

NIH Public Access

Author Manuscript

Stroke. Author manuscript; available in PMC 2009 October 1.

Published in final edited form as:

Stroke. 2009 April ; 40(4): 1098–1104. doi:10.1161/STROKEAHA.108.539692.

General and Abdominal Adiposity and Risk of Stroke in Chinese Women

Xianglan Zhang, MD, MPH, Xiao-Ou Shu, MD, PhD, Yu-Tang Gao, MD, Gong Yang, MD, MPH, Honglan Li, MD, and Wei Zheng, MD, PhD

Department of Medicine, Vanderbilt Epidemiology Center, Vanderbilt University School of Medicine, Nashville, TN 37232, USA (Drs Zhang, Shu, Yang, and Zheng) and Department of Epidemiology, Shanghai Cancer Institute, Shanghai 200032, China (Drs Gao and Li)

Abstract

Background and Purpose—Although both general and abdominal adiposity are well-established risk factors for coronary heart disease, their associations with stroke are less well characterized, particularly in generally lean Asian populations.

Methods—We evaluated associations of body mass index (BMI), waist-hip ratio (WHR), waist circumference (WC), and waist-height ratio (WHR) with stroke risk in the Shanghai Women's Health Study, a population-based, prospective cohort study of 74 942 Chinese women aged 40–70 years with anthropometric measurement taken at recruitment in 1996–2000. For this analysis, we included 67 083 women with no prior history of stroke, coronary heart disease, rheumatic heart disease, cardiac surgery, or cancer at recruitment. Incident stroke was ascertained by biennial home visits and linkage with vital statistics registries.

Results—Cutpoints for the highest quintiles of BMI, WHR, WC, and WHtR among this cohort were 26.6 (kg/m²), 0.85 (cm/cm), 84.1 (cm), and 0.54 (cm/cm), respectively. During a mean follow-up of 7.3 years, 2403 incident stroke cases were identified. All selected anthropometric measurements were positively and significantly associated with risk of total, ischemic, and hemorrhagic stroke in a dose-response manner (all *P* values for trend <0.01). The multivariable-adjusted hazard ratios (95% confidence intervals) for total stroke comparing the highest vs. lowest quintiles of these measurements were 1.71 (1.49–1.97), 1.59 (1.37–1.85), 1.77 (1.53–2.05), and 1.91 (1.61–2.27) for BMI, WHR, WC, and WHtR, respectively.

Conclusion—Increasing levels of general or abdominal adiposity consistently predict increased risk of stroke in predominantly non-obese Chinese women.

Keywords

adiposity; stroke; women

Disclosure of conflicts of interests: None reported.

To whom correspondence and requests for reprints should be addressed: Xianglan Zhang, MD, MPH, Vanderbilt Epidemiology Center, Institute for Medicine & Public Health, Vanderbilt University Medical Center, Sixth Floor, Suite 600, 2525 West End Avenue, Nashville, TN 37203-1738, Telephone: 615-936-0956, Fax: 615-936-8291, E-mail: xianglan.zhang@vanderbilt.edu.

Publisher's Disclaimer: This is an un-copyedited author manuscript that was accepted for publication in Stroke, copyright: TheAmerican Heart Association. This may not be duplicated or reproduced, other than for personal use orwithin the "Fair Use of Copyrighted Materials" (section 107, title 17, U.S. Code) without prior permission of the copyright owner, The American Heart Association. The final copyedited article, which is the version frecord, can be found at Stroke. The American Heart Association disclaims any responsibility or liability for errors or omissions in this version of the manuscript or in any version derived from it by the NationalInstitutes of Health or other parties.

Both general adiposity, measured by body mass index (BMI), and abdominal adiposity, measured by waist-hip ratio (WHR), are well-documented risk factors for coronary heart disease; 1^{-3} their associations with stroke, however, are less well characterized. Several studies have shown a significant positive association between BMI and risk of stroke, 4^{-6} while others suggest that high WHR, but not BMI, is associated with an increased risk of stroke.^{7, 8} These findings are primarily related to ischemic stroke. The association between BMI or WHR and risk of hemorrhagic stroke remains largely unclear.

Most epidemiologic investigations of adiposity and fat distribution in relation to stroke have been conducted in Western populations, where overweight and obesity are highly prevalent. Few studies to date have evaluated stroke incidence associated with excess adiposity, particularly abdominal obesity, in Asian populations, which are generally on the lower end of the BMI spectrum. Given the observation that some Asian populations develop vascular risk factors, including type 2 diabetes, hypertension, and dyslipidemia, at relatively lower levels of BMI, as compared with their Western counterparts,⁹, ¹⁰ it is important to examine whether high levels of general and abdominal adiposity contribute to the development of stroke in Asian populations.

We examined associations of BMI, WHR, and other measures of abdominal adiposity, including waist circumference (WC) and waist-height ratio (WHtR), with risk of total stroke and major stroke subtypes in a large cohort of Chinese women with an average BMI of 23.9 at the time of enrollment in the Shanghai Women's Health Study (SWHS).

