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Hemorheology, ankle brachial pressure index (ABPI) and toe brachial pressure index (TBPI) in metabolic syndrome

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ABSTRACT

Introduction: Microvascular dysfunction is associated with metabolic syndrome (MetS) and its components. The objective of our study was to assess macro and microvascular abnormalities in MetS and compare the strength of association of the ankle brachial pressure index (ABPI), toe brachial pressure index (TBPI) and hemorheological parameters with MetS.
Materials and methods: 100 participants were recruited from a rural Australian town. Anthropometric measurements were taken along with blood pressures (BP) at the arm, the ankle and the big toe for calculating ABPI and TBPI. Whole blood viscosity (WBV), erythrocyte aggregation, erythrocyte deformability, lipid profile and blood sugar level were analyzed. Recruited participants were classified into MetS and non-MetS following National Cholesterol Education Program Adult Treatment Panel III definition. Data were analyzed by IBM SPSS 20 software.
Results: WBV and erythrocyte aggregation were higher whereas erythrocyte deformability was lower in participants with MetS when compared to participants without MetS. Age, sex and diabetes mellitus adjusted odds ratio for predicting MetS was not significant for ABPI and TBPI whereas it was significant for hemorheological parameters. Receiver Operating Characteristics curve showed that TBPI better classified MetS than ABPI but association of hemorheological parameters was superior to that of ABPI and TBPI with MetS.
Conclusions: Both microcirculation defects and macrovascular circulation defects were present in MetS. The concurrences of the components of MetS could have an additive effect in enhancing alterations in hemorheological parameters which may give rise to severe microvasculopathy. The association of hemorheological parameters was stronger than the association of TBPI and ABPI with MetS.

Introduction

Metabolic syndrome (MetS) is the constellation of risk factors, the presence of which is associated with increased risk of developing cardiovascular diseases (CVD) (Isomaa et al., 2001; Lakka et al., 2002). Microvascular dysfunction is associated with MetS and its components (Czernichow et al., 2010; Serné et al., 2007; Vykoukal and Davies, 2011). The experiment of Frisbee and Stepp, on the obese zucker rat model, demonstrated reduced vasodilation of skeletal muscle to nitric oxide stimuli (Frisbee and Stepp, 2001). Same authors through series of experiments showed chronic reductions in the blood flow in a hind limb of obese Zucker rat model with MetS. Wall thickness and lumen of the vessels supplying hind limb were reduced and the compliance of the vessels wall was lost (Frisbee and Stepp, 2001; Stepp and Frisbee, 2002; Stepp et al., 2004). Microvascular abnormalities affect the pressure and the flow of the blood (Levy et al., 2001; Serné et al., 2007). Another important aspect of microcirculation that affects the pressure and flow of blood is hemorheology (Baskurt and Meiselman, 2003; Pirrelli, 1999; Sandhagen, 1999). Hemorheological parameters such as increased whole blood viscosity (WBV), reduced erythrocyte deformability, increased erythrocyte aggregation and altered erythrocyte morphology have been associated with MetS (Gyawali et al., 2012a, 2012b, 2014). Altered hemorheology has been shown to negatively affect microcirculation (Konstantinova et al., 2004).

Measurement of ankle brachial pressure index (ABPI) by using Doppler ultrasound device is the commonly used clinical method of assessing peripheral arterial disease and circulation in the lower limb (Vowden et al., 1996). However, the validity of measuring ABPI in diabetic subjects due to lower limb artery calcification has been questioned (Brooks et al., 2001; Mayfield et al., 1998). Recent literature has supported the use of the toe brachial pressure index (TBPI) for assessing circulation as it overcomes the medium vessel calcification problem seen, in the lower limb of patients with type II diabetes

Abbreviations: ABPI, ankle brachial pressure index; TBPI, toe brachial pressure index; MetS, metabolic syndrome; DM, diabetes mellitus; WBV, whole blood viscosity; EImax, maximum erythrocyte deformability; $SS_{1/2}$, half maximal deformability; ROC curve, receiver operating characteristics curve; HDL-C, high density lipoprotein cholesterol; TG, triglyceride; FBG, fasting blood glucose.

