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RESEARCH ARTICLE

Importance of Both Fatness and Aerobic Fitness on Metabolic Syndrome Risk in Japanese Children

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Abstract

Associations between body mass index (BMI), peak oxygen consumption (VO_{2peak}), and metabolic syndrome (MetS) risk factors have not been adequately studied in Japanese children. Here the relationships between these parameters and the threshold aerobic fitness level necessary for low MetS risk were determined. The participants (299 children; 140 boys and 159 girls, aged 9.1 ± 0.3 years) were divided into four groups using the medians of predicted VO_{2peak} ($_{p}VO_{2peak}$) and BMI. MetS risk scores were calculated using z-scores. Receiver Operating Characteristic analysis was used to determine the threshold aerobic fitness level necessary for low MetS risk. The MetS risk score of the High BMI group was significantly higher than that of the Low BMI group for both sexes (p < 0.0001). However, the High BMI/High Fitness group had a significantly lower MetS risk score than the High BMI/ Low Fitness group for both sexes. The $_{p}VO_{2peak}$ cut-off values for low MetS risk were 47.9 and 44.9 ml/kg/min for boys and girls, respectively. Our results suggest that improvements in both fatness and aerobic fitness are important for decreasing MetS risk. We also confirmed the $_{p}VO_{2peak}$ of cut-off values necessary for low MetS risk in Japanese children.

Introduction

Metabolic syndrome (MetS) causes serious health issues in adults, including type 2 diabetes and cardiovascular disease [1-3]. According to the Third National Health and Nutrition Examination (NHANES III) and the NHANES 1999–2006 survey, the age-adjusted prevalence of MetS increased from 29.2% (1988–1994) to 34.2% (1999–2006) in U.S. adults [4]. In contrast, the prevalence of MetS among Japanese males and females from 2005 survey had been reported to be 19% and 7%, respectively [5].

The components of MetS, such as obesity, hyperglycemia, dyslipidemia, hypertension, and insulin resistance, in children and adolescents are similar to those in adults [6]. Although MetS occurs less often in children than in adults, several previous studies have established the prevalence of MetS (approximately 3.0%-4.0%) among children and adolescents [7–9]. These phenomena have also been reported in Japanese children [10–12].

MetS is associated with aerobic fitness and/or obesity in children [13,14]. The prevalence of MetS in overweight Hispanic children, for example, has been reported to be 30% [13]. The prevalence of MetS among overweight and obese Japanese children has been shown to be 8.7% and 17.7%, respectively [14]. Moreover, several studies have shown that higher aerobic fitness decreases MetS risk [15–19].

However, very few studies have demonstrated that MetS risk is associated with both fatness and aerobic fitness [20-23]. These studies have reported differences in MetS risk among four fatness and aerobic fitness groups in American, Australian, and Canadian children and adolescents [20-23]. Eisenmann et al. [20] showed that MetS risk was significantly lower in the high fitness and high fatness than in the low fitness and high fatness group in both boys and girls. However, a similar tendency was not consistently observed in other studies [21-23]. Thus, the MetS risk of children displaying high aerobic fitness with high fatness remains unclear.

Furthermore, the aerobic fitness level necessary for a low MetS risk needs to be studied. The aerobic fitness levels necessary for low MetS risk have been published for American, European, and Canadian children [16,24,25]. These studies determined the aerobic fitness threshold from aerobic fitness and MetS risk data using a receiver operating characteristic (ROC) analysis. Ruiz et al. [16] determined the aerobic fitness threshold (42.1 mL/kg/min and 37.0 mL/kg/min for 9–10 years old boys and girls, respectively) associated with low MetS risk using European (Estonia and Sweden) data. Adegboye et al. [24] (43.6 mL/kg/min and 37.4 mL/kg/min for 8–11 years old boys and girls, respectively) and Boddy et al. [25] (46.6 mL/kg/min and 41.9 mL/kg/min for 9–10.9 years old boys and girls, respectively) also determined the aerobic fitness thresholds associated with low MetS risk using European (Denmark, Estonia, Portugal, Norway, and U.K.) data. Although the 20-m shuttle run test level was relatively higher among Japanese children than among the children from 37 countries worldwide [26], the aerobic fitness level necessary for low MetS risk has not been determined for Japanese children.

