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Original article

Can we early diagnose metabolic syndrome using brachial-ankle pulse wave velocity in community population?

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Background　The prevalence of metabolic syndrome (MetS) increased recently and there was still not a screening index to predict MetS. The aim of this study was to estimate whether brachial-ankle pulse wave velocity (baPWV), a novel marker for systemic arterial stiffness, could predict MetS in Chinese community population.

Methods　A total of 2 191 participants were recruited and underwent medical examination including 1 455 men and 756 women from June 2011 to January 2012. MetS was diagnosed according to the criteria of the International Diabetes Federation (IDF). Multiple Logistic regressions were conducted to explore the risk factors of MetS. Receiver operating characteristic (ROC) curve was performed to estimate the ideal diagnostic cutoff point of baPWV to predict MetS.

Results　The mean age was (45.35±8.27) years old. In multiple Logistic regression analysis, the gender, baPWV and smoking status were risk factors to MetS after adjusting age, gender, baPWV, walk time and sleeping time. The prevalence of MetS was 17.48% in 30-year age population in Shanghai. There were significant differences (χ^2=96.46, P <0.05) between male and female participants on MetS prevalence. According to the ROC analyses, the ideal cutoff point of baPWV was 1 358.50 cm/s (AUC=60.20%) to predict MetS among male group and 1 350.00 cm/s (AUC=70.90%) among female group.

Conclusion　BaPWV may be considered as a screening marker to predict MetS in community Chinese population and the diagnostic value of 1 350.00 cm/s was more significant for the female group.

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Metabolic syndrome (MetS), consisting of abdominal obesity, atherogenic dyslipidemia, high blood pressure, and hyperglycemia, has now received a great interest because its number is increasing in broad area of the world.[1-3] Although it has been a controversial topic, MetS has been identified as an important and common cluster of risk factors of cardiovascular diseases (CVD) and coronary heart disease (CHD) by some organizations[4-6] such as the International Diabetes Federation (IDF), the World Health Organization (WHO), and the National Cholesterol Education Program's Adult Treatment Panel (NCEP). In recent years, MetS has been commonly used in large-scale studies around the world.[7,8]

With the development in economy and changes in life style, the prevalence of MetS has been on the rise over the past few decades in China.[9-11] The prevalence of MetS is 16.5% in the mainland of China[11] and 15.8% in Taiwan, China[12] among adult population according to IDF definition. Currently, MetS has become a serious disease to the society and families not only in China, but also in other countries. However, there is still no precise data on total prevalence in Chinese, especially among middle aged and elderly population due to the lack of useful diagnostic tool. Therefore, it is necessary to establish a measure to early diagnose MetS. Arterial stiffness is a vascular marker including whole cardiovascular risks[3] and could be a diagnostic tool for Mets. In the present study, brachial-ankle pulse wave velocity (baPWV), a novel measure for

systemic arterial stiffness, was employed[13] to predict MetS.

METHODS

Study population

Participants were included if they met the following criteria: (1) Subjects aged ≥30 years; (2) Individuals who were community residents in Lujiazui, Shanghai; (3) Participants without hypertension crisis, multiple system organ failure, or other disease that was unavailable to measure baPWV. Pregnant women were excluded from the

present study. From June 2011 to January 2012, a total of 2 191 participants were recruited and underwent medical examination including 1 455 male and 756 female. The protocol was approved by the Ethical Committee of Tongji University Medical School. All participants gave written informed consent.

Laboratory measurements

Systolic blood pressure (SBP), diastolic blood pressure (DBP), body mass index (BMI), levels of fasting plasma glucose (FPG), hemoglobin A1c (HbA1c) and high-density lipoprotein (HDL) were measured in all subjects. Plasma total cholesterol, HDL cholesterol, HbA1c and blood glucose were measured enzymatically.[9] All blood samples were obtained in the morning after fasting overnight.

BaPWV measurement

A clinical device (Colin VP1000, Komaki, Japan) has been developed to automatically and simultaneously measure blood pressure (BP) in both ankles and arms, as record pulse waves of the brachial and posterior tibial arteries using an automated oscillometric method.[14,15] Using this device, we can easily obtain the baPWV values. It was measured after the subject had rested for at least 5 minutes. Validation of this method has been previously reported.[16-18] We adopted the value of right baPWV in the present study.