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mellitus (DM) (Brooks et al., 2001; Mayfield et al., 1998). The objective of our study was to assess macro and microvascular abnormalities in MetS and compare the strength of association of the ABPI, TBPI and hemorheological parameters with MetS.

Materials and methods

Subjects

One hundred (100) participants were recruited from a rural town of Australia from June to Dec, 2013. Pregnant women, non-ambulatory patients and children under 18 years of age were excluded from the study. Recruited participants were divided into three groups on the basis of the absence or presence of MetS and its components. A modified NCEP-ATPIII guideline was referred to define MetS (Expert panel on detection evaluation treatment of high blood cholesterol in adults, 2001; Grundy et al., 2004). As per the definition, the participants having three or more risk factors (components) among the following five are said to be under the state of MetS. 1) Abdominal obesity (waist circumference > 102 cm for men, >88 cm for women) 2) Triglycerides ≥ 1.7 mmol/L or drug treatment for elevated triglycerides 3) HDL-cholesterol < 1.04 for men and <1.29 for women or drug treatment to increase HDL-cholesterol 4) Fasting blood glucose level ≥ 5.6 mmol/L or drug treatment for elevated glucose or diagnosed diabetes and 5) Systolic blood pressure ≥ 130 mm Hg, diastolic blood pressure ≥ 85 mm Hg or on hypertensive treatment. Unlike world health organization (WHO) and international diabetes federation definition of MetS, an NCEP ATP III guideline avoids emphasis on a single cause for the diagnosis of MetS. The definition is less glucocentric in comparison to definition given by WHO and European Group for the study of Insulin Resistance.

Group I consists of the participants without any positive components of MetS (healthy controls), group II consists of the participants with one or two positive components and group III consists of the participants with three or more positive components. The participants under groups I and II are non-MetS whereas the participants of group III are with MetS. The study was approved by the university human research ethics committee (2012/131).

Anthropometric and blood pressure measurement

Waist circumference of the participants was measured from the upper margin of the posterior iliac crest at the end of normal expiration directly above the skin. Brachial blood pressure was measured with an automated BP machine (Welch Allyn®) in a supine position from both arms. Toe brachial pressure was measured from the great toe of both legs using SysToe (ATYS medical) that uses photoplethysmography (PPG) analyzed by a unique patented algorithm designed by Atys Medical. TBPI was calculated by dividing higher toe pressure with higher brachial systolic pressure. Ankle pressure was measured from dorsalis pedis from both legs by the hand held doppler probe (Doppler ultrasound, Hadeco, Inc.). ABPI was calculated by dividing higher ankle pressure with higher brachial systolic pressure.

Laboratory analysis

Twenty mL of blood was taken from the participants. Blood was collected into EDTA and plain vials. All analysis was carried out according to the manufacturer's instructions. Erythrocyte deformability and aggregation measurements were carried out using a RheoScan-And 300 system (RheoMeditech, Inc., Korea). Measurements were performed in duplicate for each sample and within 1½ hours of blood collection. For the measurement of erythrocyte deformability, 6 μL of EDTA blood was mixed with 600 μL of Poly Vinyl Pyrrolidone (PVP) solution (MW: 360,000; final viscosity: 30–32 mPa·s at 37 °C, Osmolality: 300 mOsm/kg). 500 μL of mixed blood was transferred into the provided test kit and loaded in the instrument for the analysis. The instrument used laser diffraction for the measurement of erythrocyte deformability. Erythrocytes in a medium were deformed by the range of shear stresses (0.5–20 Pa). When the laser beam passes through the erythrocytes suspended in a viscous PVP medium; a diffraction pattern of light is obtained. The image analysis program determines the elongation index (EI) to represent the cell deformability of the sample. EI is defined according to the formula $(L - W) / (L + W) \times 100$, where L = length of major axis in the ellipsoidal diffraction image and W = length of minor axis in the ellipsoidal diffraction image. Two measurement indices were used to define erythrocyte deformability: EI_{max} and $SS_{1/2}$ (Baskurt et al., 2009; Simmonds et al., 2012). EI_{max} is the maximum erythrocyte elongation index at the infinite shear stress and $SS_{1/2}$ is the shear stress required for the half of maximal deformation.

