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Metabolic syndrome burden in apparently healthy adolescents are adversely associated with cardiac autonomic modulation-Penn State Children Cohort

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Abstract

Background—Reduced cardiac autonomic modulation (CAM) has been associated with metabolic syndrome (MetS) in adults. However, the association between MetS component cluster and CAM has not been examined in adolescents.

Methods—We conducted a cross-sectional analysis using data from the Penn State Child Cohort follow-up examination. CAM was assessed by heart rate variability (HRV) analysis of 39-hour RR intervals, including frequency (high frequency, HF; low frequency, LF; and LF/HF ratio) and time (SDNN, standard deviation of all RR intervals; RMSSD, square root of the mean of the sum of the squares of differences between adjacent RR intervals; and HR, heart rate) domain variables. To assess the MetS burden, we used continuous MetS score (cMetS)–sum of the age and sex-adjusted standardized residual (Z-score) of five established MetS components. Linear mixed-effect models were used to analyze the association between cMetS and CAM in the entire population and stratified by gender.

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Conflict of interest:
None

Author Contributions
Sol M. Rodriguez-Colon collected the data, did the analysis, interpreted the data, and drafted the manuscript. Fan He collected the data, did the analysis, and interpreted the data. Edward O. Bixler participated in the writing of the manuscript. Julio Fernandez-Mendoza provided comments for the revision of the manuscript. Alexandros N. Vgontzas provided comments for the revision of the manuscript. Susan Calhoun provided comments for the revision of the manuscript. Zhi-Jie Zheng provided comments for the revision of the manuscript. Duanping Liao provided overall direction of the manuscript, participated in the interpretation of the study data, and the writing of the manuscript. All authors read and approved the final manuscript.

Results—After adjusting for age, sex, and race, cMetS was significantly associated with reduced HRV and higher HR. With 1 standard deviation increase in cMetS, there was a significant decrease in HF(−0.10(SE=0.02)), LF(−0.07(SE=0.01)), SDNN(−1.97(SE=0.50)), and RMSSD(−1.70(SE=0.72)), and increase in LF/HF(0.08(SE=0.02)) and HR(1.40(SE=0.26)). All cMetS components, with the exception of high-density lipoprotein (HDL), were associated with significantly decreased HRV and increased HR. High blood pressure (MAP) and triglyceride (TG) levels were also associated with an increase in LF/HF and decrease in RMSSD. An increase in high-density lipoprotein was only associated with higher LF and SDNN. Moreover, cMetS and HRV associations were more pronounced in males than in females. The associations between HRV and. MAP, TG, and HDL were more pronounced in females.

Conclusions—cMetS score is associated with lower HRV, suggesting an adverse impact on CAM, even in apparently healthy adolescents.

Keywords

Cardiovascular diseases; Metabolic Syndrome; Central Obesity; Hypertension; Insulin Resistance

1. Introduction

The metabolic syndrome (MetS) is a constellation of adverse cardiovascular disease (CVD) and metabolic risk factors that include central obesity, elevated blood pressure, elevated triglycerides, hyperglycemia or insulin resistance, and low levels of high-density lipoprotein-cholesterol [1]. The prevalence of MetS in adults in the United States is 40.1% [2]. However, in children and adolescents, the prevalence of MetS is considerably lower. Comparing data in adolescents from the 1988–1994 to 2001–2006 U.S. National Health and Nutrition Examination Survey, the prevalence of MetS increased from 4% to 9% [3]. And for those who are obese, the prevalence of MetS varies from 30–50% [4]. Although MetS has been well-defined in the adult population, there is no current universal definition for Mets in adolescents. Therefore, these results were not comparable. In addition, due to the low MetS prevalence reported, a large sample size is required to assess the MetS burden and study the risk factors in the youth. Several epidemiological studies have attempted to define MetS in children and adolescents [5–9] and have suggested the use of a continuous MetS score (cMetS). Given the higher statistical power of a continuous score compared to categorical MetS criteria; it is more practical to investigate the association between cMetS and different health outcomes in adolescents.

