Metabolic Syndrome

Systolic Blood Pressure as an Independent Predictor of Metabolic Syndrome in Male Adolescents

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Background: Recent evidence has shown that adults with metabolic syndrome (MetS) have significantly higher systolic blood pressure (SBP) than normal during childhood. However, it has not been well-documented the extent to which systolic blood pressure predicts metabolic syndrome in male adolescents.

Methods: We retrospectively studied a total of 614 male adolescents 10 to 15 years of age who received a health examination at a private health screening center from 1999 to 2008 (mean follow-up time is 2.71 years). These examinations included anthropometric, blood pressure, and biochemical measurements such as fasting plasma glucose and lipid profiles. All subjects were normotensive and refrained from taking any medications known to affect MetS components. Only adolescent boys were included in this study because the incidence of MetS for girls in this cohort was considered too low to perform further analysis. We divided our subjects into 3 groups according to baseline SBP. Multivariate linear regression analysis and multivariate logistic regression analysis were used to identify the association of anthropometric parameters with the SBP at baseline.

Results: Among 614 subjects, the incidence of metabolic syndrome in boys is 3.1%. Boys with baseline SBP $\geqq$ 120 mmHg have a higher risk of developing MetS than boys with baseline SBP < 110 mmHg (odds ratio: 31.78; 95% confidence interval for the difference = 4.16-243.07, $p < 0.001$). Age, waist circumference, body mass index, fasting plasma glucose, low serum high-density lipoprotein-cholesterol and high triglyceride correlated significantly with baseline SBP ($p < 0.001$). Among all the parameters, body mass index had the strongest association with baseline SBP in male adolescents. Waist circumference was the strongest independent contributor to baseline SBP in male adolescents.

Conclusion: SBP in male adolescents is an independent predictor for metabolic syndrome in male adolescents and could be included in routine metabolic risk assessment.

Key Words: Adolescents • Metabolic syndrome • Predictor

INTRODUCTION

Metabolic syndrome (MetS) in adults results from a cluster of risk factors, including hypertension, dyslipidemia, abdominal obesity, and hyperglycemia.[1] This syndrome develops in individuals at risk for developing cardiovascular disease and type 2 diabetes.[2,3] Early treatment of MetS components decreases morbidity and mortality.[4] The obesity epidemic has spread in children around the world and may lead to an increased incidence of MetS.[5-7] Furthermore, some evidence suggests that this metabolic derangement persists into adulthood.[8-10] Therefore, identification of children at risk of developing MetS later in life can be critical in the overall

Received: January 22, 2011 Accepted: January 19, 2012
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effort to reduce mortality. Mattson et al. identified childhood obesity, high triglyceride (TG) levels, hyperinsulinemia, high C-reactive protein (CRP) level, and a family history of hypertension or diabetes as determinants of adult MetS.[11] Burns et al. showed that, during childhood, the adults with MetS had significantly higher systolic blood pressure (SBP) than that of normal adults at that age.[12] Researchers from Japan showed that elevated SBP in obese children is associated with hyperinsulinemia and visceral fat accumulation regardless of family history of hypertension.[13] However, the potential of SBP in male adolescents to predict the incidence pf MetS later in life remains unknown. To answer this question, we retrospectively assessed longitudinal data regarding SBP during the patients' first visits, and review ongoing MetS components during follow-up to explore the potential value of baseline SBP as a predictor for MetS in male adolescents.

METHODS

Study population

Data was retrospectively collected from the MJ Health Screening Center in Taiwan from 1999 to 2008. The MJ Health Screening Center is a membership-oriented private medical check-up clinic that provides periodic health examinations to its members, and all screening activities are standardized under a detailed protocol. All personnel performing measurements received similar training and certification. A detailed description of the MJ Health Screening Center Study is described in an earlier publication.[14] The protocol for this study was approved by a review crommittee at the MJ Health Screening Center. Ten- to 15-year-old adolescents who had completed at least two medical checkups were included in the study. We excluded girls and individuals with MetS, diabetes, hypertension, hyperlipidemia, and cardiovascular disease at baseline. Individuals who were receiving medications known to affect MetS components were also excluded. A total of 614 male subjects were available for analysis. Follow-up time was 2-4 years (mean follow up time is 2.71 years). Examinations included anthropometric, blood pressure, and biochemical measurements.