Erythrocyte aggregation was measured by light transmission. The test kit was filled with 500 μL of 40% hematocrit adjusted whole blood and loaded in the instrument. While the blood was flowing through the microchannel, a laser beam emitted from the laser diode traversed the diluted erythrocyte suspension and was scattered by the erythrocytes in the suspension. The backscattered light was captured by two photodiodes, linked to a computer. When a high pressure differential was initially applied, a strong shear flow occurred through the microchannel and the erythrocyte aggregates started to disaggregate, as was indicated by the corresponding increase in light intensity. As the pressure differential decreased exponentially, the shear flow also decreased and the disaggregated erythrocytes tended to re-aggregate resulting in a decrease in the corresponding light intensity. Two measurement indices were used to define erythrocyte aggregation; critical time and critical stress: Critical time is the maximum point of back scattered light and indicates the starting point of the erythrocyte re-aggregation, which is strongly dependent on shear stress and time. The time and shear stress values corresponding to the maximum point of backscattered light are defined as the critical time and the critical shear stress. Before and after critical time and critical shear stress, there is a critical transition period from dis-aggregation to re-aggregation of the erythrocytes that is associated with a decreasing shear flow. The lesser the critical time, the faster the erythrocyte aggregation process and the higher the critical stress, the faster the erythrocyte aggregation (Hou and Shin, 2008).

Whole blood viscosity measurement was carried out using a Brookfield DV-II + programmable viscometer (MA, USA), using a CP40 spindle. A 40% hematocrit adjusted whole blood was used for the measurement. This viscometer measures blood viscosity at different given shear rates. The WBV measured at a shear rate of 150 s^{-1} has been presented in the results section and the 'WBV' used in this paper hereafter indicates WBV at the shear rate of 150 s^{-1}.

Lipid profile was measured in a fully automated clinical chemistry analyzer.

Statistical analysis

Data were analyzed by IBM SPSS Statistics version 20. Normality of the data was tested by Shapiro–Wilk test. ANOVA with post-hoc analysis was used to compare means between the three groups for normally distributed data and Kruskal–Wallis test with post-hoc analysis was used to compare median between the three groups for non-normal data. Correlation was performed among hemorheological parameters, ABPI, TBPI and components of MetS. Regression analysis was performed to find the association of MetS and hemorheology. Logistic regression analysis was applied to estimate odds ratio (OR) and the 95% Confidence interval (CI) for each MetS components on hyperviscosity, erythrocyte hyperaggregability and low erythrocyte deformability. The values of WBV and critical stress at the highest quartile and erythrocyte deformability values at the lowest quartile were considered as rheologically altered values. Receiver operating characteristics (ROC) curve was

constructed to determine the diagnostic capacity of the hemorheological parameters, ABPI and TBPI for MetS. All the *P*-values were two-tailed, and those < 0.05 (95% CI) were considered statistically significant.

Results

Thirty-one participants formed group I, thirty-three formed group II and thirty-six formed group III. Mean age of the participants was compared into the three groups of classification using ANOVA tests. The difference in mean age between the three groups (45.48 ± 8.974, 56.52 ± 12.94 and 63.06 ± 12.13 years) was statistically significant ($P < 0.0005$). Tukey post-hoc analysis revealed that the increase from group I to II ($P = 0.001$) and from group I to III ($P < 0.0005$) was significant but age difference in groups II and III was not significant ($P = 0.054$). Baseline characteristics of the participants' with and without MetS (Group I + II Vs Group III) are given in Table 1.

WBV, critical stress and EI_{max} were normally distributed among the three groups ($P > 0.05$) whereas distribution of critical time, $SS_{1/2}$, TBPI and ABPI were not normal ($P < 0.05$) as assessed by Shapiro–Wilk test.

