BRIEF REPORT

## Emergence of Cardiovascular Risk Factors From Mild Obesity in Japanese Elementary School Children

Masao Yoshinaga, md<sup>1</sup> Koji Sameshima, md<sup>2</sup> Michihisa Jougasaki, md<sup>1</sup> Hideki Yoshikawa, md<sup>1</sup> Yuji Tanaka, md<sup>1</sup> Jun Hashiguchi, md² Hirofumi Tahara, md² Takeo Ichiki, md² Shinichiro Shimizu, md² Kazuhiko Nakamura, md¹

lustering of individual cardiovascular risk factors, such as central obesity, insulin resistance, hypertension, and dyslipidemia, together known as metabolic syndrome, is largely confined to obese populations in both children and adults (1,2). The underlying pathophysiology of metabolic syndrome is thought to be related to insulin resistance (3).

In Asian countries, especially Japan, obesity-associated disorders arise in mildly to moderately obese adults (4,5). The association between mild obesity in children and individual risk factors in Asian countries is not well defined. The purpose of the present study is to determine the prevalence of, and sex differences in, abdominal obesity and insulin resistance, key features of metabolic syndrome, and assess whether risk of these factors is associated with mild obesity in Japanese elementary school children.

## **RESEARCH DESIGN AND**

**METHODS** — Subjects were elementary school children aged 6–12 years who were screened as having a percent relative body weight (%RBW) ≥35% (6). A total of 863 children (561 boys, 302 girls) participated in a screening program for comorbidity of obesity conducted in 2002 and 2003 by the Kagoshima City Board of Education and Kagoshima City Medical Association, Japan. Of these, 754 obese

children (490 boys, 264 girls) were included in the present study. One hundred nine subjects were excluded: 9 subjects (6 boys, 3 girls) were excluded because they had normal %RBW, and 100 subjects (65 boys, 35 girls) were excluded because of incomplete information. For 146 subjects (93 boys, 53 girls) who participated in the program in both years, only the 2002 data were used.

We obtained permission to use and analyze these data from the committees for ethics of Kagoshima City Medical Association and the National Hospital Organization Kyushu Cardiovascular Center under the condition that confidentiality regarding all personal data would be maintained. The components of the screening program have been described elsewhere (7).

Of the parameters examined in the programs, waist circumference, an index of obesity, and homeostasis model assessment of insulin resistance (HOMA-IR) were used in this study. Height, weight, and waist circumference were measured by each subject's home doctor. Height and waist circumference were measured to the nearest 0.1 cm and weight to the nearest 0.1 kg (7). Blood samples were collected at each clinic the morning after an overnight fast. Insulin concentrations were measured by means of a chemiluminescence immunological assay (Chemi-

lumi Insulin; Kyowa Medics, Tokyo, Japan). HOMA-IR was used as a measure of insulin resistance (8).

As a measure of obesity, we computed the %RBW: (individual body weight)/ (age-, sex-, and height-specific body weight from a reference population)  $\times$  100 (6). Obesity was classified as follows: mild, %RBW  $\geq$ 20 to <30%; moderate, %RBW  $\geq$ 30 to <50%; and severe, %RBW  $\geq$ 50% (12). Subjects were divided into four groups: those with %RBW  $\geq$ 20 to <30%,  $\geq$ 30 to <40%,  $\geq$ 40 to <50%, and  $\geq$ 50%. The data for levels of waist circumference, fasting insulin, and HOMA-IR of nonobese children (%RBW  $\geq$ -20% and <20%) were obtained from previous studies (9–11).

Statistical testing for the difference in mean values between two groups was performed using the Mann-Whitney test. A level of P < 0.05 was considered statistically significant.

**RESULTS** — The mean waist circumference value of boys  $(78.6 \pm 8.3 \text{ cm})$  was significantly higher than that of girls  $(74.5 \pm 8.3 \text{ cm})$  (P < 0.0001). On the other hand, the mean HOMA-IR level of girls (3.07 [95% CI 2.79 - 3.34]) was significantly higher than that of boys (2.65 [2.48 - 2.82]) (P < 0.0001).

