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Editorial

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Pediatric Metabolic Syndrome and the Marker of Abdominal Obesity

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Dyslipidemia in Obese Children

Blood biochemical abnormal values induced by being overweight are often seen in children and in adults. The most frequent complications in obese children are fatty liver, insulin resistance (hyperinsulinemia), and hypertriglyceridemia.

The criteria of dyslipidemia for Japanese children (fasting test) have been defined as total cholesterol (TC) levels of ≥ 220 mg/dL, LDL cholesterol (LDL-C) levels of ≥ 140 mg/dL, triglyceride (TG) levels of ≥ 140 mg/dL, HDL cholesterol (HDL-C) levels of $<$40 mg/dL, and non-HDL-C levels of ≥ 150 mg/dL[1]. The cutoff value of HDL-C is based on the 5th percentile value, and those for other lipids are each on the 95th percentile value.

Maeda *et al.* studied the secular trends in terms of body size and serum lipid levels of 10-year-old children by analyzing a 27-year data from Oita Prefecture in Kyushu, Japan, and showed that the frequency of high TG, low HDL-C, and high non-HDL-C was 4%–7%, 1%–1.5%, and 6%–8%, respectively[2]. The frequency of low HDL-C was lower than the expected value. They also reported that the frequency of high TG, low HDL-C, and high non-HDL-C in obese children, estimated by the percentage of overweight (POW) ≥ 20%, was 15%–25%, 3%–7%, and 15%–25%, respectively[2]. In our children's obesity clinic, the frequency of high TG, low HDL-C, and high TC is approximately 24%, 8%, and 10%, respectively. From these data, the percentage of dyslipidemia is not high even in obesity. Thus, when we see an obese child with dyslipidemia, we must always consider genetic or other factors.

POW is commonly used in Japan[3]. The criterion for obesity is POW ≥ 20% (≥ 120% of the standard weight) for school-age children. We do not distinguish between obesity and overweight. A POW of ≥ 20% is defined as mild obesity and ≥ 50% as severe obesity. The standard weight is the age- and sex-specific weight for height based on the 2000 national data[3].

In obesity-related dyslipidemias, TG and HDL-C levels are significantly associated with both visceral adipose tissue (VAT) area and waist circumference (WC), but TC, LDL-C, nor non-HDL-C are not **(Table 1)**[4, 5]. Either or both high TG and low HDL-C are one of the important components of metabolic syndrome (MS) in both adults and children.

Accumulation of VAT and MS

Complications of obesity are more frequent in severe obesity than in mild obesity[6]. Some complications are associated with the total fat amount, but many complications are more related to the accumulation of VAT[4-6]. Hypertrophic adipocytes induce metabolic malfunction of other cells and tissues mainly by inappropriate secretion of adipocytokines (adipokines) even in children[7]. The expression and production of adipocytokines are more in VAT than in subcutaneous adipose tissue. Therefore, the excessive accumulation of VAT itself, in the absence of other complications, should be the target of medical intervention. If dyslipidemia, hypertension, or hyperglycemia is added to excess VAT, this kind of obesity becomes a more powerful risk state, which must be MS.

MS is a risk of not only atherosclerosis but also diabetes mellitus and is defined by a cluster of some risk factors, except high LDL-C. This concept is accepted worldwide but is confusing because several definitions of MS have been made for children. Suppose that there are two children, one is a lean child

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Table 1. Correlation between four abdominal indices and other obesity-related indices and complications in Japanese obese children

	WC (cm)	Hip (cm)	WC/Ht	WC/Hip
POW (%)	0.558§	0.410§	0.879§	0.397§
BMI percentile	0.260*	0.235*	0.564§	0.110
BMI-SD	0.142	0.021	0.686§	0.274**
Hip (cm)	0.875§			
WC/Ht	0.615§	0.303***		
WC/Hip	0.459§	-0.025	0.699§	
Total AT area (cm^2)	0.937§	0.846§	0.661§	0.328**
VAT area (cm^2)	0.675§	0.569§	0.416§	0.337**
SAT area (cm^2)	0.916§	0.840§	0.666§	0.290*
TC (mg/dl)	-0.064	-0.038	-0.036	-0.065
TG (mg/dl)	0.221*	0.214*	0.070	0.084
HDL-C (mg/dl)	-0.317***	-0.214*	-0.273**	-0.289**
LDL-C (mg/dl)	-0.018	-0.033	0.054	0.023
non HDL-C (mg/dl)	0.063	0.048	0.074	0.050
ALT (U/L)	0.210*	0.139	0.163	0.189
Insulin (μU/L)	0.513§	0.526§	0.161	0.093

This table is made by our data[4)] in 55 boys and 35 girls, the mean age was 9.92 years and the mean percentage overweight (POW) was 51.6 %. The adipose tissue (AT) area was measured by computed tomography at the umbilical level[5)].
BMI; body mass index, SD; standard deviation, WC; waist circumference measured at umbilicus level, Ht; height, Hip; hip circumference at the maximum level, VAT; visceral AT, SAT; subcutaneous AT, ALT; alanine aminotransferase. §; $p<0.001$, ***; $p<0.005$, **; $p<0.01$, *; $p<0.05$.

with hypertension, high TG, and low HDL-C, and another is a child with abdominal obesity, hypertension, and high TG. Does the lean child have MS? The lean child probably has hypertension and dyslipidemia by chance; whose future metabolic risk may be half or less than that of the child with abdominal obesity.

