Investigating the definitions of metabolic syndrome among urban high-school students in Taipei City in Taiwan and the optimal cutoff points of relevant risk factors

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Research

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Abstract

Background: A comparison of different definitions of metabolic syndrome (MetS) on its prevalence among a sample of urban high-school students in Taipei City in Taiwan was examined. The differences in the discriminatory power and the optimal cutoff points of relevant risk factors were analyzed in this study.

Methods: A total of 45,756 health checkup data sets from 2011 to 2014 of high-school students aged between 15 to 17 years were sourced in Taipei city in Taiwan. The database included the students' gender, age, height, weight, waist circumference (WC), systolic and diastolic blood pressure, as well as biochemical markers such as triglycerides (TG), high-density lipoprotein cholesterol, and fasting glucose (FG) levels. The receiver operating characteristic (ROC) curve statistical approach was used to analyze the discriminatory power and optimal cutoff points of the relevant MetS risk factors.

Results: The prevalence of MetS among adolescents in Taipei City in Taiwan was 2.3% and 1.2%, according to the criteria of the modified National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) and the International Diabetes Federation (IDF) respectively. The prevalence increased to 4.3% when this study's criteria were used. Among the components of MetS analyzed, WC and TG had stronger discriminatory powers, while FG had the weakest. The optimal cutoff point for WC was approximately the 90^{th} percentile, while that for the TG was similar to the criteria of the modified NCEP ATP III. About 44.6% of adolescents had at least one MetS component. Body mass index also had good discriminatory power.

Conclusions: The prevalence of MetS differs depending on the diagnostic criteria used. Redefining the cutoff points for the components of MetS in adolescents in different regions, as well as further screening and intervention, is crucial to prevent cardiovascular disease and type 2 diabetes mellitus in adulthood.

Introduction

Childhood and adolescent overweight and obesity are major concerns in developed countries [1]. According to the 2010-2011 Nutrition and Health Survey in Taiwan (NAHSIT), the prevalence among Taiwanese adolescents aged between 11 and 18 years of overweight and obesity was 12.4% and 16.8%, respectively [2]. With the number of overweight and obese adolescents on the rise, the prevalence of metabolic syndrome (MetS) has also escalated, and has a positive correlation with obesity [3]. From 1988 to 1994, the prevalence of MetS among American adolescents aged 12 to 19 years was 28.7% in overweight subjects (BMI ≥ 95th percentile), which was significantly higher than the prevalence of 6.8% and 0.1% in subjects with a BMI in the 85th to 95th percentile and low-risk subjects (BMI < 85^{th} percentile), respectively [3]. Research has shown that cardiometabolic risk factors identified in childhood and adolescence are associated with subclinical atherosclerosis in adulthood [4]. The presence of MetS during childhood exacerbates the risk of having adulthood MetS, cardiovascular disease (CVD), and type 2 diabetes mellitus (T2DM) [5,6]. Therefore, screening of MetS and obesity during childhood and adolescence, as well as further interventions (especially changes in diet and increase physical activity), are important factors to improve the future health of the adult population [7].

MetS comprises of the risk factors for CVD and T2DM [8]. It represents the association between obesity, insulin resistance, hypertension, dyslipidemia, T2DM, and CVD [9]. In 1988, Reaven first proposed the notion of insulin resistance (IR), and named the cluster of risk factors for CVD and diabetes as "Syndrome X" [10]. In 1998, the World Health Organization (WHO) formally named the syndrome as MetS and defined its criteria [11]. Afterwards, various definitions were proposed, such as that of the European Group for the Study of Insulin Resistance (EGIR) in 1999 [12]; the National Cholesterol Education Program Adult Treatment Panel III(NCEP ATP III) in 2001 [13]; the International

Diabetes Federation (IDF) [14] and the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) [15] in 2005. Early studies suggested IR as the primary cause of MetS [16], but subsequent studies deduced that the interaction between obesity, IR, and inflammation plays a crucial role in the development of MetS [17]. Moreover, MetS is influenced by other metabolic and pathological factors such as inflammatory factors, adipocytokines, cortisol, oxidative stress, vascular factors, inheritance, and lifestyle factors [9]..

The unified criteria for diagnosing MetS in adults have been determined [8] and successfully applied in clinical practice and research [9]. However, due to the growing concern about MetS in children and adolescents, many studies have attempted to define MetS in these groups [9]. At present, as there are no unified diagnostic criteria, the difficulty in defining the condition may be associated with physiological changes during growth, racial differences, lack of CVD cases, and lack of clinical trials[18]. Consequently, the discrepancies in the prevalence of MetS in children and adolescents is remarkably large as there is no unified diagnostic criteria. Many studies have modified the NCEP ATP III's definition of MetS in adults [19], while recent studies commonly adopt the modified NCEP ATP III criteria and the 2007 IDF criteria [20]. Based on the modified NCEP ATP III criteria, the prevalence of MetS in American, Korean, and Chinese adolescents was 8.6% (2001– 2006) [21], 5.7% (2010– 2012) [22], and 3.7% (2008) [23], respectively. It must be noted, however, that cutoff points for abnormal MetS factors had different sources in these three studies. Based on the IDF criteria, the prevalence of MetS in Taiwanese, Korean, and American adolescents was 3% (2010–2011) [24], 2.1% (2010–2012) [22], and 4.24% (2011– 2016) [25], respectively.