Definition of varaibles

MetS was defined according to the following criteria: (1) required criteria: BMI ≥ 25 kg/m^2 (the waist circumference was not available in this study). (2) Plus any two of the following four factors: elevated triglyceride level: ≥ 1.7 mmol/L (or 150 mg/dl); reduced HDL cholesterol: <40 mg/dl (male) or 50 mg/dl (female); elevated blood pressure ($\geq 130/85$ mmHg), and fasting plasma glucose ≥ 5.6 mmol/L (or 100 mg/dl). Or they had been diagnosed as dyslipidemia, hypertension and diabetes mellitus with specific treatment for these abnormalities.[19-21]

Statistical analysis

Continuous data were expressed as the mean±standard deviation (SD). For the continuous variables, *t*-test was employed to analyze the difference between groups. For the categorized variables, χ^2-test was conducted to show the ratio difference between two groups. ROC curve analysis was also performed to discriminate patients with or without MetS disease by baPWV. Then, the values with the highest sum of sensitivity and specificity were identified as the cutoff values. The step-wise Logistic regression analysis was conducted to explore risk factors of MetS. All statistical analysis was performed using the SAS (SAS Institute, USA) and SPSS (SPSS Inc., USA) software package. $P < 0.05$ was considered as statistically significant.

RESULTS

A total of 2 191 subjects were enrolled in our study between June 2011 and January 2012 in Shanghai. The demographic data, physical characteristics, and mean

values of biochemical indictors of two groups (MetS group and non-MetS group) are shown in Table 1. The baseline demography of target population showed that mean age of patients was (45.35±8.27) years and the age of the MetS group was higher than the control group (*t*=5.42, *P* <0.05). There were significant differences in the constituent ratio of, education level, smoking, alchohol, diabetes history, hypertension history and CHD history between two groups (*P* <0.05), but no differences in folk and marriage status between two groups (*P* >0.05).

Table 1 also revealed the laboratory test value and clinical characteristics of research participants. The BMI value of

Table 1. Basic demographic character of MetS group and non-MetS group in Shanghai

Variables	MetS (*n*=383)	non-MetS (*n*=1 808)	*t*/χ^2	*P* values
Age (years)	47.37±7.95	44.86±8.27	5.42	0.001
Folk (*n* (%))			3.23	0.072
Han	371 (98.40)	1 782 (99.30)		
Other	6 (1.60)	12 (0.70)		
Marriage status			0.145	0.704
Single	8 (2.10)	44 (2.50)		
Other	368 (97.90)	1 746 (97.50)		
Education level			4.48	0.034
Low	249 (65.5)	1 271 (29.0)		
High	131 (34.5)	519 (71.0)		
Smoking (*n* (%))			45.53	0.001
Yes	174 (45.70)	504 (28.00)		
No	207 (54.30)	1 293 (72.00)		
Alcohol (*n* (%))			39.80	0.001
Yes	172 (45.50)	519 (28.85)		
No	206 (54.50)	1 278 (71.15)		
Walking time (h/d)	2.07±0.81	2.05±0.79	0.53	0.590
Sleeping time (h/d)	7.24±3.91	7.25±2.50	–0.04	0.950
Diabetes (*n* (%))			112.24	0.001
Yes	127 (33.16)	126 (6.97)		
No	256 (66.84)	1 682 (93.03)		
Hypertension (*n* (%))			218.25	0.001
Yes	254 (66.32)	488 (26.99)		
No	129 (3.68)	1 320 (73.01)		
CHD history (*n* (%))			55.23	0.001
Yes	66 (17.05)	104 (5.80)		
No	323 (82.95)	1 685 (94.20)		
BMI (kg/m^2)	27.53±2.21	23.31±2.74	28.24	0.001
SBP (mmHg)	136.86±16.33	122.12±15.53	16.70	0.001
HR (beats/min)	73.59±11.30	73.10±10.79	0.81	0.419
HbA1c (%)	5.74±1.12	5.27±0.75	7.76[*]	0.001
FPG (mmol/L)	5.42±1.51	4.79±0.95	7.81	0.001
LDL-C (mmol/L)	3.03±0.81	2.85±0.70	4.19	0.001
HDL-C (mmol/L)	1.13±0.44	1.27±0.34	–7.76	0.001
UA (μmol/L)	388.61±83.76	321.60±87.90	13.66	0.001
UN (mmol/L)	5.24±1.13	5.11±1.20	2.02	0.054
AST (U/L)	28.13±19.71	22.69±10.81	4.20[*]	0.001
ALT (U/L)	35.21±11.93	23.84±21.39	9.26[*]	0.001
baPWV (cm/s)	1 431.75±247.90	1 315.53±212.01	5.59	0.001
ABI	1.08±0.07	1.05±0.08	3.37	0.001

