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Original Article

Association between metabolic syndrome and risk of cardiovascular disease, using different criteria and stratified by sex

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ABSTRACT

Aim: The purpose of this study is to determine the association between the components used to define metabolic syndrome and cardiovascular risk using different criteria stratified by sex.
Methods: A cross-sectional study with 608 subjects enrolled at the out-patients department of the Thai Internal Medicine Clinic was performed between October 2006 and September 2007. Included subjects had metabolic syndrome as defined by WHO, NCEP III, or IDF. The demographic and laboratory characteristic of the subjects including BMI, waist circumference, waist/hip ratio, fasting blood glucose, 2 h postprandial blood glucose, triglyceride, HDL, blood pressure, and microalbuminuria, were measured and recorded by chart review. Cardiovascular risk was determined by pulse wave velocity. The sensitivity and specificity of the component of metabolic syndrome according to the three criteria were stratified by sex.
Results: The HDL sensitivity was higher in females than in males. Among the different component of metabolic syndrome, blood pressure gave the strongest association with cardiovascular risk, with odds ratios of 13.6, 11.97, and 10.5 for the criteria of IDF, NCEP III, and WHO, respectively. Moreover, when analyzing by sex, the odds ratio for female subjects were about two times higher than that of males. The rest of the components in each of criteria exceptional HDL gave odds ratios of 2–4.
Conclusions: The appropriate components to predict cardiovascular risks are: high blood pressure and cut off point of waist circumference in females, as defined by the IDF criterion, and high triglyceride in males, as defined by the IDF criterion.

1. Introduction

Metabolic syndrome (Mts) is defined by a cluster of metabolic risk factors including: central obesity, hypertension (HT), impaired fasting glucose (IFG) or impaired glucose tolerance (IGT), diabetes mellitus (DM), and dyslipidemia (DLD), which predispose an individual to develop cardiovascular disease and type 2 diabetes [1–3]. Mts is important because recent advances in science and technology have brought significant changes to the environment, social behaviour and lifestyle. Such transformations have resulted in an increased risk of metabolic syndrome and cardiovascular diseases [4–7]. Accordingly, the high prevalence of Mts around the world, including Asia, has significantly increased in association with a number of the components currently used to diagnose Mts [8,9].

Clinically, Mts can be defined by different criteria such as that of the National Cholesterol Educational Program Adult Treatment Panel (NCEP III) [10] and the International Diabetes Foundation (IDF) [11], which differ slightly from the NCEP III in the cut off point of waist circumference and the level of fasting blood glucose (FBG). The WHO criterion [12], however, differs from the above criteria in two components, impaired glucose tolerance (IGT) and positive microalbuminuria (MAU). The original purpose to diagnose Mts by each of these criteria was to identify important components of Mts that relate to cardiovascular risk [13]. However, such metabolic components have not been identified unequivocally. The present study uses different criteria stratified sex to determine the association between Mts components and cardiovascular risk.

2. Methods

We did a cross-sectional study to compare the components of Mts according to different criteria of cardiovascular risks, and the presence of metabolic components such as diabetes mellitus, IFG/IGT, dyslipidemia and hypertension in 608 subjects recruited from

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the Internal Medicine Clinic at the university hospital of the Faculty of Medicine, Srinakharinwirot University. Mts was used as defined by WHO, NCEP III, and IDF criteria during October 2006 to September 2007. The study protocol was approved by the Ethics Committee of the faculty and informed consent was obtained from all subjects participating in the study. We studied the demographic and laboratory characteristic among subjects, including BMI, waist circumference (WC), waist/hip ratio (W/H), fasting blood glucose (FBG), 2 h postprandial blood glucose (IGT), triglyceride (TG), HDL, blood pressure (BP), MAU and associated medication through chart review. The data were cross-sectionally collected at the beginning of 2006 and at the end of 2007, approximately 12 months apart. Active exercise was defined by subjects engaging in aerobic exercise more than 3 days per week and at least 15 min per day.

