA [10]. Similarly, Shim introduced a new marker called CosinorAge, which analyzes the relationship between aging and mortality, in addition to Corsinor-based indices such as MESOR, amplitude, and acrophase [12]. In this study, we proposed a time-frequency analysis-based circadian rhythm indicator called CCE and compared it with indicators used in previous studies.

Table 4. Previous studies on sleep and circadian rhythm indicator analysis based on wrist wearable devices

Author	Target	Device	Indicator	Methodology
Kiss et al., 2024	Obey	Fitbit Charge HR 2	sleep onset, sleep offset, sleep duration, sleep onset latency, sleep inertia, MST, Total step count, Sleeping HR, Resting HR	Explainable Boosting Machine
Zhang et al., 2024	major depressive disorder	Fitbit Charge HR 2 or 3	Sleep duration, sleep onset, sleep offset, sleep variability, Daily step, step IV, step IS, L5 onset, M10 onset, HR MESOR, HR amplitude, HR acrophase	Linear mixed-effects models
Ali et al., 2023	major depressive disorder	Actigraphy ActiCal (Philips)	MESOR, Amplitude, CQ, Acrophase, M10, L5, RA, IV, IS	Two tailed t-test and Mann-whitney U test, Kolmogorov-Smirnov test
Cui et al.,	Cognitive	AX3 (Activity)	CARE, RA	Regression

2023	Function			models
Ravindra et al., 2023	Prematurity	Motionwatch8 (CamNTech)	RA, IS, IV	Deep Learning, novel interpretability algorithms
Shim et al., 2024	Aging and Mortality	AX3 (Axivity) or GT3X+ (ActiGraph)	MESOR, Amplitude, Acrophase, CosinorAge	Harrel's concordance index, Akaike information
Kim et al., 2022	MetS	GalaxyWatch Active1	Walking hours, Physical activity hours, Step counts-	Paired t test, χ^2test
Yamaga et al., 2023	MetS	Fitbit Versa	TST, Total step count, Total activity minutes	Multilevel mixed-effects logistic regression
Ours	MetS	Fitbit Versa or Inspire 2	MST, TST, MESOR, Amplitude, Acrophase, CQ, L5, M10, RA, IS, IV, CARE, CCE	XAI models such as SHAP, EBM, and TabNet

Existing statistical analysis methods may have limitations in detecting complex temporal patterns or interactions. In contrast, XAI offers clearer insights into hidden data patterns by making the predictions of complex models explainable [29]. Kiss analyzed the relationship between sleep and heart rate indicators and obesity through EBM [7], while Ravindra investigated circadian rhythm indicators for prematurity using novel interpretability algorithms that integrate unsupervised clustering, model error analysis, feature attribution, and automated actigraphy analysis [11]. This highlights the growing importance of using XAI to analyze target diseases and circadian markers. Our study aims to address the limitations of previous research by examining the significance of circadian rhythm indicators related to MetS using XAI models such as SHAP, EBM, and TabNet. Analyzing the contribution and significance of circadian rhythm indicators across various models enhances the development of objective markers that more effectively explain MetS.

XAI-based analysis of circadian rhythm indicators revealed that CCE_MF is the most crucial marker for identifying circadian patterns related to MetS. A decrease in CCE_MF with a 1h cycle correlated with an increased contribution to MetS. The heart rate variability observed in the 1h cycle can be related to exercise, physical activity, eating, digestion, and fluctuations in the autonomic nervous system [30,31]. A low energy level in the 1h cycle indicates minimal amplitude or frequency components, suggesting strong physical activity, low metabolic changes, or an absence of exercise. Our study also noted low step counts in the same cycle. Additionally, the RA_HR consistently ranked high across all models and displayed low values in MetS. A low RA_HR indicates reduced heart rate variability, which can act as a cardiovascular risk factor. For example, heart rate variability tends to decrease in conditions such as hypertension, MetS, or heart failure [32].

XAI methods, including SHAP, EBM, and TabNet, enabled us to comprehensively understand the contribution of individual indicators to MetS prediction. While SHAP and EBM, both tree-based models, identified similar heart rate and sleep-related indicators, TabNet, a deep learning approach, highlighted a different set of significant sleep-related indicators. Notably, some sleep-related indicators that did not achieve statistical significance in traditional analyses emerged among the top indicators in the XAI method. This underscores the limitations of conventional statistical approaches that may overlook essential relationships and interactions among variables. The ability of XAI to uncover these hidden patterns suggests its valuable role in advancing research on MetS and related

diseases.