METHODS

Study population

The SWHS is a population-based, prospective cohort study of adult Chinese women. The study methods have been described in detail elsewhere.¹¹ Briefly, all eligible women 40 to 70 years of age and living in seven typical urban communities of Shanghai were invited to participate in the study. Between December 1996 and May 2000, a total of 74 942 women were enrolled, with a participation rate of 92.7%. Baseline surveys and anthropometric measurements were conducted at participants' homes by trained interviewers. Structured questionnaires were used during the surveys to obtain information on demographics, diet and other lifestyle habits, menstrual and reproductive history, use of oral contraceptives and hormone therapy, medical history, and other characteristics. The food-frequency and physical-activity questionnaires used in the SWHS have been validated.¹², ¹³

Anthropometry

Participants were asked to wear light indoor clothing when they were measured for weight, height, and circumferences of the waist and hips by trained interviewers who were retired health professionals. Measurements were taken uniformly according to a standard protocol. Weight was measured to the nearest 0.1 kg, using a digital weight scale that was calibrated every 6 months. Waist circumference was measured at 2.5 cm above the umbilicus and hip circumference at the level of maximum width of the buttocks with the subject in a standing position. Circumferences and height were measured to the nearest 0.1 cm. All measurements were taken twice. A tolerance limit of 1 kg was set for weight measurement and 1 cm for height and circumference measurements. A third measurement was taken if the difference of the first two measurements was greater than the tolerance limit. Using the average of the two closest measurements, BMI (weight in kilograms divided by the square of height in meters), WHR (waist circumference divided by hip circumference), and WHtR (waist circumference divided by height) were then calculated for the analysis.

Outcome ascertainment

The primary outcome for the present analysis was incident stroke, defined as the first nonfatal stroke or stroke death that occurred after the baseline survey. Participants were followed through biennial home visits and record linkage to the Shanghai Cancer Registry and the Shanghai Vital Statistics Registry. During the biennial home visits, trained study interviewers conducted an in-person interview using a structured questionnaire that captured information on newly diagnosed major chronic diseases. For deceased subjects, an adult family member (next of kin) was interviewed to complete the disease outcome survey. The occurrence of stroke was ascertained by asking the following question: "Since our last visit, have you suffered a stroke that was confirmed by a doctor?" For each positive response, information on the date and hospital of first diagnosis was obtained. Information on major stroke subtypes, including ischemic stroke and intracerebral hemorrhage, was also collected through in-person interviews starting with the second follow-up. In addition to biennial home visits, disease outcomes and deaths were also ascertained through record linkages. The underlying cause of death was determined on the basis of death certificates and information gathered from the next of kin.

To evaluate the validity of stroke ascertainment via structured in-person interviews in this cohort, medical records were obtained and reviewed by independent physicians for 225 participants who reported a first-ever stroke during follow-up interviews. Brain imaging, including computed tomography or magnetic resonance imaging, was available for 95% of these reported stroke cases. The diagnosis of stroke was confirmed according to the criteria of the U.S. National Survey of Stroke, which requires evidence of sudden or rapid onset of neurologic deficits that persist for more than 24 hours or until death, and have no apparent nonvascular causes such as trauma, tumor, or infection.¹⁴ Based on review of clinical information and imaging data, 203 (90.2%) stroke cases were confirmed, including 177 cases of ischemic stroke, 22 intracerebral hemorrhage, and 4 subarachnoid hemorrhage. Nine (4.0%) reported stroke cases did not meet the defined criteria for confirmation. Medical documentation was lacking or insufficient to confirm the diagnosis for the remaining 13 (5.8%) cases.

Statistical analysis

For the present analysis, we excluded women who reported a prior history of stroke, coronary heart disease, rheumatic heart disease, cardiac surgery, or cancer at baseline (n=7813). We also excluded those who were pregnant (n=10), were lost to follow-up shortly after enrollment (n=8), or had missing data for anthropometric measurements (n=39). After these exclusions (not mutually exclusive), 67 083 women remained for the analysis. Women were categorized according to quintiles of BMI, WHR, WC, and WHtR, with the lowest quintile serving as the reference category. Cox proportional hazards models were used, with age as the time scale, to estimate hazard ratios (HRs) of stroke associated with various anthropometric measures and 95% confidence intervals (CIs), and to adjust for potential confounders.¹⁵ Entry time was defined as the age at enrollment, and exit time was defined as the age at stroke diagnosis, death or censoring. Covariates included age (continuous); education level (four categories); occupation (three categories); annual family income (four categories); menopausal status (preor post-menopausal); use of oral contraceptives, hormone therapy, and aspirin (yes or no); amount of regular exercise (hours/week, four categories); cigarette smoking (yes or no); alcohol consumption (yes or no); and intakes of saturated fat, vegetables, fruits, and sodium (continuous). Considering that hypertension, diabetes, and dyslipidemia are in the causal pathway between adiposity and stroke, these factors were not adjusted for in primary analyses. Tests for linear trend across categories of anthropometric measurements were performed by using the median value for each category of the measurements and modeling them as continuous variables. In addition, we evaluated the joint effect of BMI and WHR on stroke risk. Finally, we calculated c statistics for various selected measures of adiposity to compare their predictive values. Statistical analyses were performed using SAS statistical software

(version 9.1; SAS Institute Inc., Cary, NC, USA). All statistical tests were based on two-sided probability.