Regarding waist circumference, significant differences were present among neighboring subgroups in both boys and girls; however, the greatest significance was between normal and mildly obese boys (Fig. 1). The difference in levels of HOMA-IR between normal and mildly obese children was more prominent in boys (Fig. 2). On the other hand, HOMA-IR levels gradually increased until the 40–50% RBW grouping in girls (Fig. 2).

**CONCLUSIONS** — Previous studies have shown that significant differences were found in the levels of systolic and diastolic blood pressure, HDL cholesterol, triglyceride, insulin, and HOMA-IR between overweight at-risk (BMI 23.0–24.9 kg/m²) and normal adults (BMI 18.5–22.9) in Japan (4). On the other hand, no significant differences in these

From the <sup>1</sup>National Hospital Organization Kyushu Cardiovascular Center, Kagoshima, Japan; and the <sup>2</sup>Kagoshima City Medical Association, Kagoshima, Japan.

Address correspondence and reprint requests to Masao Yoshinaga, MD, Department of Pediatrics, National Hospital Organization Kyushu Cardiovascular Center, Shiroyama-cho 8-1, Kagoshima, 892-0853, Japan. E-mail: m-yoshi@q-jun2.hosp.go.jp.

Received for publication 26 December 2005 and accepted in revised form 23 February 2006.

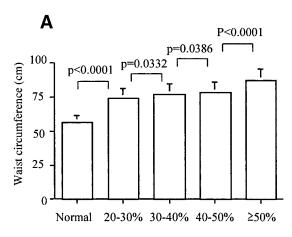
**Abbreviations:** HOMA-IR, homeostasis model assessment of insulin resistance; %RBW, percent relative body weight.

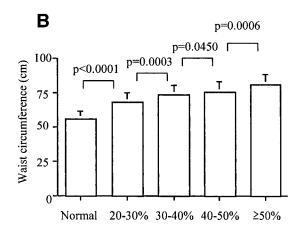
A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

DOI: 10.2337/dc06-2538

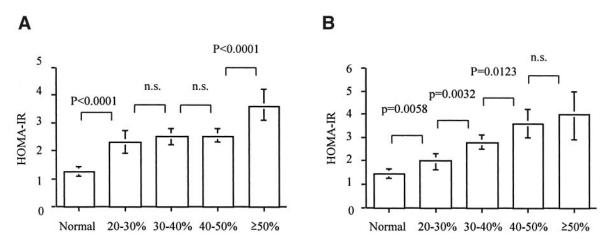
© 2006 by the American Diabetes Association.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.





**Figure 1**—Changes in waist circumference among normal and obese boys (A) and girls (B) with %RBW of 20–30, 30–40, 40–50, and ≥50%. The greatest significance was present between normal and mildly obese boys (20–30% RBW group). In boys, the z values between normal control subjects and the 20–30% RBW group and between the 40–50 and ≥50% RBW groups were -12.143 and -6.488, respectively. Waist circumference gradually increased with increasing obesity in girls.



**Figure 2**—Changes in HOMA-IR levels among normal and obese boys (A) and girls (B) with %RBW of 20–30, 30-40, 40-50, and ≥50%. HOMA-IR data are expressed as the mean and 95% CI because values were skewed. The greatest significance was present between normal and mildly obese boys (20–30% RBW group); the z values between normal control subjects and the 20–30% RBW group and between the 40–50 and ≥50% RBW groups were -4.949 and -4.381, respectively. The HOMA-IR level gradually increased until the 40-50% RBW grouping in girls.

risk factors, except diastolic blood pressure, have been shown between overweight at-risk and normal adults in Mongol (4). In Japan, BMI slightly increased in men and slightly decreased in women during the period 1976-1995, according to national surveys; however, the prevalence of diabetes and dyslipidemia has been rapidly increasing (5). These previous findings and the present data indicate a tendency toward early development of cardiovascular risk factors from mild obesity, not only in adults, but also in children aged 6–12 years in Japan. An important feature in boys is that an abrupt worsening of insulin resistance can emerge from both mild and severe obesity. This suggests that primary prevention is extremely important among preteen Japanese boys.

