Prospective Associations of Waist-to-Height Ratio With Cardiovascular Events in Postmenopausal Women: Results From the Women’s Health Initiative

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Clinicians and global health workers need valid, reliable, readily accessible, and cost-effective indicators to screen for individuals at risk for adverse cardiometabolic events in diverse populations, particularly in resource-poor settings. Waist-to-height ratio (WHR) has recently emerged as one such promising index in assessing cardiovascular disease (CVD) risk. Meta-analyses of receiver operating characteristic curves showed that WHR had better power than BMI and waist circumference (WC) in classifying CVD risk factors among adults and children (1,2). However, the role of WHR in relation to the incidence of CVD has not been examined adequately in well-characterized populations of diverse ethnicities, nor has the strength of association been compared with conventional anthropometric indicators in high-quality prospective cohorts.

The national Women’s Health Initiative (WHI) includes 161,808 postmenopausal women across 40 clinical centers in the U.S. who were enrolled at baseline from 1994 to 1998; occurrence of CVD events or death were determined during follow-up (3). Incident CVD events were adjudicated by trained physicians following a standardized protocol. The current study excluded participants with self-reported CVD or cancer at baseline and those who developed CVD or were lost to follow-up within 3 years of enrollment. WHtR, BMI, WC, and waist-to-hip ratio (WHR) were measured at baseline. Changes in body weight were examined using data collected at year 3 and baseline. WHtR was categorized as 1) per 0.1 unit increment and treated as a continuous variable and 2) “elevated,” defined as >0.5 at baseline (1). Overweight and obesity were defined as BMI >25 and >30, respectively, while abdominal obesity was defined as WC >88 cm and/or WHR ≥0.85; all cutoff values were based on the World Health Organization guidelines (4). Changes in body weight were categorized into three groups: weight gain ≥5 kg, weight loss ≥5 kg, and weight change <5 kg.

The independent effect of each anthropometric index on the risk of CVD events was estimated using Cox models and testing the proportional hazard assumption using Schoenfeld residuals (no evidence for violation of assumption). Data analysis was conducted using R 3.6.0. Two models with different sets of covariates were fitted. Model 1 included age at baseline, region in the U.S., race/ethnicity, and WHI subcohort indicators (participating in the observational study or clinical trials). Model 2 additionally adjusted for education, family income, alcohol intake, smoking status, energy expenditure from recreational physical activity, dietary energy, total carbohydrate/sugar/protein intake, dietary glycemic index, use of hormone replacement therapy, history of diabetes/hypertension/high cholesterol requiring medication/hysterectomy at baseline, and family history of diabetes/stroke/heart attack. We additionally performed sensitivity analysis to assess the robustness of findings by excluding participants with incident cancer or diabetes. Last, we assessed potential interactions between WHtR and other anthropometric indexes.

Overall, 109,536 participants were included in the analysis with a median follow-up of 17.9 years. In the fully adjusted model, elevated WHtR (WHR >0.5) was significantly associated with increased CVD risk (hazard ratio [HR] 1.29 [95% CI 1.22, 1.36]). Moreover, CVD risk increased 15% for every 0.1-unit increment of WHR (HR 1.15 [1.11, 1.18]). BMI-classified overweight and obesity were significantly associated with CVD events (HR 1.16 [1.09, 1.23] and HR 1.19 [1.11, 1.27], respectively). Other significant associations with CVD events included WC >88 cm (HR 1.23 [1.17, 1.30]),
Table 1—Associations between anthropometric indexes and CVD events among participants in the WHI study (1994–2017)