Data were expressed as mean±SD or *n* (percent). [*]The variances were not equal between two groups. Folk: Study participants was divided into Han and other minor ethic people. Education level, Low: less than education of 12 years; High: more than education of 12 years. BMI: body mass index; SBP: systolic blood pressure; HR: heart rate; HbA1c: hemoglobin A1c; FPG: fasting plasma glucose; LDL-C: low density lipoprotein cholesterol; HDL-C: how density lipoprotein cholesterol; UA: uric acid; UN: urine nitrogen; AST: aspartate aminotransferase; ALT: alanine aminotransferase; BaPWV: brachial-ankle pulse wave velocity; ABI: ankle-brachial index. Walking time: the walking time outdoor.
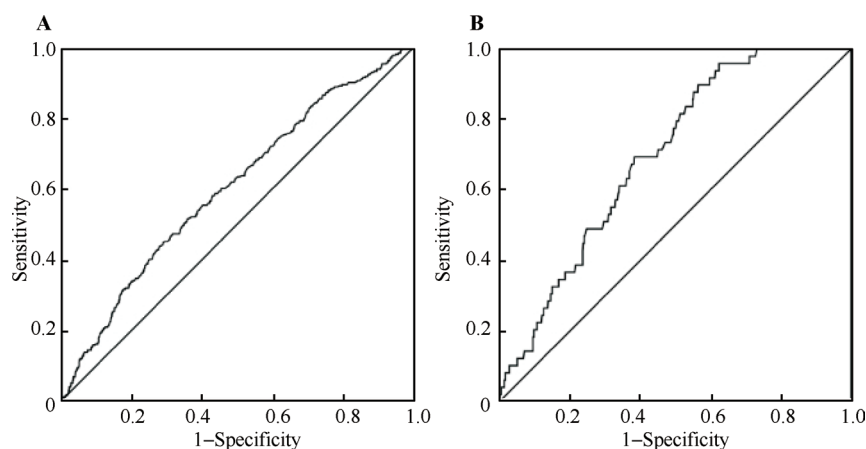
A

B

Figure 1. The ROC curves to predict MetS according to gender. **A:** Male group. Cutoff point=1 358.5 cm/s. AUC=0.60, 95% *CI*: 0.568, 0.637. Sensitivity=58.7%; Specificity=57.3%. **B:** Female group. Cutoff point=1 350cm/s. AUC=0.71, 95% *CI*: 0.636, 0.795. Sensitivity=50.5%; Specificity=74.5%.

MetS group was higher than that of control group (*t*=28.24, *P* <0.05). The lab test items SBP, HbA1c and other variables were significant higher in MetS group. However, HDL cholesterol was higher in the female group (*t*= −7.76, *P* <0.05).

In total, ROC curve analysis indicated that the cutoff point was 1 350 cm/s and AUC was 0.65 (95% *CI*: 0.568, 0.637) for the whole groups. However, the ROC curve analysis revealed there were different diagnosis effects for different gender groups (Figure 1). AUC was 0.60 (95% *CI*: 0.568, 0.637) in male group and 0.71 (95% *CI*: 0.636, 0.795) in female group respectively. Compared with the male group, the diagnosis value of baPWV cutoff point was more significant to predict MetS in female group.

In present study, 1 350 cm/s was considered as a point to divide baPWV into high value and low value according to ROC analysis results in total group. The Logistic regression model indicated that baPWV was an important risk of MetS in three models not only for the men but also for the women. Among model 2, baPWV and smoking were entered into the final regression model for men. Their *OR* value were 1.82 and 1.14 (Table 2). Among model 3, baPWV and smoking also were risk factors for the men while age and walking time were risk factors for the women.