RESULTS

Table 1 presents selected characteristics of the study population. The mean age (standard deviation [SD]) of the study population was 51 years (8.8) at baseline. The mean values (SD) for BMI, WHR, WC, and WHtR were 23.9 (3.4) kg/m², 0.81 (0.05) cm/cm, 77.4 (8.6) cm, and 0.49 (0.06) cm/cm, respectively. The prevalence of overweight or obesity (BMI \ge 25 kg/m²) was 33.7%, and the prevalence of obesity (BMI \ge 30 kg/m²) was 4.6%. Very few women ever smoked cigarettes, drank alcohol, or used hormone therapy. WHR was moderately correlated with BMI (Pearson correlation, r=0.46), whereas the correlations of both WC (r=0.84) and WHtR (r=0.83) with BMI were high.

During a mean follow-up of 7.3 years, we identified 2403 incident cases of stroke, including 2260 nonfatal strokes and 143 deaths from stroke. These cases were further classified as ischemic stroke (n=1737), intracerebral hemorrhage (n=205), and undefined stroke (n=461). Table 2 summarizes the HRs and 95% CIs of total stroke by quintiles of various measures of adiposity. In both age- and multivariable-adjusted analyses, BMI, WHR, WC, and WHtR were all positively and significantly associated with risk of total stroke in a dose-response fashion (all *P* values for trend <0.0001). The multivariable-adjusted HRs (95% CIs) for total stroke comparing the highest vs. lowest quintiles of these measurements were 1.71 (1.49–1.97) for BMI, 1.59 (1.37–1.85) for WHR, 1.77 (1.53–2.05) for WC, and 1.91 (1.61–2.27) for WHtR. Further adjustment for history of hypertension, diabetes, and dyslipidemia reduced the risk estimates to 1.31 (1.14–1.51), 1.30 (1.12–1.51), 1.34 (1.16–1.56), and 1.46 (1.22–1.74) for BMI, WHR, WC, and WHtR, respectively.

When anthropometric measures were analyzed as continuous variables, for each 1-unit increase in BMI and WC, stroke risk increased by 5% (HR=1.05; 95% CI, 1.04–1.07) and 2% (HR=1.02; 95% CI, 1.02–1.03), respectively, after adjusting for potential confounders. For each 0.01-unit increase in WHR and WHtR, the risk increased by 3% (HR=1.03; 95% CI, 1.02–1.03) and 4% (HR=1.03; 95% CI, 1.03–1.05), respectively. These results were essentially unchanged when the analyses were confined to women with a BMI <25 kg/m².

As shown in Table 2, the associations with measures of abdominal adiposity were attenuated, but all remained statistically significant after adjustment for BMI. The association with BMI, on the other hand, was no longer significant when WHtR was controlled for, but remained significant following adjustment for WHR or WC. Table 3 presents the joint effect of BMI and WHR on the risk of total stroke. Within each category of BMI, the HRs of stroke increased steadily with increasing tertiles of WHR; likewise, BMI was positively associated with risk of stroke across all levels of WHR. Women in the top tertiles of both BMI and WHR had the highest HR of stroke. A test for interaction between BMI and WHR was not statistically significant (P=0.90).

Table 4 presents the multivariable-adjusted HRs of major stroke subtypes associated with selected measures of adiposity. Consistent with the findings for total stroke, the HRs for both ischemic stroke and intracerebral hemorrhage also increased monotonically with increasing levels of BMI, WHR, WC, and WHtR. The positive association of each measure of adiposity with intracerebral hemorrhage appeared to be stronger than that for ischemic stroke, although the effect estimates for the former were less precise because of the small number of cases. Strong positive associations with all anthropometric measures were also observed for undefined stroke, many of which were likely to be hemorrhagic. Multinomial logistic regression analyses also showed stronger associations with hemorrhagic than with ischemic

stroke. The adjusted regression coefficients for intracerebral hemorrhage and ischemic stroke were 0.09 vs. 0.05 for BMI, 0.04 vs. 0.02 for both WHR and WC, and 0.06 vs. 0.03 for WHtR.

Finally, analyses with *c* statistics showed no difference in the predictive value for stroke among various measures of adiposity; the *c* statistics were 0.804, 0.803, 0.805, and 0.806 for multivariable models of total stroke that included BMI, WHR, WC, and WHtR, respectively.

DISCUSSION

In this large prospective cohort study of Chinese women, we found that high levels of BMI, WHR, WC, and WHtR were all associated with significantly increased risk of total, ischemic, and hemorrhagic stroke. To our knowledge, this is the first cohort study that has evaluated the contributions of both general and abdominal adiposity to the risk of stroke in Asian women. Two thirds of the study population had a BMI below 25.0, the cut-off point for overweight. Despite this normal/low weight range, a consistent, monotonic dose-response relationship was observed between stroke and various anthropometric variables that capture different aspects of adiposity. Our results suggest that the increased risk of stroke associated with increasing adiposity may exist on a continuum.