This study aimed to examine the performance of selected existing MetS definitions and a new set of criteria of MetS on its prevalence among a sample of urban high-school students in Taipei City in Taiwan. Also, optimal cutoff points of relevant risk factors of MetS components were examined. Findings from this study may serve as a reference to accurately estimate MetS prevalence among Taiwanese adolescence.

Methods

Study population and data collection

This study was approved by the institutional review board of the Taipei City Hospital (TCHIRB-10811003-E). The personal health data of urban high-school students aged between 15 to 17 years who underwent health checkups at a district hospital from 2011 to 2014 was sourced from the hospital's database. There were 50,280 sets of data. After omitting those with missing information, a total of 45,756 sets of data were included in this study.

The database of this study included the subjects' gender, age, height, weight, systolic blood pressure (SBP), diastolic blood pressure (DBP), and waist circumference (WC), as well as biochemical markers such as triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and fasting glucose (FG) levels.

Height and weight were measured using automatic height and weight scale(HW-3050; Kongho Instruments Co.,Ltd., Taipei, Taiwan), and measured height (in cm) and weight(in kg) were rounded to the first decimal place. To measure blood pressure (BP), a subject was told to sit in a relaxed manner, and their BP was measured by placing their left arm into a tunnel-type electronic sphygmomanometer(ES-P2000; TERUMO, Japan). The recorded BP was taken as the mean of two measurements. To measure WC, a measuring tape was kept parallel to the ground and was wrapped around a subject's waist, starting from a point midway between the upper iliac crest margin and the lower rib margin. The recorded WC was taken after the subject had breathed out. A subject's body mass index (BMI) was taken as their weight in kilograms divided by the square of their height in meters. Blood samples were drawn from the antecubital vein for biochemical analysis after at least 8 hours of fasting. Plasma was separated from the blood within 3 hours and then stored in a refrigerator. Blood samples were examined within 24 hours after transfer to the examination

center. Plasma FG, TG and HDL-C levels were analyzed in plasma using an automatic analyzer (cobas c 702; Roche Diagnostics GmbH, Mannheim, Germany).

Definition of MetS

In this study, three definitions for the prevalence of MetS were compared: the modified NCEP ATP III proposed by Ford et al. [26]; the 2007 IDF [20]; and the new criteria based on the cutoff points of this study's receiver operating characteristic (ROC) curves. All of these diagnostic criteria include the five components of WC, TG, HDL-C, BP, and FG. The modified NCEP ATP III served as a baseline for the criteria of this study, in which the optimal cutoff point of each MetS component with an area under the ROC curve (AUC) greater than 0.8 were taken as new components (modified WC, TG, and HDL-C). The components of BP and FG remained unchanged (see Table 1).

Statistics

The statistical approaches used to analyze the discriminatory power and optimal cutoff points of relevant MetS risk factors in this study included descriptive statistics, chi-squared tests, independent sample t-tests, and ROC curves.

Table 1 Comparison of definitions for MetS criteria

	Modified NCEP ATP III	IDF		This study[a]
Diagnostic criteria	Present with three or more of the five components	Present with central obesity and two or more of the four components		Present with three or more of the five components
		< 16 years old	≧ 16 years old	
WC	≧ 90th percentile (adjusted for age and gender)	≧ 90th percentile (adjusted for age and gender)	≧ 90 cm for males; ≧ 80 cm for females	≧ 86.8 cm for males ≧ 76.25 cm for females
TG	≧ 110 mg/dL	≧ 150 mg/dL	≧ 150 mg/dL or currently under drug treatment	≧ 108 mg/dL for males ≧ 104.05 mg/dL for females
HDL-C	< 40 mg/dL	< 40 mg/dL	< 40mg/dL for males and < 50mg/dL for females, or is currently under drug treatment	< 46.5 mg/dL for males < 54.5 mg/dL for females
BP	≧ 90th percentile (adjusted for age, gender, and height)	≧ 130/85 mmHg	≧ 130/85 mmHg or currently under drug treatment	≧ 90th percentile (adjusted for age, gender, and height)
FG	≧ 100 mg/dL	≧ 100 mg/dL or diagnosed with T2DM		≧ 100 mg/dL

BP: blood pressure; FG: fasting glucose; HDL-C: high-density lipoprotein cholesterol; IDF: International Diabetes Federation; MetS: metabolic syndrome; NCEP ATP III: National Cholesterol Education Program, Adult Treatment Panel III; ROC curve: receiver operating characteristic curve; TG: triglycerides; T2DM: type 2 diabetes mellitus; WC: waist circumference.

[a] ROC curve cutoff points were used as new criteria in this study (AUC > 0.8).

Results

The results of this study are shown in Table 2. The male subjects had a mean age of 15.18 ± 0.41 years; a mean height of 170.63 ± 6.14 cm; a mean weight of 63.74 ± 13.54 kg; a mean BMI of 21.81 ± 4.33 kg/m^2; a mean WC of 72.29 ± 10.66 cm; a mean SBP of 117.23 ± 15.18 mmHg; a mean DBP of 61.75 ± 11.23 mmHg; a mean TG level of 72.87 ± 36.20 mg/dL; a mean HDL-C level of 56.66 ± 11.37 mg/dL; and a mean FG level of 84.76 ± 9.55 mg/dL.

