# Waist Circumference predicting Cardiovascular Disease in Korean Men and Women

Running title: Waist Circumference and Cardiovascular Disease

Sat Byul Park<sup>1, 2</sup>, M.D., Ph.D., Ji Eun Yun<sup>3</sup>, Ph. D., Anastasia Georgiades<sup>1</sup>, Ph.D., James A.

Blumenthal<sup>1</sup>, Ph.D., Soon Young Lee<sup>4</sup>, M.D., Ph.D., Sun Ha Jee<sup>3†</sup>, Ph.D.

<sup>1</sup> Department of Psychiatry and Behavioral Sciences, Duke University Medical Center,

Durham, NC 27710, USA

<sup>2</sup> Department of Family Practice and Community Health, Ajou University School of

Medicine, Suwon, Korea

<sup>3</sup> Department of Epidemiology and Health Promotion, Institute for Health Promotion

Graduate School of Public Health, Yonsei University, Seoul, Korea

<sup>4</sup> Department of Preventive Medicine, Ajou University School of Medicine, Suwon, Korea

**†Corresponding Author:** Sun Ha Jee, MPH, Ph.D.

Address: 250 Seongsanno Seodaemon-gu, Seoul, 120-719,

Korea

Fax:	+82-2-365-5118
Office:	+82-2-2228-1523

E-mail: jsunha@yuhs.ac

#### Abstract

**Objective:** Obesity and cardiovascular disease (CVD) are closely related and have become increasingly prevalent in Korea. Asians are more prone to obesity-related co-morbidities than Caucasians, even at lower body mass index (BMI) and/or smaller waist circumference (WC) values. Nevertheless, little is known regarding the association of WC with the risk of CVD in non-Caucasian populations. The authors conducted a prospective cohort study of WC and the risk of CVD in the Korean Heart Study.

**Methods:** We examined the association of WC to CVD incidence among 53,026 Korean adults (30,152 men, 22,874 women) with no history of CVD and/or cancer. During a mean follow-up of 8.6 years, 2,722 incident cases of atherosclerotic cardiovascular disease (ASCVD) including 1,383 cases of ischemic heart disease (IHD) and 1,012 cases of stroke were documented. **Results:** Average WC at baseline was 84.0±8.2 cm in men and 75.2±8.9 cm in women. After adjustment for age and BMI, WC was significantly associated with cardiovascular risk factors (*P* <.001). In men, a WC of  $\geq$ 91 cm was associated with an ASCVD hazard ratio (HR) of 1.62 (95% confidence interval (CI): 1.25, 2.10) and an IHD HR of 1.70 (95% CI: 1.19, 2.42) in comparison with a WC of <78 cm even after further adjustment for BMI and traditional risk factors (*P* for trend = 0.0118, 0.0139 respectively). In women, the progressive associations of WC with ASCVD, IHD and stroke were observed. These associations were however attenuated after further adjustment for BMI and traditional risk factory. IHD, and stroke increased with higher WC in both men and women.

**Conclusions:** Central obesity significantly and independently contributes to cardiovascular outcomes in Korean men and women.

### Key words: Waist Circumference, Central Obesity, Cardiovascular Disease

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### **INTRODUCTION**

The prevalence and incidence of obesity are increasing rapidly in both developed and developing countries (1). Abdominal obesity has also been found to be an independent contributor to cardiovascular disease (CVD) at a given level of obesity (2-4). Moreover, abdominal obesity promotes insulin resistance and leads to metabolic syndrome (MetS) (5). MetS is recognized as a cluster of cardiovascular risk factors that frequently coincide with insulin resistance and hyperglycemia (6). Recently, the World Health Organization (WHO) established a different criteria for the clinical diagnosis of the MetS, compared to the National Cholesterol Education Program (NCEP), with lower waist circumference (WC) levels in Asian populations compared to Caucasian populations (7-9). Asians are more prone to obesity-related co-morbidities than Caucasians, even at lower BMI and/or smaller WC values (10, 11).

In Korea, proportionate morbidity and mortality from ASCVD have increased markedly between 1981 and 2003 (12). The death rates from stroke ranked second in mortality for both men and women in Korea. The death rate from IHD has increased by 122.8% over the last decade (13). Nevertheless, little information is available on the association of WC with CVD incidence in Korean population. Therefore, we had collected to form the study population for a cohort study from 19 heath promotion centers nationwide where those additional CVD risk factors were available. We have labeled this study as the Korean Heart Study (KHS). The KHS conducted by Korean metabolic syndrome research initiatives (KMSRI) which commenced in December 1<sup>st</sup> 2005, were to develop the Korean Cardiovascular Disease Prediction Model using previously collected data from 19 health promotion centers, collaborating with the Korean society of cardiology and the National Health Insurance Corporation. The objective of the study was to address the relation between the level of WC and the risk of CVD in the subgroup of the KHS.