Consistent with previous studies,^{4, 6} our analyses showed that the positive associations between measures of adiposity and stroke were attenuated substantially but remained statistically significant after accounting for hypertension, diabetes, and dyslipidemia, all of which are well-established vascular risk factors closely related to adiposity. These findings suggest that although the established risk factors play an important role in mediating the adverse effects of adiposity on stroke, other mechanisms may also be involved. It has been shown that obesity is associated with elevated levels of prothrombotic factors, such as fibrinogen and plasminogen activator inhibitor-1, and inflammatory biomarkers, such as C-reactive protein, interleukin-6, and tumor necrosis factor- α .^{16–18} The prothrombotic and proinflammatory state induced by excess adiposity is believed to be an important contributor to the development of stroke.¹⁹

Despite the strong biologic plausibility that excess adiposity may confer an increased risk of stroke, epidemiologic investigations of the relationship between adiposity and stroke have yielded conflicting results. In the Nurses' Health Study⁴ and the Women's Health Study,⁶ high BMI was associated with a significantly increased risk of total and ischemic stroke, but not hemorrhagic stroke. In contrast, a consistent positive association was observed between BMI and risk of total, ischemic, and hemorrhagic stroke in the Physicians' Health Study,⁵ similar to our finding. High BMI was also found to predict stroke incidence and stroke mortality regardless of stroke subtypes in two large studies of Korean and Chinese men.²⁰, ²¹ No association between BMI and risk of total stroke or stroke subtypes, however, was observed in several other studies.⁷, ⁸, ²² In addition, there are also few reports of an inverse association between BMI and stroke.²³ Although the reasons for the inconsistency of the BMI and stroke relationship remain unclear, the inherent limitations of BMI as a surrogate measure of overall adiposity, which provides no direct information regarding body composition or fat distribution, may be a contributing factor.⁷

It has been increasingly recognized that the adverse effects of obesity relate not only to the amount but also to the distribution of excess body fat.^{24–26} There are several studies that, while they failed to link BMI levels with stroke risk, did find a significant association between measures of abdominal obesity and risk of stroke.^{7, 8} For example, in the Health Professionals Follow-up Study, WHR, but not BMI, was found to be a significant independent predictor of total stroke in men.⁷ Similar results were also observed in both men and women in the Northern Manhattan Stroke Study involving ischemic stroke only.⁸ In a recent cohort study of Swedish

women, all measures of abdominal adiposity, including WHR, WC, and WHtR, showed significant positive associations with risk of total and ischemic stroke and a less significant association with intracerebral hemorrhage.²⁷ No previous studies have investigated abdominal adiposity in relation to stroke in Asian populations.

Unlike many previous studies showing a complex relationship between adiposity and risk of stroke, our study found that higher degrees of adiposity consistently predicted an increased risk of stroke, regardless of the obesity measures used or the stroke subtypes included. The observed positive association between adiposity and stroke in our study also appeared to be stronger than those positive associations seen in studies of Caucasian women. For example, a 1-unit increase in BMI was associated with a 5% increase in total stroke in our study, whereas the increase was 3% in the Nurses' Health Study.⁴ The finding of an increased risk of hemorrhagic stroke with increasing adiposity from our study and others provides evidence against the hypothesis that low BMI may contribute to high incidence of hemorrhagic stroke in Asian populations.⁶

Limitations of our study, however, need to be kept in mind when interpreting the results. Although all anthropometric variables used in our study were accurately measured rather than self-reported, stroke outcome was assessed through a structured in-person interview without further verification by review of medical records, raising concern about misclassification of stroke. However, our validation study indicated that stroke assessment via in-person interview in our cohort was accurate. Previous studies have also shown that even with a self-administered questionnaire, stroke, a life-threatening medical emergency, could be assessed reasonably well. ²⁸ In addition, the age-standardized incidence rate of first-ever stroke (141.1/100 000) observed in our cohort was comparable to rates reported for the Sino-MONICA-Beijing project (138.7/100 000-169.4/100 000 during 2000–2004), which involved women 25–74 years of age in Beijing.²⁹ Another concern is the possible presence of residual confounding due to inaccurately measured or unmeasured covariates. Although we cannot rule out this possibility, we have carefully adjusted for a range of potential confounders and found results similar to analyses adjusted for age only, suggesting that residual confounding is unlikely to have seriously affected our results.

In summary, our study indicates that even in a relatively lean population, increasing levels of general or abdominal adiposity were associated with a significant increase in the risk of stroke. Our findings, along with those observed from mostly overweight Western populations, emphasize the importance of preventing excess adiposity for primary prevention of stroke.