Anthropometric measurements and general data

Medical histories were obtained by the nursing staff using a questionnaire, and complete physical examinations were also performed. Subjects' body weight, waist circumference (WC), and height were measured barefoot and with light indoor clothing. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Blood pressure was measured by the nursing staff by using standard mercury sphygmomanometers: the blood pressure cuff was applied on the right arm, with the subjects in a sitting position. To determine the potential value of blood pressure as a predictor for MetS in male adolescents, we divided the subjects into 3 groups according to SBP and DBP during the first visits (SBP-1 group: SBP < 110 mmHg; SBP-2 group: 110 mmHg ≤ SBP < 120 mmHg; SBP-3 group: SBP ≥ 120 mmHg; DBP-1 group: DBP ≤ 55 mmHg; DBP-2 group: 55 mmHg < DBP ≤ 65 mmHg; DBP-3 group: DBP > 65 mmHg).

Biochemical parameter measurements

We collected a 10-h fasting blood sample from the subjects during the first visit and also upon follow-up. Plasma was separated from blood within 1 hour and stored at -30 °C. Fasting plasma glucose (FPG) was detected using the glucose oxidase method (YSI 203 Glucose Analyzer, Scientific Division, Yellow Spring Instruments, Yellow Spring, OH, USA). Total cholesterol (TC) and TG levels were measured using the dry, multilayer, analytical slide method by using a Fuji Dri-Chem 3000 Analyzer (Fuji Photo Film, Minato-Ku, Tokyo, Japan). Serum high-density lipoprotein-cholesterol (HDL-C) and low-density lipoprotein-cholesterol (LDL-C) concentrations were analyzed enzymatically.[15,16]

Metabolic syndrome definition

The International Diabetes Federation (IDF) consensus definition of MetS in children and adolescents was used to define MetS in the study.[17] We defined MetS as the presence of at least 3 of the following abnormalities: abdominal obesity[18] (WC ≥ 90th percentile); TG level ≥ 150 mg/dl; HDL-C < 40 mg/dl; hypertension (SBP ≥ 130/DBP ≥ 85 mmHg); and FPG concentration ≥ 100 mg/dl.

Statistical analysis

To determine the potential of baseline blood pressure to predict MetS components in male adolescence, we divided the subjects into 3 groups according to SBP and DBP during the first visits (SBP-1, SBP-2, and SBP-3 groups; DBP-1, DBP-2, and DBP-3 groups). All statistical analyses were performed using SPSS 17.0 software (SPSS Inc., Chicago, IL, USA). Data are presented as means ± standard deviation (SD), Additionally, baseline and follow-up data were compared using a paired *t* test. We assessed the differences between the 3 SBP and 3 DBP groups using one-way analysis of variance (ANOVA) test and the Bonferroni test as a post-hoc test. Furthermore, we used Pearson's correlation to examine the correlation between each metabolic component with SBP and DBP. The TG level was not normally distributed and was, therefore, logarithmically transformed before analyses. Multivariate linear regression analysis was applied to investigate which of the significant MetS components were truly independent. Finally, logistic regression analysis was used to calculate odds ratios (ORs) for increased risk of developing MetS or abnormal MetS components between the 3 groups.