In adults, MetS increases the risk of CVD and diabetes [10–11] and alters the function of the cardiovascular system [12]. The autonomic nervous system plays an important role in the cardiovascular regulation [13]. Heart rate variability (HRV), a noninvasive measurement of cardiac autonomic modulation (CAM) [14], is regulated by the balance of sympathetic and parasympathetic modulation. An imbalance between the these two results in impairment of CAM [13,15], which has been reported as an independent risk factor for CVD [13,15–16]. Lower HRV calculated from short-term normal RR intervals has been associated with CVD mortality and CVD morbidity in various adults populations [11,16–23]. Several studies in adults have examined the association between MetS and HRV [23–27]. However most of these studies analyzed the clustering of MetS disorders, which is not applicable in young

populations due to the lack of binary defintion of MetS. A number of other studies have evaluated the association between each individual MetS component and HRV indices in children [28–35].Only one particular study examined the relationships between each component of MetS, as continuous variable, and the change of HRV in young adults (18–21 years) [28]. However, to our knowledge, no study has examined the association between MetS component cluster and HRV in children/adolescents. Several methods, including principle component analysis [7], Z scores [5,8], and rankings [6], have been used to derive a cMetS score and represent an aggregated burden for MetS in adolescents. This cMetS score enables examinations of preclinical MetS burden in children and adolescents, much earlier than the development of clinical symptoms of MetS. Thus, the main objective of the study is to investigate the association between cMetS score and the CAM as measured by HRV in a population-based sample of adolescents.

2. Material and Methods

2.1. Study population

We used data from 421 adolescents who completed the follow-up examination of the Penn State Children Cohort (PSCC) study. The recruitment and examination procedures for the baseline study have been published elsewhere [36,37]. During 2010–2013, a follow-up examination for 700 participants from phase II of PSCC was conducted. Among these subjects, 421 of them completed the follow-up with a response rate of 60% and a mean follow-up time of 7.7-year. The loss to follow-up was mainly due to subjects moving out of central Pennsylvania. However, no major difference in baseline characteristics was observed between subjects who did or did not participate. During the study period, participants were evaluated overnight in the Clinical Research Center at the Pennsylvania State University College of Medicine (COM) including a complete physical examination, a whole body dual-energy x-ray absorptiometry, and a 9-hour fixed-time polysomngraphy (PSG) recording, and overnight fasting blood, saliva, and urine samples. The study protocol was approved by Pennsylvania State University COM IRB. Written informed consents were obtained from participants and their parents if participant was a minor (<18 years old).

2.2. Continuous Metabolic Syndrome Score (cMetS)

MetS burden was assessed by the cMetS–the sum of the age and sex adjusted standardized residual (Z-score) of the following parameters: waist circumference (WC), mean arterial pressure (MAP), homeostasis model assessment of insulin resistance (HOMA-IR), triglycerides (TG), and high-density lipoprotein (HDL). WC and seated blood pressure (BP) were assessed during physical exam by a trained investigator. The average of the 2^{nd} and 3^{rd} BP was used in the analysis. MAP was calculated as diastolic pressure+1/3 systolic pressure. Glucose, insulin, and lipid profiles were obtained from venous blood drawn from subjects in fasted status. HOMA-IR was calculated as the product of fasting insulin level (in μU/ml) and fasting glucose level (in mmol/L) divided by 22.5. Because HDL level is inversely related to metabolic risk, it was multiplied by -1. The five components were age and gender-adjusted based on separate regressions on age and gender. The five adjusted components were converted to Z-score and summed to create cMetS. A higher score is indicative of less favorable cardiometabolic profile and higher MetS burden.

