Cardiovascular and Metabolic Risk

Age-Dependent Decline of Association Between Obesity and Hyperglycemia in Men and Women

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OBJECTIVE—The purpose of this study was to determine whether age influences the association between obesity and hyperglycemia.

RESEARCH DESIGN AND METHODS—The subjects were 57,576 Japanese male and female workers aged 35–70 years. The associations of adiposity indices, including BMI, waist circumference, and waist-to-height ratio, with risk for hyperglycemia were compared among different age groups (35–39, 40–49, 50–59, and 60–70 years) using odds ratios (ORs).

RESULTS—There were significant trends for the crude ORs of obese subjects versus non-obese subjects for hyperglycemia to be lower as age increased in men and women. Multivariate logistic regression analysis showed these trends of age-dependent decreases in ORs for hyperglycemia to be lower as age increased in men and women. Multivariable logistic regression analysis showed these trends of age-dependent decreases in ORs for hyperglycemia were not altered by adjustment for confounders such as smoking, alcohol drinking, and habitual exercise.

CONCLUSIONS—The results suggest that the association between obesity and hyperglycemia declines with age in men and women.

A J- or U-shaped relationship is known to exist between BMI and all-cause mortality (1,2). Excess mortality in obese people is mainly due to vascular disease (3) and has been shown to decline with age (4–7). Type 2 diabetes is a major risk factor for cardiovascular disease and is induced by lifestyle-related modifiable risk factors such as obesity and low physical activity. The association between obesity and the risk for coronary heart disease has been shown to be weaker in older men than in younger men (8,9). The incidence of type 2 diabetes increases with age (10); however, the effects of age on the relationship between obesity and glycemic status have not been confirmed. Therefore, the aim of this study was to clarify whether the association between obesity and hyperglycemia differs by age in men and women.

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RESEARCH DESIGN AND METHODS

Subjects

The subjects were Japanese workers (37,686 men and 19,890 women), aged 35–70 years, who had received periodic health examinations at workplaces in Yamagata Prefecture in Japan and were divided into four groups by age (35–39, 40–49, 50–59, and 60–70 years). Histories of alcohol consumption, cigarette smoking, habitual exercise, and treatment for any illnesses were surveyed by questionnaires. This study was approved by the Yamagata University School of Medicine Ethics Committee.

Measurements

BMI was calculated as weight in kilograms divided by the square of height in meters. The criterion for obesity evaluated by using each adiposity index was defined as BMI ≥25 kg/m², waist circumference ≥85 cm for men and ≥80 cm for women, and waist-to-height ratio (WHtR) ≥0.5. Fasted blood was sampled from each subject, and hemoglobin A1c, triglycerides, and LDL cholesterol were determined. The hemoglobin A1c values were calibrated by using a formula proposed by the Japan Diabetes Society (11) as hemoglobin A1c (National Glycohemoglobin Standardization Program) (%) = hemoglobin A1c (Japan Diabetes Society) (%) + 0.4%. Hyperglycemia including diabetes and prediabetes was defined as hemoglobin A1c ≥5.7% (12) and/or current history of drug therapy for diabetes.

Statistical analysis

Statistical analyses were performed using SPSS 16.0 J software (SPSS Inc., Chicago, IL). Crude odds ratios (ORs) and ORs after adjustment for age, smoking, alcohol intake, and habitual exercise were calculated by using logistic regression. Trends for crude ORs across the age groups were tested by using the Breslow-Day test. P values < 0.05 were defined as significant.

RESULTS—Prevalences of hyperglycemia, high triglycerides, and high LDL cholesterol were, respectively, 24.2, 36.0, and 21.3% in men and 19.3, 14.1, and 19.4% in women. Prevalences of high BMI, large waist circumference, and high WHtR were, respectively, 30.8, 44.2, and 46.5% in men and 20.6, 41.3, and 47.8% in women.

In all of the age groups of men and women, crude and adjusted ORs for hyperglycemia of subjects with a high or large adiposity index versus subjects without a high or large adiposity index were significantly higher compared with a reference level of 1.00 (Table 1). There were significant trends for the crude ORs to be lower in higher age groups, and the adjusted ORs also tended to be lower as age increased. Crude and adjusted ORs for high triglycerides and high LDL cholesterol of subjects with a high or large adiposity index versus subjects without a high or large adiposity index also tended to decrease with age in men and women (Table 1).
Table 1—ORs for hyperglycemia, high triglycerides, and high LDL cholesterol of subjects with a high or large adiposity index versus subjects without a high or large adiposity index in men and women