RESULTS

A total of 614 subjects were studied. MetS incidence in boys was 3.1% during a mean follow-up of 2.7 ± 0.97 years. In our follow-up, all studied subjects had significantly ($p < 0.001$) higher WC, BMI, SBP and DBP, but lower lipid profiles than the corresponding baseline values (Table 1). For each component of MetS, we found that age, WC, BMI, FPG, HDL-C, and TG correlated significantly ($p < 0.001$) with SBP at the baseline (Table 2). The WC, BMI, and TG correlated signifi-

Table 1. Characteristics of the study participants at baseline and follow-up

	Baseline	Follow-up	p value*
Age (years)	12.9 ± 1.6	15.6 ± 1.4	< 0.001
Waist circumference (cm)	69.2 ± 10.3	73.1 ± 9.9	< 0.001
Body mass index (kg/m^2)	20.5 ± 4	21.7 ± 4.1	< 0.001
Systolic blood pressure (mmHg)	110.5 ± 12.2	115.2 ± 13.0	< 0.001
Diastolic blood pressure (mmHg)	59.6 ± 8.2	61.4 ± 9.0	< 0.001
Fasting plasma sugar (mg/dL)	94.9 ± 6.6	95.6 ± 6.4	0.020
Total cholesterol (mg/dL)	162.4 ± 28.8	155.9 ± 26.5	< 0.001
HDL-C (mg/dL)	55.8 ± 13.4	53.4 ± 12.3	< 0.001
LDL-C (mg/dL)	90.9 ± 24.0	87.2 ± 22.8	< 0.001
Triglycerides (mg/dL)	79.0 ± 38.1	77.2 ± 39.9	0.269

HDL-C, serum high-density lipoprotein-cholesterol; LDL-C, serum low-density lipoprotein-cholesterol.
Mean follow-up time = 2.71 years; Number of subjects = 614 male adolescents.
* compared with baseline by paired t-test.

Table 2. Pearson correlation coefficients (*r*) between baseline systolic blood pressure, diastolic blood pressure and other metabolic parameters

Parameter	Systolic blood pressure (mmHg)		Diastolic blood pressure (mmHg)	
	r	p value	*r*	p value
Age (years)	0.261	< 0.001	0.101	0.013
Waist circumference (cm)	0.359	< 0.001	0.244	< 0.001
Body mass index (kg/m^2)	0.389	< 0.001	0.238	< 0.001
Fasting plasma glucose (mg/dL)	0.143	< 0.001	0.024	0.551
HDL-C (mg/dL)	-0.191	< 0.001	-0.046	< 0.259
LDL-C (mg/dL)	0.064	0.114	0.023	0.575
Triglyceride* (mg/dL)	0.202	< 0.001	0.145	< 0.001

HDL-C, serum high-density lipoprotein-cholesterol; LDL-C, serum low-density lipoprotein-cholesterol.
* Data were log-transformed.
Number of subjects = 614 male adolescents.

cantly ($p < 0.001$) with DBP at the baseline (Table 2). The two strongest associations were between BMI and SBP (BMI and SBP, $r = 0.389$, $p < 0.001$), and also between WC and DBPt (WC and DBP, $r = 0.244$, $p < 0.001$). We used multivariate regression analysis to investigate the independent BP (SBP or DBP) contributions and MetS components. Age, WC, high TG, and FPG levels were independently correlated with SBP (Table 3). On the other hand, age, WC, and high TG were independently correlated with DBP (Table 3). Among them, WC had the greatest β value, indicating that it is the strongest independent contributor to both SBP and DBP in male adolescents (Table 3). Boys with higher SBP (Group SBP-3: SBP ≥ 120 mmHg) were found to have a higher risk of developing MetS than those with lower SBP (Group SBP-1: SBP < 110 mmHg) (OR, 31.78, 95% confidence interval = 4.16-243.07, $p < 0.001$). The subjects in group SBP-3 had significantly higher ORs for WC, high TG level, and lower HDL-C level, but not for FPG (Table 4). Boys with higher DBP

Table 3. Multivariate regression analysis between baseline systolic blood pressure, diastolic blood pressure and metabolic components