The International Diabetes Federation (IDF) proposed the diagnostic criteria of MS for children in 2007 [8)]. This is based on abdominal obesity and a WC of ≥ 90th percentile value as the essential components of the criteria. However, the IDF definition for adult MS was changed. In Japan, pediatric MS is also based on VAT accumulation, which is the same as that of adult MS.

What is the Best Abdominal Index?

The measurement site of VAT and WC is important. Calculating the VAT area using computed tomography (CT) at the umbilical level is the gold standard method. This slice is the best area because no perirenal fats exist. The measured VAT area is highly associated with the total VAT volume estimated by multi-slice CT[5, 6)].

Until now, many different criteria of WC, from the 75th to the 95th percentile value by age and gender, have been proposed for abdominal obesity and are used in many countries. Subsequently, a waist-to-height ratio (WC/Ht) of ≥ 0.5 has been proposed as a predictor of cardiovascular disease risk and used recently as a marker for VAT, even in Japan.

WC/Ht ≥ 0.5 looks attractive because it has the factor of one's height and is easy to remember. Interestingly, WC/Ht almost completely matches POW[4)] and is highly related to body mass index (BMI) for age **(Table 1)**. POW and BMI for age are the markers for total body fat than VAT. WC/Ht=0.5 line is also reported to well match the 90th percentile WC line in healthy Japanese boys[9)]. Statistically, the correlation of umbilical WC with VAT area is higher than that of WC/Ht, POW, or BMI for age **(Table 1)**.

Asayama *et al.*[6)] showed in their study that the percentage of biochemical complications was 46% in younger obese children (<10.5 years) and 75% in older obese children (≥ 10.5 years). Almost all pediatricians have clinically experienced that obesity-related complications rarely occur in early elementary school children, whereas common in junior high school students, even if their obesity levels are the same. I believe that this fact is the key to determining the cutoff value of the marker.

In a child with an average built, WC is linearly increased by approximately 3 cm per 10 cm of height growth during school age[3, 10)] **(Fig. 1)**. Both inclinations of the WC/Ht=0.5 line and the 90th

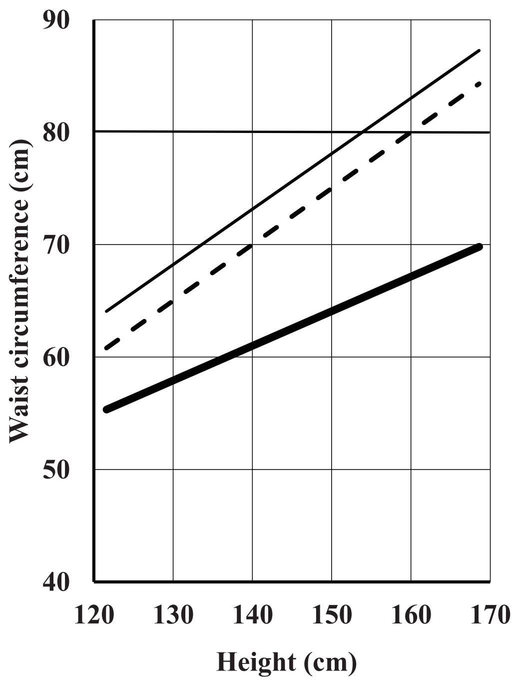

Fig. 1. Average WC line in Japanese school-age boys

Thick line; average WC line, thin line; average WC + 2 standard deviation (SD) line, and dot line; WC to height (Ht) ratio = 0.5 line. This graph was made based on 10803 healthy elementary and junior high school boys in the west side of Japan, reported by Fujiwara *et al.*[10]. WC was measured at the umbilical level. The average WC line is calculated as 0.31 × Ht + 18. The WC + 2SD line almost completely matches the 0.52 × Ht line.

percentile WC line are higher than the average WC line. A cutoff value of 0.5 for WC/Ht is too mild. The sensitivity to detect a child with a metabolic complication is very high, but the specificity is extremely low. Therefore, WC/Ht > 0.5 is considered inappropriate as a marker of the excessive accumulation of VAT. The same applies to the 90th percentile WC.

For these reasons, WC at the umbilical level itself is thought to be the best surrogate marker. In Japan, the cutoff for WC for 6–15-year-olds is originally set to the constant line of 80 cm **(Fig. 1)**, corresponding to approximately 60 cm^2 of VAT area by CT[5, 6]. The sensitivity and specificity of the WC of 80 cm at umbilical level to detect children with at least one complication are > 70% for both. Then, a WC of 75 cm has also been proposed for elementary school pupils to prevent underdiagnosis of MS in younger children. The criterion may not be perfect, but it is better than others at this time.

The WC cutoff as the essential component of pediatric MS should be able to well predict biochemical complications. I hope the more age-specific WC cutoff or the new surrogate marker is created for school-age children.

Conflicts of Interest

I have no conflicts of interest to declare.

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