#### **METHODS**

## **Study Population**

The KHS cohort includes the 476,529 Korean (290,509 men and 186,020 women) over the age of 20 who had undertaken medical examinations. Of the study participants, 11,141 participants (2.3%) between 1993 and 1995, 24,226 participants (5.1%) in 1996, 38,159 participants (8.0%) in 1997, 39,906 participants (8.4%) in 1998, 42,417 participants (8.9%) in 1999, 73,883 participants (15.5%) in 2000, 90,051 participants (18.9%) in 2001, 52,057 participants (10.9%) in 2002, 47,543 participants (10.0%) in 2003 and 57,146 participants (12.0%) in 2004 were enrolled. Of the 476,529 participants, 57,708 people who had data on waist circumference were included for the present study.

To avoid confounding of the association between WC and the risk of preexisting disease, 4,329 individuals who reported history of cancer or ASCVD (IHD or stroke) were excluded. In addition, 353 individuals with missing information about gender, smoking status, alcohol intake or exercise were excluded. The final sample included 53,026 subjects.

Because the study involved data that were routinely collected, consent was not specifically obtained. The institutional review boards of Yonsei University and each institution participated to this study approved the study.

## **Data Collection**

Sociodemographic characteristics, smoking status, alcohol intake, and exercise habits were assessed by questionnaire. Height and weight were measured using bioelectrical impedance analysis (Inbody 3.0, Biospace, Korea, 2001) following overnight fast. BMI was calculated as weight divided by height squared ( $kg/m^2$ ) (14). WC was measured at middle part between the

lower rib and iliac crest by a trained nurse. Blood pressure was measured by a semi-automated blood pressure monitor (TM-2650A, PMS Instruments, Tokyo, Japan) after a rest of at least 15 min.

Venous blood was drawn following an 8-h overnight fast and 24-h abstinence from vigorous activity. Standard enzymatic measurements of total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol, and fasting glucose were made on fresh serum samples by oxidase–peroxidase enzymatic assay (TBA-200FR, Toshiba, Tokyo, Japan).

### **Outcome definition and follow-up procedures**

We followed the NCEP-ATP III guidelines to define central obesity ( $\geq 102$  cm of WC for men and  $\geq 88$  cm of WC for women) (8). We also evaluated the WC according to the report of the joint WHO/IASO/IOTF committee, who propose that the WC values of 90 cm for men and 80 cm for women be used as Asian-specific WC cutoff points for central obesity (15). We also used the WC cutoff recently established as ethnically appropriate for central obesity specifically in Korean adults which was set at 90 cm for men and 85 cm for women (16).

The principal outcome variables were morbidity from: (1) total ASCVD included by hypertensive disease (ICD 9 codes 401–405), IHD (410–414), hemorrhagic stroke (430–432), thrombotic stroke (433–434), other stroke (435–438), other heart disease likely related to ASCVD (426–429), and other vascular disease (440–444). (2) IHD alone (ICD 9 codes 410–414), along with acute myocardial infarction (AMI) alone (410) and angina pectoris (AP) alone (413), and (3) Stroke alone (ICD 9 codes 430–438).

In Korea, professionally trained and certified medical chart recorders abstracted charts and assigned discharge diagnoses in a standardized fashion using WHO codes for common diseases such as stroke and myocardial infarction. The mean follow-up period was 8.59 years, through 30 June 2009. Consequently, follow-up accrual began on 1 January of the calendar year (2005) following the year (2004) in which the survey form was completed.

## **Statistical Analysis**

We examined the bivariate relationship between WC and traditional cardiovascular risk factors using Pearsons correlation analyses and partial correlations, controlling for age and BMI. Cox proportional hazards models were used to assess the independent effects of WC on ASCVD, IHD, and stroke. All models included adjustment for age, smoking status, alcohol consumption and exercise. In addition, we also fitted models with further adjustment for BMI, and traditional risk factors such as systolic blood pressure, fasting glucose and total cholesterol levels to evaluate the effect of WC that is not explained by BMI and cardiovascular risk factors. We also used Cox proportional hazards models to compare the guidelines of central obesity on ASCVD, IHD, and stroke, controlling for age, smoking status, alcohol consumption and exercise. In all analyses, a two-sided  $\alpha$  level of 0.05 was considered statistically significant. All analyses were conducted with the use of SAS software, version 9 (SAS institute Inc., Cary, NC, USA).

