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Correlation among Poincare plot and traditional heart rate variability indices in adults with different risk levels of metabolic syndrome: a cross-sectional approach from Southern India

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Abstract

Objectives: Heart rate variability (HRV) is an important marker of cardiac autonomic modulation. Metabolic syndrome (MetS) can alter cardiac autonomic modulation, raising the risk of cardiovascular disease (CVD). Poincaré plot analysis (PPA) is a robust scatter plot-based depiction of HRV and carries similar information to the traditional HRV measures. However, no prior studies have examined the relationship between PPA and traditional HRV measures among different risk levels of MetS. We evaluated the association between the Poincare plot and traditional heart rate variability indices among adults with different risk levels of MetS.
Methods: We measured anthropometric data and collected fasting blood samples to diagnose MetS. The MetS risk was assessed in 223 participants based on the number of MetS components and was classified as control (n=64), pre-MetS (n=49), MetS (n=56), and severe MetS (n=54). We calculated the Poincaré plot (PP) and traditional HRV measures from a 5 min HRV recording.
Results: Besides the traditional HRV measures, we found that various HRV indices of PPA showed significant differences among the groups. The severe MetS group had significantly lower S (total HRV), SD1 (short-term HRV), SD2 (long-term HRV), and higher SD2/SD1. The values of S, SD1, SD2, and SD2/SD1 were significantly correlated with most traditional HRV measures.
Conclusions: We found gradual changes in HRV patterns as lower parasympathetic and higher sympathetic activity alongside the rising number of MetS components. The HRV indices of PPA integrating the benefits of traditional HRV indices distinguish successfully between different risk levels of MetS and control subjects.

Keywords: autonomic modulation; heart rate variability; metabolic syndrome; Poincare plot analysis; risk stratification.

Introduction

Metabolic syndrome (MetS) is a complex combination of predisposing variables which increase the risk of type 2 diabetes (T2DM) and adversely affect cardiovascular health [1, 2]. Insulin resistance (IR), atherogenic dyslipidemia, abdominal obesity, and hypertension are the major determinants of MetS, which are interrelated and confer more significant cardiovascular disease (CVD) risk in combination than individually [3]. Currently, MetS is receiving considerable attention from the medical community as a major modifiable determinant of CVD and T2DM. The growing prevalence of MetS is a concern in both developed and developing countries [4, 5]. About one-quarter of the world's population is estimated to have MetS [6]. Studies report that the prevalence of MetS ranges from 7.9 to 39% in developed countries, while in India, it varies from 9.2 to 43.2% [7–9].

Studies have suggested that MetS-related cardiac autonomic dysfunction (CAD) manifests as a sympathovagal imbalance, accelerating CVD outcomes [10–12]. Heart rate variability (HRV) has proven to be a simple, reliable, and non-invasive method for evaluating autonomic modulation

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[13]. HRV is a valuable tool for monitoring CVD progression in MetS patients due to its predictive power [14–16]. The CAD in MetS is linked to lower overall HRV that predicts T2DM, coronary heart disease, and all-cause mortality [10–17]. Analyzing HRV signals involves a variety of approaches and methodologies for quantitative evaluation of the autonomic activity over the chronotropic property. Traditional HRV measures involving temporal (time-domain) and spectral (frequency-domain) analyses are widely accepted due to their strong physiological basis. It is easy to measure time domain variables, and their utility has been demonstrated in various cardiac and noncardiac pathological conditions and in normal individuals [18]. As a more robust and easier-to-interpret measure of autonomic activity than time analysis, frequency-domain HRV analysis provides more accessible measures to interpret when considering physiological regulation. Although traditional HRV methods provide reliable information about the sympathetic and parasympathetic activity, these methods can fail to account for the non-stationary properties of HRV signals [18]. They only offer limited information about HRV because nonlinear mechanisms are likely to play a role in heart rate dynamics.

The Poincaré plot analysis (PPA) is one of the most popular methods of HRV analysis. In addition to being called return maps, it is considered nonlinear because it describes the nonlinear dynamics of a phenomenon by recognizing hidden correlation patterns [19]. Poincaré plots depict temporal correlations within the RR interval as elliptic-shaped graphs. Each RR interval in this plot is a function of the preceding RR interval, which means the duration of the current cardiac beat (RRn) is represented on the x-axis, and the duration of the next beat (RRn+1) is represented on the y-axis. As a result, each point (RRn, RRn+1) on the plot corresponds to two consecutive heartbeats. Various descriptors such as S, SD1, SD2, and SD2/SD1 are associated with this plot, some of which have an interesting physiological interpretation [20]. Recent trends favor PPA since nonstationary and nonlinear dynamics of HRV measurements are simplified by nonlinear analysis. However, Brennan et al. [21] raised the question of whether existing measures of Poincaré plot geometry actually reflect nonlinear HRV features. According to them, SD1 and SD2 computed from Poincaré plots are linear markers and cannot be used to describe nonlinear dynamics associated with HRV. Another study tested this statement by analyzing the correlations of descriptors of PPA with classical linear and nonlinear indexes [22]. They reported a strong relationship of SD1/SD2 ratio with nonlinear variables, Hurst Exponent, and detrended fluctuation analysis (DFA) α1, both in patients with coronary artery disease and healthy subjects. At the same time, isolated SD1 and SD2 indexes were strongly related to linear time and frequency domains. This supported the notion of Brennan et al. [21] and verified the presence of nonlinear information hidden in the SD1/SD2 ratio.

Prior studies regarding MetS relied only on traditional parameters (such as time domain or spectral analysis) to measure HRV [10–17]. It has been shown that Poincaré plots have been able to combine the advantages of both time and frequency domain methods in a very promising way [23]. The correlation between the Poincare plot and traditional HRV indices indicated that an increased respiratory rate decreases the long term HRV measures indicating increase in high frequency [24]. Strength of correlation between the lagged Poincare with the spectral indices are useful to delineate normal from pathological HRV. The PPA reflects the trendline in the form of spectral sensitivity on dynamic autonomic basis which would enable maintenance of homeostasis [25]. Interestingly, only a few studies have investigated HRV dynamics by PPA to assess autonomic modulation in MetS [24, 26–30]. Furthermore, no studies have compared cardiac autonomic activity set by PPA with traditional HRV indices among MetS patients with different risk levels. We hypothesize that both PPA and traditional HRV indices can assist in stratifying MetS risk. In addition, we expect the PPA descriptors to be highly correlated with traditional time- and frequency-domain measurements generated by the same processes. Thus, this study sought to compare and correlate four different descriptors of PPA with traditional HRV parameters and spontaneous baroreflex sensitivity (BRS) among different MetS risk levels.

Materials and methods

Study participants

We performed a cross-sectional study in a tertiary care teaching hospital in Puducherry, India. The Institutional Ethical Committee approved the study protocol for human studies (JIP/IEC/2018/0301). A power analysis was performed before the study using OpenEpi, version 3. Based on the previous report with a difference of 7.39 between two independent means of SD1 of PPA, the sample size obtained was 66 subjects with 33 in each group, resulting from 95% confidence interval and 90% power [28]. However, we enrolled 223 subjects aged 18–65 years of either gender who volunteered to participate in this study. Before participating, all participants signed informed consent.