Acknowledgements

This study was supported by research grants R01CA70867 and R01HL079123 from the National Institutes of Health. Dr. Zhang was supported by an NIH-sponsored Building Interdisciplinary Research Careers in Women's Health (BIRCWH) Program at Vanderbilt University (2K12HD043483-06). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

References

- Willett WC, Manson JE, Stampfer MJ, Colditz GA, Rosner B, Speizer FE, Hennekens CH. Weight, weight change, and coronary heart disease in women. Risk within the 'normal' weight range. JAMA 1995;273(6):461–5. [PubMed: 7654270]
- Rexrode KM, Carey VJ, Hennekens CH, Walters EE, Colditz GA, Stampfer MJ, Willett WC, Manson JE. Abdominal adiposity and coronary heart disease in women. JAMA 1998;280(21):1843–8. [PubMed: 9846779]

- Zhang X, Shu XO, Gao YT, Yang G, Matthews CE, Li Q, Li H, Jin F, Zheng W. Anthropometric predictors of coronary heart disease in Chinese women. Int J Obes Relat Metab Disord 2004;28(6): 734–40. [PubMed: 15052279]
- Rexrode KM, Hennekens CH, Willett WC, Colditz GA, Stampfer MJ, Rich-Edwards JW, Speizer FE, Manson JE. A prospective study of body mass index, weight change, and risk of stroke in women. JAMA 1997;277(19):1539–45. [PubMed: 9153368]
- Kurth T, Gaziano JM, Berger K, Kase CS, Rexrode KM, Cook NR, Buring JE, Manson JE. Body mass index and the risk of stroke in men. Arch Intern Med 2002;162(22):2557–62. [PubMed: 12456227]
- Kurth T, Gaziano JM, Rexrode KM, Kase CS, Cook NR, Manson JE, Buring JE. Prospective study of body mass index and risk of stroke in apparently healthy women. Circulation 2005;111(15):1992–8. [PubMed: 15837954]
- Walker SP, Rimm EB, Ascherio A, Kawachi I, Stampfer MJ, Willett WC. Body size and fat distribution as predictors of stroke among US men. Am J Epidemiol 1996;144(12):1143–50. [PubMed: 8956626]
- Suk SH, Sacco RL, Boden-Albala B, Cheun JF, Pittman JG, Elkind MS, Paik MC. Abdominal obesity and risk of ischemic stroke: the Northern Manhattan Stroke Study. Stroke 2003;34(7):1586–92. [PubMed: 12775882]
- 9. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. The Lancet 2004;363(9403):157–63.
- Hu FB, Wang B, Chen C, Jin Y, Yang J, Stampfer MJ, Xu X. Body mass index and cardiovascular risk factors in a rural Chinese population. Am J Epidemiol 2000;151(1):88–97. [PubMed: 10625178]
- Zheng W, Chow WH, Yang G, Jin F, Rothman N, Blair A, Li HL, Wen W, Ji BT, Li Q, Shu XO, Gao YT. The Shanghai Women's Health Study: rationale, study design, and baseline characteristics. Am J Epidemiol 2005;162(11):1123–31. [PubMed: 16236996]
- Shu XO, Yang G, Jin F, Liu D, Kushi L, Wen W, Gao YT, Zheng W. Validity and reproducibility of the food frequency questionnaire used in the Shanghai Women's Health Study. Eur J Clin Nutr 2004;58(1):17–23. [PubMed: 14679362]
- Matthews CE, Shu XO, Yang G, Jin F, Ainsworth BE, Liu D, Gao YT, Zheng W. Reproducibility and validity of the Shanghai Women's Health Study physical activity questionnaire. Am J Epidemiol 2003;158(11):1114–22. [PubMed: 14630608]
- Walker AE, Robins M, Weinfeld FD. The National Survey of Stroke. Clinical findings. Stroke 1981;12(2 Pt 2 Suppl 1):I13–I44. [PubMed: 7222164]
- 15. Korn EL, Graubard BI, Midthune D. Time-to-event analysis of longitudinal follow-up of a survey: choice of the time-scale. Am J Epidemiol 1997;145(1):72–80. [PubMed: 8982025]
- Van Gaal LF, Mertens IL, De Block CE. Mechanisms linking obesity with cardiovascular disease. Nature 2006;444(7121):875–80. [PubMed: 17167476]
- Berg AH, Scherer PE. Adipose Tissue, Inflammation, and Cardiovascular Disease. Circ Res 2005;96 (9):939–49. [PubMed: 15890981]
- Mora S, Lee IM, Buring JE, Ridker PM. Association of Physical Activity and Body Mass Index With Novel and Traditional Cardiovascular Biomarkers in Women. JAMA 2006;295(12):1412–9. [PubMed: 16551713]
- Ridker PM. Inflammatory Biomarkers, Statins, and the Risk of Stroke: Cracking a Clinical Conundrum. Circulation 2002;105(22):2583–5. [PubMed: 12045159]
- Song YM, Sung J, Davey SG, Ebrahim S. Body mass index and ischemic and hemorrhagic stroke: a prospective study in Korean men. Stroke 2004;35(4):831–6. [PubMed: 15001798]
- Zhou M, Offer A, Yang G, Smith M, Hui G, Whitlock G, Collins R, Huang Z, Peto R, Chen Z. Body mass index, blood pressure, and mortality from stroke: a nationally representative prospective study of 212,000 Chinese men. Stroke 2008;39(3):753–9. [PubMed: 18239175]
- 22. Folsom AR, Rasmussen ML, Chambless LE, Howard G, Cooper LS, Schmidt MI, Heiss G. Prospective associations of fasting insulin, body fat distribution, and diabetes with risk of ischemic stroke. The Atherosclerosis Risk in Communities (ARIC) Study Investigators. Diabetes Care 1999;22 (7):1077–83. [PubMed: 10388971]
- 23. Cui R, Iso H, Toyoshima H, Date C, Yamamoto A, Kikuchi S, Kondo T, Watanabe Y, Koizumi A, Wada Y, Inaba Y, Tamakoshi A. Body mass index and mortality from cardiovascular disease among Japanese men and women: the JACC study. Stroke 2005;36(7):1377–82. [PubMed: 15920029]

