Associations of visceral and subcutaneous fat areas with the prevalence of metabolic risk factor clustering in 6292 Japanese individuals: the Hitachi Health Study

Running head: Association of fat depot with metabolic syndrome

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Background. We examined the relationships of visceral fat area (VFA), subcutaneous fat area, and waist circumference determined using computed tomography (CT), and BMI, on the metabolic risk factors in a large Japanese population.

Research Design and Methods. Study subjects were 6292 men and women who participated in Hitachi Health Study, received CT examination in 2007 and 2008.

Results. Regarding the clustering of metabolic risk factors, the odds ratios for the VFA quintiles were 1.0 (ref.), 2.4, 3.4, 5.0, and 9.7, for men and 1.0 (ref.), 1.5, 2.6, 4.6, and 10.0, for women, respectively (P < 0.001 for trends in both sexes). For the highest quintiles, the odds ratio for the VFA was 1.5 to 2 times higher than those of the other anthropometric indices in both sexes.

Conclusions. We clearly demonstrated a superior performance of VFA to predict the clustering of metabolic risk factors compared to other anthropometric indices.
Metabolic syndrome (MS) has been growing globally with the clusters of obesity, high blood pressure, impaired lipid metabolism, and hyperglycemia. Individuals with MS have a higher risk of cardiovascular disease and a subsequent increase in disease mortality or morbidity (1-3). For the diagnosis of MS, waist circumference (WC) is almost always used as one of the criteria, and this measure is typically used as a simplified measure of the visceral fat area (VFA) (4-7). Visceral fat is regarded as an endocrine organ, which secretes adipocytokines and other vasoactive substances that can influence the risk of developing traits of MS (8). A few studies have shown the impact of visceral fat on MS and its components in large-scale epidemiological research efforts (9). The present study analyzed the epidemiological impact of VFA, compared with that of the subcutaneous fat area (SFA), WC, and body mass index (BMI), against the clustering of metabolic risk factors and its components.

RESEARCH DESIGN AND METHODS

Of 17606 employees and their spouses who, after more than 12 hours of fasting, underwent a health examination in Hitachi, Ibaraki Prefecture between 2007 and 2008, we analyzed data for 6292 subjects (5606 men and 686 women), aged from 26 to 75 years, who underwent a computed tomography (CT) examination, answered a questionnaire on lifestyle and health, and did not have a history of serious illness (cancer, cerebrovascular disease, myocardial infarction). The VFA, SFA, and WC were measured using a CT scanner according to a protocol described elsewhere (10). The present study was approved by the ethics review committee of the International Medical Center of Japan. Written informed consent was obtained from all subjects.

In this study, subjects with two or more of the four risk factors (high blood pressure, high triglyceride, low HDL-cholesterol, hyperglycemia) defined in the criteria of the National Cholesterol Education Program’s Adult Treatment Panel III guidelines in 2005 (6) except for WC were defined as having the clustering of metabolic risk factors. Subjects currently receiving treatment for hyperlipidemia, hypertension, or diabetes were deemed as having the respective risk factors, regardless of the biochemical values.

We divided the subjects into quintiles (Q1 to Q5) according to each anthropometric value and calculated the odds ratio (OR) of the clustering of metabolic risk factors and its components adjusted for age, smoking habits, alcohol consumption, and regular physical activity using a logistic regression analysis, with Q1 as the reference. All analyses were performed using SPSS for Windows, Version 15.0 (SPSS Inc., IL, USA).

RESULTS

The mean VFA was 123.7 ± 51.2 cm² in men and 85.1 ± 45.2 cm² in women. The mean SFA was 134.8 ± 56.6 cm² in men and 182.5 ± 72.9 cm² in women. The ratio of VFA to SFA was approximately 1:1 for men and 1:2 for women. The mean WC was 86.4 ± 8.3 cm in men and 83.2 ± 9.2 cm in women. The mean BMI was 24.1 ± 3.0 kg/m² in men and 23.0 ± 3.3 kg/m² in women. The prevalence of the clustering of metabolic risk factors was 46.0 % in men and 30.0 % in women.