#### RESULTS

## **Demographic Characteristics**

Demographic characteristics are presented in Table 1. A total of 53,026 individuals participated, 30,152 men (56.9%) and 22,874 women (43.1%). The mean age of the study participants was  $43.9 \pm 10.5$  yr. About 36% of the men were among 40- to 49-year old and 33% of the women were among 30- to 39-year old. The mean WC was  $84.0\pm8.2$  cm in men and  $75.2\pm8.9$  cm in women. Almost 46% of men had WC of 80-89 cm and 43% of women had WC of 70-79 cm (Fig. 1). Men, in comparison to women, had higher smoking and alcohol drinking rates.

Over 8.6 years of follow-up, there were 2,722 incident cases of ASCVD (1,676 in men, 1,046 in women), including 1,383 cases of IHD (914 in men, 469 in women) and 1,012 cases of stroke (601 in men, 411 in women).

#### Correlation between cardiovascular risk factors and waist circumference

Systolic blood pressure and diastolic blood pressure were positively correlated with WC in men and women, and these associations persisted after controlling for age and BMI. In both men and women, the negative relation of HDL cholesterol to WC remained significant even after adjusting for age and BMI. The levels of total cholesterol, triglyceride and fasting glucose still increased progressively with WC after adjustment for age and BMI in men and women (Table 2).

#### Hazard Ratios of cardiovascular disease by waist circumference categories in men

The independent effects of WC on ASCVD, IHD, and stroke were examined in Cox proportional hazards models that simultaneously controlled for age, smoking status, alcohol

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consumption and exercise, and with further adjustment for BMI and traditional risk factors in men. To assess the relationship between WC and ASCVD by level of WC, we divided the cohort into quintiles of WC (<78, 78-82.9, 83-86.9, 87-90.9,  $\geq$ 91 cm). In these quintiles, the number of IHD events was 82, 159, 169, 226, and 278 respectively, while the number of ASCVD events was 164, 320, 328, 374, and 490 respectively.

As Table 3 shows, the HR (95% CI) for any ASCVD event was 2.32 (1.94-2.78) in the highest quintile of WC compared to the lowest quintile of WC after controlling for age, smoking status, alcohol consumption and exercise. Additional adjustment for BMI and traditional risk factors remained highly significant, albeit attenuated in men (HR = 1.62, 95% CI: 1.25-2.10).

Compared to the lowest quintile of WC, the HR (95% CI) for any IHD event was 2.68 (2.09-3.44) in the highest quintile of WC after controlling for age and behavioral factors, still significant after further adjustment for BMI and traditional risk factors (HR = 1.70, 95% CI: 1.19-2.42). For stroke, the corresponding HR (95% CI) was 1.82 (1.37-2.43) in the highest quintile of WC. Additional adjustment for BMI and traditional risk factors however altered the HR results for stroke. There were strong and graded relations of increasing WC with ASCVD and IHD in men, as shown in Table 3 (P for trend = 0.0118, 0.0139 respectively).

### Hazard Ratios of cardiovascular disease by waist circumference categories in women

In women, the independent effects of WC on ASCVD, IHD, and stroke were examined in Cox proportional hazards models that simultaneously controlled for age, smoking status, alcohol consumption and exercise as well. In addition, the models were further adjusted for BMI and traditional risk factors. To assess the relationship between WC and ASCVD by level of WC, we divided the cohort into quintiles of WC (<68, 68-71.9, 72-75.9, 76-81.9,  $\geq$ 82 cm). In these

quintiles, the number of ASCVD events was 77, 96, 186, 288, and 399 respectively, while the number of stroke events was 32, 37, 75, 112, and 155 respectively.

As Table 4 shows, the HR (95% CI) for any ASCVD event was 2.09 (1.61-2.70) in the highest quintile of WC compared to the lowest quintile of WC after controlling for age, smoking status, alcohol consumption and exercise. Additional adjustment for BMI and traditional risk factors attenuated the HR results for ASCVD in women.

Compared to the lowest quintile of WC, the HR (95% CI) for IHD was 2.34 (1.59-3.44) in the highest quintile of WC after controlling for age and behavioral factors. Further adjustment for BMI and traditional risk factors altered the HR results for IHD, non-significant. For stroke, the corresponding HR (95% CI) was 1.74 (1.16-2.59) in the highest quintile of WC. However, additional adjustment for BMI and traditional risk factors also attenuated the results for stroke in women. As shown in Table 4, the progressive associations of WC with ASCVD, IHD and stroke were observed in women., These associations were however attenuated after further adjustment for BMI and traditional risk factors.