- Despres JP, Lemieux I. Abdominal obesity and metabolic syndrome. Nature 2006;444(7121):881– 7. [PubMed: 17167477]
- de KL, Merchant AT, Pogue J, Anand SS. Waist circumference and waist-to-hip ratio as predictors of cardiovascular events: meta-regression analysis of prospective studies. Eur Heart J 2007;28(7): 850–6. [PubMed: 17403720]
- 26. Zhang X, Shu XO, Yang G, Li H, Cai H, Gao YT, Zheng W. Abdominal Adiposity and Mortality in Chinese Women. Arch Intern Med 2007;167(9):886–92. [PubMed: 17502529]
- 27. Lu M, Ye W, Adami HO, Weiderpass E. Prospective study of body size and risk for stroke amongst women below age 60. J Intern Med 2006;260(5):442–50. [PubMed: 17040250]
- Engstad T, Bonaa KH, Viitanen M. Validity of Self-Reported Stroke: The Tromso Study. Stroke 2000;31(7):1602–7. [PubMed: 10884460]
- Zhao D, Liu J, Wang W, Zeng Z, Cheng J, Liu J, Sun J, Wu Z. Epidemiological transition of stroke in China: twenty-one-year observational study from the Sino-MONICA-Beijing Project. Stroke 2008;39(6):1668–74. [PubMed: 18309149]

Table 1

Selected characteristics of the study population

Variable	
Age (y), mean (SD)	51.3 (8.8)
Body mass index (kg/m ²), mean (SD)	23.9 (3.4)
Waist-hip ratio, mean (SD)	0.81 (0.05)
Waist circumference, mean (SD)	77.4 (8.6)
Waist-height ratio, mean (SD)	0.49 (0.06)
Regular exercise (h/week), mean (SD)	1.9 (3.6)
Education level, %	
≤Elementary school	19.6
Middle school	38.3
High school	28.6
≥College	13.5
Occupation, %	
Professionals, technicians, administrators	28.3
Clerical and service workers	21.0
Manufacturing and agricultural workers	50.7
Annual family income (yuan), %	
< 10,000	15.6
10,000 to < 20,000	38.1
20,000 to < 30,000	28.5
\geq 30,000	17.8
Postmenopausal, %	45.2
Hormone therapy, %	2.0
Oral contraceptive use, %	20.3
Aspirin use, %	1.3
Ever smoked cigarettes, %	2.7
Ever drank alcohol, %	2.3

_
_
_
_
U
<u> </u>
~
-
_
<u> </u>
_
_
\mathbf{O}
<u> </u>
_
_
<
0
L L
_
_
0)
ä
0

NIH-PA Author Manuscript

NIH-PA Author Manuscript

 Table 2

 Hazard ratios (HRs) of total stroke according to quintiles of body mass index, waist-hip ratio, waist circumference, and waist-height ratio

		0	juintiles of anthropometric m	easures		
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P for trend
Body mass index, kg/m ²						
Quintile cutoffs	<21.1	21.1–22.7	22.8–24.3	24.4–26.5	≥26.6	
No. of subjects	13420	13391	13514	13341	13417	
No. of cases	269	320	403	584	827	
Age-adjusted HR	1.00	1.16 (0.99–1.36)	1.26 (1.08–1.47)	1.56 (1.35–1.81)	1.82 (1.59–2.10)	< 0.0001
Multivariate HR [*]	1.00	1.16 (0.98–1.36)	1.24 (1.06–1.45)	1.51 (1.30–1.74)	1.71 (1.49–1.97)	< 0.0001
Additionally adjusted for WHR	1.00	1.10 (0.93–1.29)	1.15 (0.98–1.34)	1.37 (1.17–1.59)	1.53 (1.32–1.78)	< 0.0001
Additionally adjusted for WC	1.00	1.08 (0.91–1.30)	1.08 (0.89–1.30)	1.20 (0.99–1.47)	1.24 (1.01–1.53)	0.03
Additionally adjusted for WHtR	1.00	1.01 (0.85–1.22)	0.97 (0.80–1.17)	1.06 (0.87–1.30)	1.10 (0.89–1.36)	0.17
Waist-hip ratio, cm/cm						
Quintile cutoffs	<0.77	0.77 - 0.78	0.79 - 0.81	0.82 - 0.84	≥0.85	
No. of subjects	13430	13495	13319	13345	13494	
No. of cases	231	322	416	576	858	
Age-adjusted HR	1.00	1.22 (1.03–1.45)	1.33 (1.13–1.56)	1.56 (1.34–1.82)	1.71 (1.48–1.98)	< 0.0001
Multivariate HR*	1.00	1.21 (1.02–1.43)	1.29 (1.10–1.52)	1.49 (1.28–1.74)	1.59 (1.37–1.85)	< 0.0001
Additionally adjusted for BMI	1.00	1.15 (0.97–1.36)	1.18 (1.00–1.39)	1.32 (1.12–1.55)	1.34 (1.15–1.57)	< 0.0001
Waist circumference, cm						
Quintile cutoffs	<70.1	70.1–75.0	75.1–79.0	79.1–84.0	≥84.1	
No. of subjects	14941	14755	11482	12590	13315	
No. of cases	237	311	336	549	970	
Age-adjusted HR	1.00	1.09 (0.92–1.29)	1.24 (1.05–1.47)	1.48 (1.27–1.73)	1.90 (1.64–2.19)	< 0.0001
Multivariate HR*	1.00	1.09 (0.92–1.30)	1.23 (1.04–1.45)	1.43 (1.22–1.67)	1.77 (1.53–2.05)	< 0.0001
Additionally adjusted for BMI	1.00	1.04 (0.87–1.26)	1.13 (0.92–1.38)	1.26 (1.03–1.55)	1.50 (1.21–1.86)	< 0.0001
Waist-height ratio, cm/cm						
Quintile cutoffs	<0.44	0.44-0.46	0.47 - 0.49	0.50 - 0.53	≥0.54	