We followed National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) [3, 4] guidelines to stratify the study participants with different risk levels of MetS based on the number of MetS components (Table 1). The 223 study participants were divided into 64 subjects in the control group (none or any one MetS component), 49 subjects in pre-MetS (any two components), 56 subjects in the MetS (any three MetS components), and 54 subjects in the severe MetS group (more than three MetS components). We excluded many subjects with a

Table 1: National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines for the diagnosis of MetS.

MetS component	Cut-off or reference value
Waist circumference	≥90 cm in Asian men, ≥80 cm in Asian women.
Fasting plasma glucose	≥100 mg/dL (5.6 mmol/L) or previously diagnosed with type-2 diabetes or on medication for type-2 diabetes.
Serum triglyceride	≥150 mg/dL (1.7 mmol/L) or on specific treatment for dyslipidemia.
HDL cholesterol	≤40 mg/dL (1.03 mmol/L) in men, ≤50 mg/dL (1.29 mmol/L) in women or on specific treatment for dyslipidemia.
Blood pressure (BP)	Systolic blood pressure ≥130 mmHg, diastolic blood pressure ≥85 mmHg, or receiving antihypertensive medication.

medical history of cardiac disorders, cancer, neurological, psychiatric, and other endocrine ailments, and medication use for any chronic condition during the screening procedure.

Anthropometric, clinical, and biochemical data collection

Anthropometric measurements were performed using the World Health Organization (WHO) guidelines [31, 32]. The body fat percentage (BF%) was assessed using Quadscan 4000 analyzer from Bodystat 1500 UK with a bioelectrical impedance analysis (BIA) approach. Blood pressure (BP) was measured in the right arm using an Omron automated BP device after 10 min of rest in a sitting posture. We obtained a minimum of three recordings at 1 min intervals. Three BP readings were averaged. Fasting blood samples were obtained by vein puncture and processed using assay kits designed for clinical chemistry self-analyzer (Olympus 400, Beckman Coulter, Orlando, FL, USA) for biochemical parameters. Friedwald's formula was used to estimate other lipid profile parameters [33]. Lipid-to-lipoprotein ratios were computed using lipid parameters. We have utilized commercially available immunosorbent assay kits (ELISA) for assessing insulin, hs-CRP, and adiponectin as directed by the manufacturer (Calbiotech, CA). Homeostatic model assessment of IR (HOMA-IR) was calculated as fasting plasma insulin (μU/mL) × FPG (mmol/L)/22.5.

Measures of cardiac autonomic modulation

Short-term heart rate variability (HRV): We used BIOPAC MP 150 data acquisition system (BIOPAC Inc., Goleta, CA), Acknowledge (version 4.2), and Kubios HRV analysis software (Version 2.0., Biomedical Signal Analysis Group, University of Kuopio, Finland) to record and analyze the lead II ECG. Previously, a complete description was given regarding the apparatus, procedure, and protocol for measurement [34]. Following the standard guidelines of the Task Force of European and North American society for HRV, lead II electrocardiography (ECG) was recorded for 15 min. Participants were instructed not to talk or move and to relax as much as possible. The participants were in a supine position for 10 min before the start of the HRV test [18]. The recorded resting lead II ECG using a bandpass filter (2–40 Hz) was carefully analyzed for artifacts and ectopic beats, which were removed thoroughly. Data recordings of 15 min were divided into three equal segments of 5 min each and ensured that the sampling RR intervals (R–Ri) were sufficiently long for analysis, preferably stationary, and of good quality. Conventionally, short-term recordings of HRV are considered stationary because of well-controlled experimental conditions that ensure transients are absent. However, we performed a stationarity test and compared the mean and variance of short HRV series (about 300 beats) to differentiate stationary from nonstationary periods. In this study, we performed the stationarity test recommended by Magagnin et al. to avoid nonstationarities, potentially biasing HRV indices [35]. We calculated the percentage of mean and standard deviation differences within each pair of segments of the selected R–Ri series to test their stability/stationarity. A stationarity check was conducted on all the 5 min segments to determine the most suitable for the study. This distribution was assessed for normality using Kolmogorov–Smirnov goodness-of-fit ($p<0.05$). A log transformation was applied to the data if the null hypothesis of normality was rejected. The null hypothesis of normality was finally invalidated if it was rejected a second time.

Poincaré plot analysis (PPA): It has been shown in clinical studies that Poincaré plots can be used to analyze HRV data, and they yield good results [26]. Research suggests the transversal axis represents vagal-mediated short-term variability since it develops faster than sympathetically induced changes in RR intervals. On the other hand, the longitudinal axis represents global variability as an inverse function of sympathetic modulation. Based on quantification of the RR intervals scattered over the transversal and longitudinal axes of the Poincare plot, researchers compared them to spectral or temporal analysis in several maneuvers (daily activity, exercise, supine, sitting, and standing), with or without pharmacological blocking [26, 36]. They found that Poincare plot indexes more reliably and conveniently recorded the autonomic activity, providing useful information that would otherwise be challenging to detect. Consequently, we chose Poincaré plot markers to test their effectiveness in distinguishing different MetS risk levels. The PPA quantified from the 5 min ECG recordings provides four indicators when the ellipse-fitting technique modifies the plot. S constitutes the ellipse area and is strongly linked with total HRV and BRS. We have estimated S ($\pi \times SD1 \times SD2$) as per published sources. The S increases either with SD1 or SD2 and remains constant when SD1 increases at the rate SD2 declines. SD1 refers to scattered points perpendicular to the line of identity, serves as an index of short-term HRV, and is directly related to parasympathetic activity. SD2 refers to the scattered points along the identity line, representing both short- and long-term HRV, and seems to be inversely related to sympathetic activity. The ratio of SD2/SD1 expressed the complexity of HRV, thus suggesting the delicate equilibrium between sympathovagal systems in the heart [24].

Baroreflex sensitivity (BRS): Like HRV, power spectral analysis also assesses blood pressure variability (BPV) [37]. It contains high-frequency oscillations considered respiration-mediated and low-frequency oscillations called "Mayer waves," which reflect sympathetic vascular activity. Among all the BPV parameters, baroreceptor reflex sensitivity (BRS) has been considered vital in assessing cardiovascular function and dysfunction and cardiovascular risks in health and various clinical disorders [38]. We used Finapres hemodynamic cardiovascular monitor (Finometer version 1.22a; Finapres Medical Systems BV, Amsterdam, Netherlands) and BeatScope Easy software to assess BRS. Finapres measures finger arterial pressure continuously by using a finger cuff. It

rebuilds brachial artery pressure from finger pressure using generalized waveform inverse modeling and level correction based on the volume clamp method of Penaz and the physical criteria of Wesseling [39]. The significant advantage of Finapres is the return-to-flow (RTF) calibration, which computes reconstructed brachial pressure nearly identical to the intrabrachial pressure. Rate-pressure product (RPP) determines the myocardial oxygen consumption and workload [40]. RPP was obtained using the formula RPP=10–2 × (BHR × SBP).