The approach used in this study has some limitations. First, data from former studies (9-11) were used as controls. Although these studies (9-11) were conducted using data of Japanese children, and although the control data for fasting glucose and insulin were obtained from an elementary school in the same city (10,11), future studies should include a subject control group. Possible limitations also include the use of HOMA-IR and waist circumference for surrogate assessment of insulin resistance and abdominal obesity, respectively. In addition, the present study included a larger percentage of boys than girls. However, recent increases in the prevalence of obesity during elementary school years have been shown in boys but not girls in Japan (12), indicating that a focus on boys is justified.

The reason for this rapid increase in boys needs investigation in the future.

Acknowledgments— This work was supported by grants from the Foundation of Health and Labor Sciences Research (Comprehensive Research on Cardiovascular Diseases [17160501]) and Foundation of Tanita Healthy Weight Promotion (2004).

## References

- 1. Weiss R, Dziura J, Burgert TS, Tamborlane WV, Taksali SE, Yeckel CW, Allen K, Lopes M, Savoye M, Morrison J, Sherwin RS, Caprio S: Obesity and the metabolic syndrome in children and adolescents. *N Engl J Med* 350:2362–2374, 2004
- Park YW, Zhu S, Palaniappan L, Heshka S, Carnethon MR, Heymsfield SB: The metabolic syndrome: prevalence and as-

## Cardiovascular risk factors in obese children

- sociated risk factor findings in the US population from the Third National Health and Nutrition Examination Survey, 1988–1994. *Arch Intern Med* 163: 427–436, 2003
- 3. Kahn R, Buse J, Ferrannini E, Stern M: The metabolic syndrome: time for a critical appraisal: joint statement from the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care* 28:2289–2304, 2005
- 4. Shiwaku K, Anuurad E, Enkhmaa B, Nogi A, Kitajima K, Shimono K, Yamane Y, Oyunsuren T: Overweight Japanese with body mass indexes of 23.0–24.9 have higher risks for obesity-associated disorders: a comparison of Japanese and Mongolians. *Int J Obes Relat Metab Disord* 28: 152–158, 2004
- 5. Yoshiike N, Seino F, Tajima S, Arai Y, Kawano M, Furuhata T, Inoue S: Twentyyear changes in the prevalence of over-

- weight in Japanese adults: the National Nutrition Survey 1976–95. *Obes Rev* 3:183–190, 2002
- 6. Murata M, Yamazaki K, Itani A, Inaba M: Standard body weight for height for age between 5 years and 17 years. *J Child Health* 93–96, 1980 (in Japanese)
- Yoshinaga M, Sameshima K, Miyata K, Hashiguchi J, Imamura M: Prevention of mildly overweight children from development of more overweight condition. *Prev* Med 38:172–174, 2004
- Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC: Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 28:412– 419, 1985
- 9. Asayama K, Hayashi K, Kawada Y, Nakane T, Uchida N, Hayashibe H, Kawasaki K, Nakazawa S: New age-adjusted measure of body fat distribution in chil-

- dren and adolescents: standardization of waist-hip ratio using multivariate analysis. *Int J Obes Relat Metab Disord* 21:594–599, 1997
- Hashiguchi J, Sameshima K, Arima K, Shimizu S, Ichiki K, Yoshinaga M: Metabolic syndrome develops from insulin resistance in obese children. *J Kagoshima* City Med Assoc 43:104–106, 2004 (in Japanese)
- Yoshinaga M, Tanaka S, Shimago A, Sameshima K, Nishi J, Nomura Y, Kawano Y, Hashiguchi J, Ichiki T, Shimizu S: Metabolic syndrome in overweight and obese Japanese children. *Obes Res* 13:1135– 1140, 2005
- 12. Yoshinaga M, Shimago A, Koriyama C, Nomura Y, Miyata K, Hashiguchi J, Arima K: Rapid increase in the prevalence of obesity in elementary school children. *Int J Obes Relat Metab Disord* 28(4):494–499, 2004