Quintile 1 Quintile 3 Quintile 4 Quintile 5 Pfor No. of subjects 13404 13411 13642 13205 13421 13421 No. of subjects 163 220 363 581 1076 1076 No. of cases 163 220 363 581 1076 60: Age-adjusted HR 1.00 1.05 (0.86-1.28) 1.30 (1.08-1.57) 1.62 (1.36-1.94) 2.07 (1.75-2.46) <0: Multivariate HR* 1.00 1.05 (0.86-1.28) 1.27 (1.06-1.53) 1.55 (1.30-1.89) 1.91 (1.61-2.27) <0: Additionally adjusted for 1.00 1.05 (0.84-1.30) 1.26 (1.01-1.57) 1.50 (1.19-1.89) 1.77 (1.38-2.26) <0:			0	uintiles of anthropometric m	easures		
No. of subjects 13404 13411 13642 13205 13421 No. of subjects 163 220 363 581 1076 No. of cases 163 220 363 581 1076 Age-adjusted HR 1.00 1.05 (0.86-1.28) 1.30 (1.08-1.57) 1.62 (1.36-1.94) 2.07 (1.75-2.46) <0. Multivariate HR* 1.00 1.05 (0.86-1.28) 1.27 (1.06-1.53) 1.65 (1.30-1.85) 1.91 (1.61-2.27) <0. Additionally adjusted for 1.00 1.05 (0.84-1.30) 1.26 (1.01-1.57) 1.50 (1.19-1.89) 1.77 (1.38-2.26) <0.		Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P for trend
No. of cases 163 220 363 581 1076 Age-adjusted HR 1.00 1.05 (0.86–1.28) 1.30 (1.08–1.57) 1.62 (1.36–1.94) 2.07 (1.75–2.46) <0.	No. of subjects	13404	13411	13642	13205	13421	
Age-adjusted HR 1.00 1.05 (0.86-1.28) 1.30 (1.08-1.57) 1.62 (1.36-1.94) 2.07 (1.75-2.46) < 0. Multivariate HR* 1.00 1.05 (0.86-1.28) 1.27 (1.06-1.53) 1.55 (1.30-1.85) 1.91 (1.61-2.27) < 0.	No. of cases	163	220	363	581	1076	
Multivariate HR [*] 1.00 1.05 (0.86–1.28) 1.27 (1.06–1.53) 1.55 (1.30–1.85) 1.91 (1.61–2.27) < 0. Additionally adjusted for 1.00 1.05 (0.84–1.30) 1.26 (1.01–1.57) 1.50 (1.19–1.89) 1.77 (1.38–2.26) < 0. BMI	Age-adjusted HR	1.00	1.05 (0.86–1.28)	1.30 (1.08–1.57)	1.62 (1.36–1.94)	2.07 (1.75–2.46)	< 0.0001
Additionally adjusted for 1.00 1.05 (0.84–1.30) 1.26 (1.01–1.57) 1.50 (1.19–1.89) 1.77 (1.38–2.26) < 0. BMI	Multivariate HR [*]	1.00	1.05 (0.86–1.28)	1.27 (1.06–1.53)	1.55 (1.30–1.85)	1.91 (1.61–2.27)	< 0.0001
	Additionally adjusted for BMI	1.00	1.05 (0.84–1.30)	1.26 (1.01–1.57)	1.50 (1.19–1.89)	1.77 (1.38–2.26)	< 0.0001

Zhang et al.

intakes of saturated fat, vegetables, fruits, and sodium. 'n

Table 3 Joint effect of body mass index and waist-hip ratio on the risk of total stroke