|                      | Primary analysis, HR (95% CI) | Sensitivity analysis, HR (95% CI) |
|----------------------|-------------------------------|----------------------------------|
|                      | Model 1 (N = 109,536)c         | Model 2 (N = 82,370)c             | Model 1 (N = 79,641)c         | Model 2 (N = 59,835)c |
| WHR >0.5             | 1.61 (1.54, 1.68)              | 1.29 (1.22, 1.36)                | 1.50 (1.42, 1.58)             | 1.29 (1.21, 1.38)               |
| Per 0.1-increment    | 1.31 (1.29, 1.34)              | 1.15 (1.11, 1.18)                | 1.28 (1.24, 1.32)             | 1.17 (1.12, 1.21)               |
| BMI                  |                               |                                  |                                |                               |
| Normal               |                               |                                  |                                |                               |
| Underweight          | 1.07 (0.83, 1.38)              | 1.10 (0.82, 1.48)                | 0.95 (0.70, 1.28)             | 1.03 (0.73, 1.45)               |
| Overweight           | 1.27 (1.21, 1.33)              | 1.16 (1.09, 1.23)                | 1.24 (1.17, 1.32)             | 1.19 (1.11, 1.27)               |
| Obese                | 1.58 (1.50, 1.67)              | 1.19 (1.11, 1.27)                | 1.47 (1.38, 1.57)             | 1.22 (1.12, 1.32)               |
| Interaction with WHtR (P value) | 0.15                           |                                  |                               | 0.16                           |
| WC >88 cm            | 1.57 (1.50, 1.63)              | 1.23 (1.17, 1.30)                | 1.46 (1.39, 1.54)             | 1.23 (1.16, 1.31)               |
| Interaction with WHtR (P value) | 0.02                           |                                  |                               | 0.02                           |
| WHR ≥0.85            | 1.61 (1.54, 1.67)              | 1.25 (1.19, 1.32)                | 1.50 (1.42, 1.58)             | 1.25 (1.17, 1.34)               |
| Interaction with WHtR (P value) | <0.01                          |                                  |                               | <0.01                          |
| Weight change in kg  |                               |                                  |                                |                               |
| <5 kg                |                               |                                  |                                |                               |
| Loss ≥5 kg           | 1.28 (1.20, 1.37)              | 1.19 (1.10, 1.29)                | 1.30 (1.19, 1.41)             | 1.23 (1.11, 1.36)               |
| Gain ≥5 kg           | 1.16 (1.09, 1.25)              | 1.03 (0.95, 1.12)                | 1.17 (1.07, 1.27)             | 1.05 (0.95, 1.16)               |
| Interaction with WHtR (P value) | 0.84                           |                                  |                               | 0.52                           |

*Adjusted for baseline diabetes status; excluded CVD and cancer cases at baseline. †Excluded diabetes and cancer cases at baseline and follow-up. ‡Covariates in model 1: age at baseline, region in the U.S., race/ethnicity, and subcohort indicators (participating in observational study or clinical trials). Model 2: covariates in model 1 plus alcohol intake, smoking status, energy expenditure from recreational physical activity, dietary energy, total carbohydrates/sugar/protein, dietary glycemic index, hysterectomy history, use of hormone replacement therapy, personal history of diabetes, personal history of hypertension, personal history of high cholesterol requiring medication, family history of diabetes, family history of stroke or heart attack, education, and family income. ‡P value for interaction with WHtR. ‡Due to missing anthropometric data at year 3 follow-up, 95,696 participants were included in model 1 and 72,451 participants were included in model 2; for sensitivity analysis, 69,240 participants were included in model 1 and 52,381 participants were included in model 2.

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References

1. Ashwell M, Gunn P, Gibson S. Waist-to-height ratio is a better screening tool than waist circumference and BMI for adult cardiometabolic risk factors: systematic review and meta-analysis. Obes Rev 2012;13:275–286
2. Lo K, Wong M, Khalechelvam P, Tam W. Waist-to-height ratio, body mass index and waist circumference for screening paediatric cardio-metabolic risk factors: a meta-analysis. Obes Rev 2016;17:1258–1275
3. Song Y, Huang YT, Song Y, et al. Birthweight, mediating biomarkers and the development of type 2 diabetes later in life: a prospective study of multi-ethnic women. Diabetologia 2015;58:1220–1230
4. World Health Organization. Waist circumference and waist:hip ratio: report of a WHO expert consultation, Geneva, 8-11 December 2008. Available from https://www.who.int/nutrition/publications/obesity/WHO_report_waistcircumference_and_waisthip_ratio/en/ Accessed 12 March 2019
5. Cederholm T, Bosaues I, Barazoni R, et al. Diagnostic criteria for malnutrition – an ESPEN Consensus Statement. Clin Nutr 2015;34:335–340
6. Rothman KJ. BMI-related errors in the measurement of obesity. Int J Obes 2008;32(Suppl. 3):S56–S59