The purposes of this study were to determine: 1) the differences in MetS risk among Japanese children categorized into four groups by fatness and aerobic fitness; and 2) the aerobic fitness level necessary to achieve a low MetS risk. We hypothesized that: 1) the risk of MetS is highest in Japanese children with low $_{\rm p}VO_{\rm 2peak}$ and high BMI; and 2) The $_{\rm p}VO_{\rm 2peak}$ level necessary for Japanese children to achieve a low MetS risk is higher than those observed in previous studies.

Materials and Methods

Participants

This cross-sectional, school-based study included 299 elementary school children. This group included 140 boys and 159 girls from 13 elementary schools in Japan. Data were collected from on 2008 in Ibara city, Okayama prefecture, Japan. The procedure conformed to the principles of the Declaration of Helsinki and was approved by the Institutional Review Board of the Okayama University. All participating children and their parents provided a written informed consent before participation.

Instruments and Procedure

Anthropometric characteristics. Height and weight were measured in light clothing without shoes. Body mass index (BMI) was calculated using the ratio of weight (kg) to height (m^2) . Waist circumference (WC) was measured with a metal anthropometric tape midway between the lower rib margin and iliac crest. The WC to height ratio was calculated and reported as waist/height (W/H).

Aerobic fitness. Aerobic fitness was defined as the predicted peak oxygen consumption $({}_{p}VO_{2peak})$ from a 20-m shuttle run test [27]. ${}_{p}VO_{2peak}$ was calculated using the method reported in a previous study [28].

Blood pressure. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured from the right arm using an automatic oscillometric method. SBP and DBP were taken from children in a seated, relaxed position after at least 10 min rest. Measurements were conducted between 9:30 and 12:00 h.

Blood samples. Plasma triglycerides (TG) and high-density lipoprotein cholesterol (HDLc) levels were measured in a nonfasted state, between 9:30 and 12:00, when children were in elementary school using the Wako L-Type method (Wako Chemical, Japan).

Data Analysis

Participant characteristics and MetS scores are reported as the mean \pm S.D. MetS risk scores were calculated from the sums of sex-standardized values (z-scores) of the following six parameters: WC, W/H, TG, HDL-c, SBP, and DBP. A lower score indicates a lower MetS risk. Participants were divided into four groups using a median split of $_{\rm p}VO_{\rm 2peak}$ and BMI; Low BMI/High Fitness (LB/HF), Low BMI/Low Fitness (LB/LH), High BMI/High Fitness (HB/HF), and High BMI/Low Fitness (HB/LF) groups. The association between the obtained variables was analyzed using the Pearson's correlation coefficient. One-way analysis of variance (ANOVA) was used to compare the MetS risk factors between the LB/HF, LB/LH, HB/HF, and HB/LF groups. Post-hoc analysis was performed using the Games–Howell test. Receiver Operating Characteristic (ROC) analysis was used to identify the threshold of aerobic fitness necessary to achieve a low MetS risk. A risk score in the bottom 75th percentile was considered to indicate a low MetS risk. All analyses were performed using the SPSS Statistics software, version 20.0 (IBM, Armonk, NY). The level of significance was set to $\alpha = 0.05$.

Results

Participants Characteristics

The descriptive characteristics of the study participants were 140 boys and 159 girls. Descriptive characteristics among two groups, or four groups, are shown in Tables $\underline{1}$ and $\underline{2}$, respectively (<u>S1 Dataset</u>).