The WHO criteria [12] consists of the identification of insulin resistance, e.g. type 2 diabetes or impaired fasting glucose (IFG) or IGT, plus any two of the following: elevated blood pressure (⩾140/90 mm Hg or drug therapy), plasma TG ⩾ 150 mg/dl, HDL <35 mg/dl (men) or <40 mg/dl (women), BMI >30 kg/m^2 and/or W/H ratio >0.9 (men) or >0.85 (women), urinary albumin >20 g/min; Alb/Cr >30 mg/g.

The NECP III [10] defines Mts by the presence of three or more of the following risk determinants: central obesity [WC >100 cm or, 40 inches (men); >88 cm or >35 inches (women)]; elevated TG (⩾150 mg/dl), low HDL cholesterol (<40 mg/dl in men, <50 mg/dl in women), HT (⩾130/85 mm/Hg), IFG (⩾110 mg/dl) [13]. Subjects were defined as Mts by IDF [11] if central obesity was present, and any two of the following: elevated TG (⩾150 mg/dl), low HDL cholesterol (<40 mg/dl in men, <50 mg/dl in women), HT (⩾130/85 mm/Hg), IFG (⩾100 mg/dl). The WC ⩾ 90 cm in men or ⩾80 cm in women was defined as central obesity in Japanese Asian patients [11]. The WC was measured by a tape in the direction of the horizontal plane, midway between the inferior margin of the risk and the superior border of the iliac crest [11,13,14].

Cardiovascular risk was determined by pulse wave velocity (PWV) [15] measured by Colin Medical Technology (VP-1000), and analyzed by pulse wave diagnosis results. Peripheral PWV (ba PWV) represented as volume waveforms for the brachium and ankle was measured using a VP-1000 pulse wave analyzer (Colin Medical Technology), as previously described [16]. In brief, the PWV measurement system recorded electrocardiogram, phonocardiogram and three pulse waves from the brachial and dorsalis pedis arteries. Pressure pulse sensors were used to measure pulse waves, and amplifier, filter, and isolation circuits were used to detect accurate signals. The intersecting tangent algorithm, using the least square mean (LSM) method, was adapted to determine upstroke points. Regional PWV values, brachial and dorsalis pedis were calculated automatically after collecting 10 s of data. For baPWV, brachial-dorsalis pedis transit time and PWV were calculated from the brachial-dorsalis pedis path length divided by transit time. Path length was estimated from the linear distance from the sternal notch to the dorsalis pedis artery at the point of applanation.

In a previous study, these analyses demonstrated that baPWV equal to or over 1400 cm/s was an independent variable for assessing risk stratification. According to the Framingham score, and for discriminating between patients with either stroke or coronary heart disease in both genders although our study referred to a cut off of baPWV equal to or over 1400 cm/s as a surrogate to arterial stiffness and representative of cardiovascular risks.

Logistic regression was used to determine the association of the components of Mts according to different criteria with of cardiovascular risk by measurement of PWV. Multivariate analyses were performed to adjust for all components of metabolic syndrome in the same criteria, including age, sex, LDL, cholesterol, and smoking. The prevalence rate of Mts using the three criteria and also for each component within each were calculated with 95% confidence intervals for males and females and overall. Sensitivity and specificity for determining Mts for individual components were computed using the respective criteria as gold standards and presented separately for both sexes. The results were considered statistically significant if the p-value was less than 0.05 Data analyses were performed using SPSS package for windows, version 11.

3. Results

A total of 608 subjects were included in the study. About 56% of them had been diagnosed with diabetes, 21.7% had IFG or IGT, and the rest were normal. About 30% of the subjects were males. Eighty five percent were non-smokers and 82% percent were non-drinkers. Thirty two percent had regular exercise. Average values for age, weight, body mass index, waist circumference, and W–H ratio were 57.79, 68.02, 27.08, 90.94, and 0.91, respectively (Table 1).

The overall prevalence rate (%) with 95% confidence intervals of metabolic syndrome in this population was found to be 69.6 (65.9–73.3), 71.1 (67.5–74.7), and 67.4 (63.7–71.1), when using the criteria of NCEP III, WHO, and IDF, respectively (Table 2).

Table 1
Baseline characteristics of patients.