The female subjects had a mean age of 15.19 ± 0.41 years; a mean height of 159.28 ± 5.53 cm; a mean weight of 52.60 ± 9.35 kg; a mean BMI of 20.67 ± 3.43 kg/m^2; a mean WC of 67.02 ± 7.80 cm; a mean SBP of 106.13 ± 13.33 mmHg; a mean DBP of 62.82 ± 9.81 mmHg; a mean TG level of 68.89 ± 27.16 mg/dL; a mean HDL-C level of 63.38 ± 12.74 mg/dL; and a mean FG level of 83.73 ± 9.09 mg/dL.

Among metabolic components, WC、SBP、TG and FG were significantly higher, while DBP and HDL-C were significantly lower, in males than in females($p < 0.001$). There are already significant differences in height and weight between boys and girls, and compared with other indicators, we need to pay more attention to BMI. BMI, a reference value of overweight and obesity, was significantly higher in males than in females ($p < 0.001$).

Table 2 Comparison of relevant data and biochemical markers in male and female subjects

Variable	Males (n = 27,168) Mean ± SD	Females (n = 18,588) Mean ± SD	P [a]
Age (years)	15.18	15.19	**
Height (cm)	170.63	159.28	***
Weight (kg)	63.74	52.60	***
BMI(kg/m^2)	21.81	20.67	***
WC (cm)	72.29	67.02	***
SBP (mmHg)	117.23	106.13	***
DBP (mmHg)	61.75	62.82	***
TG (mg/dL)	72.87	68.89	***
HDL-C (mg/dL)	56.66	63.38	***
FG (mg/dL)	84.76	83.73	***

BMI: body mass index; DBP: diastolic blood pressure; FG: fasting glucose; HDL-C: high-density lipoprotein cholesterol; SBP: systolic blood pressure; TG: triglycerides; WC: waist circumference.

[a] Independent sample t-tests used for data analysis; **: $p < 0.01$, *** $p < 0.001$.

The relevant MetS risk factors of high-school students have different discriminatory powers toward the diagnosis of MetS (Fig. 1 and Table 3). Table 3 lists the discriminatory power of each MetS component in descending order according to their AUC values. The top four components with the highest AUC values in the male subjects were WC (AUC = 0.942, sensitivity = 0.89, specificity = 0.917); BMI (AUC = 0.926, sensitivity = 0.9, specificity = 0.85); TG (AUC = 0.924, sensitivity = 0.87, specificity = 0.902); and HDL-C (AUC = 0.825, sensitivity = 0.674, specificity = 0.832). The top four components with the highest AUC values in the female subjects were WC (AUC = 0.937, sensitivity = 0.918, specificity = 0.904); TG (AUC = 0.931, sensitivity = 0.883, specificity = 0.922); BMI (AUC = 0.915, sensitivity = 0.817, specificity = 0.902); and HDL-C (AUC = 0.827, sensitivity = 0.763, specificity = 0.752). Generally speaking, the subjects' WC, BMI, and TG had the highest discriminatory power, sensitivity, and specificity.

For the male subjects, the cutoff points for the main components of MetS were WC, TG, HDL-C, SBP, DBP, and FG was 86.8 cm, 108 mg/dL, 46.5 mg/dL, 128 mmHg, 67.5 mmHg, and 91.5 mg/dL, respectively. For the female subjects, their WC, TG, HDL-C, SBP, DBP, and FG was 76.25 cm, 104.05 mg/dL, 54.5 mg/dL, 117.5 mmHg, 72.5 mmHg, and 93.5 mg/dL, respectively.

Table 3 Optimal cutoff points of the ROC curves of relevant MetS components

	AUC	Youden index	Optimal cutoff point	Sensitivity (%)	Specificity (%)
Males					
WC	0.942	0.81	86.8	0.89	0.917
TG	0.924	0.772	108	0.87	0.902
BMI	0.926	0.75	25.6	0.9	0.85
HDL-C	0.825	0.507	46.5	0.674	0.832
SBP	0.767	0.413	128	0.65	0.763
DBP	0.709	0.338	67.5	0.602	0.736
FG	0.629	0.192	91.5	0.361	0.831
Females					
WC	0.937	0.823	76.25	0.918	0.904
TG	0.931	0.805	104.05	0.883	0.922
BMI	0.915	0.719	24.65	0.817	0.902
HDL-C	0.827	0.515	54.5	0.763	0.752
SBP	0.791	0.483	117.5	0.665	0.818
DBP	0.786	0.478	72.5	0.615	0.863
FG	0.64	0.266	93.5	0.346	0.919

BMI: body mass index; DBP: diastolic blood pressure; FG: fasting glucose; HDL-C: high-density lipoprotein cholesterol; MetS: metabolic syndrome; SBP: systolic blood pressure; TG: triglycerides; WC: waist circumference.

The prevalence of MetS among urban high-school students in Taipei City in Taiwan was 2.3%, 1.2%, and 4.3% according to the criteria of the modified NCEP ATP III, the IDF, and this study, respectively (Table 4). Using the modified ATP III criteria, the prevalence of each MetS component was, in decreasing order, 18.6% for BP; 10.6% for WC; 9.7% for TG; 4.2% for HDL-C; and 2.9% for FG; 34.4% of the students had at least one component. Using the IDF criteria, the prevalence of each MetS component was, in decreasing order, 15.7% for BP; 10.1% for WC; 5.1% for HDL-C; 2.9% for FG; and 2.9% for TG; 28.3% of adolescents had at least one component. Applying the criteria developed in this study, the prevalence of each MetS component was, in decreasing order, 21.2% for HDL-C; 18.6% for BP; 10.8% for TG; 10.7% for WC; and 2.9% for FG; 44.6% of adolescents had at least one component. For all three of the diagnostic criteria (modified NCEP ATP III, the IDF, and this study), except WC, the differences in the prevalence of MetS and the MetS components (TG, HDL-C, BP, and FG) between male and female subjects were all statistically significant ($p < 0.001$).