| Variable     | Hyperglycemia | High triglycerides | High LDL cholesterol |
|--------------|---------------|--------------------|----------------------|
|              | High BMI      | Large WC           | High WHtR            | High BMI      | Large WC           | High WHtR            |
| **Men**      |               |                    |                      |               |                    |                      |
| 35–39 years  |               |                    |                      |               |                    |                      |
| Crude        | 4.45 (3.73–5.32)* | 4.06 (3.38–4.88)* | 4.47 (3.73–5.35)* | 3.69 (3.28–4.15)* | 3.40 (3.03–3.81)* | 3.70 (3.30–4.16)* |
| Adjusted     | 4.16 (3.47–4.97)* | 3.92 (3.26–4.71)* | 4.25 (3.55–5.11)* | 3.74 (3.32–4.22)* | 3.39 (3.02–3.80)* | 3.71 (3.29–4.17)* |
| 40–49 years  |               |                    |                      |               |                    |                      |
| Crude        | 3.41 (3.08–3.76)* | 2.96 (2.68–3.27)* | 3.13 (2.84–3.45)* | 2.83 (2.62–3.06)* | 3.05 (2.82–3.28)* | 2.92 (2.71–3.15)* |
| Adjusted     | 3.39 (3.08–3.73)* | 2.95 (2.67–3.26)* | 3.07 (2.78–3.38)* | 2.87 (2.65–3.10)* | 3.02 (2.80–3.26)* | 2.91 (2.70–3.14)* |
| 50–59 years  |               |                    |                      |               |                    |                      |
| Crude        | 2.50 (2.31–2.70)* | 2.21 (2.05–2.42)* | 2.25 (2.09–2.42)* | 2.35 (2.18–2.53)* | 2.75 (2.56–2.95)* | 2.74 (2.55–2.95)* |
| Adjusted     | 2.49 (2.31–2.69)* | 2.24 (2.08–2.41)* | 2.23 (2.07–2.40)* | 2.37 (2.19–2.55)* | 2.74 (2.55–2.95)* | 2.80 (2.60–3.01)* |
| 60–70 years  |               |                    |                      |               |                    |                      |
| Crude        | 1.80 (1.60–2.02)* | 1.75 (1.57–1.95)* | 1.73 (1.54–1.93)* | 2.23 (1.98–2.51)* | 2.64 (2.35–2.96)* | 2.96 (2.61–3.36)* |
| Adjusted     | 1.78 (1.59–2.00)* | 1.76 (1.58–1.97)* | 1.72 (1.54–1.93)* | 2.22 (1.96–2.50)* | 2.63 (2.34–2.96)* | 3.06 (2.70–3.48)* |
| Trend (P)    | < 0.001       | < 0.001            | < 0.001              | < 0.001       | < 0.001            | < 0.001              |
| **Women**    |               |                    |                      |               |                    |                      |
| 35–39 years  |               |                    |                      |               |                    |                      |
| Crude        | 5.91 (4.24–8.24)* | 4.66 (3.34–6.51)* | 4.79 (3.42–6.71)* | 5.87 (4.30–8.00)* | 4.82 (3.53–6.57)* | 5.17 (3.77–7.08)* |
| Adjusted     | 5.83 (4.17–8.14)* | 4.68 (3.34–6.54)* | 4.76 (3.39–6.67)* | 5.93 (4.34–8.11)* | 4.81 (3.52–6.57)* | 5.17 (3.78–7.09)* |
| 40–49 years  |               |                    |                      |               |                    |                      |
| Crude        | 4.04 (3.49–4.68)* | 3.42 (2.96–3.95)* | 3.47 (3.00–4.02)* | 4.32 (3.70–5.03)* | 4.09 (3.50–4.77)* | 3.84 (3.28–4.49)* |
| Adjusted     | 4.01 (3.46–4.65)* | 3.37 (2.92–3.89)* | 3.35 (2.89–3.88)* | 4.15 (3.55–4.85)* | 3.99 (3.41–4.66)* | 3.71 (3.16–4.35)* |
| 50–59 years  |               |                    |                      |               |                    |                      |
| Crude        | 2.56 (2.29–2.87)* | 2.23 (2.01–2.47)* | 2.29 (2.05–2.55)* | 2.55 (2.25–2.89)* | 2.60 (2.31–2.94)* | 3.02 (2.64–3.45)* |
| Adjusted     | 2.56 (2.28–2.86)* | 2.18 (1.96–2.41)* | 2.19 (1.97–2.45)* | 2.50 (2.20–2.83)* | 2.56 (2.26–2.89)* | 2.98 (2.60–3.41)* |
| 60–70 years  |               |                    |                      |               |                    |                      |
| Crude        | 2.16 (1.74–2.69)* | 1.68 (1.38–2.04)* | 1.50 (1.21–1.86)* | 1.96 (1.54–2.49)* | 2.26 (1.78–2.87)* | 2.16 (1.64–2.84)* |
| Adjusted     | 2.10 (1.68–2.62)* | 1.65 (1.36–2.02)* | 1.46 (1.17–1.82)* | 1.91 (1.49–2.43)* | 2.25 (1.76–2.87)* | 2.16 (1.63–2.87)* |
| Trend (P)    | < 0.001       | < 0.001            | < 0.001              | < 0.001       | < 0.001            | < 0.001              |