Associations between aerobic fitness/BMI and each risk factor

Pearson's correlation analysis revealed that BMI was associated with WC (r = 0.933, P < 0.0001), W/H (r = 0.909, p < 0.0001), TG (r = 0.383, p < 0.0001), HDL-c (r = -0.430, p < 0.0001), and SBP (r = 0.372, p < 0.0001) in boys. In girls, BMI was also associated with WC (r = 0.871, p < 0.0001), W/H (r = 0.860, p < 0.0001), TG (r = 0.277, p < 0.0001), HDL-c (r = -0.266, p = 0.0007), and SBP (r = 0.165, p = 0.0381). Also, we confirmed similar results in the High BMI group but the Low BMI group was only associated with WC and W/H in boys and with WC, W/H and SBP in girls. Aerobic fitness in boys was associated with WC (r = -0.784, p < 0.0001), W/H (r = -0.771, p < 0.0001), TG (r = -0.318, p < 0.0001), SBP (r = -0.288, p = 0.0006), and HDL-c (r = 0.421, p < 0.0001). Aerobic fitness in girls was also associated with WC (r = -0.652, p < 0.0001), W/H (r = -0.709, p < 0.0001), TG (r = -0.377, p < 0.0001), and HDL-c (r = 0.322, P < 0.0001). However, both aerobic fitness and BMI were not associated with DBP in boys or girls. In addition, aerobic fitness was not associated with SBP in girls.

Table 1. Participants characteristics and MetS risk factors by BMI categories.

		B	oys	Girls			
		Low BMI	High BMI	Low BMI	High BMI		
		n = 70	n = 70	n = 80	n = 79		
Age	(years)	9.2	9.1	9.1	9.1		
		(0.4)	(0.3)	(0.3)	(0.3)		
Height	(cm)	133.2	138.0	135.2	136.9		
		(4.9)	(5.9)	(5.4)	(5.4)		
Weight	(kg)	27.0	37.5	27.6	34.5		
		(2.7)	(8.6)	(2.8)	(5.2)		
BMI	(kg/m ²)	15.2	19.6	15.1	18.4		
		(0.9)	(3.4)	(0.9)	(2.0)		
vO _{2peak}	(ml/kg/min)	53.6	48.5	48.3	44.4		
		(3.6)	(5.6)	(2.8)	(3.5)		
WC	(cm)	54.5*	65.6	54.3*	62.0		
		(3.1)	(9.6)	(3.3)	(6.4)		
Waist / height		0.41*	0.47	0.40*	0.45		
		(0.03)	(0.06)	(0.02)	(0.04)		
TG	(mg/dl)	67.0*	84.7	76.1	88.7		
		(37.2)	(47.5)	(42.2)	(59.0)		
HDL-c	(mg/dl)	74.7*	66.5	69.9*	62.6		
		(14.4)	(14.6)	(14.0)	(13.1)		
SBP	(mmHg)	106.2*	110.5	108.4	109.6		
		(8.5)	(8.3)	(9.6)	(9.8)		
DBP	(mmHg)	60.0	60.8	61.8	61.4		
		(9.0)	(7.6)	(8.1)	(8.5)		

Values are means (S.D.)

Participants were divided into two groups using a median split of BMI; Low BMI and High BMI groups in each gender.

BMI; Body Mass Index, MetS risk score; metabolic syndrome risk score, WC; waist circumference

Waist / height; Waist to height ratio, TG; Triglycerides, HDL-c; high density lipoprotein cholesterol

SBP; systolic blood pressure, DBP; diastolic blood pressure

*; p<0.05 for differences between Low BMI and High BMI.

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MetS risk factors and scores by BMI category

Results comparing MetS risk factors by BMI category are shown in <u>Table 1</u>. WC and W/H were significantly higher in the High BMI group than in the Low BMI group and HDL-c was significantly lower in the High BMI group than in the Low BMI group for boys and girls. TG and SBP were significantly higher in the High BMI group than in the Low BMI group for boys. Fig 1 shows the MetS risk scores by BMI category. The MetS risk score of the High BMI group was significantly higher than that of the Low BMI group for both genders (p < 0.0001).