Parameter	Systolic blood pressure		Diastolic blood pressure	
	β (95% CI)	p value	β (95% CI)	p value
Age (years)	0.224 (1.110-2.251)	< 0.001	0.094 (0.091-0.985)	0.018
Waist circumference (cm)	0.262 (0.218-0.406)	< 0.001	0.216 (0.112-0.248)	< 0.001
Fasting plasma glucose (mg/dL)	0.128 (0.106-0.372)	< 0.001	0.022 (-0.072-0.128)	0.582
Triglyceride* (mg/dL)	0.144 (4.230-14.528)	< 0.001	0.101 (0.863-7.731)	0.014
HDL-C (mg/dL)	-0.018 (-0.089-0.056)	0.661	0.033 (-0.032-0.076)	0.416

CI, confidence interval; HDL-C, serum high-density lipoprotein-cholesterol; SBP, systolic blood pressure.
* Data were log-transformed.
Number of subjects = 614 male adolescents.

Table 4. Prevalence and odds ratios (95% CI) for each component of metabolic syndrome criteria at follow-up of different baseline systolic and diastolic blood pressure groups

		SBP-1	DBP-1	SBP-2	DBP-2	SBP-3	DBP-3
	n	196	212	213	268	205	134
WC	Prevalence (%)	2.8	4.7	6.3	4.9	16.7	16.4
	ORs (95% CI)	1 (Ref)	1 (Ref)	2.33 (0.92-5.90)	1.15 (0.48-2.74)	6.98 (3.06-15.89)†	4.43 (1.91-9.95)#
FPG	Prevalence (%)	24	25.9	26.7	26.9	29.3	24.6
	ORs (95% CI)	1 (Ref)	1 (Ref)	1.15 (0.75-1.77)	1.05 (0.70-1.58)	1.31 (0.84-2.04)	0.933 (0.57-1.54)
HDL-C	Prevalence (%)	10.8	15.1	8.5	8.6	18.0	14.2
	ORs (95% CI)	1 (Ref)	1 (Ref)	0.769 (0.40-1.47)	0.53 (0.30-0.93)‡	1.81 (1.04-3.17)*	0.93 (0.50-1.72)
TG	Prevalence (%)	3.1	2.4	7.4	5.6	8.7	11.2
	ORs (95% CI)	1 (Ref)	1 (Ref)	2.46 (1.03-5.89)*	2.46 (0.88-6.89)	2.93 (1.22-7.03)*	5.22 (1.85-14.72)‡
MetS	Prevalence (%)	0.3	1.4	1.7	2.2	10.0	7.5
	ORs (95% CI)	1 (Ref)	1 (Ref)	4.96 (0.51-48.06)	1.60 (0.39-6.46)	31.778 (4.16-243.07)†	5.618 (1.52-20.81)‡

SBP-1, SBP < 110 mmHg; SBP-2, 110 mmHg ≤ SBP < 120 mmHg; SBP-3, SBP ≥ 120 mmHg; DBP-1, DBP ≤ 55 mmHg; DBP-2, 55 mmHg < DBP ≤ 65 mmHg; DBP-3, DBP > 65 mmHg.
CI, confident interval; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL-C, serum high-density lipoprotein-cholesterol; MetS, metabolic syndrome; OR, odd ratio; SBP, systolic blood pressure; TG, triglycerides; WC, waist circumference.
* $p < 0.05$ vs. SBP-1; † $p < 0.001$ vs. SBP-1; ‡ $p < 0.05$ vs. DBP-1; # $p < 0.001$ vs. DBP-1.
Number of subjects = 614 male adolescents.

(Group DBP-3: DBP > 65 mmHg) were also found to have a higher risk of developing MetS than those with lower DBP (Group DBP-1: DBP ≦ 55 mmHg) (OR, 5.62, 95% confidence interval = 1.52-20.81, p < 0.05) (Table 4). Finally, we used multivariate logistic regression analysis to investigate the independent contributions of each MetS component and MetS. We found SBP, DBP and WC were independently correlated with MetS. Among them, WC was the strongest independent contributor to MetS in male adolescents, followed by SBP and DBP (Tables 5-1 and 5-2).