## Comparison of waist circumference by using various guidelines for central obesity

To assess the relationship between central obesity and CVD, we divided the cohort into two groups of WC using different criteria for central obesity among men and women. Hazard ratios of various guidelines for central obesity on ASCVD, IHD, and stroke events were analyzed after controlling for age, smoking status, alcohol intake and exercise. According to Korean guideline for central obesity, the HR for ASCVD was 1.47 (95% CI 1.33-1.63) in men and 1.56 (95% CI 1.36-1.78) in women. As Table 5 shows, the multivariable HRs increased with higher WC for events from ASCVD, IHD and stroke in both men and women. The HR of IHD to WC tended to be higher than those of ASCVD and stroke.

#### DISCUSSION

Our results show that WC is significantly associated to CVD risk factors in this Korean cohort, over and above what can be explained by BMI alone. Results also show that central obesity is an important and independent contributor to future CVD in this Asian population. The importance of metabolic risk factors and central obesity has been recognized recently and many diagnostic criteria have been established for MetS. The IDF proposed that central obesity, as assessed by WC cutoff values specific for ethnicity and gender, should be an essential component for the diagnosis of MetS (17). As above mentioned, Asian populations may have a different fat distribution pattern than Western populations and may be more prone to central obesity, even at low BMI levels (10, 18). While the precise reasons for these differences are not completely understood (18), at similar BMI, Asians will tend do have less muscle mass and connective tissue than Caucasian subjects and more fat mass (19).

A previous study according to obesity type indicated that any type of obesity may be metabolically harmful (20), and serves as a signal of a constellation of insulin-resistance related abnormalities in both genders (21-26). Cross-sectional studies conducted in the Asia Pacific region (27, 28) have found a continuous relationship between central obesity and CVD risk factors including blood pressure, plasma glucose, plasma lipids, and insulin levels. In the present study, we also found the relations of cardiovascular risk factors to WC remained significant even after adjusting for age and BMI. Therefore, a combination of obesity and abdominal adiposity, i.e. central obesity, may be used as a distinctive marker for MetS, a clustering of many insulinresistance related risk factors (21, 29).

Obesity, often cited as a CVD risk factor, has long been sidelined as a useful practical prediction tool (30). The multinational INTERHEART case-control study confirmed the

importance of obesity, particularly abdominal adiposity, as a potent risk factor for myocardial infarction (31, 32). In addition, International Day for the Evaluation of Abdominal Obesity (IDEA) Study reported that BMI and particularly WC were both strongly linked to CVD and especially to diabetes mellitus among men and women (33). In a recent large cohort study of South Korean men and women, BMI was strongly related the incidence of ASCVD, including acute myocardial infarction, throughout its entire range (34). However, measures of BMI do not reveal the distribution of body fat (35). Cohort studies in the United States have found that higher waist-to- hip ratio (WHR) or WC are strongly associated with increased risk of IHD in women (36), and stroke in men (37). Swedish cohort studies have also found that the relationship with acute myocardial infarction (38), as well as stroke and IHD (39), is stronger for WHR than BMI. Our results indicate the strong and graded relation between WC and ASCVD incidence without specific thresholds of abrupt change in both men and women. Also, WC was significantly associated with the risk of IHD in men, while the association of WC to IHD was attenuated after further adjustment in women. The progressive association of WC with stroke was also observed in men and women. It is in line with some earlier studies suggesting that central obesity may partly explain the risk profile of coronary heart disease (35, 40, 41).

A recent meta-analysis of MetS and risk of incident cardiovascular events and death suggests that people with MetS are at increased risk of cardiovascular events (42). Moreover, results from several studies have shown that the presence of MetS using different definitions is associated with a significantly increased risk of total mortality and cardiovascular morbidity and mortality (43).We also found that the hazard ratios of various guidelines for central obesity increased with higher WC for events from ASCVD, IHD and stroke in both men and women. Our findings are thus consistent with those of available studies on the relation between MetS and CVD (44-46), and MetS is even a significant predictor of subclinical carotid atherosclerosis (47). In addition, Dhaliwal SS et al. (35) evaluated the role of measurements of central obesity in the multivariable prediction for cardiovascular risk using the Framingham risk scores. According to the results, WHR and WC were independent predictors of CVD deaths.

The limitation of this study was that the prevalence of central obesity in our data does not reflect the general population. However, we performed the study with a large number of subjects relatively and the baseline characteristics of the study population were similar to the Korea Medical Insurance Corporation Study (34). Also, we didn't measure hormonal status, especially for women, so that we could not evaluate a hormonal difference that might affect cardiovascular outcomes among this population.

In conclusion, the results of the present study suggest that the association of WC with CVD in this cohort of Korean population was progressive over the range of WC values. As expected, central obesity significantly and independently contributes to cardiovascular outcomes in Korean men and women.