Statistical analysis

The SPSS software (version 22) was used to perform statistical analyses (Chicago, IL, USA). The Kolmogorov–Smirnov test was employed to check the normality of data. Skewed data were reported as median (interquartile range), whereas normal distribution data were described as mean ± SD. The percentages and frequencies were provided for categorical data, and a chi-square test ($\chi 2$) was employed to determine differences among groups. One-way ANOVA made the intergroup comparison of parameters, and post hoc analysis was done by Tukey for parametric and the Kruskal–Wallis test for nonparametric data. Spearman's rank correlation analysis was applied to assess the degree of correlation among parameters. All analyses were two-tailed, and the study employed $p<0.05$ as a level of statistical significance.

Results

The groups were similar in age, gender distribution, smoking and alcohol intake, family history of high BP, and T2DM. In contrast, family history of CVD, abdominal obesity, hyperglycemia, high TG, low HDL-C, and elevated BP were substantially higher among Groups III and IV. The anthropometric parameters, including weight, BMI, WC, HC, WHR, and WHtR, were pointedly greater in Group III and IV participants than in Group I (Table 2). The participants in Group II showed significantly higher WHR and WHtR than Group I. In addition, the post-hoc analysis confirms that weight and BMI were considerably higher in Groups III and IV than in Group II. However, WC and WHtR were suggestively more significant only in Group IV. Body fat percentage values are substantially higher, while the lean fat percentage was pointedly lesser in Groups III and IV than in Group I.

Groups III and IV participants had an impaired glycemic profile with significantly higher FPG, insulin, and HOMA-IR than Groups I and II (Table 3). Moreover, we further

Table 2: Comparison of demographic, anthropometric, and body composition data between healthy control, pre-MetS, MetS, and severe MetS subjects.

Variables	Group I (n=64)	Group II (n=49)	Group III (n=56)	Group IV (n=54)	p-Value[a]
Demographic data					
Age (years) **þ**	46 (44–52)	51 (41–55)	48.50 (41–52)	51 (43.75–53)	0.206
Gender (male/female) ¶	30/34	28/21	31/25	29/25	0.697
Smoking: n, % ¶	6 (9.4)	9 (18.4)	11 (19.6)	12 (22.2)	0.260
Alcohol intake: n, % ¶	13 (20.3)	17 (34.7)	16 (28.6)	18 (33.3)	0.305
Family H/O HTN: n, % ¶	20 (31.2)	19 (38.8)	24 (42.9)	29 (53.7)	0.099
Family H/O T2D: n, % ¶	28 (43.8)	26 (53.1)	32 (57.1)	37 (68.5)	0.059
Family H/O CVD: n, % ¶	2 (3.1)	4 (8.2)	9 (16.1)	11 (20.4)	0.017
Increased WC: n, % ¶	25 (39.1)	23 (46.9)	33 (58.9)	37 (68.5)	0.008
Hyperglycemia: n, % ¶	6 (9.4)	24 (49)	44 (78.6)	54 (100)	0.001
High TG: n, % ¶	2 (3.1)	10 (20.4)	27 (48.2)	45 (83.3)	0.001
Low HDL-c: n, % ¶	4 (6.2)	18 (36.7)	32 (57.1)	45 (83.3)	0.001
Raised BP: n, % ¶	4 (6.2)	9 (18.4)	24 (42.9)	39 (72.2)	0.001
Anthropometric measures					
Height, cm **þ**	164 (158.2–171)	162 (154.15–166.9)	160 (155–165.9)	160.75 (153.5–170)	0.059
Weight, kg **þ**	66.5 (58–75.75)	66.0 (63–72)	71 (65–76)[b,c]	72 (69–75)[b,c]	0.001
Body mass index, kg/M^2 **þ**	25.25 (23.65–27.85)	26 (23.75–27.90)	26.85 (25.72–29.17)[b,c]	27.40 (25.9–29.80)[b,c]	0.001
Waist circumference, cm **§**	90.01 ± 9.34	93.55 ± 8.20	97.11 ± 8.72[b]	99.58 ± 8.69[b,c]	0.001
Hip circumference, cms **§**	98.32 ± 9.63	99.36 ± 9.82	101.91 ± 8.78[b]	103.30 ± 9.14[b]	0.021
Waist-to-hip ratio **þ**	0.91 (0.89–0.94)	0.94 (0.90–0.98)[b]	0.95 (0.92–0.99)[b]	0.95 (0.92–0.99)[b]	0.001
Waist-to-height ratio **þ**	0.54 (0.51–0.58)	0.58 (0.54–0.60)[b]	0.60 (0.56–0.64)[b]	0.61 (0.58–0.67)[b,c]	0.001
Body composition					
Body fat, % **þ**	23.85 (17.7–30.5)	25.40 (22.15–35.75)	28.60 (24.02–38.42)[b]	29.50 (25.10–38.37)[b]	0.001
Body lean, % **þ**	76.15 (69.2–81.6)	74.60 (64.25–77.85)	71.40 (65.57–75.85)[b]	70.50 (61.12–74.90)[b]	0.001

Participants were allocated to four groups: Group I – healthy control subjects; Group II – pre-MetS subjects; Group III – MetS subjects and Group IV – severe MetS subjects. Results are expressed as mean ± standard deviation for variables with a normal distribution (**§**), median, and interquartile range for variables with a skewed distribution (**þ**) based on normality testing by Kolmogorov–Smirnov test, and number with percentage for categorical variables (¶). [a]p-Value indicates the differences between the groups by one-way ANOVA. [b]p-Value is significant compared to Group I. [c]p-Value is significant compared to Group II. H/O HTN, history of hypertension; H/O T2D, history of type 2 diabetes mellitus; H/O CVD, history of cardiovascular disease; TG, triglycerides; HDL-c, high-density-lipoprotein cholesterol.

Table 3: Comparison of biochemical profile between healthy control, pre-MetS, MetS, and severe MetS subjects.