2.3. Continuous ECG recording and CAM measures

A high-fidelity (sampling frequency 1,000 Hz) 12-lead HScribe Holter System (Mortara Instrument, Inc., Milwaukee, WI) was used for 39-hour beat-to-beat ECG data collection. The standardized operation procedures for the PSCC study were followed in the data collection, offline processes, HRV analysis, and interpretation processes. We followed the Holter ECG Data Collection and Analysis Procedures previously described [19], but using 39-hour recording instead of 24-hour.

The complete 39-hour data recordings (from 5:00PM of Day-1 to 8:00AM of Day-3) were used for this particular analysis. The 39-hour normal beat-to-beat RR interval data was divided into 30-minute segments of RR data. Thus, each individual provided 78 segments of 30-minute RR data. The RR data for HRV analysis were processed according to current recommendations [19]. Within each segment, any RR interval ≤300ms, ≥1600ms, or where the ratio from two adjacent RR intervals was <0.75 or >1.33 were excluded from the HRV analysis. The time and frequency-domain HRV analysis were performed on the remaining normal RR interval data if the total length of such normal RR intervals was greater than 22.5 minutes (75% of original data), using the HRV Analysis Software v1.1 [38]. For the frequency-domain HRV analysis we used Fast Fourier Transformation (FFT). Briefly, the adjacent RR interval data was interpolated using a piecewise cubic spline approach, with a 2Hz sampling rate. The FFT was performed on the equidistantly interpolated RR time series. The following HRV indices were calculated as measures of CAM: power in the high frequency range (HF, 0.15–0.40Hz), power in the low frequency range (LF, 0.04–0.15Hz), the ratio of LF to HF (LF/HF), standard deviation of all RR intervals (SDNN, ms), and the square root of the mean of the sum of the squares of differences between adjacent RR intervals (RMSSD, ms).

2.4. Covariables

Demographic information of population attributes, such as age, race, gender, and medical history were collected by an experienced investigator. Body mass index (BMI) was calculated by dividing weight in kilograms by height in meters squared; and age and sex adjusted BMI percentile was calculated based on the 2000 CDC Growth Charts.

2.5. Statistical analysis

The characteristics of the study population (mean, standard deviation (SD) or proportions) were calculated. From the 421 adolescents who completed the follow-up examination, 7 had insufficient ECG data, 49 were excluded due to incomplete information on any of the 5 MetS components, and 7 were excluded due to diabetes diagnosis or a high risk of diabetes or other cardiovascular conditions. As a result, the effective sample size for this report is 368 adolescents (87% of the original 421). Each individual contributed up to 78 segments of 30-minute RR interval data, resulting in 21,863 segments of HRV data. To assess the effect of the cMets on the HRV variables, we used adjusted (age, sex, and race) linear mixed-effect models. Logarithmic transformation was performed on HOMA-IR, to achieve a normal distribution when analyzing its relationship to HRV variables. HF, and LF were also log-transformed according to current recommendation [19]. All results from the regression models were expressed as the associated change in HRV of 1 SD increase in cMetS and its

components. We tested the interactions between gender and cMetS, and each of its components. A p-value of ≤0.05 was used to determine statistical significance. All analyses were performed using SAS version 9.3 software (SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Characteristics of study population

The characteristics of the study population, overall and stratified by gender, are shown in Table 1. Out of the 368 adolescents, 54.1% (N=199) were males, and 77.7% (N=286) were non-Hispanics whites. The age and BMI percentile of the entire cohort was 16.90(2.24) years and 65.94(28.05), respectively. The prevalence of obesity (BMI percentile ≥95) in this population was 15.5%. The cMetS for males and females were 0.07(2.71) and 0.17(2.72), respectively. Males had significantly higher WC, and lower HDL than females (all with p-value of <0.01). The average MAP, TG, and HOMA of the entire population were 82.42(9.10), 93.96(46.53), and 1.07(1.34), respectively. All HRV indices, with the exception of HR, were lower in females.