# References

- 1. World Health Organization. Obesity: Preventing and managing the global epidemic. Report of the WHO consultation on obesity. Geneva: Geneva, 1998.
- 2. Bjorntorp P. Abdominal fat distribution and disease: an overview of epidemiological data. *Ann Med* 1992; **24**: 15-18.
- 3. Bjorntorp P. Abdominal fat distribution and the metabolic syndrome. *J Cardiovasc Pharmacol* 1992; **20**: S26-28.
- Despres JP, Moorjani S, Lupien PJ, Tremblay A, Nadeau A, Bouchard C. Regional distribution of body fat, plasma lipoproteins, and CVD disease. *Arteriosclerosis* 1990; 10: 497-511.
- 5. Grundy SM. Hypertriglyceridemia, insulin resistance, and the metabolic syndrome. *Am J Cardiol* 1999; **83**: 25F-29F.
- 6. Meigs JB. Invited commentary: insulin resistance syndrome? Syndrome X? Multiple metabolic syndrome? A syndrome at all? Factor analysis reveals patterns in the fabric of correlated metabolic risk factors. *Am J Epidemiol* 2000; **152**: 908-11; discussion 912.
- Isomaa B, Almgren P, Tuomi T, Forsén B, Lahti K, Nissén M, et al. Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care* 2001; 24: 683-9.
- 8. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001; **285**: 2486-97.
- 9. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications: Part 1. Diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med* 1998; **15**: 539- 53.
- McKeigue PM, Shah B, Marmot MG. Relation of central obesity and insulin resistance with high diabetes prevalence and cardiovascular risk in South Asians. *Lancet* 1991; **337**: 382-6.
- Deurenberg-Yap M, Chew SK, Lin VF, Tan BY, van Staveren WA, Deurenberg P. Relationships between indices of obesity and its co-morbidities in multi-ethnic Singapore. *Int J Obes Relat Metab Disord*. 2001; 25: 1554-62.
- 12. National Statistical Office. Annual report on the cause of death statistics. Republic of Korea; 2003
- 13. Korea National Statistical Office. 2007 Report of Statistics of Mortality in Koreans, 2008
- Clinical Guidelines on the Identification. Evaluation and treatment of overweight and obesity in adults-the evidence report. National Institutes of Health. *Obes Res* 1998; 6: 51S-209S.
- 15. International Obesity Task Force. Asia-Pacific perspective: redefining obesity and its treatment. Western Pacific Region, Sydney, Australia, 2000.
- Lee SY, Park HS, Kim DJ, Han JH, Kim SM, Cho GJ, et al. Appropriate waist circumference cutoff points for central obesity in Korean adults. *Diabetes Res Clin Pract* 2007; **75**: 72-80.
- 17. K.G. Alberti, P. Zimmet, J. Shaw, IDF Epidemiology Task Force Consensus Group. The metabolic syndrome-a new worldwide definition. *Lancet* 2005; **366**: 1059-1062.
- 18. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* 2004; **363**: 157-63.

- 19. Deurenberg P, Deurenberg Yap M, Wang J, Lin FP, Schmidt G. The impact of body build on the relationship between body mass index and percent body fat. Int J Obes Relat Metab Disord 1999; 23: 537-42.
- 20. Vanhala MJ, Pitkäjärvi TK, Kumpusalo EA, Takala JK. Obesity type and clustering of insulin resistance-associated cardiovascular risk factors in middle-aged men and women. *Int J Obes Relat Metab Disord* 1998; **22**:369-74.
- 21. BjoÈrntorp P. Abdominal obesity and the metabolic syndrome. *Ann Med* 1992; **24**: 465-468.
- 22. Reaven GM. Banting lecture 1988: Role of insulin resistance in human disease. *Diabetes* 1988; **37**: 1595-1607.
- 23. DeFronzo RA, Ferrannini E. Insulin resistance. A multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. *Diab Care* 1991; **14**: 173-194.
- 24. Reaven GM. A syndrome of resistance to insulin stimulated glucose uptake (Syndrome-X): Defnitions and implications. *Cardiovascular Risk Factors* 1993; **1**: 2-11.
- 25. Haffner SM, Valdez RA, Hazuda HP, Mitchell BD, Morales PA, Stern MP. Prospective analysis of the insulin-resistance syndrome (Syndrome-X). *Diabetes* 1992; **41**: 715-722.
- 26. Laakso M. The possible pathophysiology of insulin resistance syndrome. *Cardiovascular Risk Factors* 1993; **1**: 55-66.
- 27. Thomas GN, Ho SY, Lam KSL, Janus ED, Hedley AJ, Lam TH. Impact of obesity and body fat distribution on cardiovascular risk factors in Hong Kong Chinese. *Obesity Research* 2004; **12**: 1805-13.
- 28. Lin W-Y, Lee L-T, Chen C-Y, Lo H, Hsia H-H, Liu I-L, et al. Optimal cut-off values for obesity: using simple anthropometric indices to predict cardiovascular risk factors in Taiwan. *Int J Obesity* 2002; **26**: 1232-8.
- 29. BjoÈrntorp P. ``Portal" adipose tissue as a generator of risk factors for cardiovascular disease and diabetes. *Arteriosclerosis* 1990; **10**: 493-496.
- 30. Kannel WB, Larson M. Long-term epidemiologic prediction of coronary disease. The Framingham experience. *Cardiology* 1993; **82**: 137-52.
- 31. Yusuf S, Hawken S, Ounpuu S, Bautista L, Franzosi MG, Commerford P, et al.; and the INTERHEART Study Investigators. Obesity and the risk of myocardial infarction in 27 000 participants from 52 countries: a case-control study. *Lancet* 2005; **366**: 1640-1649.
- 32. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al.; and the INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): casecontrol study. *Lancet* 2004; **364**: 937-952.
- 33. Balkau B, Deanfield JE, Després JP, Bassand JP, Fox KA, Smith SC Jr, et al. International Day for the Evaluation of Abdominal Obesity (IDEA): a study of waist circumference, cardiovascular disease, and diabetes mellitus in 168,000 primary care patients in 63 countries. *Circulation* 2007; **116**: 1942-51.
- 34. Jee SH, Pastor-Barriuso R, Appel LJ, Suh I, Miller ER 3rd, Guallar E. Body mass index and incident ischemic heart disease in South Korean men and women. *Am J Epidemiol* 2005; **162**: 42-8.
- 35. Dhaliwal SS, Welborn TA. Central obesity and multivariable cardiovascular risk as assessed by the Framingham prediction scores. *Am J Cardiol* 2009; **103**: 1403-7.