Table 4 Comparison of the prevalence of MetS and its components

	Total			Modified NCEP ATP III			IDF			This study		
	Modified NCEP ATP III	IDF	This study	Males	Females	P[a]	Males	Females	P[a]	Males	Females	P[a]
MetS (%)	2.3	1.2	4.3	3	1.4	<0.001	1.8	0.5	<0.001	4.6	3.8	<0.001
MetS components												
Central obesity (elevated WC) (%)	10.6	10.1	10.7	10.8	10.4	0.222	10.3	9.8	0.089	10.8	10.7	0.833
High TG (%)	9.7	2.9	10.8	11.4	7.3	<0.001	3.7	1.6	<0.001	12.1	8.9	<0.001
Low HDL-C (%)	4.2	5.1	21.2	5.8	2	<0.001	5.8	4.2	<0.001	18.3	25.5	<0.001
Elevated BP (%)	18.6	15.7	18.6	19.3	17.7	<0.001	22.3	6.1	<0.001	19.3	17.7	<0.001
Elevated FG (%)	2.9	2.9	2.9	3.4	2.3	<0.001	3.4	2.3	<0.001	3.4	2.3	<0.001
Numbers of MetS components												
1	25.4	22.1	30.2	26	24.4	<0.001	26.2	16.5	<0.001	29	32.1	<0.001
2	6.6	5	10.1	7.5	5.4		6.6	3		9.9	10.3	
3	1.9	1	3.3	2.5	1.1		1.6	0.4		3.5	2.9	
4	0.4	0.2	0.9	0.5	0.3		0.3	0.1		1	0.8	
5	0	0	0.1	0	0		0	0		0.1	0.1	

BMI: body mass index; BP: blood pressure; FG: fasting glucose; HDL-C: high-density lipoprotein cholesterol; IDF: International Diabetes Federation; MetS: metabolic syndrome; NCEP ATP III: National Cholesterol Education Program, Adult Treatment Panel III; TG: triglycerides; WC: waist circumference.

[a] Data analyzed by chi-squared tests.

Discussion

MetS in adolescents and the prevalence of its components

At present, there are no unified criteria for diagnosing MetS in adolescents, which makes it difficult to compare between studies in the literature. The prevalence of MetS differs across studies, which could be associated with differences in diagnostic criteria, age (especially IR in adolescents), gender, regions, and races [7]. In this study, the prevalence of MetS as measured using the modified NCEP ATP III and IDF criteria was 2.3% and 1.2% respectively, and increase to 4.3% by using this study's criteria. Low prevalence of MetS was also found among adolescents(mainly in urban area) in southern Brazil(1.9% to 5.0% by using different criteria) and in many studies(1.6% to 6.3% by using the IDF criteria) [27].

Differences in the percentage of abnormal measures of MetS components are a result of different diagnostic criteria. According to this study's criteria, 10.7% of high-school students had a slightly large WC, 10.8% had high TG, and 21.2% had low HDL-C. The study population had a higher percentage of individuals with abnormal measures for these three components than for the other two components (elevated BP and elevated FG).

The criteria developed in this study identified a significantly higher percentage of subjects with low HDL-C (21.2%), compared to that seen using the modified NCEP ATP III (4.2%) and the IDF (5.1%). A possible explanation could be that a unified criterion (< 40 mg/dL) was used in the modified NCEP ATP III (in which subjects were 12 to 19 years old) and the IDF (in which subjects were below 16 years old), which gender differences were not adjusted for in the cutoff values, which resulted in a low prevalence among females. This has also been observed in another study [24].

Differences were observed between the results from the modified NCEP ATP III and IDF in the percentage of individuals with abnormal measures for TG (9.7% vs. 2.9%) and BP (18.6% vs. 15.7%). This may be because the modified NCEP ATP III criteria define elevated BP as ≧ 90^{th} percentile after adjusting for age, gender, and height, while high TG are defined as ≧ 110 mg/dL after adjusting for age [3], whereas the IDF criteria define elevated BP in adults as ≧ 130/85 mmHg and high TG as ≧ 150mg/dL.

Compared with the modified NCEP ATP III criteria adjusted by Ford et al.[26], the percentage of subjects identified as having a large WC in this study(10.6%) was similar to that in a Korean population (9.7%) [22], but lower than that in an American population (19.1%) [21]; the percentage of subjects with elevated BP in this study(18.6%) was also similar to that in a Korean population (20.4%), but higher than that in an American population (6.9%). These differences could due to differences in the populations, which indicates the importance of establishing a large database on the WC and BP of people in different regions. The percentage of subjects with high TG in this study(9.7%) was lower than that in studies conducted in Korea (21.2%) and the USA (25.6%); the percentage of subjects with low HDL-C in this study(4.2%) was lower than that in Korea (11.6%) and the USA (19.3%); and the percentage of subjects with elevated FG was 2.9%, which is significantly lower than that in the USA (14%) and Korea (11.4%) [21,22]. The components of MetS in adolescents must be adjusted for racial and regional differences. This highlights the importance of the results of this study.