In Figure 1, the ORs for the clustering of metabolic risk factors are shown according to each anthropometric index. The OR was 1.5 to 2 times higher for the Q5 VFA category than for the other Q5 categories for both men and women. The OR (95% confidence interval [CI]) of the VFA quintiles
were 1.0, 2.4 (2.0-2.9), 3.4 (2.8-4.2), 5.0 (4.1-6.0), and 9.7 (8.0-11.9) for men and 1.0, 1.5 (0.7-3.2), 2.6 (1.3-5.3), 4.6 (2.3-9.1), and 10.0 (5.0-19.9) for women, respectively (P <0.001 for trends in both sexes). According to the SFA quintiles, OR were 1.0, 1.8 (1.5-2.2), 2.6 (2.2-3.1), 3.1 (2.6-3.7), and 4.8 (4.0-5.8) for men and 1.0, 1.3 (0.7-2.5), 2.3 (1.3-4.3), 3.5 (1.9-6.4), and 4.5 (2.5-8.4) for women, respectively (P <0.001 for trends in both sexes).

The OR for a high triglyceride level, a low HDL level, high blood pressure, and hyperglycemia increased with increasing quintile categories of each anthropometric index. The OR (95%CI) of the Q5 VFA category for a high triglyceride level was 9.0 (7.3-11.1) in men and for a low HDL level was 7.1 (4.8-10.5) in men and 11.0 (4.0-30.1) in women, which exhibited extremely high OR.

The slope for VFA is significantly steeper than those for SFA, WC, and BMI on high triglyceride and on clustering of metabolic risk factors (p <0.05) except for that for on the clustering of metabolic risk factors in women.

CONCLUSIONS

In the present study, a stronger association between an increasing VFA and the clustering of metabolic risk factors and its components than for an increasing SFA, WC, or BMI was observed. Among metabolic risk factors, a high triglyceride level in men and a low HDL cholesterol level in both men and women showed particularly strong associations with VFA.

BMI and WC are used clinically to measure obesity, but do not exactly reflect visceral adiposity. Previous report showed that some individuals with a normal BMI and WC actually had an excessive amount of visceral fat and metabolic risk factors (11). In our study, the OR for the clustering of metabolic risk factors were similar for BMI and WC in men, but for WC was lower than that for BMI (which was similar to that for SFA) in women. The OR of VFA and SFA differed according to sex. Furthermore, a stronger correlation was observed between WC and SFA than between WC and VFA. Fox et al. reported similar results (9). These findings suggest that WC measurements in women may have the same meaning as SFA measurements, explaining the similarity of the OR for the clustering of metabolic risk factors in WC and SFA.

The present study adds evidence to support an important role of VFA in the pathogenesis of metabolic risk factor clustering in Japanese adults. Further studies are needed to confirm this association prospectively and to examine the impact of VFA on the risk of cardiovascular disease.

Author Contributions. Y.M. derived the hypothesis, collated data from the Hitachi Health Study trials, planned and did the analyses, and wrote the paper. T.N. and S.Y. collected data. T.Y. advised on analyses and commented on drafts of the report. T.N., Y.T., T.Y., M.N., and T.M. contributed to interpretation of results and discussion of the results. This report was critically reviewed and subsequently approved by all authors.

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REFERENCES
Legend for Figure 1.
Odds ratios for high triglyceride and the clustering of metabolic risk factors according to the quintiles (Q1-Q5) of VFA, SFA, WC, and BMI adjusted for age, smoking habits (never, current, past), alcohol consumption (nondrinker, drinker consuming 2 go or less per day [one go contains approximately 23 g of ethanol], or consuming more than 2 go per day), and regular fitness habit (yes/no). The symbols are the estimated odds ratios using Q1 as the reference category. The curves are fitted by the logistic regression models. The slope for VFA is significantly steeper than those for SFA, WC, and BMI on high triglyceride and on clustering of metabolic risk factors (p <0.05) except for that on the clustering of metabolic risk factors in women.