Variables	Group I (n=64)	Group II (n=49)	Group III (n=56)	Group IV (n=54)	p-Value[a]
Glucose profile					
FPG, mg/dL **β**	81 (71.25–88)	97 (82–121.52)[b]	120 (106.25–135.50)[b,c]	133 (120–145.5)[b,c,d]	0.001
Insulin, µU/mL **β**	10.12 (8.91–11)	12.12 (10.25–15.19)[b]	15 (13.28–16.93)[b,c]	16.62 (15–18.18)[b,c,d]	0.001
HOMA1-IR **β**	2.02 (1.57–2.39)	2.90 (2.08–4.55)[b]	4.4 (3.48–5.66)[b,c]	5.46 (4.44–6.53)[b,c,d]	0.001
Lipid profile and lipid ratios (risk factors)					
TC, mg/dL **β**	166.50 (154.2–185.7)	172 (162.5–189.0)	177.50 (167.0–187.0)	184.50 (171.7–206.5)[b]	0.001
TG, mg/dL **β**	123.50 (112–141.75)	134 (123.5–143)[b]	149 (123.75–171)[b,c]	164 (152.75–188)[b,c,d]	0.001
HDL-c, mg/dL **§**	46.14 ± 5.01	40.95 ± 8.11[b]	38.61 ± 7.22[b]	35.87 ± 5.69[b,c]	0.001
LDL-c, mg/dL **β**	101.0 (88.25–112.0)	106.0 (88.0–124.0)	107.5 (85.25–118.75)	111.0 (98.0–128.5)[b]	0.024
VLDL-c, mg/dL **β**	21.0 (15.0–29.0)	24.0 (19.0–28.50)	27.5 (20.0–34.0)[b]	32.0 (26.0–37.75)[b,c]	0.001
LDL/HDL **β**	2.29 (1.83–2.54)	2.41 (2.02–3.22)[b]	2.72 (1.99–3.19)[b]	3.10 (2.51–3.96)[b,c,d]	0.001
TC/HDL **β**	3.79 (3.32–4.11)	3.97 (3.55–5.02)[b]	4.41 (4.1–4.96)[b,c]	5.10 (4.23–6.15)[b,c,d]	0.001
TG/HDL **β**	2.76 (2.49–2.99)	3.21 (2.86–3.89)[b]	3.82 (3.12–4.92)[b,c]	4.64 (4.23–5.56)[b,c,d]	0.001
Non-HDL/HDL **β**	1.76 (1.49–1.99)	2.21 (1.86–2.89)[b]	2.82 (2.12–3.92)[b,c]	3.64 (3.23–4.56)[b,c,d]	0.001
AIP **β**	0.44 (0.40–0.447)	0.51 (0.46–0.59)[b]	0.58 (0.49–0.69)[b,c]	0.66 (0.62–0.74)[b,c,d]	0.009
Biomarkers					
Hs-CRP, mg/L **β**	8.41 (7.88–9.28)	8.66 (7.91–9.26)	8.95 (8.57–9.72)[b,c]	9.13 (8.65–9.60)[b,c]	0.001
Adiponectin, µg/mL **β**	15.33 (14.20–16.58)	14.0 (12.33–15.33)[b]	13.0 (11.33–14.58)[b]	11.83 (10.91–12.66)[b,c]	0.001

Participants were allocated to four groups: Group I – healthy control subjects; Group II – pre-MetS subjects; Group III – MetS subjects and Group IV – severe MetS subjects. Results are expressed as mean ± standard deviation for variables with a normal distribution (**§**), median, and interquartile range for variables with a skewed distribution (**β**) based on normality testing by Kolmogorov–Smirnov test. [a]p-Value indicates the differences between the groups by one-way ANOVA. [b]p-Value is significant compared to Group I. [c]p-Value is significant compared to Group II. [d]p-Value is significant compared to Group III. FPG, fasting plasma glucose; HOMA-IR, homeostatic model assessment of insulin resistance; TC, total cholesterol; TG, triglyceride; HDL-c, high-density-lipoprotein cholesterol; LDL-c, low-density-lipoprotein cholesterol; VLDL-c, very-low-density lipoprotein cholesterol; AIP, atherogenic index of plasma; hs-CRP, high-sensitive C reactive protein.

identified substantial glycemic profile changes based on post hoc findings. This could show that IR gradually increases as the number of MetS components increases. Groups II–IV participants showed significantly higher TG, LDL/HDL, TC/HDL, TG/HDL, non-HDL/HDL, AIP, and markedly lower HDL-C compared to Group I (Table 3), indicating atherogenic dyslipidemia in them. Moreover, the post-hoc results showed more significant atherogenic dyslipidemia in Group IV. Compared to Group I, Group II–IV participants showed substantially higher hs-CRP and lower adiponectin. Similarly, we found significant relative differences in hs-CRP and adiponectin between Groups II and IV.

The BPV parameters differed among the groups with significantly higher BHR, SBP, DBP, MAP, RPP, and TPR in Groups III and IV. BRS was markedly lesser in Groups II–IV than in Group I (Table 4). Among the HRV indices, Groups III and IV participants had significantly lower mean RR, SDNN, RMSSD, NN50, and pNN50, suggesting lower overall HRV with decreased parasympathetic activity. We observed a declining trend for SDNN, RMSSD, NN50, and PNN50 among Group IV compared to Group II and III. In addition, we found lower TP, HF, LF, VLF, HFnu, and greater LF/HF ratio in Groups III and IV than in Group I (Table 4), suggesting probable silent CAD and sympathovagal imbalance. Based on the PPA of HRV, we observed substantially lower S, SD, SD2, and higher SD2/SD1 in Groups II–IV than in Group I (Figure 1). The post-hoc results showed that in comparison with Groups II and III, the participants in Group IV showed markedly lower S, SD1, and SD2 (Figure 1).

There were significant relationships of S and SD2 with BRS and all standard HRV indices except LF and LF/HF for Group I. The association of S and SD2 with SDNN was relatively high (Table 5). TP also correlated well with both S and SD2. SD1 was substantially associated with BRS and all the standard HRV indices except for mean RR, LF, and LF/HF (Table 5). We identified similar correlations of S, SD1, and SD2 with RMSSD, even though there is a natural consequence of a known association between RMSSD and SD1. The association of SD2/SD1 with most of the standard HRV measures was statistically significant, except for mean RR and SDNN (Table 5). In addition, SD2/SD1 was significantly and negatively correlated with BRS, RMSSD, and HF. Although of moderate strength, we observed a significant and positive association of SD2/SD1 with LF/HF (r=0.359) and LF (r=0.275).

There were significant correlations of S with BRS in Group II subjects and all the traditional HRV indices except