MetS risk factors and MetS risk score across BMI/pVO_{2peak} groups

Results comparing MetS risk factors across the four BMI/_pVO_{2peak} groups are shown in Table 2. Significant differences in WC, W/H, HDL-c, and SBP were observed among these four groups in boys. In boys, the WC in the HB/LF group was significantly higher than that in the other three groups (p < 0.0001). W/H in the HB/LF group was also significantly higher than

Table 2. Participants characteristics and MetS risk factors among BMI and pVO_{2peak} groups.

		Boys						Girls							
			Low	v BMI High B		ЗМІ	Low BMI				High BMI				
-		High Fit		Low Fit		High Fit	Low Fit	High Fit		Low Fit		High Fit		Low Fit	
		n = 47		n = 23		n = 23	3	n = 47	n = 58		n = 22		n = 21		n = 58
Age	(years)	9.2		9.1		9.1		9.1	9.1		9.2		9.1		9.1
		(0.4)		(0.3)		(0.3)		(0.2)	(0.3)		(0.4)		(0.4)		(0.3)
Height	(cm)	133.9		131.9		135.5		139.2	135.6		133.9		138.8		136.2
		(5.1)		(4.4)		(6.2)		(5.3)	(5.4)		(5.3)		(4.8)		(5.4)
Weight	(kg)	27.4		26.4		32.1		40.2	27.5		28.1		32.9		35.1
		(2.9)		(2.0)		(4.2)		(8.9)	(3.0)		(2.4)		(3.1)		(5.7)
BMI	(kg/m²)	15.2		15.2		17.4		20.6	14.9		15.6		17.1		18.8
		(0.9)		(0.8)		(0.9)		(3.7)	(0.9)		(0.4)		(0.8)		(2.1)
₽ ^{VO} 2peak	(ml/kg/min)	55.6		49.6		54.1		45.7	49.5		45.3		48.8		42.9
		(2.6)		(1.4)		(1.8)		(4.7)	(2.4)		(0.8)		(1.7)		(2.5)
WC	(cm)	54.4	†,‡	54.9	§,	59.2	¶	68.7	53.9	†, ‡	55.6	§,	58.6	¶	63.2
		(2.8)		(3.5)		(3.8)		(10.0)	(3.4)		(2.6)		(3.5)		(6.7)
Waist / height		0.41	†,‡	0.42	§,	0.44	¶	0.49	0.40	*,†,‡	0.42		0.42	¶	0.46
		(0.02)		(0.03)		(0.02)		(0.07)	(0.03)		(0.02)		(0.02)		(0.04)
TG	(mg/dl)	67.7		65.6		73.8		90.0	76.6		74.8		62.6	¶	98.1
		(37.8)		(36.6)		(30.2)		(53.4)	(41.9)		(43.9)		(21.3)		(65.3)
HDL-c	(mg/dl)	75.7	‡	72.6		70.1		64.7	70.4	‡	68.6		69.9	¶	60.0
		(14.1)		(15.2)		(15.2)		(14.1)	(14.6)		(12.3)		(13.5)		(12.0)
SBP	(mmHg)	107.0	‡	104.6		107.0		112.1	107.3		111.5		110.2		109.3
		(7.9)		(9.4)		(8.2)		(7.9)	(9.4)		(9.4)		(9.4)		(10.0)
DBP	(mmHg)	59.9		60.2		59.7		61.3	61.2		63.2		58.9		62.3
		(10.0)		(6.8)		(8.1)		(7.3)	(7.3)		(10.0)		(8.1)		(8.5)

Values are means (S.D.)

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Participants were divided into four groups using a median split of _pVO_{2peak} and BMI; Low BMI/High Fitness (LH), Low BMI/Low Fitness (LL), High BMI/ High Fitness (HH), and High BMI/Low Fitness (HL) groups.