The growing prevalence of wearable devices, such as smart bands and watches, is fostering an environment where individuals' everyday health information can be collected and analyzed in real-time. These data could be instrumental in personalized healthcare, particularly in the early detection and prevention of chronic diseases such as MetS. Keshet provided an overview of wearable and digital devices capable of alerting individuals to specific metabolic outcomes, emphasizing the unique opportunities for creating personalized prevention and treatment strategies for cardiometabolic diseases [2]. This study may contribute to the healthcare landscape by developing wearable data-based circadian rhythm markers, addressing the need for technologies aimed at preventing and treating MetS in everyday life.

This study has some limitations. The dataset used was limited in size and was collected from specific regions or population groups, making the generalization challenging. Further research should delve deeper into investigating the stability and generalizability of the model when considering real-world medical applications. Additionally, there was an issue of data imbalance for MetS and metabolic diseases, potentially leading to model bias toward the majority class.

Conclusions

In this study, we detected and analyzed digital biomarkers related to MetS using wearable wrist sensor data. Overall, 26 indicators were analyzed, including the newly proposed CCE indicator in this study. To evaluate the contribution and importance of each indicator, we applied the XAI technique and used SHAP, EBM, and TabNet. The high importance of the same indicator in various models means that the indicator is robust as a digital biomarker of MetS. CCE showed the highest contribution in all three models, and RA_HR also showed consistently high importance in all three models. This proved that CCE and RA_HR are useful biomarkers for tracking and predicting MetS.

Previous studies mainly used markers based on sleep patterns and physical activity, but this study confirmed the possibility that wearable-based circadian rhythm analysis can be used in MetS research. These results enable real-time tracking and management of MetS using wearable devices such as smartwatches and bands. This approach holds significant potential for personalized health management and chronic disease prevention. Future research should focus on developing long-term tracking and management strategies for MetS using the proposed markers, including larger datasets and various health indicators.

Acknowledgements

Funding

The Development of Korean Medicine Original Technology for Preventive Treatment Based on Integrative Big Data (grant number KSN1731121) from the Korea Institute of Oriental Medicine.

Author contributions

JK Kim: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Validation, Visualization Writing – original draft, Writing – review & editing. S Mun: Conceptualization, Investigation, Writing – review & editing. S Lee: Funding acquisition, Project administration, Supervision.

Conflicts of Interest

None declared.

Data availability

The data supporting this study's findings were provided by the Korean Medicine Data Center of the Korea Institute of Oriental Medicine under license and cannot be freely shared. Requests for access should be directed to the Korean Medicine Data Center at http://kdc.kiom.re.kr/.

Abbreviations

CARE: circadian activity rhythm energy
CCE: circadian rhythm energy
CWT: continuous wavelet transform
EBM: explainable boosting machine
GAM: generalized additive model
HRV: heart rate variability
IV: intradaily variability
KDDC: knowledge discovery in data classification
LIME: local interpretable model-agnostic explanation
MST: mid-sleep time
MetS: metabolic syndrome
RA: relative amplitude
RA_HR: relative amplitude for heart rate
SHAP: shapley additive explanations
SVD: singular value decomposition
TabNet: tabular neural networks
TST: total sleep time
WASO: wake after sleep onset
WT: wavelet transform
XAI: explainable artificial intelligence

References

1. Dobrowolski, P., Prejbisz, A., Kuryłowicz, A., et al. (2022). Metabolic syndrome—A new definition and management guidelines. Arterial Hypertension, 26(3), 99-121. https://doi.org/10.5114/aoms/152921. PMID:36160355.
2. Keshet, A., Reicher, L., Bar, N., & Segal, E. (2023). Wearable and digital devices to monitor and treat metabolic diseases. Nature Metabolism, 5(4), 563–571. https://doi.org/10.1038/s42255-023-00778-y. PMID:37100995.
3. Alkhulaifi, F., & Darkoh, C. (2022). Meal timing, meal frequency and metabolic syndrome. Nutrients, 14(9), 1719. https://doi.org/10.3390/nu14091719. PMID:35565686.
4. Manogaran, G., Alazab, M., Song, H., & Kumar, N. (2021). CDP-UA: Cognitive data processing method wearable sensor data uncertainty analysis in the internet of things assisted smart medical healthcare systems. IEEE Journal of Biomedical and Health Informatics, 25(10), 3691-3699. https://doi.org/10.1109/JBHI.2021.3051288. PMID:33439849.
5. Kim, J. K., Lee, K., & Hong, S. G. (2023). Detection of important features and comparison of datasets for fall detection based on wrist-wearable devices. Expert Systems with Applications, 234, 121034. https://doi.org/10.1016/j.eswa.2023.121034.
6. Meng, Y., Speier, W., Shufelt, C., et al. (2020). A machine learning approach to classifying self-reported health status in a cohort of patients with heart disease using activity tracker data. IEEE Journal of Biomedical and Health Informatics, 24(3), 878-884. https://doi.org/10.1109/JBHI.2019.2922178. PMID:31199276.
7. Kiss, O., Baker, F. C., Palovics, R., Dooley, E. E., Pettee Gabriel, K., & Nagata, J. M. (2024). Using explainable machine learning and Fitbit data to investigate predictors of adolescent