- Rexrode KM, Carey VJ, Hennekens CH, Walters EE, Colditz GA, Stampfer MJ, et al. Abdominal obesity and coronary heart disease in women. *J Am Med Assoc* 1998; 280: 1843-8.
- 37. 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 Epidem* 1996; **144**:1143-50.
- Lapidus L, Bengtsson C, Larsson B, Pennert K, Rybo E, Sjostrom L. Distribution of adipose tissue and risk of cardiovascular disease and death: a 12 year follow up of participants in the population study of women in Gothenburg, Sweden. *Br Med J* 1984; 289: 1257-61.
- 39. Larsson B, Svardsudd K, Welin L, Wilhelmsen L, Bjorntorp P, Tibblin G. Abdominal tissue distribution, obesity, and risk of cardiovascular disease and death: 13 year follow up of participants in the study of men born in 1913. *Br Med J* 1984; **288**: 1401-4.
- Ammar KA. Redfield MM. Mahoney DW. Johnson M. Jacobsen SJ. Rodeheffer RJ. Central obesity: association with left ventricular dysfunction and mortality in the community. *American Heart Journal* 2008; **156**: 975-81.
- 41. Asia Pacific Cohort Studies Collaboration. Central obesity and risk of cardiovascular disease in the Asia Pacific Region. *Asia Pacific Journal of Clinical Nutrition* 2006; **5**: 287-92.
- 42. Gami AS, Witt BJ, Howard DE, Erwin PJ, Gami LA, Somers VK, et al. Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. *J Am Coll Cardiol* 2007; **49**: 403-14.
- 43. Hu G, Qiao Q, Tuomilehto J. The metabolic syndrome and cardiovascular risk. *Curr Diabetes Rev* 2005; **1**: 137-43.
- 44. Zhang WW, Liu CY, Wang YJ, Xu ZQ, Chen Y, Zhou HD. Metabolic syndrome increases the risk of stroke: a 5-year follow-up study in a Chinese population. *J Neurol* 2009; **256**: 1493-9.
- 45. Wang J, Ruotsalainen S, Moilanen L, Lepistö P, Laakso M, Kuusisto J. The metabolic syndrome predicts incident stroke: a 14-year follow-up study in elderly people in Finland. *Stroke* 2008; **39**: 1078-83.
- 46. Noda H, Iso H, Saito I, Konishi M, Inoue M, Tsugane S; JPHC Study Group. The impact of the metabolic syndrome and its components on the incidence of ischemic heart disease and stroke: the Japan public health center-based study. *Hypertens Res* 2009; **32**: 289-98.
- 47. Rundek T, White H, Boden-Albala B, Jin Z, Elkind MS, Sacco RL. The metabolic syndrome and subclinical carotid atherosclerosis: the Northern Manhattan Study. *J Cardiometab Syndr* 2007; **2**: 24-9.