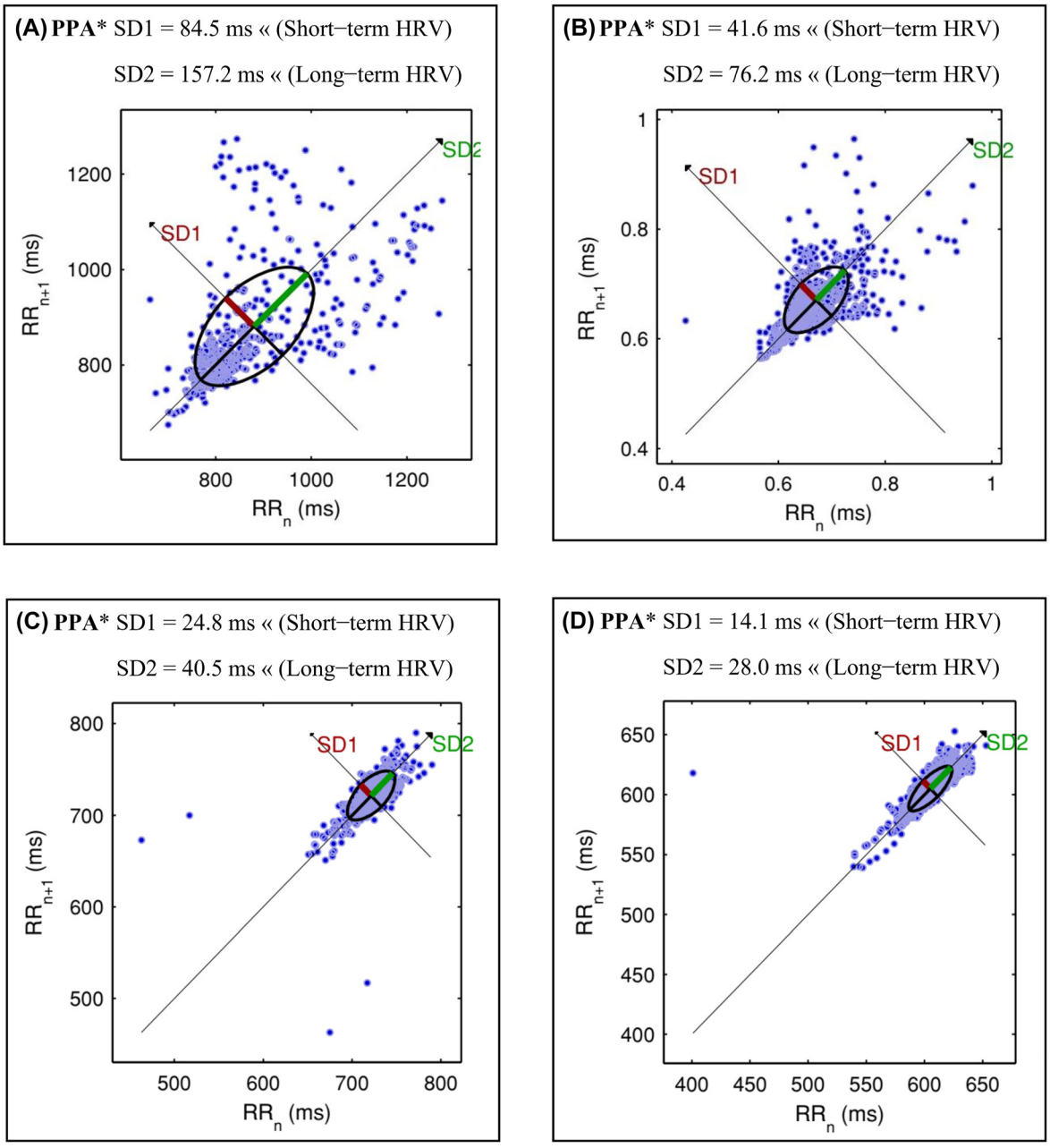

Figure 1: The Poincaré plots of RR intervals recorded from a 5 min ECG recording in a healthy person from the control group (A) and participants from the pre-MetS group (B), MetS group (C) and severe MetS group (D). SD1 and SD2, minor and major axes of Poincaré plot; RRn, time between two successive R peaks; RRn+1, time between the next two successive R peaks.

LF/HF. We found an extremely high correlation of S with RMSSD and SDNN (Table 5). SD1 correlated significantly with BRS, and all the traditional HRV indices studied, except LF and LF/HF (Table 5). SD2 is also linked substantially with BRS, and all the traditional HRV indices studied, except LF/HF. We found a significantly higher association of SD2 with SDNN, RMSSD, TP, and HF. SD2/SD1 exhibits a substantial inverse relationship with mean RR, RMSSD, and HF and a positive relationship with LF and LF/HF (Table 5).

The descriptor S is strongly associated with BRS and all the traditional HRV indices except LF/HF in Group III subjects (Table 6). We found a highly superior correlation of S with RMSSD, SDNN, and TP. SD1 showed significant positive correlations with all traditional HRV indices, and BRS studied, except LF/HF, negatively correlated. We found an immensely higher association of SD1 with RMSSD and HF (Table 6). SD2 correlated with all the traditional HRV indices and BRS except LF/HF. SDNN, RMSSD, and TP showed the

Table 4: Comparison of blood pressure and heart rate variability (traditional and PP) parameters between healthy control, pre-MetS, MetS, and severe MetS subjects.

Variables	Group I (n=64)	Group II (n=49)	Group III (n=56)	Group IV (n=54)	p-Value[a]
BPV parameters					
BHR, per min §	71.75 ± 8.34	74.55 ± 10.02	78.65 ± 11.29[b]	79.74 ± 12.89[b]	0.001
SBP, mmHg §	116.57 ± 9.556	119.79 ± 10.28	125.44 ± 13.77[b]	134.61 ± 12.05[b,c,d]	0.001
DBP, mmHg §	74.45 ± 8.89	77.57 ± 9.06	80.91 ± 8.20[b]	84.53 ± 9.53[b,c]	0.001
MAP, mmHg §	88.29 ± 8.51	91.63 ± 8.89	95.75 ± 9.13[b]	101.10 ± 9.48[b,c,d]	0.001
RPP, mmHg/min þ	81.05 (72.77–90.52)	84.20 (73.80–96.25)	95.35 (81.92–113.45)[b,c]	102.05 (91.7–116.8)[b,c]	0.001
SV, mL þ	83.30 (68.77–93.85)	84.96 (73.49–97.87)	85.75 (74.69–94.18)	86.57 (73.88–97.81)	0.563
LVET, ms §	314.69 ± 25.30	320.15 ± 22.88	323.25 ± 18.08	323.83 ± 25.97	0.123
CO, L/min §	6.16 ± 1.57	6.35 ± 1.15	6.38 ± 1.51	6.60 ± 1.54	0.504
TPR, mmHg.min/L þ	0.83 (0.75–0.96)	0.93 (0.78–1.13)	0.94 (0.79–1.18)[b]	1.02 (0.78–1.54)[b]	0.020
BRS, ms/mmHg þ	15.31 (12.7–19.22)	10.99 (7.35–16.38)[b]	9.71 (5.85–14.95)[b]	4.71 (3.91–8.1)[b,c,d]	0.001
Time-domain indices of HRV					
Mean RR, ms þ	875.4 (771.35–949.72)	828.0 (759.1–903.65)	778.5 (684.0–886.0)[b]	757.35 (705–858.7)[b,c]	0.001
SDNN, ms þ	44.75 (35.70–58.50)	39.90 (26.75–48.65)	33.30 (17.02–47.30)[b]	19.70 (11.97–35)[b,c,d]	0.001
RMSSD, ms þ	36.80 (28.05–55.85)	27.80 (18.05–47.60)[b]	23.60 (12.4–48.95)[b]	17.30 (9.47–24.92)[b,c,d]	0.001
NN50 þ	40.00 (14.5–67.5)	27.00 (6.01–58.0)	17.00 (6.01–18.75)[b]	10.00 (7.0–18.5)[b,c]	0.001
pNN50, % þ	11.5 (3.73–18.72)	8.30 (4.45–16.85)	4.9 (2.50–14.40)[b]	3.0 (1.09–7.00)[b,c,d]	0.001
Frequency-domain indices of HRV					
TP, ms^2 þ	1675.0 (1141.5–2105.5)	1197.0 (678.0–1740.0)[b]	788.5 (621.2–1558.7)[b]	687.0 (608.2–825.25)[b,c,d]	0.001
HF, ms^2 þ	474.0 (314.0–721.0)	307.5 (161.5–640.0)[b]	255.5 (199.7–543.2)[b]	229.5 (170.2–265)[b,c,d]	0.001
LF, ms^2 þ	502.0 (320.5–657.25)	413.0 (221.0–630.5)	277.0 (192.25–555.50)[b]	262.0 (223.75–378.5)[b,c]	0.001
VLF, ms^2 þ	446.5 (221.5–688.0)	207.0 (148.0–462.5)[b]	203.0 (128.0–447.0)[b]	188.0 (132.7–272.2)[b]	0.001
HF (nu) §	53.39 (45.79–62.99)	51.0 (33.69–64.53)	51.12 (40.74–55.25)	44.27 (40.47–48.19)[b,c,d]	0.001
LF, nu §	45.53 (36.39–62.94)	52.0 (39.15–64.03)	54.12 (47.06–60.40)[b]	63.75 (53.16–69.24)[b,c,d]	0.001
LF/HF §	0.77 (0.64–1.15)	1.05 (0.66–1.66)[b]	1.06 (0.87–1.35)[b]	1.41 (1.21–1.63)[b,c,d]	0.001
Poincare plot indices of HRV					
S þ	6850.73 (2968.9–10991.3)	3246.14 (1418.8–5357)[b]	2140.3 (1229.7–6110)[b]	1306.14 (1077–1922)[b,c,d]	0.001
SD1, **ms** þ	41.70 (26.75–51.87)	32.50 (20.15–39.80)[b]	19.05 (14.92–34.6)[b,c]	15.55 (13.05–18.67)[b,c,d]	0.001
SD2, **ms** þ	53.0 (36.27–69.40)	42.80 (29.70–54.75)[b]	38.65 (26.12–53.10)[b]	28.75 (24.17–38.32)[b,c,d]	0.001
SD2/SD1 §	1.44 ± 0.29	1.79 ± 0.45[b]	1.88 ± 0.77[b]	1.97 ± 0.65[b]	0.001