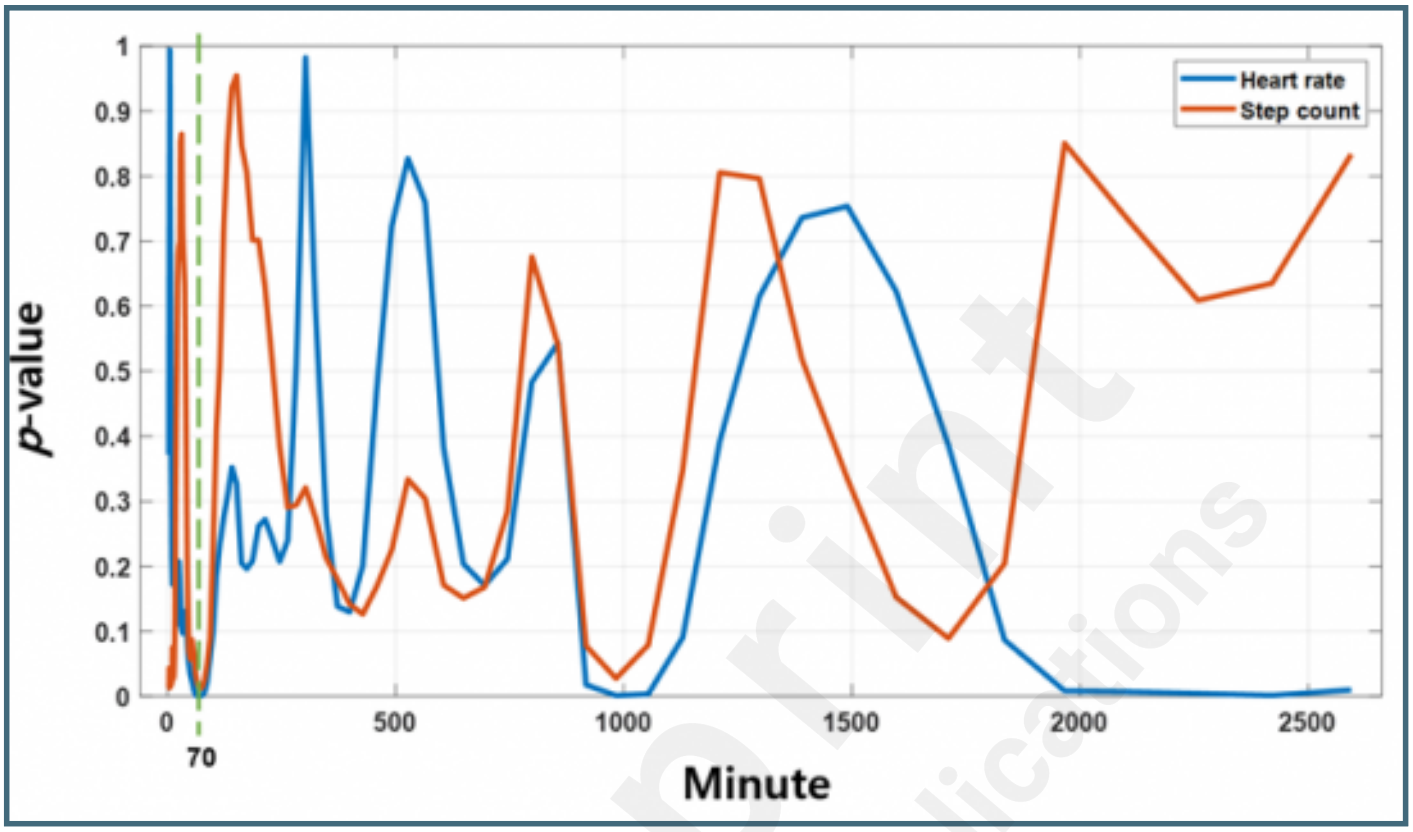
obesity. Scientific Reports, 14(1), 12563. https://doi.org/10.1038/s41598-024-60811-2. PMID:38821981.
8. Zhang, Y., Folarin, A. A., Sun, S., et al. (2024). Longitudinal assessment of seasonal impacts and depression associations on circadian rhythm using multimodal wearable sensing: Retrospective analysis. Journal of Medical Internet Research, 26, e55302. https://doi.org/10.2196/55302. PMID:38941600.
9. Ali, F. Z., Parsey, R. V., Lin, S., Schwartz, J., & DeLorenzo, C. (2023). Circadian rhythm biomarker from wearable device data is related to concurrent antidepressant treatment response. NPJ Digital Medicine, 6(1), 81. https://doi.org/10.1038/s41746-023-00827-6. PMID:37120493.10. Cui, S., Lin, Q., Gui, Y., et al. (2023). CARE as a wearable derived feature linking circadian amplitude to human cognitive functions. NPJ Digital Medicine, 6(1), 123. https://doi.org/10.1038/s41746-023-00865-0. PMID:37433859.
11. Ravindra, N. G., Espinosa, C., Berson, E., et al. (2023). Deep representation learning identifies associations between physical activity and sleep patterns during pregnancy and prematurity. NPJ Digital Medicine, 6(1), 171. https://doi.org/10.1038/s41746-023-00911-x. PMID:37770643.
12. Shim, J., Fleisch, E., & Barata, F. (2024). Circadian rhythm analysis using wearable-based accelerometry as a digital biomarker of aging and healthspan. NPJ Digital Medicine, 7(1), 146. https://doi.org/10.1038/s41746-024-01111-x. PMID:38834756.
13. Rangayyan RM, Krishnan S. Biomedical signal analysis. John Wiley & Sons; 2024. ISBN:9781119825876
14. Kim, J., Bae, M. N., Lee, K. B., & Hong, S. G. (2020). Gait event detection algorithm based on smart insoles. ETRI Journal, 42(1), 46-53. https://doi.org/10.4218/etrij.2018-0639
15. Mun, S., Park, K., Kim, J. K., Kim, J., & Lee, S. (2024). Assessment of heart rate measurements by commercial wearable fitness trackers for early identification of metabolic syndrome risk. Scientific Reports, 14(1), 1–9. https://doi.org/10.1038/s41598-024-74619-7