3.2. cMetS and its components effect on HRV indices

The association between cMetS and its components and HRV indices are presented in Table 2. The age, race, and sex adjusted regression coefficients from the linear mixed-effect models were used to associate cMetS and each of its components, in relationship to HRV indices. In summary, after adjustment for major covariables, 1 SD increase in cMetS was significantly associated with lower HF, LF, SDNN, and RMSSD, and higher LF/HF and HR. As to the cMets component, increase in each of the cMetS components, with the exception of HDL, was associated with a significant decrease of HF, LF, SDNN, and increase of HR. Higher MAP and TG were also associated with higher LF/HF and lower RMSSD. Higher HDL was associated with high LF and SDNN; but not associated with other HRV indices.

3.3. Effect modification by gender

After establishing the main associations between HRV and cMetS, as well as its individual components, we further tested the interactions between gender and cMetS, and each of its components to elucidate any gender differences in the main effects, given the development stage of our study population. Because of the significant (at the <0.05 level) interaction terms between sex and cMetS, and sex and several individual components of cMetS, we stratified the main associations according to gender and presented the gender-specific associations in Table 3, adjusting for age and race. In general, the associations between HRV and overall cMetS, WC, and HOMA-IR were significantly more pronounced in males than in females. However, the association between several individual components, such as MAP, TG, and HDL cholesterol, and HRV were more pronounced in females.

4. Discussion

We examined the cross-sectional associations between cMetS and its components and CAM as measured by HRV indices and HR. In this population-based sample of apparently healthy

adolescents, cMetS is adversely associated with CAM, in the direction of lower HRV and higher HR. Similar patterns of association were also observed for each cMetS component. Moreover, there is a significant gender effect modification in our data.

In adult populations, it is well known that MetS is associated with adverse HRV profile. However, in children, the clinical manifestation of MetS as defined by traditional adult criteria is very rare. This may explain the limited published data showing the association between measures of MetS and HRV in children/adolescents. At individual MetS component level, one particular study in young adults (ages 18–21) found that the increases in most MetS components were associated with lower HF, SDNN, RMSSD and higher HR. Specifically, increased levels of systolic BP, glucose, and TG were associated with lower HF and higher HR. In addition, increased systolic BP has been also associated with lower SDNN, and RMSSD [28]. Other studies in children have only evaluated the association between some of the five individual components of MetS and HRV [29–35]. For WC, a measure of central obesity, very limited data is available to assess its association with HRV in children [29,30]. Previously published data from our group, using baseline data from the PSCC study, demonstrated that an increase of 1 SD in WC was significantly associated with lower HF, LF, RMSSD, SDNN, and higher LF/HF and HR [29]. In addition, Luisa and colleagues studied a sample of 16 overweight/obese girls (ages 8–16) and found an association between increase of central fat and lower HF and higher LF/HF [30]. The findings of these previous studies on WC and HRV are consistent with our current results, which showed that higher WC is associated with impairment of CAM. In addition, several studies have examined the association between BP and HRV in children [31–35]. A study performed in 105 healthy children found that those high systolic BP displayed significant lower HF and RMSSD [32]. Also, Fitzgibbon et al. found that children with high BP have significantly lower HF, LF, and higher LF/HF than those with normal levels [33]. In another study of children (ages 15–16), high normal BP was also correlated with a reduced HF of HRV [34]. Our finding that increased MAP is associated with low HF, LF, SDNN, RMSSD, and higher LF/HF and HR, combined with these previous studies, provides evidence that increased BP is associated with reduced HRV in children.

The relationship between HOMA-IR and CAM has been studied in children [31]. In a study of 36 children (mean age of 11.5 years), Kaufman et al. found that LF/HF was positively related, whereas HF was negatively related to HOMA-IR. However, after adjustment for fat mass, this relationship was no longer significant [31]. A subgroup analysis of children classified by HOMA-IR values demonstrated that those in the insulin-resistance group had lower HF and higher LF/HF than the non-resistant group [35]. In our data, HOMA-IR is significantly associated with decreased HF, LF, SDNN, RMSSD, and increased HR, whereas no association was found with the LF/HF. No data in children is available on the association of TG or HDL with HRV. However, a study in young adults (ages18–21) found that TG was associated with lower HF, and higher LF/HF and HR [28]. Our findings confirmed their results. In addition, we also found a significant association between TG and lower LF, SDNN, RMSSD. A study on adults demonstrated that HDL was associated with low LF/HF, and high LF, even after adjustment for type 2 diabetes, depression, and smoking [46]. Our data on HDL demonstrate that it is positively related with all HRV variables, and negatively related with HR. In adults, others have reported gender differences in the