Participants were allocated to four groups: Group I – healthy control subjects; Group II – pre-MetS subjects; Group III – MetS subjects and Group IV – severe MetS subjects. Results are expressed as mean ± standard deviation for variables with a normal distribution (§), median and interquartile range for variables with a skewed distribution (þ) based on normality testing by Kolmogorov–Smirnov test. [a]p-Value indicates the differences between the groups by one-way ANOVA. [b]p-Value is significant compared to Group I. [c]p-Value is significant compared to Group II. [d]p-Value is significant compared to Group III. BHR, basal heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; RPP, rate pressure product; SV, stroke volume; LVET, left ventricular ejection time; CO, cardiac output; TPR, total peripheral resistance; BRS, baroreflex sensitivity; Mean RR, mean-RR interval; SDNN, standard deviation of normal to normal interval; RMSSD, square root of the mean squared differences of successive normal to normal intervals; NN50, the number of interval differences of successive NN intervals greater than 50 ms; PNN50, the proportion derived by dividing NN50 by the total number of NN intervals; TP, total power; HF, high-frequency power; HF nu, HF power in normalized units (HF/(TP − VLF)*100); LF, low-frequency power; LF nu, LF power in normalized units (LF/(TP − VLF)*100); VLF, very-low-frequency; LF/HF, a ratio of the low-frequency component to the high-frequency; S, SD1, SD2, and SD2/SD1, descriptors of Poincare plot analysis of HRV.

highest correlation with SD2. SD2/SD1 in Group III has a significant inverse association with HF and a positive association with LF and LF/HF. In Group IV subjects, we found a few associations between descriptors of PPA and BRS and traditional HRV indices, but with smaller r and larger p values. The descriptors S, SD1, and SD2 were correlated significantly and commonly with SDNN, RMSSD, and TP. Additionally, SD1 showed a profound positive association with HF, while SD2 showed an association with BRS and LF. The ratio of SD2/SD1 was associated significantly and positively with LF and LF/HF.

Discussion

Traditionally, HRV is an easy, non-invasive way to measure cardiac autonomic function. Lower HRV has been associated with CVD morbidity and mortality [41]. Many studies have demonstrated altered HRV indices in MetS [12–17, 42] and reported autonomic dysfunction as a critical connection between MetS and CVD. However, variance in duration and body position during HRV recording, research population, influencing factors, and HRV analysis methodologies generated disparities among different investigations.

Table 5: Spearman correlation analysis of the relationship between descriptors of Poincare plot and traditional HRV parameters as well as BRS in healthy control and pre-MetS subjects.

	Group I (control subjects n: 64)				Group II (pre-MetS subjects n: 49)			
Risk variables	**S**	**SD1**	**SD2**	**SD2/SD1**	**S**	**SD1**	**SD2**	**SD2/SD1**
BRS, r	0.327	0.353	0.297	−0.288	0.564	0.357	0.520	−0.168
p-Value	**0.008**	**0.005**	**0.017**	**0.021**	**0.001**	**0.012**	**0.001**	0.250
Mean RR, r	0.269	0.240	0.260	−0.021	0.509	0.456	0.471	−0.349
p-Value	**0.032**	0.058	**0.038**	0.868	**0.001**	**0.001**	**0.016**	**0.014**
SDNN, r	0.782	0.721	0.808	0.172	0.788	0.689	0.746	0.238
p-Value	**0.001**	**0.001**	**0.001**	0.175	**0.001**	**0.001**	**0.002**	0.099
RMSSD, r	0.496	0.520	0.481	−0.283	0.944	0.667	0.842	−0.513
p-Value	**0.001**	**0.001**	**0.001**	**0.023**	**0.001**	**0.001**	**0.001**	**0.001**
TP, r	0.460	0.388	0.498	0.263	0.555	0.286	0.669	0.181
p-Value	**0.001**	**0.002**	**0.001**	**0.036**	**0.001**	**0.047**	**0.001**	0.212
HF, r	0.576	0.590	0.556	−0.284	0.736	0.439	0.659	−0.487
p-Value	**0.001**	**0.001**	**0.001**	**0.023**	**0.001**	**0.002**	**0.001**	**0.001**
LF, r	0.202	0.133	0.251	0.359	0.336	0.181	0.519	0.347
p-Value	0.109	0.297	**0.045**	**0.004**	**0.018**	0.212	**0.001**	**0.015**
LF/HF, r	0.074	0.018	0.100	0.275	−0.246	−0.249	−0.069	0.584
p-Value	0.563	0.890	0.433	**0.028**	0.089	0.084	0.639	**0.001**

r, coefficient of correlation. The values in bold indicate a significant p-value. Correlation is significant at $p<0.05$, $p<0.01$, and $p<0.001$. **Abbreviations** as in Table 4.