BMI; Body Mass Index, MetS risk score; metabolic syndrome risk score, WC; waist circumference

Waist / height; Waist to height ratio, TG; Triglycerides, HDL-c; high density lipoprotein cholesterol

SBP; systolic blood pressure, DBP; diastolic blood pressure

*; p<0.05 Low BMI/High fit significantly different from Low BMI/Low fit

 $\dagger;$ p<0.05 Low BMI/High fit significantly different from High BMI/High fit

 $\ddagger;$ p<0.05 Low BMI/High fit significantly different from High BMI/Low fit

 $; p<0.05 \ Low BMI/Low fit significantly different from High BMI/High fit$

||; p<0.05 Low BMI/Low fit significantly different from High BMI/Low fit

 \prescript{s} ; p<0.05 High BMI/High fit significantly different from High BMI/Low fit.

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that in the other three groups (p < 0.0001). The HDL-c level in the HB/LF group was significantly lower than that in the LB/HF group. Finally, the SBP of the HB/LF group was significantly higher than that of the LB/HF and LB/LF groups. We also confirmed significant differences in WC, W/H, TG, and HDL-c in girls. The TG level in the HB/HF group was significantly lower than that in the HB/LF group. Fig 2 shows the results of the MetS risk score calculations. The HB/LF group had the highest MetS risk score in both boys (p < 0.0001) and girls (vs. LB/HF, p < 0.0001; vs. LB/LF, p = 0.0003; vs. HB/HF, p = 0.0002). In addition, the MetS









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Fig 3. Receiver operating characteristic (ROC) analysis to identify low/high metabolic risk score in boys and girls. ROC curves showing the optimal $_pVO_{2peak}$ cut-off point for metabolic syndrome risk score of <75% ile in boys and girls. AUC indicates the area under the curve (95% confidence interval). In boys, the optimal pair of true- and false-positive rates were 0.92 and 0.66, respectively (AUC = 0.80%; 95% confidence interval (CI): 0.70–0.90; p < 0.0001). In girls, these parameters were 0.82 and 0.74, respectively (AUC = 0.85%; 95% CI: 0.74–0.92; p < 0.0001). $_pVO_{2peak}$ of cut-off value for low metabolic risk was 47.9 and 44.9 mL/kg/min in boys and girls, respectively.

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risk score of the HB/HF group was significantly lower than that of the HB/LF group in both boys and girls.

ROC analysis

Fig 3 shows the results of the ROC analysis. The ROC analysis demonstrated the significant discriminating ability of $_{\rm p}VO_{\rm 2peak}$ for identifying low versus high MetS risk scores in boys (AUC = 0.80%; 95% confidence interval CI: 0.70–0.90; p < 0.0001), and girls (AUC = 0.85%; 95% CI: 0.74–0.92; p < 0.0001). $_{\rm p}VO_{\rm 2peak}$ at these points were 47.9 and 44.9 ml/kg/min in boys and girls, respectively.

Discussion

The purposes of this study were to investigate the relationships between BMI, aerobic fitness, and MetS risk factors and determine the threshold aerobic fitness level necessary to achieve a low MetS risk in Japanese children. The results demonstrate that the High BMI/Low fitness group had the highest MetS risk score in both boys and girls. The MetS risk score of the High BMI/High fitness group was significantly lower than that of the High BMI/Low fitness group in both genders. The $_{\rm p}VO_{\rm 2peak}$ cut-off values for low metabolic risk was 47.9 and 44.9 mL/kg/ min for boys and girls, respectively.

In addition, the results demonstrate that children in the Low BMI group had lower MetS risk factors and MetS risk scores, on average, than those in children in the High BMI group from Pearson's correlation analysis and ANOVA. This finding is consistent with those of

previous studies assessing the relationship between BMI/%Fat and MetS risk in European, American, Australian and Canadian children and adolescents [20–23,29]. We confirmed that an increase in BMI was associated with higher MetS risk.