The prevalence of MetS was 17.48% in present study population in Shanghai. The prevalence of MetS was more common in men than in women in all generations (Table 3, *P* <0.05). The Chi-square test for trend indicated prevalence of MetS in different gender groups was closer with the increasing age group (χ^2=10.40, *P* <0.05). The prevalence of MetS was rapidly rising with age increasing in female group, but not in male group.

Table 4 demonstrates the changing trend of positive/ negative likelihood ratio and Yodan index according to

different BaPWV cutoff point. When BaPWV was equal to 1 350 cm/s, the results were ideal. These results confirmed the cutoff value coming from ROC analysis. Its positive likelihood ratio and negative likelihood ratio was 1.35 and 0.73 for the men (2.12 and 0.64 for the women) respectively.

DISCUSSION

Previous studies have indicated that MetS was strongly associated with significant coronary artery stenosis, mixed plaque formation and multivessel involvement.[3,4] In present study, CHD history in MetS group was higher than that in control group and this result was consistent with above conclusion. At the same time, baPWV might predict the development of atherosclerosis and it has been verified by several studies. Then we assumed that baPWV could be a screening index to predict the MetS.

ROC analysis showed that baPWV may be considered as a screening marker to predict MetS among middle-aged and

Table 2. Risk factors of MetS in Logistic regression analysis according to three models

Variables	β	SE	Wald	*P* values	*OR*	95% *CI*
Men						
Model 1						
baPWV	0.56	0.12	19.79	0.000	1.75	1.37, 2.25
Model 2						
Age group	−0.03	0.08	0.19	0.655	0.96	0.80, 1.14
baPWV	0.59	0.13	19.56	0.000	1.82	1.39, 2.37
Marriage	−0.19	0.47	0.16	0.682	0.82	0.32, 2.09
Smoking	0.13	0.06	4.40	0.035	1.14	1.01, 1.30
Model 3						
Age group	−0.05	0.08	0.28	0.596	0.95	0.80, 1.13
baPWV	0.63	0.13	21.70	0.000	1.89	1.44, 2.47
Marriage	−0.20	0.47	0.18	0.671	0.81	0.32, 2.08
Smoking	0.15	0.06	5.24	0.022	1.16	1.02, 1.32
Walking time	0.02	0.08	0.07	0.781	1.02	0.86, 1.21
Sleeping time	0.01	0.02	0.07	0.786	1.00	0.96, 1.04
Women						
Model 1						
baPWV	0.73	0.30	5.68	0.017	2.07	1.13, 3.78
Model 2						
Age group	0.81	0.21	13.82	0.111	2.26	1.47, 3.47
baPWV	0.38	0.32	1.39	0.237	1.46	0.77, 2.77
Marriage	−1.04	0.73	2.00	0.157	0.35	0.08, 1.49
Smoking	0.21	0.55	0.15	0.694	1.24	0.42, 3.67
Model 3						
Age group	0.83	0.23	13.03	0.000	2.29	1.46, 3.60
baPWV	0.43	0.33	1.67	0.195	1.54	0.80, 2.98
Marriage	−1.32	0.78	2.83	0.092	0.26	0.05, 1.24
Smoking	0.16	0.58	0.08	0.771	1.18	0.37, 3.73
Walking time	0.51	0.17	8.28	0.004	1.66	1.17, 2.36
Sleeping time	−0.00	0.05	0.00	0.939	0.99	0.89, 1.11

BaPWV (men): high value (baPWV≥1 350 cm/s), low value (baPWV<1 350 cm/s). BaPWV (women): high value (baPWV≥1 350 cm/s), low value (baPWV<1 350 cm/s). Adjusted variable in model 1: baPWV. Adjusted variables in model 2: age, baPWV, marriage, smoking. Adjusted variables in model 3: age, baPWV, marriage, smoking, walking time, sleeping time.

Table 3. Prevalence of MetS among different age groups according to gender

Age	Men		Women		χ^2	P values
(years)	MetS (%)	Non-MetS (%)	MetS (%)	Non-MetS (%)		
30–39	65 (19.88)	262 (80.12)	7 (1.15)	276 (97.53)	44.14	0.000
40–49	131 (24.86)	396 (75.14)	25 (7.65)	302 (92.35)	40.04	0.000
50–	138 (23.71)	444 (76.29)	17 (11.72)	128 (88.28)	9.94	0.001
Total	334 (23.26)	1 102 (76.74)	49 (6.49)	706 (82.52)	96.46	0.000

Chi-square test for trend: χ^2=10.40, P <0.05.