Moreover, according to the criteria of the modified NCEP ATP III, the IDF, and this study, about 34.4%, 28.3%, and 44.6% of adolescents, respectively, had at least one MetS component. The fewer of these components that are present during childhood, the lower the cardiovascular risk in the future [28]. Some researchers [29] have emphasized that the effects of metabolic risk factor clustering are more important than diagnosing MetS in children. Based on these

arguments, it is not only crucial to detect MetS in adolescents, but those present with MetS components despite not yet reaching the diagnostic criteria should receive attention as well, to provide prompt intervention and prevention [7,28].

Gender difference among prevalences of MetS and MetS components abnormalities

The prevalence of MetS was significantly higher in males than females in our study with the modified NCEP ATP III, IDF and our study's criteria separately(see Table 4, $P < 0.001$). However, previous studies showed inconclusive results. In USA adolescents, one study showed the same result in different criteria(males vs females - Cook et al.: 5.09% vs 2.17%, $P = 0.04$; de Ferranti et al.: 11.4% vs 8.63%, $P = 0.19$; IDF: 6.04% vs 2.28%, $P < 0.01$)[7], but another study showed the prevalence of MetS differed in different races (males vs females - Hispanic: 12.9% vs 9.4%; White: 11.8% vs 5.8%; Black: 3.9% vs 4.2%, all within 95% CI)[21]. In Chinese adolescents, the prevalence of MetS differed in different region (males vs females - in urban: 5.8% vs 3.5%; in rural: 2.9% vs 3.7%) [23]. In Korean adolescents, there was no statistically significant between gender [22].

Among all the MetS components, in our study, the prevalence of elevated BP, high TG, low HDL-C and elevated FG were significantly higher in males than females, while the prevalence of central abesity showed no statistically difference between gender when applying the modified NCEP ATP III and IDF criteria separately. Similar results were noted when applying our study's criteria except the prevalence of low HDL-C, which was higher in females(25.5%) than in males(18.3%), and increased significantly in both gender comparing with the modified NCEP ATP III and the IDF criteria(see Table 4). However, previous studies showed inconclusive results. In USA adolescents, the prevalence of high TG, low HDL-C and elevated FG were higher, while central obesity and elevated BP were lower, in males than in females(all within 95% CI)[21]. In Korean adolescents, there were no statistically significant between gender among MetS components in the modified NCEP ATP III criteria, and similar results were noted in the IDF criteria except for the prevalence of elevated BP, which was significantly higher in males than in females(males 3.4%, females 1.2%, $P < 0.001$)[22]. Furthermore, according to the IDF criteria, the prevalence of elevated BP was significantly higher in males (22.3%) than females (6.1%), which showed only mild difference according to the modified NCEP ATP III criteria(male: 19.3%, female: 17.7%) This could be because the IDF criteria use fixed values($\geq$ 130 mmHg for SBP and/or $\geq$ 85 mmHg for DBP) to define elevated BP, instead of $\geq 90^{th}$ percentile by modified NCEP ATP III and our study(adjusted for age, gender, and height).

As stated above, the prevalence of MetS and MetS components abnormalities could differ due to the differences in race, region and diagnostic criteria.

The predictive power of MetS components

According to the results of this study, WC has the highest predictive power, sensitivity, and specificity, regardless of gender. This is in agreement with other studies which have suggested that WC is a good indicator for predicting MetS during adolescence [25,29,30] and adulthood [32]. A study on American adolescents between 12 and 19 years of age revealed that abdominal obesity was closely associated with MetS and other MetS components [25]. Another study on 15-year old Greek teenagers showed that a WC at the 75th percentile or higher is closely related to the phenotypes of MetS [30]; while a study on Chinese adolescents between 11 and 16 years old indicated that WC has the best predictive power toward MetS [31].

To determine the optimal cutoff point for WC, Cook et al. (2003) [3] took into account the differences between adolescents and adults, and defined abdominal obesity as at the 90^{th} percentile or higher; in 2004, de Ferranti et al.[33] adopted a value at the 75^{th} percentile or higher as their standard; afterward, in 2007, the IDF study (in which subjects

were below 16 years of age) [20] and numerous studies [21,22,26] adopted a WC at the 90th percentile or higher as their standards. A Chinese study on children and adolescents between 7 and 18 years of age found that a WC at the 75th percentile and the 90th percentile was the optimal cutoff point for predicting the risk of cardiovascular risk [34]. The optimal cutoff point for WC specified in this study was 86.8 cm for males and 76.25 cm for females, which was around the 90th percentile and similar to that of the previous studies.

In this study, TG level also had adequate predictive power, with an optimal cutoff point of 108 mg/dL for males and 104.05 mg/dL for females, similar to that of the modified NCEP ATP III criteria (< 110 mg/dL).

SBP, DBP, and FG had weaker predictive powers. In particular, FG had the weakest predictive power, which was also observed in other studies with adolescents [31] and adult [32] subjects.

In this study, the cutoff points for MetS components were redefined based on the results of urban high-school students in Taipei City in Taiwan. This indicates that it is necessary to take into account regional differences when determining definition criteria.

The predictive power of BMI

Based on the results of this study, BMI also had good predictive power on MetS in adolescents, after that of WC and TG. The optimal cutoff point for males was between the 80th to 85th percentile (25.6 kg/m^2) for males and approximately the 90th percentile (24.65 kg/m^2) for females.