associations between MetS and HRV [24,47], and between MetS or type 2 diabetes and coronary heart disease [48,49]. To our knowledge, there is no published data that systematically investigate gender effect modification of MetS and HRV relationship in children and adolescents. One large epidemiological study performed in young adults found an association between MetS and lower HRV [24]. The authors also reported that although higher BP was associated with lower HRV in both genders, higher WC was associated with lower HRV in males only, whereas higher TG was associated with lower HRV in females only. After systematically examining the significant effect modifications by gender, we reported significantly more pronounced associations between cMetS, WC, HOMA-IR and HRV in males. Whereas, the associations between MAP, TG, and HDL and HRV were more pronounced in females. These significant gender differences could be related to differences in fat distribution between genders [50], and/or the changes of insulin resistance during the prepubertal to pubertal stages, which are known to relate to hormonal changes in both genders [48,51–52].

There is limited data available on the association between cMetS and other health outcomes in children, especially CVD [53–56]. A study in Indian children investigating the association between cMetS and risk of carotid arterial stiffness, found a graded relationship between cMetS and risk factors of MetS, and that children with higher cMetS had higher risk of carotid arterial stiffness than those with lower cMetS [54]. Due to the limited data available on the cMetS in adolescence, to the best of our knowledge, this is the first study to demonstrate that cMetS and its components are associated with impairment of CAM, even in apparently healthy adolescents without symptomatic metabolic abnormalities or clinically abnormal cMetS components. However, it would be crucial to further evaluate this association in children using longitudinal data, in order to prevent the onset of CVD in later life. Recently, a 3-year longitudinal study on 163 young healthy adults demonstrated that the MetS components, including WC, systolic BP, TG, glucose, and HDL, were inversely associated with vagal indices, suggesting that these components of MetS are associated with lower vagal modulation even in a population with no metabolic abnormalities [28].

A few limitations of this study should be recognized. First, the five cMetS components were equally weighted and treated independently when summing-up the individual z-score. Thus, the true association between each individual risk factor and MetS risk may not be detected, since, for example, HOMA-IR may play the most critical role in the association. Second, the cMetS derived in this study cannot be compared to other study, since it is sample specific. However, we may argue that the present population-based sample of adolescents represents the demographic characteristics of central Pennsylvania. Therefore, our results are generalizable and comparable to other studies targeting adolescent population. Third, we used cross-sectional data limiting our ability to establish a temporal relationship.

Several strengths of this study are worth mentioning. First, it is the first population-based sample of adolescents investigating the association between cMetS and its components on CAM. Second, we were able to collect a ECG recording of long duration (39-hours of data). Third, because of the low prevalence of MetS in adolescents, the MetS criteria developed for adults may not be applicable for adolescent. Therefore, we use cMetS score to represent the MetS burden in our population. However, the five components used to calculate cMetS are

the same risk factors used in the adult MetS definition. The consistency enables the possibility of tracking the MetS risk across the lifespan. Meanwhile, the z-score accounted for the influences of age and sex on each individual risk factor and subsequently overall MetS burden. These strengths enhance the validity of our findings.

In conclusion, in apparently healthy adolescents higher cMetS score, a measure of preclinical MetS burden, is already associated with reduced HRV and higher HR, suggesting an adverse impact on CAM. This finding suggests the potential damage to the cardiac system from the overall metabolic burden as well as from each individual MetS components.