Table 4. Cutoff point of BaPWV and its positive/negative likelihood ratio by gender

BaPWV	Sensitivity	Specificity	LR+	LR–	Youden index
Men					
1 250	0.83	0.30	1.17	0.59	0.12
1 300	0.70	0.42	1.21	0.71	0.12
1 350[*]	0.58	0.57	1.35	0.73	0.15
1 400	0.50	0.65	1.43	0.77	0.15
1 450	0.42	0.73	1.58	0.56	0.15
Women					
1 250	0.67	0.57	1.55	0.57	0.22
1 300	0.56	0.68	1.75	0.64	0.24
1 350[*]	0.51	0.76	2.12	0.64	0.27
1 400	0.32	0.84	2.00	0.81	0.16
1 450	0.22	0.88	1.83	0.89	0.10

LR+: positive likelihood ratio; LR–: negative likelihood ratio. [*]Best cutoff point of baPWV.

elderly population. Its diagnosis value was more significant in the female group. The cutoff point was 1 358.50 cm/s for the men and 1 350 cm/s for the women while it was 1 350 cm/s for the whole group. When considered 1 350 cm/s as the best cutoff value in total groups, multiple logistic regression results revealed that baPWV and smoking were risk factors causing to MetS for the men while age and walking time were risk factors for the women.

Using the IDF definition, we assessed the prevalence of MetS among 30-year old population in Shanghai. Approximately 17.48% of participants met the criteria of MetS. This result was higher than the prevalence of 12.1% reported by Wang et al[22] and 14.6% reported by Li et al.[23] In contrast, it was lower than the results (prevalence of 19.4%) made by Weng et al.[24] On the other hand, we are aware that the study group is not necessarily representative of the general population since it is a selective elderly based community population. Therefore, we assume that the prevalence of MetS in the general population in Shanghai might be even lower than present results.

It was interesting that there were significant differences in prevalence among the different gender groups in the present study. The prevalence of male group was higher than female group among all age groups. Above results suggested that male group have higher risk to MetS than female group. This means that females may be a protective factor to MetS. We propose the main reason being the arterial stiffness of male participants was worse than female group for the present research. It also means that the degree of inflammation was higher in the male group. At the same time, the BMI, blood press, glucose and low-density lipoprotein cholesterol were lower among female group.

With an increase in age, the trend became closer on prevalence. Different researches had controversial results to this conclusion. In researches reported by Zhao et al,[25,26] they also showed the prevalence of MetS was higher in men than in women. While the research conducted by Gu et al[11] indicated the opposite results.

Although MetS has attracted the attention coming from several international organizations, there was still not a suitable diagnosed marker to predict this disease. As a good marker of atherosclerosis, baPWV may be a potential diagnose tool to the MetS, especially to the 30-year old individuals.

There was a strong relationship between MetS and atherosclerosis in previous studies.[27] The mechanisms underlying the association between MetS and arterial stiffness[28] were likely that they have the same important pre-steps (inflammation and oxidative stress appearance). Several researches[28-31] indicated that inflammation and oxidative stress could contribute to the progress of MetS and atherosclerosis.

As we acknowledge, there were few researches to consider baPWV as a screening tool to predict the MetS among middle-aged and elderly population and ROC analysis indicated its diagnosis value was more significant in the female group. Another novel finding was that females could be a protective factor to causing MetS. The positive/negative likelihood ratio and Youden index also confirmed the 1 350 cm/s was the best cutoff value not only for men but for women.

There were also several limitations in present studies. Firstly, we could overestimate the prevalence of male group since its mean age was higher than female group. Secondly, our discoveries could not definitively prove a cause link underlying the association described above since it was a cross-sectional study. Thirdly, we could not promise that we have ruled out residual confounding of other unknown factors. Therefore, it is necessary to have further prospective studies for a better explanation.

In conclusion, baPWV may be considered as a screening marker to predict the MetS among middle-aged and elderly population and the diagnosis value was more significant to the female group (cutoff point=1 350 cm/s). In our daily life, we should pay attention in preventing MetS through controlling baPWV and quitting smoking, especially in men.

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