A one way ANOVA was conducted to determine if WBV, critical stress and EI_{max} were different between the three different groups. WBV, critical stress and EI_{max} values were significantly different between the three groups, $P < 0.005$. Mean WBV value increased from group I (3.99 ± 0.33) to group II (4.10 ± 0.50) and group III (4.56 ± 0.36), in that order. Tukey post-hoc analysis revealed that the difference between groups I and III ($P < 0.0005$) and II and III ($P = 0.042$) were significant. Similarly, for critical stress mean value increased from group I (274.23 ± 48.44) to group II (343.48 ± 101.34) and group III (505.68 ± 186.49), in that order. Games–Howell post-hoc analysis revealed that the increase from group I to group II (69.24, 95% CI: 21.62 to 116.86) was significant ($P = 0.003$) as well as from group II to group III (162.20, 95% CI: 76.11 to 248.29), $P < 0.0005$. In the same way, mean EI_{max} values decreased from group I (0.561 ± 0.02) to group II (0.557 ± 0.022) and further decreased in group III (0.534 ± 0.214). Tukey post-hoc analysis revealed that the decrease from group II to III ($P = 0.001$) and I to III ($P < 0.0005$) was significant but the decrease from group I to group II was non-significant ($P = 0.766$).

Since the distribution of ABPI, TBPI, critical time, and $SS_{1/2}$ were not normal; Kruskal–Wallis test was used to compare the median between the three groups (Table 2).

For the variables with a significant Kruskal–Wallis test, pairwise post-hoc test was performed. The pairwise comparisons were performed with a Bonferroni correction for multiple comparisons. The alpha level was reduced with a new adjusted *P*-value = 0.05/3 = 0.016. Post-hoc analysis revealed that critical time differs between groups I and III ($P < 0.0005$) and II and III ($P = 0.002$), ABPI differs between groups II and III ($P = 0.008$) and TBPI differs between groups I and III ($P < 0.0005$) and groups II and III ($P = 0.005$).

TBPI and ABPI were correlated with hemorheological parameters. ABPI was significantly correlated with WBV only ($P = 0.029$) whereas TBPI was significantly correlated with WBV ($P < 0.0005$) and erythrocyte aggregation parameters (Critical stress $P = 0.003$ and critical time $P = 0.002$). None of them correlated with erythrocyte deformability parameters ($P > 0.05$). Correlation analysis of hemorheological parameters, ABPI and TBPI with components of MetS is given in Table 3.

The WBV, critical stress and EI_{max} were divided into four groups (quartiles) using 25th, 50th and 75th percentiles. The values at 25th, 50th, and 75th percentiles were: WBV (3.9, 4.17, 4.43 mPa.s); critical stress (259.85, 329.25 and 476.9 Pa) and EI_{max} (0.525, 0.551 and 0.569). Ordinal logistic regression analysis was used through Generalized Linear Model to find out the association of MetS (group III) with the highest quartile of WBV and critical stress and the lowest quartile of EI_{max}. Ordinal logistic regression analysis showed that the highest quartile of WBV values occurred 7.958 (95% CI, 2.556 to 24.775) times more frequently than the lowest quartile values in subjects under MetS, a statistically significant effect, χ^2 (1) = 12.816, $P < 0.0005$. Similarly, the highest quartile of critical stress values occurred 44.293 (95% CI, 10.680 to 183.696) times more frequently than the lowest quartile values in subjects under MetS, a statistically significant effect, χ^2 (1) = 27.283, $P < 0.0005$. In the same way, the lowest quartile of EI_{max} values occurred 6.795 (95% CI, 2.244 to 20.573) times more frequently than the lowest quartile values in subjects under MetS, a statistically significant effect, χ^2 (1) = 11.494, $P = 0.001$. None of the MetS components constitute an independent predictor of hyperviscosity and low erythrocyte deformability ($P > 0.05$). Systolic blood pressure (OR: 1.055; 95% CI: 1.025 to 1.085; $P < 0.0001$), fasting blood glucose (OR: 1.367; 95% CI: 1.047 to 1.786; $P = 0.022$), waist circumference (OR: 1.052; 95% CI: 1.022 to 1.084; $P = 0.001$), triglyceride (OR: 1.020; 95% CI: 1.011 to 1.030; $P < 0.0001$) and HDL-C (OR: 1.121; 95% CI: 1.052 to 1.194; $P < 0.0001$) independently predicted erythrocyte hyperaggregability.