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Abbreviations

BMI	body mass index
CAM	cardiac autonomic modulation
cMetS	continuous metabolic syndrome score
CVD	cardiovascular diseases
ECG	electrocardiography
HDL	high-density lipoprotein
HF	high frequency range
HR	heart rate
HRV	Heart rate variability
LF	Low frequency range
LF/HF	the ratio of LF to HF
MAP	mean arterial pressure
MetS	metabolic syndrome
PSCC	Penn State Children Cohort
RMSSD	square root of the mean of the sum of the squares of differences between adjacent RR intervals
SDNN	Standard deviation of all RR intervals
TG	triglycerides
WC	waist circumference

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Table 1

The study population characteristics and summaries of HRV indices.

Demographics	All (N=368)	Male (N=199)	Female (N=169)
Age (years)	16.90 (2.24)	16.80 (2.23)	17.03 (2.24)
Non-Hispanics White (%)	77.72	79.40	75.74
BMI percentile	65.94 (28.05)	64.85 (29.36)	67.22 (26.46)
cMetS	0.04 (2.71)	0.07 (2.71)	0.17 (2.72)
WC (cm)	80.48 (13.48)	82.63 (14.09)	77.95 (12.28)
MAP (mm Hg)	82.42 (9.10)	83.02 (9.12)	81.72 (9.05)
TG (mg/dL)	93.96 (46.53)	94.03 (48.83)	93.88 (43.82)
HDL (mg/dL)	49.81 (12.32)	46.15 (9.67)	54.13 (13.66)
Log HOMA-IR	−0.23 (0.71)	−0.29 (0.69)	−0.21 (0.73)
HRV Indices*:			
Log of HF (ms^2)	6.18 (1.16)	6.25 (1.12)	6.09 (1.19)
Log of LF (ms^2)	6.63 (0.80)	6.73 (0.77)	6.51 (0.82)
LF/HF Ratio	2.09 (1.70)	2.12 (1.69)	2.06 (1.71)
SDNN (ms)	91.62 (35.52)	96.23 (36.54)	86.19 (33.48)
RMSSD (ms)	59.20 (34.10)	61.09 (33.96)	56.97 (34.13)
Heart Rate (BPM)	75.68 (16.38)	74.57 (16.40)	76.99 (16.26)

Abbreviations: BMI, body mass index; cMetS, continuous metabolic syndrome score; HDL, high-density lipoprotein; HF, high frequency power; HOMA-IR, homeostasis model assessment of insulin resistance; HRV, heart rate variability; LF, low frequency power; Log, logarithm; MAP, mean arterial pressure; RMSSD, square root of the mean of the sum of the squares of differences between adjacent RR intervals; SDNN, standard deviation of all RR intervals; TG, triglycerides; WC, waist circumference. Continuous variables reported as mean ± SD; binary variables reported as %.

*:Overall average of the intra-subject means.

Table 2

Adjusted regression coefficient of HRV in association with 1SD increase in cMetS and its components.

	HRV Index					
	Log-HF (ms^2) β (SE)	**Log LF (ms^2) β (SE)**	**LF/HF ratio β (SE)**	**SDNN (ms) β (SE)**	**RMSSD (ms) β (SE)**	**HR (bpm) β (SE)**
cMetS	−0.10 (0.02)**	−0.07 (0.01)**	0.08 (0.02)**	−1.97 (0.50)**	−1.70 (0.72)*	1.40 (0.26)**
WC	−0.07 (0.02)**	−0.06 (0.01)**	0.03 (0.02)	−1.88 (0.53)**	−0.82 (0.77)	1.02 (0.28)**
MAP	−0.08 (0.02)**	−0.05 (0.01)**	0.06 (0.02)**	−1.98 (0.53)**	−1.80 (0.76)*	1.13 (0.27)**
Log HOMA-IR	−0.06 (0.02)**	−0.05 (0.01)**	0.01 (0.02)	−1.47 (0.52)**	−1.37 (0.75)	1.33 (0.27)**
TG	−0.14 (0.02)**	−0.09 (0.01)**	0.12 (0.02)**	−3.56 (0.50)**	−2.85 (0.73)**	2.00 (0.26)**
HDL	0.03 (0.02)	0.04 (0.01)**	0.02 (0.02)	2.59 (0.54)**	1.21 (0.80)	−0.49 (0.29)