	Men (n=30,152)	Women (n=22,874)
-	Mean ± SD	Mean ± SD
Age (yrs)	43.7±10.0	44.2±11.2
Waist circumference (cm)	84.0±8.2	75.2±8.9
Body mass index (kg/m <sup>2</sup> )	23.8±2.9	23.1±3.2
Systolic blood pressure (mm Hg)	121.9±16.6	116.0±19.1
Diastolic blood pressure (mm Hg)	75.8±11.6	72.7±11.2
Total cholesterol (mg/dL)	193.2±35.1	189.1±36.6
Triglyceride (mg/dL)	155.5±111.9	114.2±77.0
HDL cholesterol (mg/dL)	48.1±11.2	54.7±12.7
Fasting glucose (mg/dL)	100.3±23.7	96.0±19.5
	%	%
Smoking status		
Ex-smoker	19.3	1.6
Current smoker	57.9	5.4
Alcohol drinking (yes)	83.6	31.3
Regular exercise (yes)	23.1	24.3
Hypertension	26.8	21.9
Type 2 diabetes	9.8	7.4

Table 1. General characteristics of the study population at baseline

HDL, high-density lipoprotein; SD, standard deviation

	Men		Women		
	Crude	Age and BMI adjusted	Crude	Age and BMI adjusted	
Systolic blood pressure	0.313**	0.042**	0.425**	0.051**	
Diastolic blood pressure	0.298**	0.073**	0.332**	0.038**	
Total cholesterol	0.229**	0.058**	0.263**	0.027**	
Triglyceride	0.264**	0.078**	0.283**	0.059**	
HDL cholesterol	-0.237**	-0.076**	-0.194**	-0.039**	
Fasting glucose	0.157**	0.043**	0.226**	0.045**	

Table 2. Pearson correlations between waist circumference and cardiovascular risk factors

HDL, high-density lipoprotein; BMI, body mass index. Correlation coefficients were calculated using partial correlation analysis. \*p < .001

Waist circumference, cm						
	<78	78-82.9	83-86.9	87-90.9	≥91	]
Type of CVD	(n=5,650)	(n=7,015)	(n=5,828)	(n=5,537)	(n=6,122)	P value for trend
ASCVD						
Case	164	320	328	374	490	
Rate*	373.5	566.6	641.3	747.3	842.7	
HR $(95\% \text{ CI})^{\dagger}$	1.0	1.54(1.27-1.85)	1.77(1.47-2.13)	2.07(1.72-2.49)	2.32(1.94-2.78)	0.0020
HR (95% CI) <sup>‡</sup>	1.0	1.42(1.16-1.73)	1.54(1.24-1.91)	1.74(1.38-2.18)	1.82(1.40-2.35)	0.0100
HR (95% CI) <sup>§</sup>	1.0	1.33(1.09-1.62)	1.41(1.14-1.75)	1.55(1.24-1.95)	1.62(1.25-2.10)	0.0118
IHD						
Case	82	159	169	226	278	
Rate*	193.0	269.5	323.9	439.8	476.7	
HR $(95\% \text{ CI})^{\dagger}$	1.0	1.52(1.16-1.98)	1.84(1.41-2.39)	2.54(1.97-3.27)	2.68(2.09-3.44)	0.0021
HR $(95\% \text{ CI})^{\ddagger}$	1.0	1.35(1.02-1.78)	1.51(1.12-2.03)	1.97(1.44-2.68)	1.89(1.33-2.68)	0.0126
HR (95% CI) <sup>§</sup>	1.0	1.27(0.96-1.67)	1.38(1.03-1.87)	1.77(1.29-2.41)	1.70(1.19-2.42)	0.0139
Stroke						
Case	66	130	115	128	162	
Rate*	142.0	235.7	223.9	254.4	259.9	
HR $(95\% \text{ CI})^{\dagger}$	1.0	1.59(1.18-2.14)	1.56(1.15-2.11)	1.76(1.31-2.37)	1.82(1.37-2.43)	0.0478
HR (95% CI) <sup>‡</sup>	1.0	1.53(1.11-2.10)	1.47(1.03-2.09)	1.63(1.12-2.37)	1.64(1.07-2.51)	0.0833
HR (95% CI) <sup>§</sup>	1.0	1.41(1.03-1.94)	1.32(0.93-1.88)	1.41(0.97-2.06)	1.43(0.93-2.20)	0.1420

Table 3. Hazard ratios (95% confidence intervals) of CVD by waist circumference quintiles in men

- \* Age adjusted rate per 100,000 person year
- + The Cox proportional hazards model was adjusted for age, smoking status (ex-smoker, current smoker), alcohol consumption (no, yes), and exercise (no, yes).
- ‡ The Cox proportional hazards model was adjusted for age, smoking status (ex-smoker, current smoker), alcohol consumption (no, yes), exercise (no, yes), and BMI.
- § The Cox proportional hazards model was adjusted for age, smoking status (ex-smoker, current smoker), alcohol consumption (no, yes), exercise (no, yes), BMI, systolic blood pressure, fasting glucose, and total cholesterol.