Crude and adjusted ORs (95% CI) for hyperglycemia, high triglycerides, and high LDL cholesterol are shown. Adjusted ORs were calculated using age, smoking, alcohol drinking, and habitual exercise as other explanatory variables in logistic regression analysis. Therapy for dyslipidemia was also added to explanatory variables for calculation of ORs for high triglycerides and high LDL cholesterol. P values for trends across the age groups are also shown. WC, waist circumference. *P < 0.001. †P < 0.05.
CONCLUSIONS — The association between obesity and hyperglycemia declined with age in men and women, although the association remained significant even in the highest age group. This age-dependent trend was consistent in any analyses using different adiposity-related indices. This study is, to the best of our knowledge, the first study showing an age-dependent significant attenuation of the association between obesity and glycemic status both in men and women. In addition, significant age-dependent declines were also found in the associations of obesity with dyslipidemias such as high triglycerides and high LDL cholesterol. Therefore, the associations between obesity and metabolic disorders, such as diabetes and dyslipidemia, are thought to decline with age.

There is limited information on whether and how age influences the relationship between obesity and diabetes. Two recent studies have reported results related to this topic. Effects of obesity evaluated by BMI on incidence of type 2 diabetes have been reported to decline with age in women but not in men, and the authors speculated that the sex difference observed was due to the smaller population size of male subjects than that of female subjects (13). Another study showed that the correlation coefficient between waist circumference and fasting blood glucose tended to be higher in younger (≤51 years) than in older (>51 years) men and women, although the differences in the correlation between the younger and older subjects were not significant (14). The current study clearly demonstrated significant age-dependent declines of the associations of obesity with hyperglycemia and dyslipidemia in men and women.

Taken together with these findings, our results suggest that the effect of obesity on development of diabetes is stronger in younger people than in older people. This also suggests that correction of obesity is more effective for prevention of diabetes in younger people than in older people and agrees with a consensus that young people should be encouraged to attain and maintain a weight-for-height ratio in the normal range to prevent type 2 diabetes (15). The age-dependent declines in the associations of obesity with hyperglycemia and dyslipidemia may partly explain the weaker association between obesity and the risk for coronary heart disease in older men than in younger men (8,9).

In conclusion, the association between obesity and hyperglycemia is stronger in younger men and women than in older men and women, respectively, and this finding supports a general concept of the necessity of body weight control in young people from the viewpoint of prevention of type 2 diabetes.

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I.W. researched data, performed the statistical analyses, wrote the manuscript, and is guarantor for the article. T.D. performed the statistical analyses.

References
1. Klenk J, Nagel G, Ulmer H, et al.; The VHM&PP Study Group. Body mass index and mortality: results of a cohort of 184,697 adults in Austria. Eur J Epidemiol 2009;24:83–91.
2. Berrington de Gonzalez A, Hartge P, Cerhan JR, et al. Body-mass index and mortality among 1.46 million white adults. N Engl J Med 2010;363:2211–2219.
3. Whitlock G, Lewington S, Sherliker P, et al.; Prospective Studies Collaboration. Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. Lancet 2009;373:1083–1096.
4. Bender R, Jöckel KH, Trautner C, Spraul M, Berger M. Effect of age on excess mortality in obesity. JAMA 1999;281:1498–1504.
5. Stevens J, Cai J, Juhaeri, Thun MJ, Williamson DF, Wood JL. Consequences of the use of different measures of effect to determine the impact of age on the association between obesity and mortality. Am J Epidemiol 1999;150:399–407.
6. Reuser M, Bonneux L, Willekens F. The burden of mortality of obesity at middle and old age is small. A life table analysis of the US Health and Retirement Survey. Eur J Epidemiol 2008;23:601–607.
7. Kuk JL, Ardern CI. Influence of age on the association between various measures of obesity and all-cause mortality. J Am Geriatr Soc 2009;57:2077–2084.
8. Rimm EB, Stampfer MJ, Giovannucci E, et al. Body size and fat distribution as predictors of coronary heart disease among middle-aged and older US men. Am J Epidemiol 1995;141:1117–1127.
9. Shiraishi J, Kohno Y, Sawada T, et al.; The AMI-Kyoto Multi-Center Risk Study Group. Relation of obesity to acute myocardial infarction in Japanese patients. Differences in gender and age. Circ J 2006;70:1525–1530.
10. Jack L Jr, Boeseman L, Vinicor F. Aging Americans and diabetes. A public health and clinical response. Geriatrics 2004;59:14–17.
11. The Committee of Japan Diabetes Society on the diagnostic criteria of diabetes mellitus. Report of the committee on the classification and diagnostic criteria of diabetes mellitus. J Japan Diab Soc 2010;53:450–467 [in Japanese].
12. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2011;34(Suppl. 1):S62–S69.
13. Fujita M, Ueno K, Hata A. Effect of obesity on incidence of type 2 diabetes declines with age among Japanese women. Exp Biol Med (Maywood) 2009;234:750–757.
14. Oda E, Kawai R. Age- and gender-related differences in correlations between abdominal obesity and obesity-related metabolic risk factors in Japanese. Intern Med 2009;48:497–502.
15. Bloomgarden ZT. Prevention of obesity and diabetes. Diabetes Care 2003;26:3172–3178.