16. Cornelissen, G. (2014). Cosinor-based rhythmometry. Theoretical Biology and Medical Modelling, 11, 1-24. https://doi.org/10.1186/1742-4682-11-16. PMID:24725531.
17. Castells, F., Laguna, P., Sörnmo, L., Bollmann, A., & Roig, J. M. (2007). Principal component analysis in ECG signal processing. EURASIP Journal on Advances in Signal Processing, 2007, 1-21. https://doi.org/10.1155/2007/74580
18. Sonawani, S., Patil, K., & Natarajan, P. (2023). Biomedical signal processing for health monitoring applications: A review. International Journal of Applied Systemic Studies, 10(1), 44-69. https://doi.org/10.1504/IJASS.2023.129065
19. Zhang D. Wavelet transform. In: Fundamentals of image data mining: Analysis, features, classification and retrieval (Texts in Computer Science). Springer, Cham; 2019. p. 35-44. https://doi.org/10.1007/978-3-030-17989-2_3. ISBN: 9783030179892
20. Khorrami, H., & Moavenian, M. (2010). A comparative study of DWT, CWT and DCT transformations in ECG arrhythmias classification. Expert Systems with Applications, 37(8), 5751-5757. https://doi.org/10.1016/j.eswa.2010.02.033
21. Slack D, Hilgard S, Jia E, Singh S, Lakkaraju H. Fooling LIME and SHAP: Adversarial attacks on post hoc explanation methods. In: Proceedings of the AAAI/ACM Conference on AI, Ethics, and Society; 2020. p. 180-6. https://doi.org/10.1145/3375627.3375830
22. Nori, H., Jenkins, S., Koch, P., & Caruana, R. (2019). InterpretML: A unified framework for machine learning interpretability. arXiv preprint arXiv:1909.09223. https://doi.org/10.48550/arXiv.1909.09223
23. Hastie TJ. Generalized additive models. In: Statistical models in S. Routledge; 2017. p. 249-307. ISBN:9780203738535
24. Arik SÖ, Pfister T. TabNet: Attentive interpretable tabular learning. In: Proceedings of the AAAI Conference on Artificial Intelligence 2021;35:6679-87. https://doi.org/10.1609/aaai.v35i8.16826
25. Sedgwick, P. (2015). A comparison of parametric and non-parametric statistical tests. BMJ, 350.