	Waist circumference, cm					
	<68	68-71.9	72-75.9	76-81.9	≥82	]
Type of CVD	(n=4,586)	(n=5,267)	(n=5,704)	(n=5,791)	(n=5,623)	P value for trend
ASCVD						
Case	77	96	186	288	399	
Rate*	408.6	397.1	446.7	594.8	727.1	
HR $(95\% \text{ CI})^{\dagger}$	1.0	1.07(0.79-1.44)	1.32(1.01-1.73)	1.80(1.38-2.33)	2.09(1.61-2.70)	0.0055
HR (95% CI) <sup>‡</sup>	1.0	0.96(0.71-1.31)	1.09(0.82-1.45)	1.34(1.00-1.79)	1.33(0.96-1.85)	0.0318
HR (95% CI) <sup>§</sup>	1.0	0.96(0.71-1.30)	1.06(0.79-1.40)	1.23(0.92-1.65)	1.21(0.87-1.67)	0.0421
IHD						
Case	34	41	81	118	195	
Rate*	178.0	176.3	192.4	235.8	360.0	
HR $(95\% \text{ CI})^{\dagger}$	1.0	1.05(0.66-1.65)	1.33(0.89-2.00)	1.70(1.15-2.52)	2.34(1.59-3.44)	0.0129
HR $(95\% \text{ CI})^{\ddagger}$	1.0	0.89(0.56-1.41)	0.98(0.64-1.49)	1.06(0.69-1.64)	1.14(0.70-1.84)	0.1329
HR (95% CI) <sup>§</sup>	1.0	0.88(0.55-1.39)	0.93(0.61-1.42)	0.96(0.62-1.49)	1.01(0.62-1.64)	0.6272
Stroke						
Case	32	37	75	112	155	
Rate*	185.1	161.6	179.0	228.1	252.0	
HR $(95\% \text{ CI})^{\dagger}$	1.0	0.96(0.60-1.55)	1.20(0.79-1.83)	1.51(1.01-2.27)	1.74(1.16-2.59)	0.0113
HR (95% CI) <sup>‡</sup>	1.0	0.92(0.57-1.49)	1.11(0.71-1.72)	1.33(0.84-2.11)	1.43(0.85-2.40)	0.0232
HR (95% CI) <sup>§</sup>	1.0	0.92(0.57-1.49)	1.08(0.69-1.68)	1.23(0.78-1.95)	1.30(0.77-2.18)	0.0308

Table 4. Hazard ratios (95% CI) of CVD by waist circumference quintiles in women

- \* Age adjusted rate per 100,000 person year
- + The Cox proportional hazards model was adjusted for age, smoking status (ex-smoker, current smoker), alcohol consumption (no, yes), and exercise (no, yes).
- ‡ The Cox proportional hazards model was adjusted for age, smoking status (ex-smoker, current smoker), alcohol consumption (no, yes), exercise (no, yes), and BMI.
- § The Cox proportional hazards model was adjusted for age, smoking status (ex-smoker, current smoker), alcohol consumption (no, yes), exercise (no, yes), BMI, systolic blood pressure, fasting glucose, and total cholesterol.

Guideline		WC (cm)	ASCVD	IHD	Stroke
NCEP	Men	<102	1.00	1.00	1.00
		≥102	1.79(1.36-2.36)	1.65(1.13-2.43)	1.85(1.19-2.86)
	Women	<88	1.00	1.00	1.00
		≥88	1.55(1.33-1.80)	1.93(1.56-2.39)	1.39(1.08-1.76)
APC	Men	<90	1.00	1.00	1.00
		≥90	1.47(1.33-1.63)	1.66(1.45-1.90)	1.20(1.01-1.42)
	Women	<80	1.00	1.00	1.00
		≥80	1.61(1.42-1.83)	1.74(1.44-2.11)	1.51(1.23-1.85)
Korean	Men	<90	1.00	1.00	1.00
		≥90	1.47(1.33-1.63)	1.66(1.45-1.90)	1.20(1.01-1.42)
	Women	<85	1.00	1.00	1.00
		≥85	1.56(1.36-1.78)	1.96(1.61-2.38)	1.43(1.15-1.77)

Table 5. Hazard ratios (95% CI) of various guidelines for waist circumference (WC)

\*adjusted for age, smoking status, alcohol intake and exercise.

NCEP, National Cholesterol Education Program Adult Treatment Panel III criteria; APC,

Asia-Pacific criteria