Abbreviations: BPM, beats per minute; cMetS, continuous metabolic syndrome score; HDL, high-density lipoprotein; HF, high frequency power; HOMA-IR, homeostasis model assessment of insulin resistance; HRV, heart rate variability; LF, low frequency power; Log, logarithm; MAP, mean arterial pressure; RMSSD, square root of the mean of the sum of the squares of differences between adjacent RR intervals; SDNN, standard deviation of all RR intervals; TG, triglycerides; WC, waist circumference.

The model was adjusted for age, race, and gender.

* and **, $P < 0.05$; and $P < 0.01$, respectively

Table 3

Adjusted regression coefficient of HRV in association with 1SD increase in cMetS and its components stratified by gender.

	HRV Index						
	Gender	**Log-HF (ms^2) β (SE)**	**Log LF (ms^2) β (SE)**	**LF/HF ratio β (SE)**	**SDNN (ms) β (SE)**	**RMSSD (ms) β (SE)**	**HR (bpm) β (SE)**
cMetS	M	−0.13(0.03)**	−0.08(0.01)**	0.15(0.03)**	−3.38(0.66)**	−2.74(0.97)**	1.85(0.35)**
	F	−0.05(0.03)	−0.05(0.02)**	0.01(0.03)	−0.35(0.74)	−0.32(1.08)	1.02(0.38)**
WC	M	−0.13(0.03)**	−0.08(0.01)**	0.12(0.03)**	−3.28(0.68)**	−2.60(0.99)**	1.76(0.36)**
	F	0.02(0.04)	−0.03(0.02)	−0.10(0.04)**	0.12(0.83)	1.97(1.21)	0.11(0.43)
MAP	M	−0.06(0.03)*	−0.03(0.02)*	0.07(0.03)*	−1.86(0.72)**	−0.67(1.04)	0.88(0.38)*
	F	−0.11(0.03)**	−0.08(0.02)**	0.05(0.03)	−2.43(0.75)**	−3.02(1.09)**	1.74(0.38)**
Log HOMA-IR	M	−0.13(0.03)**	−0.09(0.02)**	0.11(0.03)**	−3.78(0.73)**	−3.35(1.06)**	2.20(0.38)**
	F	0.01(0.03)	−0.02(0.02)	−0.07(0.03)*	0.83(0.72)	0.74(1.05)	0.46(0.37)
TG	M	−0.10(0.03)**	−0.08(0.01)**	0.09(0.03)**	−3.43(0.63)**	−2.22(0.93)*	2.06(0.33)**
	F	−0.18(0.03)**	−0.11(0.02)**	0.15(0.03)**	−3.48(0.75)**	–3.47(1.15)**	1.81(0.41)**
HDL	M	–0.07(0.04)	–0.002(0.02)	0.15(0.04)**	0.73(0.87)	–1.58(1.27)	–0.33(0.47)
	F	0.09(0.03)**	0.07(0.02)**	–0.05(0.03)	3.74(0.69)**	2.98(1.00)**	–0.61(0.36)

Abbreviations: BPM, beats per minute; cMetS, continuous metabolic syndrome score; F, female; HDL, high-density lipoprotein; HF, high frequency power; HOMA-IR, homeostasis model assessment of insulin resistance; HRV, heart rate variability; LF, low frequency power; Log, logarithm; M, male; MAP, mean arterial pressure; RMSSD, square root of the mean of the sum of the squares of differences between adjacent RR intervals; SDNN, standard deviation of all RR intervals; TG, triglycerides; WC, waist circumference.

The model was adjusted for age, and race.

* and **, $P < 0.05$; and $P < 0.01$, respectively.