Table 6: Spearman correlation analysis of the relationship between descriptors of Poincare plot and traditional HRV parameters as well as BRS in MetS and severe MetS subjects.

	Group III (MetS subjects n: 56)				Group IV (severe MetS subjects n: 54)			
Risk variables	**S**	**SD1**	**SD2**	**SD2/SD1**	**S**	**SD1**	**SD2**	**SD2/SD1**
BRS, r	0.427	0.312	0.508	0.119	0.229	0.145	0.327	0.226
p-Value	**0.001**	**0.019**	**0.001**	0.384	0.095	0.295	**0.016**	0.100
Mean RR, r	0.542	0.608	0.446	−0.234	0.066	0.072	0.077	−0.013
p-Value	**0.001**	**0.000**	**0.001**	0.083	0.637	0.604	0.580	0.925
SDNN, r	0.870	0.672	0.899	0.146	0.545	0.473	0.577	0.144
p-Value	**0.001**	**0.001**	**0.001**	0.283	**0.001**	**0.001**	**0.001**	0.300
RMSSD, r	0.948	0.869	0.843	−0.118	0.592	0.512	0.658	0.191
p-Value	**0.001**	**0.001**	**0.001**	0.388	**0.001**	**0.001**	**0.001**	0.166
TP, r	0.799	0.671	0.801	0.013	0.310	0.380	0.347	−0.006
p-Value	**0.001**	**0.001**	**0.000**	0.923	**0.022**	**0.005**	**0.010**	0.967
HF, r	0.657	0.758	0.541	−0.307	0.261	0.415	0.198	−0.147
p-Value	**0.001**	**0.001**	**0.001**	**0.021**	0.057	**0.002**	0.151	0.287
LF, r	0.620	0.418	0.698	0.284	0.033	−0.095	0.310	0.445
p-Value	**0.001**	**0.001**	**0.001**	**0.034**	0.811	0.495	**0.022**	**0.001**
LF/HF, r	−0.025	−0.286	0.104	0.367	−0.026	−0.183	0.244	0.385
p-Value	0.858	**0.033**	0.444	**0.005**	0.852	0.186	0.076	**0.004**

r, coefficient of correlation. The values in bold indicate a significant p-value. Correlation is significant at $p<0.05$, $p<0.01$, and $p<0.001$. **Abbreviations** as in Table 4.

Several methods have been developed for HRV evaluation, including time- and frequency-domain indices and PPA. Our previous research showed that MetS patients had reduced BRS and severely altered time- and frequency-domain HRV indices [34].

Recent HRV studies using the PPA have provided more predictive information about HRV patterns and have complemented time-domain and frequency-domain analyses. The PPA can characterize the qualitative properties of the heart rate rather than the quantitative. Also, it has been used

to measure autonomic modulation and randomness of heart rate [24]. Recent studies have reported that SD1 and SD2 of PPA were pointedly reduced in adults with MetS than in controls [28, 43]. Additionally, SD1 has been presumed to be a marker of parasympathetic activity, appearing to be significantly related to RMSSD and HF of traditional HRV measures [44]. A decrease in SD1 values indicates weakened parasympathetic regulation. In contrast, SD2 is influenced both by parasympathetic and sympathetic signals. A lower SD2 value indicates increased sympathetic activity. In this sense, the lower values of SD1 and SD2 reflect profound vagal withdrawal and enhanced sympathetic activity. The PPA descriptor proposed to assess the relationship between the sympathetic and parasympathetic activity of the ANS is the SD2/SD1 ratio. A higher SD2/SD1 ratio indicates sympathovagal imbalance. Thus SD1, SD2, and the ratio of SD2/SD1 combine the advantages of easy calculation and stability of statistical time domain parameters with the capability of expressing HRV in the same manner as expressed by frequency domain parameters. In this context, we intended to evaluate four distinct PPA descriptors of HRV and their relationship with traditional HRV indices and BRS among different risk levels of MetS. We found significant differences in the HRV pattern among MetS groups, as determined by PPA and traditional HRV indices.

Conventionally, risk factors such as abdominal obesity, hyperglycemia, dyslipidemia, and hypertension play a role in CAD and CVD development. All of these risk factors are combined to form MetS. In addition, each component of MetS raises the risk of CAD and CVD. Adiposity and abdominal obesity are significantly altered in Groups III and IV compared to Groups I and II, which predisposes individuals to CVD. An increase in WC, WHR, and WHtR indicates adiposity and abdominal obesity. WHtR has been reported to be associated with excess adiposity and early CAD [45]. As we observed in our study, subjects with MetS and severe MetS showed gradually declining cardiac autonomic functions with increased BMI, WHR, and WHtR. In the MetS and severe MetS groups, BF% and BFMI were significantly higher, which may indicate impaired glucose and lipid metabolism.

Furthermore, IR and dyslipidemia may increase CVD risk in Groups III and IV subjects through deteriorated cardiovascular autonomic function. Higher glucose levels can influence signal transmission through the baroreflex arc neuronal pathway and affect cardiac autonomic function at the myocyte level [46]. Our results support the theory that chronic low-grade inflammation and hypoadiponectinemia play a vital role in developing cardiometabolic abnormalities. Chronic low-grade inflammation, reflected by increased hs-CRP and decreased adiponectin concentrations in Groups III and IV, indicates an autonomic imbalance that favors sympathetic overactivity. There was evident immense variation in hemodynamic variables (BHR, SBP, DBP, MAP, and RPP) across the groups. The rise in heart rate, SBP, and DBP is associated with CVD morbidity and mortality [47]. Compared to controls, the significant increase in basal HR and RPP, in addition to SBP, DBP, and MAP in Groups III and IV, indicates poor CV health. An increased TPR in MetS and sever MetS groups indicate an increased hemodynamic stress and sympathetic vasoconstrictor tone. Additionally, BRS, a strong determinant of CVD mortality, was drastically reduced in Groups II–IV than in controls, confirming poor CV health and cardiac autonomic imbalance.