The WC and BMI of adolescents are good predictive indicators of cardiovascular risk factors [35]. A longitudinal study highlighted the close association between BMI and many other cardiometabolic risk factors, while changes in WC mainly have a stronger correlation with FG [36]. A study on children and adolescents between 8 and 19 years of age [37] revealed that a high BMI has strong predictive power for cardiometabolic risk factors. In addition, the sensitivity of BMI is higher among obese adolescents while its specificity is higher among overweight adolescents [38].

The definitions of overweight and obesity are currently based on a person's BMI, and their criteria differ for adolescents [37–39]. In 2007, the WHO defined overweight as having a BMI between the 85th and 95th percentiles, while obesity is defined as having a BMI greater than the 95th percentile [38]; in 2012, the International Obesity Task Force (IOTF) deduced the cutoff points for BMI in adolescents and adults after mathematical adjustments based on the definition of overweight and obesity in adults I [38,39]. One study [41] used the three aforementioned criteria (WHO; Conde and Monteiro; IOTF) to analyze Brazilian adolescents between 12 and 20 years old; it revealed that the IOTF criteria had the best predictive power for MetS (AUC = 0.75–0.89), with a sensitivity ranging from 59.4% to 84.2% and a specificity ranging from 88.2% to 93.6. In contrast, according to this study's adjusted definition of MetS, BMI had a better predictive power (AUC = 0.915–0.926) and sensitivity (0.817–0.9) for the high-school students. The differences between these results and those of the aforementioned studies could be due to the differences in the diagnostic criteria, age, region, and race in adolescents [7].

Future aspect of establishing suitable criteria of MetS for adolescents in different region

First, we already know the difference of prevalence of MetS and MetS components abnormality in adolescents among different races and regions in previous studies [7,27]. In this study, urban high-school students in Taipei City in Taiwan, which are all Asians, were included for the purpose to specify race and region.

Second, there are many version of criteria published for metabolic syndrome in adolescents. However, Reuter et al. found low agreement between different criteria, and emphasized the importance to create specific cutoff points of

MetS components for adolescents in their region [27]. In this study, despite using current main criteria (modified NCEP ATP III, IDF), we establish new criteria for urban adolescents in Taipei City in Taiwan for comparison.

Third, previous studies have showed that presence of MetS in childhood increase the risk of CVD and T2DM in adulthood [5,6], there is still no exact MetS criteria for adolescents, which has proven to predict CVD and T2DM in adults. Therefore, the new criteria in this study is not only used to compare the differences between other current main MetS criteria for adolescents, but also can be used in future cohort study, to analyze which MetS criteria for adolescents can better predict CVD and T2DM in adulthood.

Limitations

The cross-sectional research design of this study hindered observations of the causal relationships in the data. Moreover, the subjects were adolescents from Taipei City, an urban region of northern Taiwan, which limited the extrapolation of results to adolescents in rural locations as well as those with special circumstances. However, the results of this study are still valuable and can serve as a reference to define MetS in urban adolescents in Taipei City in Taiwan. First, the sample size in this study is large enough, which can serve as the representatives for urban Taipei adolescents in Taiwan, which are all Asians. Seconds, this study analyzed the differences in the discriminatory power of relevant risk factors as well as their optimal cutoff points, which could provide markers for early interventions in the future. Subsequent research could include the potential confounders of MetS, such as the influence of puberty and temporary IR during adolescence [7]; as well as taking into account more biochemical markers, and participating in cross-regional and cross-cultural cohort studies. A combination of these approaches would make the understanding of MetS in Taiwanese adolescents more comprehensive.

Conclusion

The prevalence of MetS in adolescents differs when measured using different criteria. In comparison to the results with the criteria of the modified NCEP ATP III and the IDF, the criteria defined in this study found that the prevalence of MetS among urban adolescents in Taipei City in Taiwan was higher (4.3%). Of the MetS components, WC and TG had the strongest discriminatory power, sensitivity, and specificity, while FG had the weakest discriminatory power. The optimal cutoff point for WC was approximately at the 90^{th} percentile; while the optimal cutoff point for TG was similar to the criteria of the modified NCEP ATP III. Moreover, about 44.6% of adolescents had at least one MetS component. The early detection of relevant risk factors during adolescence is a crucial issue as it provides vital information for prevention and intervention, to reducing the risk of CVD and T2DM in adulthood. For accurate detection, it is necessary to redefine the cutoff points for MetS components specific to adolescents in different regions, to establish suitable criteria for adolescents in Taiwan as a whole.

Abbreviations

AHA/NHLBI: American Heart Association/National Heart, Lung, and Blood Institute; AUC: area under the ROC curve; CVD: cardiovascular disease; BP: blood pressure; DBP: diastolic blood pressure; EGIR: European Group for the Study of Insulin Resistance; FG: fasting glucose; HDL-C: high-density lipoprotein cholesterol; IDF: International Diabetes Federation; IR: insulin resistance; MetS: metabolic syndrome; NAHSIT: Nutrition and Health Survey in Taiwan; NCEP ATP III: National Cholesterol Education Program, Adult Treatment Panel III; ROC curve: receiver operating characteristic curve; SBP: systolic blood pressure; TG: triglycerides; T2DM: type 2 diabetes mellitus; WC: waist circumference; WHO: World Health Organization .