https://doi.org/10.1136/bmj.h2053. PMID:25888112.
26. Kim, H. J., Lee, K. H., Lee, J. H., Youk, H., & Lee, H. Y. (2022). The effect of a mobile and wearable device intervention on increased physical activity to prevent metabolic syndrome: Observational study. JMIR Mhealth Uhealth, 10(2), e34059. https://doi.org/10.2196/34059. PMID:35200145.
27. Yamaga, Y., Svensson, T., Chung, U. I., & Svensson, A. K. (2023). Association between metabolic syndrome status and daily physical activity measured by a wearable device in Japanese office workers. International Journal of Environmental Research and Public Health, 20(5), 4315. https://doi.org/10.3390/ijerph20054315. PMID:36901325.
28. Nikbakht, H. A., Rezaianzadeh, A., Seif, M., et al. (2023). Physical activity and metabolic syndrome: A population-based study (forest and tree model algorithms). Clinical Nutrition ESPEN, 56, 173-179. https://doi.org/10.1016/j.clnesp.2023.05.014. PMID:37344069.
29. Khater, T., Tawfik, H., & Singh, B. (2024). Explainable artificial intelligence for investigating the effect of lifestyle factors on obesity. Intelligent Systems with Applications, 23, 200427. https://doi.org/10.1016/j.iswa.2024.200427
30. Castelli, L., Macdonald, J. H., Innominato, P. F., & Galasso, L. (2024). Circadian rhythm, athletic performance, and physical activity. Frontiers in Physiology, 15, 1466152. https://doi.org/10.3389/fphys.2024.1466152. PMID:39145108.
31. McCraty, R., Atkinson, M., Stolc, V., Alabdulgader, A. A., Vainoras, A., & Ragulskis, M. (2017). Synchronization of human autonomic nervous system rhythms with geomagnetic activity in human subjects. International Journal of Environmental Research and Public Health, 14(7), 770. https://doi.org/10.3390/ijerph14070770. PMID:28703754.
32. Azulay, N., Olsen, R. B., Nielsen, C. S., Stubhaug, A., Jenssen, T. G., Schirmer, H., et al. (2022). Reduced heart rate variability is related to the number of metabolic syndrome components and manifest diabetes in the sixth Tromsø study 2007–2008. Scientific Reports, 12(1), 11998. https://doi.org/10.1038/s41598-022-15824-0. PMID:35835836.