Furthermore, MetS risk is also associated with aerobic fitness. In adults, high levels of aerobic fitness among those with high BMI decrease cardiovascular disease risk [30,31]. However, these phenomena have not been consistently observed in children and adolescents [20–23]. Our results clearly show that, among those with high fatness, the children in the high aerobic fitness group have lower MetS risk scores. This finding was also observed for WC and W/H in boys and WC, W/H, TG, and HDL-c in girls. We suggest that a high level of aerobic fitness is important for decreasing MetS risk, even among overweight and obese children. With regard to the reason of lower MetS risk score in High BMI/High fit vs. High BMI/Low fit, it may be related to physical activity [17,32,33]. In addition, there is a possibility that body composition may have a role in MetS risk. More importantly, MetS risk score in boys was lower in High BMI/High fit than Low BMI/High fit but that in girls was not. Therefore, in children with high fitness, it is suggested that a gender difference could exist. Based on the present observations, we speculate that in high fitness groups, BMI may have a stronger relationship with MetS risk in boys compared to girls. In the future, it is necessary to investigate gender difference in MetS risk in concomitant with physical activity and/or body composition.

The aerobic fitness levels found to be necessary for a low MetS risk in this study (47.9 and 44.9 ml/kg/min for 9–10 years old in boys and girls, respectively) were relatively higher than those reported in previous studies by Ruiz et al. [16] (42.1 and 37.0 ml/kg/min for 9–10 years old boys and girls, respectively), Adegboye et al. [24] (43.6 and 37.4 ml/kg/min for 8–11 years old boys and girls, respectively) and Boddy et al. [25] (46.6 and 41.9 ml/kg/min for 9–10.9 years old boys and girls, respectively). In the studies of Ruiz et al. [16] and Adegboye et al. [24], aerobic fitness was evaluated using a cycle-ergometer test. On the other hand, in our study and that of Boddy et al. [25], aerobic fitness was evaluated using the 20-m shuttle run test. These differences in aerobic fitness threshold may reflect the method used to evaluate aerobic fitness. However, in Japanese children, the 20-m shuttle run test level was higher than that observed among 37 countries worldwide [26]. Therefore, it is reasonable to expect that our results would be higher than those observed in previous studies.

This study has several limitations. First, in terms of safety and ethical considerations, blood samples were measured in a nonfasting state. Therefore, we were not able to measure glucose or insulin. However, we believe the data are sufficient to provide the first determination of a ${}_{\rm p}{\rm VO}_{\rm 2peak}$ cut-off value for low MetS risk in Japanese children. These data are quite important for the children. Second, this study was that VO_{2peak} was predicted from a single 20-m shuttle run. Standard exercise testing methods with directly measured oxygen consumption are required to confirm our findings. Third, this study was performed in only one city in Japan. However, our study covered all 13 schools within that city. The VO_{2peak} of cut-off value we found necessary for low MetS risk in Japanese children needs to be confirmed using a large sample size. Finally, because this study is cross-sectional, a longitudinal analysis is required to better understand the importance of fatness and aerobic fitness on MetS risk.

Conclusions

This study suggests that improvements in both BMI and aerobic fitness are important for achieving a low MetS risk. Moreover, we confirm specific $_{\rm p}VO_{\rm 2peak}$ of cut-off values (47.9 and 44.9 ml/kg/min in boys and girls, respectively) for low MetS risk in Japanese children.

Supporting Information

S1 Dataset. Dataset of all parameters from140 boys and 159 girls. (XLSX)

Author Contributions

Conceived and designed the experiments: KS EO MA. Performed the experiments: KS MA. Analyzed the data: KS EO. Contributed reagents/materials/analysis tools: KS EO MA. Wrote the paper: KS EO MA.

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