Binomial logistic regression analysis showed that ABPI and TBPI were significantly associated with the presence of DM ($P = 0.009$ and <0.0005 respectively). Adjusted odds ratio for predicting MetS by rheological components is given in Table 4.

To further confirm the binomial logistic regression analysis results, the ROC curve of WBV, critical stress, EI_{max} and TBPI was plotted for the differentiation of MetS and non-MetS at various coordinate points (Figs. 1 and 2). Area under the curve (AUC) was the highest for critical stress (AUC: 0.818, 95% CI: 0.715 to 0.922, $P < 0.0005$) followed by EI_{max} (AUC: 0.782, 95% CI: 0.688 to 0.876, $P < 0.0005$), TBPI (AUC: 0.774, 95% CI: 0.679 to 0.869, $P < 0.0005$), WBV (AUC: 0.719, 95% CI: 0.616 to 0.821, $P < 0.0005$) and ABPI (AUC: 0.667, 95% CI: 0.550 to 0.784, $P = 0.006$).

Discussion

Our study showed that WBV and erythrocyte aggregation were higher whereas erythrocyte deformability (lower EI_{max}), was lower in the participants with MetS when compared to the participants without MetS. MetS was significantly associated with the highest quartile of critical stress and WBV and with the lowest quartile of erythrocyte deformability. Our findings are in line with reports from Zhang et al. which showed that the mean WBV level was progressively higher in groups with higher number of positive MetS components including that the highest quartile of WBV (shear rate 200 s^{-1}) occurred 4.8

Table 1
Baseline characteristics of participants with and without MetS.

Parameters	Non-MetS (n = 64)	MetS (n = 36)	*P*-value
Diagnosed DM	11	22	<0.0005
Diagnosed hypertension	13	29	<0.0005
Hypertriglyceridemia	9	23	<0.0005
Low HDL-C	6	19	<0.0005
High waist circumference	31	12	0.207
Mean BMI (Kg/m^2)	25.79 ± 3.89	30.89 ± 5.50	<0.0005

Table 2
Table showing median and *P*-value for Kruskal–Wallis test.

Variables	Median			Test statistic	*P*-value
	Group I	Group II	Group III		
Critical time (Sec)	8.4	7.8	7.0	29.067	<0.0005
$SS_{1/2}$	2.60	2.55	2.90	3.875	0.144
ABPI[a]	1.04	1.01	1.06	7.969	0.019
TBPI	1.0	0.96	0.85	25.311	<0.0005

[a] Although ABPI difference is significant, it is not clinically relevant in our study due to the possible calcification of the lower limb arteries in recruited participants.

Table 3
Spearman's Correlation of hemorheological parameters, ABPI and TBPI with the components of MetS.

Parameters		Systolic BP	Waist circumference	HDL-C	TG	FBG
WBV	Correlation coefficient	.264	.344	−.177	.187	.234
	P-value	.008	.000	.080	.064	.021
Crit stress	Correlation coefficient	.383	.419	−.459	.591	.200
	P-value	.000	.000	.000	.000	.049
Crit time	Correlation coefficient	−.426	−.449	.280	−.438	−.283
	P-value	.000	.000	.005	.000	.005
EI_{max}	Correlation coefficient	−.150	−.304	.362	−.388	−.321
	P-value	.136	.002	.000	.000	.001
$SS_{1/2}$	Correlation coefficient	−.067	.039	−.255	.143	−.010
	P-value	.508	.698	.011	.157	.924
ABPI	Correlation coefficient	−.023	.173	−.240	.073	.046
	P-value	.820	.085	.017	.473	.652
TBPI	Correlation coefficient	−.545	−.462	.138	−.113	−.452
	P-value	.000	.000	.173	.265	.000