DISCUSSION

In this retrospective study, we found that SBP is an independent predictor for MetS in male adolescents. A direct relationship between childhood blood pressure and MetS in adulthood was reported in the Fels Longitudinal Study.[8] In this study, we conclusively show that healthy male adolescents with higher SBP at baseline have a higher risk of developing MetS even during follow-up after only 2 years. The highest SBP group (SBP ≧ 120 mmHg) carried a 31.78-fold ORs (p < 0.001) to develop MetS than the lowest SBP group (SBP < 110 mmHg) (Table 4). We also demonstrated that SBP helps to predict several MetS components in male adolescents. One component is an increase in WC, an obesity indicator, which manifests the strongest independent contribution to elevated SBP in male adolescents. Our findings support those findings of a previous report that showed elevated blood pressure in adolescents is associated with obesity.[8,19] Among all the parameters, BMI has the strongest association with baseline SBP in male adolescents. This is consistent with the findings in the REACH registry, which found BMI, rather than waist circumference, is more closely related to metabolic syndrome and its individual components in the Chinese population.[20] In this study, we also provide evidence that DBP has a significant predictive value for MetS.

Our study has the following limitations. First, the study cohort was enrolled from a health checkup center rather than being selected randomly from a community. In other words, this was not a conscientious epidemiological study. Second, the purpose of this study was to investigate the potential value of SBP as a predictor of MetS among male adolescents. During the mean follow-up of 2.7 ± 0.97 years, the number of female subjects with MetS was not adequate to perform further analysis. The difference may result from differences be-

Table 5-1. Multivariate logistic regression analysis of different metabolic syndrome components and systolic blood pressure

Parameter	β (95% CI)	p value	Adjust p value
Waist circumference	5.151 (1.893-14.017)	0.001	0.001
Fasting plasma glucose	0.824 (0.247-2.747)	0.752	0.759
High density lipoprotein cholesterol	1.598 (0.413-6.187)	0.498	0.512
Triglyceride	1.798 (0.444-7.292)	0.411	0.358
Systolic blood pressure	4.559 (1.691-12.29)	0.003	0.003

CI, confidence interval.
* p value was age adjusted.
Number of subjects = 614 male adolescents.

Table 5-2. Multivariate logistic regression analysis of different metabolic syndrome components and diastolic blood pressure

Parameter	β (95% CI)	p value	Adjust p value
Waist circumference	6.879 (2.549-18.560)	< 0.001	< 0.001
Fasting plasma glucose	0.883 (0.266-2.931)	0.839	0.899
High density lipoprotein cholesterol	1.461 (0.382-5.592)	0.579	0.586
Triglyceride	2.240 (0.570-8.807)	0.248	0.236
Diastolic blood pressure	2.077 (1.060-4.069)	0.033	0.047

CI, confidence interval.
Number of subjects = 614 male adolescents.

tween the genders. However, further extended follow-up studies are required. Third, all subjects included in this study were Taiwanese. Therefore, the role of SBP in the MetS may be different in other ethnic groups. Finally, it is unknown whether management of hypertension among male adolescents either with life style modification or with drugs has a prognostic value for CVD in the present study.

CONCLUSION

In conclusion, we have shown that SBP is an independent predictor for MetS in male adolescents. Family history of hypertension and type 2 diabetes, hypertriglyceridemia, hyperinsulinemia, and high CRP level are helpful in pediatric metabolic risk assessment.[21] Our study shows that higher SBP can help predict MetS in male adolescents. Consequently, SBP is a simple parameter that can be used to predict MetS in male adolescents, and should be included in routine metabolic risk assessment.

ACKNOWLEDGEMENTS

The authors would like to sincerely thank MJ Health Screening Centers in Taiwan for providing the records for the present research.

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