Declarations

Ethics approval and consent to participate

The study was conducted with the approval of the Taipei City Institutional Review Board (TCHIRB-10811003-E).

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Competing interests

All the authors declared no competing interests.

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Authors' contributions

SCCL and MJC participated in study design, data analysis and interpretation. SCCL wrote the manuscript. MJC reviewed the manuscript. All authors read and approved the final manuscript.

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References

1. Wang Y, Lobstein T. Worldwide trends in childhood overweight and obesity. Int J Pediatr Obes. 2006;1(1):11–25.
2. Chen CM, Lou MF, Gau BS. Parental Body Mass Index Is Associated With Adolescent Obesity in Taiwan. Res Nurs Heal. 2016;39(6):399–405.
3. Cook S, Weitzman M, Auinger P, Nguyen M, Dietz WH. Prevalence of a Metabolic Syndrome Phenotype in Adolescents: findings from the third National Health and Nutrition Examination Survey, 1988–1994. Arch Pediatr Adolesc Med. 2003;157:821–7.
4. Juonala M, Järvisalo MJ, Mäki-Torkko N, Kähönen M, Viikari JSA, Raitakari OT. Risk factors identified in childhood and decreased carotid artery elasticity in adulthood: The cardiovascular risk in young finns study. Circulation. 2005;112(10):1486–93.
5. Morrison JA, Friedman LA, Gray-McGuire C. Metabolic syndrome in childhood predicts adult cardiovascular disease 25 years later: The Princeton lipid research clinics follow-up study. Pediatrics. 2007;120(2):340–5.

6. Morrison JA, Friedman LA, Wang P, Glueck CJ. Metabolic Syndrome in Childhood Predicts Adult Metabolic Syndrome and Type 2 Diabetes Mellitus 25 to 30 Years Later. J Pediatr. 2008;152(2):201–6.
7. Deboer MD. Assessing and managing the metabolic syndrome in children and adolescents. Nutrients. 2019;11(8):1788.
8. Alberti KGMM, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: A joint interim statement of the international diabetes federation task force on epidemiology and prevention; National heart, lung, and blood institute; American heart association; World heart federation; International. Circulation. 2009;120(16):1640–5.
9. Steinberger J, Daniels SR, Eckel RH, Hayman L, Lustig RH, McCrindle B, et al. Progress and challenges in metabolic syndrome in children and adolescents. A Scientific Statement from the American Heart Association Atherosclerosis, Hypertension, and Obesity in the Young Committee of the Council on Cardiovascular Disease in the Young; Circulation. 2009;119(4):628–47.
10. Reaven GM. Role of insulin resistance in human disease. Diabetes. 1988;37(12):1595–607.
11. Alberti KGMM, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus. Provisional report of a WHO consultation. Diabet Med. 1998;15(7):539–53.
12. Balkau B, Charles MA. Comment on the provisional report from the WHO consultation. Diabet Med. 1999;16(5):442–3.
13. Expert Panel on Detection E and T of HBC in A. Executive Summary of the Third Report (NCEP) -Adult Treatment Panel III. J Am Med Assoc. 2001;285(19):2486–97.
14. Alberti KGMM, Zimmet P, Shaw J. The metabolic syndrome - A new worldwide definition. Lancet. 2005;366(9491):1059–62.
15. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and management of the metabolic syndrome: An American Heart Association/National Heart, Lung, and Blood Institute scientific statement. Circulation. 2005;112(17):2735–52.
16. Reaven GM. Insulin Resistance: The Link Between Obesity and Cardiovascular Disease. Med Clin North Am [Internet]. 2011;95(5):875–92.
17. Wittcopp C, Conroy R. Metabolic syndrome in children and adolescents. Pediatr Rev. 2016;37(5):193–202.
18. Pérez EA, Olivares VM, Martínez-Espinosa RM, Vila MDM, García-Galbis MR. New insights about how to make an intervention in children and adolescents with metabolic syndrome: Diet, exercise vs. changes in body composition. A systematic review of RCT. Nutrients. 2018;10(7):878.
19. Ford ES, Li C. Defining the Metabolic Syndrome in Children and Adolescents: Will the Real Definition Please Stand Up? J Pediatr. 2008;152(2):160–4.
20. Zimmet P, Alberti KGM, Kaufman F, Tajima N, Silink M, Arslanian S, et al. The metabolic syndrome in children and adolescents - an IDF consensus report. Pediatr Diabetes. 2007;8:299–306.
21. Johnson WD, Kroon JJM, Greenway FL, Bouchard C, Ryan D, Katzmarzyk PT. Prevalence of Risk Factors for Metabolic Syndrome in Adolescents. Arch Pediatr Adolesc Med. 2009;163(4):371–7.
22. Kim S, So WY. Prevalence of metabolic syndrome among Korean adolescents according to the national cholesterol education program, adult treatment panel III and international diabetes federation. Nutrients. 2016;8(10):588.
23. Li Y, Yang X, Zhai F, Kok FJ, Zhao W, Piao J, et al. Prevalence of the metabolic syndrome in Chinese adolescents. Br J Nutr. 2008;99(3):565–70.