times more frequently than the lowest quartile measurement among subjects with four MetS components (Zhang et al., 2006). Our findings are also in agreement with Vaya et al. (Vaya et al., 2011), who reported higher corrected WBV, increased erythrocyte aggregation and reduced erythrocyte deformability in subjects with MetS compared to group without MetS who might have one or two components of MetS. Erythrocyte aggregates damage blood vessels (Pirrelli, 1999). Increased erythrocyte aggregation ultimately leads to increased WBV (Chien et al., 1967) and reduced microcirculatory flow (Bishop et al., 2001; Cabel et al., 1997; Soutani et al., 1995). Peripheral vascular resistance is increased when WBV increases which ultimately increases the pumping requirement of the heart (Devereux et al., 2000). This results in higher frictional force (shear stress) acting on the endothelium further increasing the risk of CVD (Kensey, 2003). Heart rate is also increased to compensate the hypoxic situation due to diminished oxygen supply to tissues as a result of erythrocyte aggregation (Connes et al., 2008). Oxygen diffusion and rate of oxygen release in peripheral tissues are affected due to slow capillary flow (Dandona et al., 2005; Tateishi et al., 2001). This chain of events may give rise to the further complications of MetS. In the Edinburgh artery study, WBV was shown to be associated with CVD complications (ischemic heart disease and stroke). The relative risk of cardiovascular events for WBV was as strong as established risk factors like low density lipoprotein and blood pressure. Plasma viscosity and fibrinogen level were also shown to be associated with CVD (Lowe et al., 1997).

Correlation analysis in our study showed significant correlation of hemorheological parameters with different components of MetS. None of the MetS components predicted hyperviscosity or low deformability but all of the individual components of MetS predicted erythrocyte hyperaggregability. After adjusting for age, sex and the presence of DM; WBV, critical stress and EI_{max} significantly predicted the likelihood of exhibiting MetS. It seems that though the individual MetS components has their own possible effect on rheological parameters (Husstedt et al., 1997; Medvedev and Skoriatina, 2012; Pirrelli, 1999; Sola et al., 2007), the combined effect due to their complex interplay is more severe and significant. The concurrences of the components of MetS could have an additive effect in enhancing alterations in hemorheological parameters which may give rise to severe microvasculopathy. Altered hemorheology might be one of the reasons for increased CVD events seen in MetS.

Contrary to the expectation, our study showed an increase in the value of ABPI in MetS. This could be explained by the fact that due to the calcification of lower limb artery in DM, ankle blood pressure readings often go beyond 200 mm Hg giving the falsely high ankle pressure (Brooks et al., 2001). Since, ABPI is not useful in vascular assessment if calcification of arteries has already progressed (Strandness and Bell, 1965), we also measured TBPI. Our study showed decreased value of TBPI in the participants with MetS. TBPI is the commonly used tools for the assessment of macrovascular functions (Mayfield et al., 1998; Vowden et al., 1996) in DM. Decreased value of this parameter indicates abnormal blood flow in larger and smaller arteries and have been shown to predict cardiovascular morbidity (Ono et al., 2003). High prevalence of MetS has been shown in patients with peripheral vascular diseases (Gorter et al., 2004; Olijhoek et al., 2004). TBPI and ABPI were significantly associated with DM in our study similar to other studies (Spångéus et al., 2013; Tapp et al., 2003). Altered hemorheology affects blood circulation at the capillaries level (microcirculation) (Pirrelli, 1999) whereas ABPI and TBPI measures vascular abnormalities of small and large arteries (macrocirculation). DM was significantly associated with parameters of both macro and microcirculation. After adjusting for the effect of DM, age and sex, ABPI and TBPI were not associated with MetS. However, this was not the case with hemorheological

Table 4
Age, sex and DM adjusted odds ratio for predicting MetS by hemorheological parameters, ABPI and TBPI.