Characteristics	Categories	Number	Percent
DM status	DM	339	55.8
	IFG/IGT	132	21.7
	Normal FBS	137	22.5
	Total	608	100
Sex	Male	180	29.6
	Female	428	70.4
	Total	608	100
Smoking status	Current smoking	33	5.4
	Ex-smoking	60	9.9
	Non-smoking	514	84.5
	Total	607	99.8
Drinking status	Current drinking	47	7.7
	Ex-drinking	60	9.9
	Non-drinking	500	82.2
	Total	607	99.8
Aerobic exercise	Active exercise	195	32.1
	Non-active exercise	413	67.9
	Total	608	100
Weight (Wt.)	68.02 ± 15.16		
Height (Ht.)	1.58 ± 0.08		
Body mass index (BMI)	27.08 ± 0.08		
Waist circumference (WC)	90.94 ± 0.08		
Hip circumference (HC)	99.89 ± 0.08		
W–H ratio	0.91 ± 0.08		

Table 2
Prevalence (percent) with 95% confidence intervals of metabolic syndrome by sex.

Criteria		Male	Female	Overall
NCEP III	Prevalence	68.3	70.1	69.6
	95% CI	61.5–75.1	65.8–74.3	65.9–73.3
	n	180	428	608
WHO	Prevalence	83.3	65.9	71.1
	95%CI	77.9–88.7	61.4–70.4	67.5–74.7
	n	180	428	608
IDF	Prevalence	61.7	69.9	67.4
	95% CI	54.6–68.8	65.6–74.2	63.7–71.1
	n	179	428	607

Table 3 shows a prevalence of metabolic syndrome components when using different criteria. The prevalence of Mts for positive waist circumference was 73.4% in IDF criteria, but it was 46.1% in NCEPT III, while the prevalence of Mts for positive BMI or W/H ratio in WHO criteria was 79.8%. Subjects who had high triglyceride were at 67.3% for WHO criteria, while only 63.2% for the other two criteria. The prevalence rates of high blood glucose were 74.8%, 63.3%, and 77.5% for IDF, NCEP III, and WHO. The prevalence of high blood pressure (HBP) was not only at a positive high level of 73.4% in the both IDF and NCEPT III, but also at a positive high level in WHO (73.2%).

Table 4 shows sensitivity and specificity for diagnosing metabolic syndrome for each component of metabolic syndrome, using the three criteria and stratified by sex. For HDL, sensitivity was higher in females than males. The specificity of blood pressure and fasting blood glucose was found to be higher in females than in males.

The association between cardiovascular risk and the components of the metabolic syndrome was calculated (Table 5). High strength of association was found for HBP with odds ratios with 95% CI of 13.6 (7.13–26.03), 11.97 (5.86–24.45), and 10.5 (5.44–20.26) for the criteria of IDF, NCEP III, and WHO, respectively. In addition, when analyzing by sex, the odds ratio for female's subjects was about two times higher than for male subjects. The waist circumferences in IDF and NCEP III has cardiovascular risk at odds ratio with 95% CI of 4.32 (2.42–7.71) and 3.92 (2.21–6.97), respectively. But the BMI or W/H ratio in WHO was associated to lesser cardiovascular risk than the others at odds ratio with 95% CI of 2.83 (1.52-5–27). Again, when this component was analyzed by sex, it was found that odds ratio for female subjects were about two times higher than for male. The high triglyceride (HTG) in IDF and NCEP III has been associated with cardiovascular risk at odds ratio with 95% CI of 3.63 (1.9–6.94) and 3.93 (2.07–7.48), respectively. When this component was analyzed by sex, it was also found that the odds ratio for male groups was about two times higher than that for female. HDL was not found to be significantly related to cardiovascular risk for any criterion. The rest of the components in each criterion were found to have an odds ratios of 2–3.

Table 3
Prevalence (percent) of components of metabolic syndrome for IDF, NCEP III, and WHO criteria.