		Tertile of body mass index, kg/m ²	
Tertile of waist-hip ratio	<22.2	22.2–24.9	≥25.0
<0.78			
No. of subjects	12491	6747	3199
No. of cases	191	128	106
Multivariate HR [*]	1.00 (reference)	1.17 (0.93–1.46)	1.40 (1.10–1.78)
0.78–0.82			
No. of subjects	6739	8429	6897
No. of cases	159	234	319
Multivariate HR [*]	1.18 (0.95–1.45)	1.36 (1.12–1.64)	1.75 (1.46–2.10)
≥0.83			
No. of subjects	3108	7165	12308
No. of cases	120	339	807
Multivariate HR [*]	1.31 (1.04–1.65)	1.53 (1.28–1.83)	1.85 (1.57–2.17)

* Adjusted for age, education, occupation, family income, menopausal status, use of oral contraceptives, hormone therapy, and aspirin, amount of exercise, cigarette smoking, alcohol consumption, and intakes of saturated fat, vegetables, fruits, and sodium.

_
_
_
=
~~
$\mathbf{\nabla}$
-
~
2
<u> </u>
t
_
=
0
-
· ·
~
\leq
É C
<u> </u>
2
0
0
<u> </u>
<u> </u>
0

Zhang et al.

Multivariate hazard ratios*(HRs) of ischemic stroke, intracerebral hemorrhage, and undefined stroke according to quintiles of body mass index, waist-hip ratio, waist circumference, and waist-height ratio Table 4

		Q	uintiles of anthropometric me	asures		
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P for trend
			Ischemic stroke			
Body mass index, kg/m ²						
No. of cases	204	232	289	430	582	
Multivariate HR	1.00	1.11 (0.92–1.34)	1.17 (0.98–1.41)	1.47 (1.24–1.74)	1.59 (1.36–1.88)	< 0.0001
Waist-hip ratio, cm/cm						
No. of cases	176	244	301	411	605	
Multivariate HR	1.00	1.20 (0.99–1.46)	1.22 (1.02–1.48)	1.39 (1.16–1.66)	1.46 (1.23–1.74)	< 0.0001
Waist circumference, cm						
No. of cases	178	231	245	396	687	
Multivariate HR	1.00	1.07 (0.88–1.31)	1.18 (0.97–1.43)	1.36 (1.14–1.63)	1.66 (1.40–1.97)	< 0.0001
Waist-height ratio, cm/cm						
No. of cases	128	155	270	427	757	
Multivariate HR	1.00	0.93(0.73 - 1.17)	1.18 (0.96–1.47)	1.42 (1.16–1.74)	1.67 (1.37–2.03)	< 0.0001
			Intracerebral hemorrhage			
Body mass index, kg/m ²						
No. of cases	20	29	40	45	71	
Multivariate HR	1.00	1.40 (0.79–2.48)	1.68 (0.98–2.88)	1.63 (0.96–2.77)	2.11 (1.27–3.50)	0.003
Waist-hip ratio, cm/cm						
No. of cases	18	25	39	47	76	
Multivariate HR	1.00	1.23 (0.67–2.26)	1.67 (0.95–2.93)	1.75 (1.01–3.02)	2.15 (1.27–3.65)	0.001
Waist circumference, cm						
No. of cases	18	27	34	41	85	
Multivariate HR	1.00	1.33 (0.73–2.42)	1.84 (1.03–3.27)	1.67 (0.95–2.94)	2.56 (1.51–4.34)	< 0.0001
Waist-height ratio, cm/cm						
No. of cases	13	17	36	50	89	
Multivariate HR	1.00	1.11 (0.54–2.29)	1.90 (1.00–3.61)	2.21 (1.18-4.14)	2.84 (1.54–5.26)	< 0.0001
			Undefined stroke			

lanuscript	
NIH-P/	
A Author Ma	
anuscript	

Zhang et al.

		Q	uintiles of anthropometric me	asures		
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P for trend
Body mass index, kg/m ²						
No. of cases	45	59	74	109	174	
Multivariate HR	1.00	1.28 (0.87–1.89)	1.35 (0.93–1.96)	1.64 (1.16–2.33)	2.06 (1.48–2.88)	< 0.0001
Waist-hip ratio, cm/cm						
No. of cases	37	53	76	118	177	
Multivariate HR	1.00	1.22 (0.80–1.86)	1.45 (0.98–2.15)	1.85 (1.27–2.68)	1.94 (1.35–2.78)	< 0.0001
Waist circumference, cm						
No. of cases	41	53	57	112	198	
Multivariate HR	1.00	1.06 (0.71–1.60)	1.17 (0.78–1.75)	1.61 (1.12–2.32)	1.95 (1.38–2.76)	< 0.0001
Waist-height ratio, cm/cm						
No. of cases	22	48	57	104	230	
Multivariate HR	1.00	1.68 (1.02–2.79)	1.43 (0.87–2.34)	1.95 (1.22–3.12)	2.79 (1.77–4.39)	< 0.0001
*						

^Adjusted for age, education, occupation, family income, menopausal status, use of oral contraceptives, hormone therapy, and aspirin, amount of exercise, cigarette smoking, alcohol consumption, and intakes of saturated fat, vegetables, fruits, and sodium.