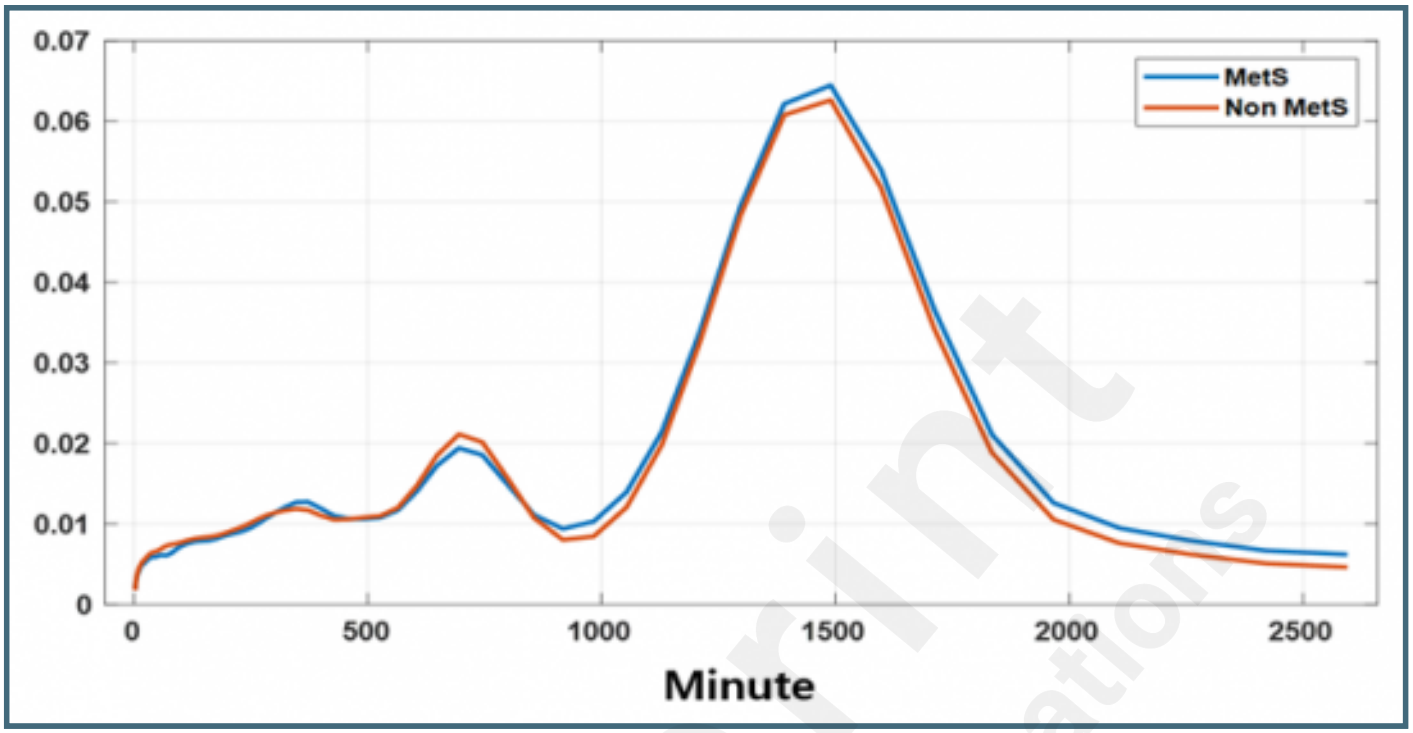
Supplementary Files

Figures

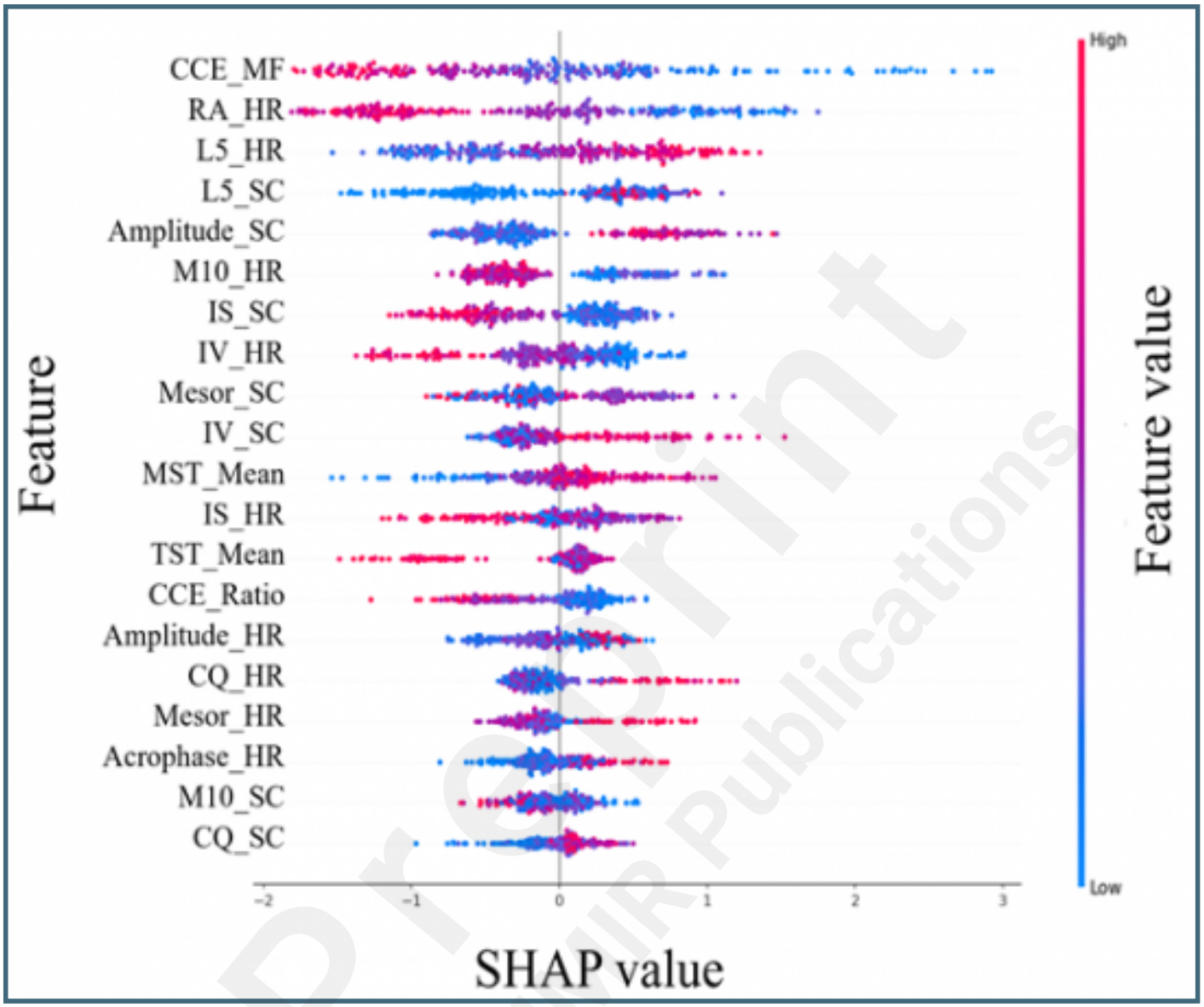
Statistical Significance of Step Count and Heart Rate CWT Based on Central Frequency in MetS.