Components of criteria	Male	Female	All
IDF			
Waist circumference	65.6	76.6	73.4
Triglyceride	64.4	62.6	63.2
HDL	49.4	77.8	69.4
Blood pressure	82.2	69.6	73.4
Fasting blood glucose	88.3	69.2	74.8
NCEP III			
Waist circumference	26.1	54.4	46.1
Triglyceride	64.4	62.6	63.2
HDL	49.4	77.8	69.4
Blood pressure	82.2	69.6	73.4
Fasting blood glucose	76.7	57.7	63.3
WHO			
Fasting blood glucose or IGT	88.9	72.7	77.5
BMI or W/H ratio	82.8	78.5	79.8
Triglyceride	68.3	66.8	67.3
Blood pressure	82.2	69.4	73.2
Microalbuminuria	53.9	46.5	48.7

Table 4
Sensitivity and specificity for diagnosing metabolic syndrome of components of metabolic syndrome for IDF, NCEP III, and WHO criteria.

Components of criteria	Sensitivity			Specificity		
	Male (%)	Female (%)	Overall (%)	Male (%)	Female (%)	Overall (%)
IDF						
Waist circumference	100.0	100.0	100.0	89.7	77.5	81.7
Triglyceride	73.0	74.2	73.9	47.8	64.3	58.7
HDL	57.7	87.0	79.0%	62.7	43.4	50.0
Blood pressure	91.0	85.9	87.3	30.3	66.9	54.4
Fasting blood glucose	100.0	82.6	87.3	30.9	62.0	51.3
NCEP III						
Waist circumference	35.8	71.3	61.0	94.7	85.2	88.1
Triglyceride	78.0	75.3	76.1	64.3	67.2	66.3
HDL	67.5	90.7	83.9	89.3	52.3	63.6
Blood pressure	97.6	91.3	93.1	50.9	81.3	71.9
Fasting blood glucose	95.1	78.3	83.2	63.2	90.6	82.2
WHO						
Fasting blood glucose or IGT	100.0	100.0	100.0	66.7	80.1	77.8
BMI or W/H ratio	90.0	88.3	88.9	53.3	40.4	42.6
Triglyceride	75.8	76.2	76.1	66.7	51.4	54.0
Blood pressure	92.7	88.7	90.0	70.0	67.8	68.2
Microalbuminuria	64.6	69.2	67.6	86.2	87.8	87.5

IGT, impaired glucose tolerance test.

4. Discussion

In the present study, we found that the components of WC in IDF and FBG in NCEP III had higher sensitivity and specificity, making them more suitable to diagnose Mts. The components of HBP in IDF and NCEP III had predominately the same effects in the female groups.

A manuscript of the author published in Journal of Diabetes and its Complications compared three criteria of Mts (WHO, NCEP III, and IDF) to predict cardiovascular risk. The results of this study show that IDF criteria were appropriate in predicting cardiovascular risks in female, whereas NCEP III was more suitable for males. For the above reasons, the author was interested in analysing each of components in the different criteria to prove which of each component among three criteria was the strongest in predicting cardiovascular risk.

Our study used baPWV represented as cardiovascular risks, since it had some previous evidence-base studies [15,16] showing correlation between baPWV and a marker of atherosclerotic vascular damage and cardiovascular risks. Our study is in agreement with studies [17,18] that the peripheral PWV or arterial stiffness was the best correlated marker to represent cardiovascular risks.

For prediction of cardiovascular risks through the components of Mts by each criteria, we observed that the first, the component of HBP, in the three criteria, was significantly associated with CVD. Since this component can directly affect the blood vessels and the cardiovascular system, it would increase the risk of CVD [19].

Second, the component of WC in the IDF and NCEP III has a higher association to cardiovascular risk than BMI or W/H ratio in the WHO, because the WC represents visceral fat, which several studies have related to an increase in the risk of CVD [20–22]. Additionally, our study has shown that not only the WC of female group in IDF significant associates with CVD risk but also the BMI or W/H ratio of female group in WHO had the same effects. From these results, it may be concluded that the WC of female group in IDF is the strongest predictor of cardiovascular risks, which is in agreement with a previous study [23]. It is interesting to note that gender differences in the relationship between Mts and subclinical atherosclerosis have been recently reported. Women showed a stronger risk factor for carotid atherosclerosis than men [24,25].

Table 5
Odds ratios with 95% confidence interval for the association between cardiovascular risk and the components of metabolic syndrome according to IDF, NCEP III, and WHO criteria.