The groups with more MetS components, particularly groups III and IV, showed lower HRV as changes in PPA (Figure 1) and traditional HRV indices. The TP, SDNN, and descriptor S of PPA represent entire autonomic activity and cardio-vagal regulation. Recently, reduced TP was associated with sudden death due to cardiac failure [48]. Consequently, this study showed a gradual drop in TP among Groups II–IV, possibly increasing CVD risk. Lower TP was accompanied by lower SDNN and S of PPA, indicating lower overall HRV. The HRV outcomes proposed to assess the parasympathetic activity are mean RR, RMSSD, NN50, PNN50, HF, HFnu, and SD1 of PPA. The LF power of HRV, LF nu, and SD2 of PPA represent sympathetic and parasympathetic modulation, with the cardiac sympathetic drive being the most prominent. However, SD2 is often debatable from a clinical perspective. The physiological implications of SD2 as an HRV outcome are controversial. Previous studies linked SD2 inversely with sympathetic activity [49]. The markedly lower values of parasympathetic (RMSSD, HF, SD1) and sympathetic modulation (LF and SD2) might result in lower TP, SDNN, and S values among Groups II, III, and IV. The HRV parameters recommended to evaluate the sympathovagal balance are LF/HF ratio and SD2/SD1 ratio [24]. As expected, we observed significantly higher LF/HF ratio and SD2/SD1 values among Groups II–IV, indicating a considerable sympathovagal imbalance in these subjects. Accordingly, this study demonstrates CAD in the form of progressive reduction in HRV due to reduced parasympathetic modulation (TP, SDNN, RMSSD, HF, HFnu, and SD1 of PPA) in conjunction with an increase in MetS components.

The PP descriptor S, which determines the total HRV, correlates best with traditional HRV indices like TP, SDNN, and RMSSD. The correlation of S with other HRV indices indicates that S is linked to BRS, parasympathetic, and sympathetic activity. Toichi et al. have already utilized a parameter equivalent to S [36]. However, there are major variations in the functional justification between the S used in this research and the variable used by Toichi et al. [36]. Furthermore, S represented by the product of SD1 and SD2 in

the Toichi et al. study reflects solely the parasympathetic tone, which is contradictory to the present report. However, Guzik et al. stated findings similar to our research and interpreted this descriptor S as a measure of total HRV [24]. The absolute association of SD1 with RMSSD implies that SD1 has the same interpretation as RMSSD, a recognized measure of short-term HRV [13, 18]. Other significant associations of SD1 with SDNN, TP, HF, and BRS substantiate that SD1 is a reliable indicator of overall HRV and parasympathetic modulation. SD1 also correlates considerably with LF and could suggest some dependence on sympathetic activity. Another explanation may be that vagal activity strongly influences LF, especially in the lying position in brief 5 min recordings [13, 18], as seen in our study. However, the link between SD1 and sympathetic activity cannot be ruled out.

The SD2 descriptor of PPA was correlated dramatically with all the traditional HRV and BRS measures, which appear to have resulted from total HRV to long-term HRV in shorter recordings [18, 23]. Additionally, the positive correlation of SD2 with RMSSD and HF strengthens the notion that SD2 appears inverse to sympathetic activation [22, 49, 50]. The correlation between SD2 and LF in MetS and severe MetS groups supports the hypothesis that SD2 is also related to sympathetic tone. Various reports have testified to the connection of SD2 with sympathetic and parasympathetic activity [22, 50, 51]. Our research reflected this as a correlation of SD2 with the sympathetic and parasympathetic HRV indices. In analogy to LF/HF, we consider the SD2/SD1 ratio to quantify the balance between long- and short-term HRV [36, 51]. The numerators in both ratios are based on both long- and short-term variability, while the denominators are based solely on short-term variability. Thus, as expected, SD2/SD1 correlates most strongly with LF/HF among the groups studied. SD2/SD1 is positively associated with LF and LF/HF and negatively with BRS, RMSSD, and HF. These results indicate that greater SD2/SD1 might indicate sympathovagal imbalance. Thus, SD2/SD1 might be considered an alternative to LF/HF. Moreover, the SD2/SD1 parameter is theoretically equivalent to the cardiac sympathetic index developed by Toichi et al. with a similar physiological interpretation [36]. Some studies have employed the reciprocal of this parameter (SD1/SD2) as an index of heart rate randomness rather than autonomic balance [22, 26, 52].

As discussed above, PP descriptors correlated well with traditional HRV indices, supporting their use in identifying subjects with MetS from those without and stratifying MetS risk. Our findings are consistent with the previous cross-sectional studies [12, 14–17, 28, 49]. They revealed that MetS and its components were linked to CAD through sympathovagal imbalance. According to a study, MetS components, when combined, confer greater CVD risk than they do individually [3]. Hyperglycemia was prevalent in most of the subjects in Groups II–IV, which adversely affected cardiovascular and metabolic outcomes. Recent research suggested that hyperglycemia may cause CAD via increased formation of advanced glycation end products, endothelial dysfunction, and oxidative stress, all of which may lead to neuronal damage and subsequent autonomic impairment [46]. In addition, the association between hyperglycemia and CAD may be bidirectional. It has been suggested that CAD causes hyperglycemia via impaired insulin release by the pancreas, increased glucose production by the liver, impaired glucose uptake, and insulin resistance in skeletal muscles [51]. Hence, CAD might be a result of, as well as a precursor to hyperglycemia, and a vicious cycle of hyperglycemia and CAD may exist. Additionally, most subjects with MetS and severe MetS have elevated BP, associated with disturbed circadian BP and decreased HRV through heightened sympathetic nervous system activity.

Thus, it must be considered that several multifaceted metabolic pathways involving glucotoxicity, lipotoxicity, altered insulin signaling, increased cytokine activity, and interstitial deposition of triacylglycerol resulting in increased circulation of glucose and FFA, which further increases pancreatic insulin secretion, can lead to enhanced sodium reabsorption and increased SNS activity, which might be the pathological basis for CAD in the form of reduced BRS and lower HRV in MetS and severe MetS subjects. Furthermore, MetS and severe MetS subjects exhibit excess adiposity, hypoadiponectinemia, and pro-inflammatory events, all of which may be linked to cardiac autonomic imbalance among different risk levels of MetS [53]. The noteworthy observation of the current study is that HRV by PPA offers valuable and applicable information similar to traditional time- and frequency-domain HRV measures. We suggest that S, SD1, SD2, and SD2/SD1 could be alternatives to or complementary to other traditional HRV measures. These descriptors of PPA provided supplementary information about individual RR intervals by the graphical representation, which cannot be obtained by traditional time- and frequency-domain measures of HRV. They help detect diseases in their early stages or determine their extent. This investigation has a few shortcomings that need to be acknowledged. Due to the cross-sectional design, we could not infer a cause-and-effect relationship. In addition, a bidirectional association between autonomic impairments and MetS components may need to be established. We need to design longitudinal studies with rigorous measurements in the future to explore these bidirectional interactions over time.

Conclusions

In summary, the sympathovagal imbalance was more apparent in the MetS and severe MetS groups than in the control group. The S, SD1, SD2, and SD2/SD1 are the more robust PPA descriptors that distinguish between MetS subjects with varying risk levels and healthy controls. They correlated significantly with most conventional HRV measures and BRS. Thus, we propose using the descriptors of PPA to assess impaired autonomic modulation in MetS groups and use them for risk stratification. Together with traditional HRV measures, they would help interpret various physiological correlates of HRV abnormalities in MetS subjects. Using PPA overcomes the major problems of other methods, such as data stationarity, and offers mathematical simplicity. Thus, research in this area is necessary to uncover the true potential of HRV analysis based on Poincaré plots and how they may predict cardiovascular risk.

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