Parameters	Odds ratio	95% CI	*P*-value
WBV	3.699	1.144 to 11.952	0.029
Critical stress	1.010	1.006 to 1.015	<0.0005
EI_{max} (lowest quartile)	4.025	1.333 to 12.147	0.013
TBPI (lowest quartile)	1.007	0.274 to 3.697	0.991
ABPI (lowest quartile)	2.090	0.699 to 6.248	0.187

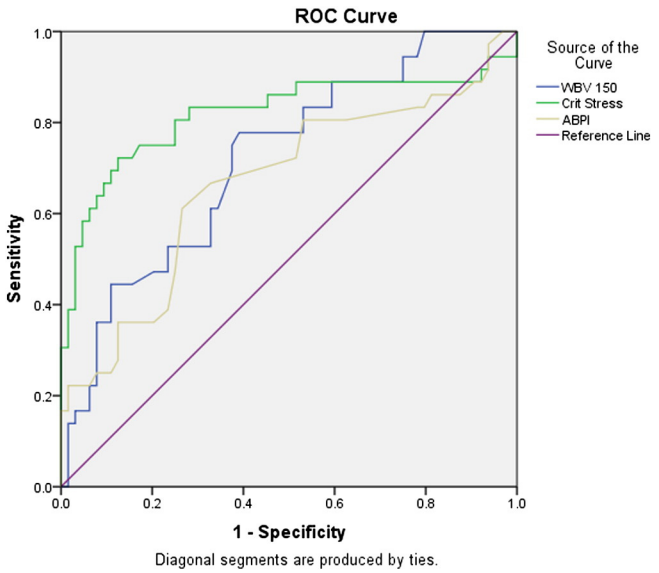

Fig. 1. ROC curve of WBV, critical stress and ABPI for differentiating MetS from non-MetS.

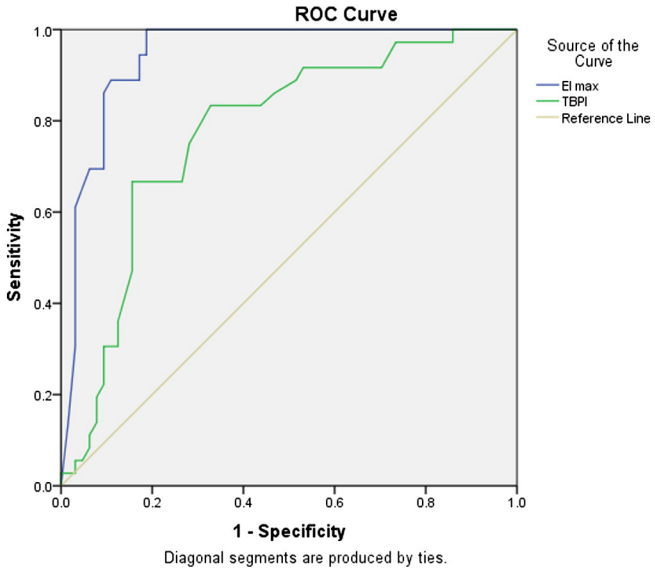

Fig. 2. ROC curve of EI_{max} and TBPI for differentiating MetS from non-MetS.

parameters. Also, ROC curve showed that two of the three hemorheological parameters (critical stress and EI_{max}) better classified MetS than TBPI. Hence, we proposed that microcirculatory defect present in MetS is beyond the affect of DM alone and alteration in microcirculation better identifies with MetS rather than alteration in macrocirculation. Peripheral artery disease of MetS is more likely due to the presence of DM whereas alteration in capillary blood flow seems to depend upon more complex pathophysiology underlying MetS. Czernichow et al. have shown microvascular dysfunction (lower functional capillary density) in MetS among subjects without DM or known CVD (Czernichow et al., 2010). The stronger association of MetS with microcirculation parameters rather than altered macrocirculation may be due to synergistic effect of different abnormalities or abnormal components underlying MetS and also could be explained by other aspects of MetS which are not routinely measured such as inflammatory and oxidative stress parameters. Richards et al. have proposed that oxidative damages lead to erythrocytes' shape changes and increase its rigidity by altering its lipid bilayer (Richards et al., 2000). These aspects need further study. We believe that assessment of microvascular abnormalities is as important as an assessment of macrovascular functions in MetS.

Conclusions

Both microcirculation defect and macrovascular circulation defect were present in MetS. All of the hemorheological parameters were significantly associated with MetS. The association of hemorheological parameters was stronger than the association of TBPI and ABPI with MetS. Altered hemorheology could be the bridge that connects MetS with increased CVD. Also, defect in microcirculation due to altered hemorheology could be one of the several pathogenic mechanisms underlying complications of MetS.

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