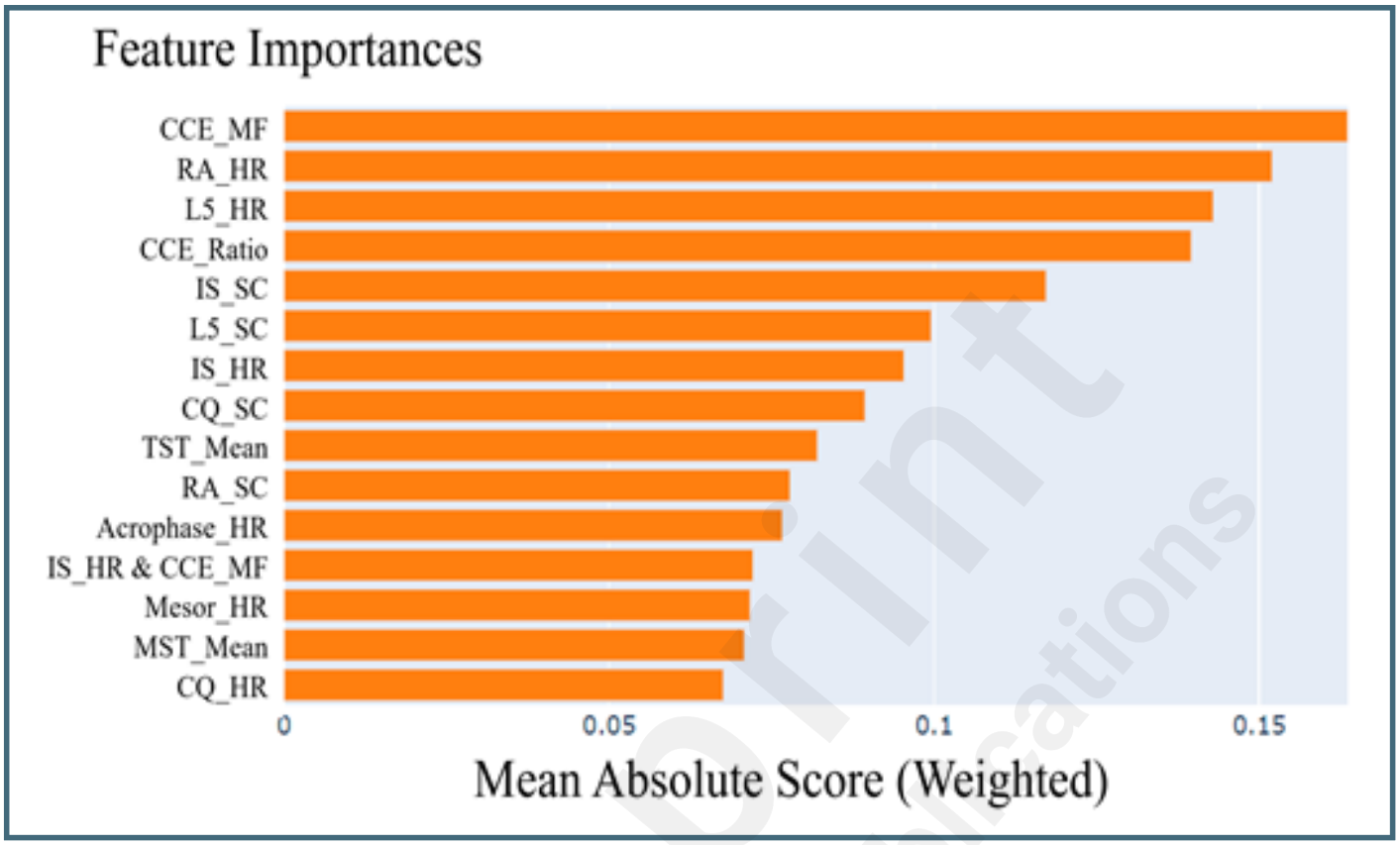
Comparison of Heart Rate Energy at Central Frequencies in MetS and Non-MetS.