	Male		Female		Overall	
	OR*	95% CI	OR*	95% CI	OR**	95% CI
IDF						
Waist circumference	1.81	0.63–5.23	6.34	3.08–13.05	4.32	2.42–7.71
Triglyceride	6.24	1.42–27.38	3.54	1.67–7.51	3.63	1.9–6.94
HDL	1.69	0.56–5.1	1.22	0.57–2.61	1.37	0.75–2.48
Blood pressure	12.6	3.02–52.47	14.5	6.73–31.14	13.6	7.13–26.03
Fasting blood glucose	1.35	0.29–6.38	2.1	1.03–4.3	1.99	1.06–3.73
NCEP III						
Waist circumference	3.83	0.96–15.29	3.97	2.08–7.57	3.92	2.21–6.97
Triglyceride	8.76	2.02–37.93	3.35	1.61–7	3.93	2.07–7.48
HDL	1.62	0.52–4.99	1.25	0.6–2.6	1.35	0.75–2.43
Blood pressure	14.63	2.29–93.59	12.93	5.78–28.92	11.97	5.86–24.45
Fasting blood glucose	1.1	0.19–6.44	2.55	1.18–5.55	2.21	1.11–4.43
WHO						
Fasting blood glucose or IGT	3.57	0.8–15.9	2.12	1.03–4.39	2.28	1.2–4.32
BMI or W/H ratio	1.82	0.56–5.92	3.36	1.6–7.08	2.83	1.52–5.27
Triglyceride	2.11	0.58–7.63	2.72	1.32–5.6	2.49	1.36–4.58
Blood pressure	7.24	1.72–30.47	13.3	6.06–29.09	10.5	5.44–20.26
Microalbuminuria	4.43	1.29–15.19	2.33	1.06–5.13	2.83	1.49–5.39

IGT, impaired glucose tolerance test.
* Adjusted for all components of metabolic syndrome in the same criteria including age, LDL, cholesterol, and smoking.
** Adjusted for all components of metabolic syndrome in the same criteria including age, sex, LDL, cholesterol, and smoking.

Finally, our study found that the component of high triglyceride (HTG) was significantly associated with cardiovascular risk in IDF and NCEP III, but this was not the case in WHO, consistent with previous studies [26,27]. The effect of HTG could be a consequence of increased visceral fat, whose relation to cardiovascular risk has already been described [20–22]. In the male group, HTG in IDF has a significant association to cardiovascular risk than in the female group, whereas a previous study has found no such a difference [27]. This study, however, includes subjects selected from the general population, rather than subjects having metabolic syndrome, as in our case.

We must acknowledge that our study has some limitations. First, as our study is based on a cross-sectional design, causal relationships between risk factors and outcomes could not be claimed at the moment [28]. Additionally, our subjects were predominantly female, in the middle age group, which might not represent the general population. Second, our cross-sectional study consisted of patients at high risk of CVD, since the most of our subjects have Mts consisting of DM, DLD, and HT, each of which has increased risk of CVD [25]. Thus, our finding relates to subjects at increased risk of both elevated levels of atherosclerosis and cardiovascular events, and might not be applicable to the general population. Finally, our study used PWV as representation of CVD risk [15–18], which is used extensively as a measure of subclinical atherosclerosis, and relates to the future risk of clinical cardiovascular events in Mts patients [15,16]. Additional prospective clinical studies are required to determine the suitability of each component using different Mts criteria in predicting the occurrence of ischemic heart disease in both males and females.

Our results may be applied in two clinical aspects: First, we found that the cut off point of WC in IDF, the level of FBG more than 110 mg/dl and the HBP over than 130/85 mm Hg in female groups, respectively, were the appropriate components to use for diagnosis of Mts. Second, we found that the HBP over than 130/85, cut off point of WC in female group by IDF criteria and HTG of male group in IDF criteria were the appropriate components to use for the prediction of cardiovascular risk.

We may summarise that the appropriate components to predict cardiovascular risks are: high blood pressure and cut off point of waist circumference in females, as defined by the IDF criterion, and high triglyceride in males, as defined by the IDF criterion.

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