24. Lin WT, Lee CY, Tsai S, Huang HL, Wu PW, Chin YT, et al. Clustering of metabolic risk components and associated lifestyle factors: A nationwide adolescent study in Taiwan. Nutrients. 2019;11(3).
25. Gaston SA, Tulve NS, Ferguson TF. Abdominal obesity, metabolic dysfunction, and metabolic syndrome in U.S. adolescents: National Health and Nutrition Examination Survey 2011–2016. Ann Epidemiol [Internet]. 2019;30:30–6.
26. Ford ES, Li C, Cook S, Choi HK. Serum concentrations of uric acid and the metabolic syndrome among US children and adolescents. Circulation. 2007;115(19):2526–32.
27. Reuter CP, Burgos MS, Barbian CD, Renner JDP, Franke SIR, deMello ED. Comparison between different criteria for metabolic syndrome in schoolchildren from southern Brazil. Eur J Pediatr. 2018;177:1471-1477.
28. Chen W, Srinivasan SR, Li S, Xu J, Berenson GS. Metabolic Syndrome Variables at Low Levels in Childhood Are Beneficially Associated With Adulthood Cardiovascular Risk. Diabetes Care. 2005;28(April 2004):138–43.
29. Magge SN, Goodman E, Armstrong SC, Daniels S, Corkins M, De Ferranti S, et al. The metabolic syndrome in children and adolescents: Shifting the focus to cardiometabolic risk factor clustering. Pediatrics. 2017;140(2):e20171603.
30. Bitsori M, Linardakis M, Tabakaki M, Kafatos A. Waist circumference as a screening tool for the identification of adolescents with the metabolic syndrome phenotype. Int J Pediatr Obes. 2009;4(4):325–31.
31. Wang ZN, Li P, Jiang RH, Li L, Li X, Li L, et al. The association between serum uric acid and metabolic syndrome among adolescents in northeast China. Int J Clin Exp Med. 2015;8(11):21122–9.
32. Chedid R, Gannagé-Yared MH, Khalifé S, Halaby G, Zoghbi F. Impact of different metabolic syndrome classifications on the metabolic syndrome prevalence in a young Middle Eastern population. Metabolism [Internet]. 2009;58(6):746–52.
33. De Ferranti SD, Gauvreau K, Ludwig DS, Neufeld EJ, Newburger JW, Rifai N. Prevalence of the metabolic syndrome in American adolescents: Findings from the Third National Health and Nutrition Examination Survey. Circulation. 2004;110(16):2494–7.
34. Ma GS, Ji CYE, Ma J, Mi J, Sung RYT, Xiong F, et al. Waist circumference reference values for screening cardiovascular risk factors in chinese children and adolescents. Biomed Environ Sci. 2010;23(1):21–31.
35. Messiah SE, Arheart KL, Lipshultz SE, Miller TL. Body Mass Index, Waist Circumference, and Cardiovascular Risk Factors in Adolescents. J Pediatr. 2008;153(6):6–12.
36. Jago R, Mendoza JA, Chen T, Baranowski T. Longitudinal associations between BMI, waist circumference, and cardiometabolic risk in US youth: Monitoring implications. Obesity. 2013;21(3):271–9.
37. Sardinha LB, Santos DA, Silva AM, Grøntved A, Andersen LB, Ekelund U. A comparison between BMI, waist circumference, and waist-to-height ratio for identifying cardio-metabolic risk in children and adolescents. PLoS One [Internet]. 2016;11(2):e0149351.
38. Onis M de, Onyango AW, Borghi E, Siyam A, Nishida C, Siekmann J. Development of a WHO growth reference for school-aged children and adolescents. Bull World Health Organ. 2007;85(9):660–7.
39. Cole TJ, Lobstein T. Extended international (IOTF) body mass index cut-offs for thinness, overweight and obesity. Pediatr Obes. 2012;7(4):284–94.
40. Conde WL, Monteiro CA. Body mass index cutoff points for evaluation of nutritional status in Brazilian children and adolescents. J Pediatr (Rio J). 2006;82(4):266–72.
41. Oliveira RG de, Guedes DP. Performance of different diagnostic criteria of overweight and obesity as predictors of metabolic syndrome in adolescents. J Pediatr (Rio J). 2017;93(5):525–31.

Figures

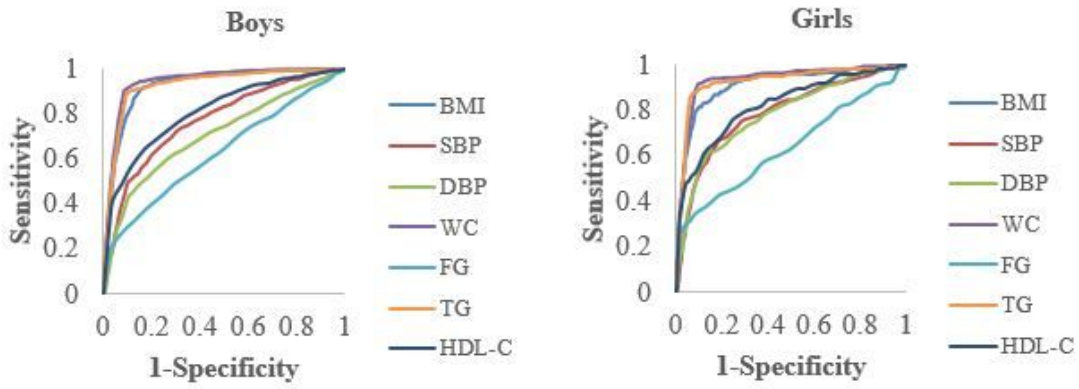

Figure 1

ROC curves of relevant MetS risk factors for boys (left) and girls (right).