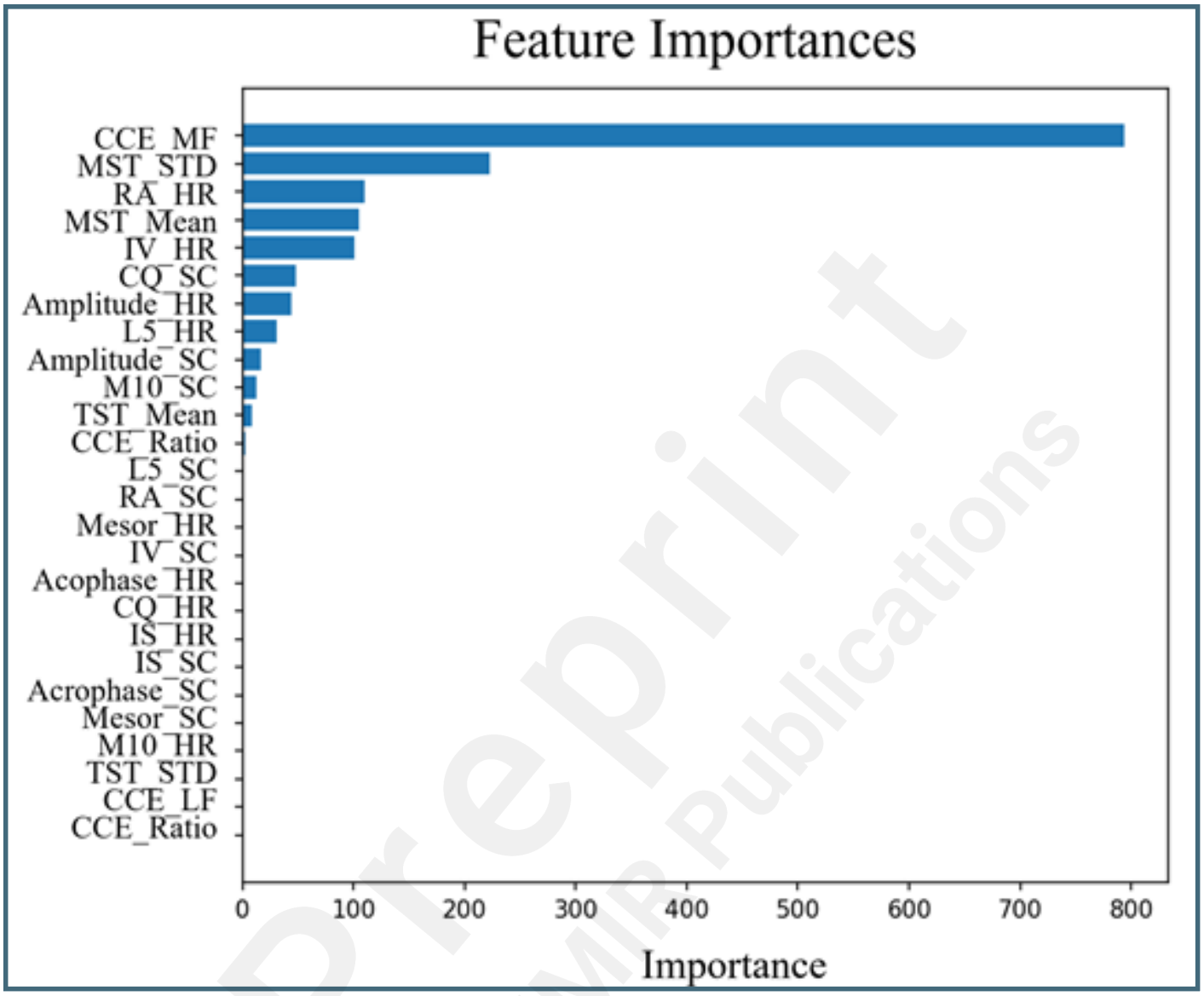
Important Indicators Identified by SHAP for MetS.



Important Indicators Identified by EBM for MetS.



Important Indicators Identified by TabNet for MetS.



Score Changes for CCE_MF and RA_HR Identified by EBM for MetS.