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Waist-to-hip ratio is better at predicting subclinical atherosclerosis than body mass index and waist circumference in postmenopausal women

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ABSTRACT

Objective: Body fat distribution becomes more central after menopause. Although some studies have identified the superiority of various anthropometric indices to assess general health outcomes, very limited studies have compared the efficacy of body mass index (BMI), waist circumference (WC), and waist-to-hip ratio (WHR) to predict subclinical atherosclerosis according to menopausal status.
Methods: In total, 442 participants (209 premenopausal women and 233 postmenopausal women) were prospectively enrolled from the Health Promotion Center of Korea University Guro Hospital. We examined subclinical atherosclerosis using carotid intima-media thickness (CIMT) and brachial-ankle pulse wave velocity (baPWV).
Results: In premenopausal women, all anthropometric parameters such as BMI, WC and WHR were positively correlated with baPWV and CIMT values, whereas in postmenopausal women, only WHR was positively correlated with baPWV values (0.27, $P < 0.01$), and WC and WHR were positively correlated with CIMT (0.15, $P < 0.05$ and 0.21, $P < 0.01$, respectively). By receiver operating characteristic (ROC) curve analyses, WHR was superior to the other anthropometric indices to predict carotid atherosclerosis in postmenopausal women. Furthermore, the normal weight (BMI < 23 kg/m^2) with higher WHR group had a significantly thicker CIMT when compared to the normal weight with lower WHR group (0.76 mm vs. 0.68 mm, $P < 0.01$) and even the overweight subjects with BMI ≥ 23 kg/m^2 (0.76 mm vs. 0.70 mm, $P < 0.01$) in postmenopausal women.
Conclusions: The present study shows that WHR has the best potential for predicting subclinical atherosclerosis compared to BMI and WC in postmenopausal women.
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1. Introduction

Cardiovascular disease (CVD) is the first leading cause of death worldwide, still accounting for 31.9% of all mortality in 2010 [1]. CVD is also the primary cause of death in women of westernized countries with more than one in two women dying from CVD [2]. However, premenopausal women appear to be protected from CVD compared with men of a similar age. Women aged <50 years rarely develop CVD, whereas by age 70, the incidence of CVD is similar in men and women [2]. This means that the transition from pre- to postmenopause is associated with a rapid increase in many features of the metabolic disturbances leading to CVD. Therefore, a more accurate understanding of these metabolic changes with menopause will help early risk stratification for postmenopausal women with future CVD.

Obesity is a well-established risk factor of atherosclerosis and cardiovascular events. However, a generalized obesity index such as body mass index (BMI) cannot fully reflect the risk of obesity-related metabolic complications [3]. Instead, waist circumference (WC) and waist-to-hip ratio (WHR) are widely used, because anthropometric measures of abdominal obesity appear to be more strongly associated with metabolic risk factors [4]. In a prospective

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cohort study from the Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation (ADVANCE) trial, BMI was not related to any CVD events, whereas WHR had the best predictive capability [5]. When compared with WC, the additional factors reflected by WHR might be influenced by gluteal subcutaneous fat, which has a protective role against metabolic disturbances by increasing lipolysis and fatty acid storage [6]. Therefore, WHR can provide more information about body fat distribution than WC.

Body fat distribution changes across menopause with a preferential increase in abdominal adiposity caused by estrogen deficiency. The abdominal to total-body fat tissue ratio measured by dual-energy X-ray absorptiometry was significantly increased in postmenopausal women, and it was independently related to years since menopause [7]. Furthermore, Poehlman et al. [8] found that natural postmenopausal women showed increased WHR when compared with age-matched premenopausal women. Therefore, the superiority of various obesity indices such as BMI, WC, and WHR to predict metabolic risk might be different according to the menopause status. Very recently, Liu et al. [9] reported that among the indicators of central obesity, WHR is the best predictive marker for metabolic syndrome development in Chinese postmenopausal women. However, no study has compared the utility of various obesity indices to predict subclinical atherosclerosis in pre- and postmenopausal women simultaneously.

Therefore, the objective of the present analyses was to compare the predictive value of each anthropometric marker (BMI, WC, and WHR) for predicting subclinical atherosclerosis, represented as carotid intima-media thickness (CIMT) and brachial-ankle pulse wave velocity (baPWV), in Korean pre- and postmenopausal women without CVD.

2. Methods

2.1. Study design and participants

Participants were prospectively recruited based on inclusion and exclusion criteria from individuals who were self-referred for a routine health check-up at the Health Promotion Center of Korea University Guro Hospital between April 2012 and May 2013. Participants were apparently healthy Korean women aged 20–80 years residing in Seoul, South Korea. Subjects were excluded from this study if they met any of the following criteria: history of CVD (myocardial infarction, unstable angina, stroke, or cardiovascular revascularization); stage 2 hypertension (resting blood pressure, ≥160/100 mmHg); history of inflammatory conditions that affect the study results; taking medications that might affect inflammatory status, including steroidal and non-steroidal anti-inflammatory drugs within 6 months; malignancy or severe renal or hepatic disease; surgical menopause; uncertain age of menopause; and history of hormone replacement therapy. Menopause was defined as at least 12 months of amenorrhea resulting in permanent cessation of ovarian function. Medical histories and lifestyle information were collected for all subjects by personal interview using a detailed questionnaire. All participants provided written informed consent, and the Korea University Institutional Review Board approved this study protocol in accordance with the Declaration of Helsinki of the World Medical Association.

2.2. Anthropometric and laboratory measurements

BMI was calculated as weight/height^2 (kg/m^2), and waist circumference (in centimeters) was measured at the midpoint between the lower border of the rib cage and the iliac crest. Hip circumference (in centimeters) was measured at the level of the widest circumference over the buttocks. Waist-to-hip ratio was calculated as waist circumference divided by hip circumference. All blood samples were obtained in the morning after a 12-h overnight fast and were immediately stored at −80 °C for subsequent assays. Serum triglyceride and high-density lipoprotein cholesterol levels were determined enzymatically using a model 747 chemistry analyzer (Hitachi, Tokyo, Japan). The glucose oxidase method was used to measure plasma glucose levels. Latex-enhanced turbidimetric immunoassay (HiSens hsCRP LTIA; HBI, Anyang, Korea) was used for measurement of high-sensitivity C-reactive protein with an interassay coefficient of variation of 7.2%.

2.3. Measurement of CIMT for analysis of carotid atherosclerosis

The IMT of the common carotid artery was determined using high-resolution B-mode ultrasonography (EnVisor; Philips Healthcare, Andover, MA, USA) with a 5- to 12-MHz transducer. CIMT measurements were made using a software (Intimascope; Media Cross Co., Tokyo, Japan) at three levels of the far wall, 1–3 cm proximal to the carotid bifurcation. The mean CIMT was the average value of 99 computer-based points in the region, and the maximal CIMT was the IMT value at a maximal point of the region. The intra-observer variability coefficient of CIMT was 0.93. In this study, carotid plaque was defined by a CIMT ≥1.5 mm or by a focal increase in thickness of 0.5 mm or 50% of the surrounding CIMT value, while carotid atherosclerosis was defined by a mean CIMT >0.9 mm or the existence of carotid plaque, all according to the 2013 European Society of Hypertension and the European Society of Cardiology guidelines for the management of arterial hypertension [10]. A single trained technician who was unaware of the subjects' anthropometric and laboratory data recorded all measurements.

2.4. Measurement of baPWV for analysis of arterial stiffness

After a subject rested in the supine position for 5 min, baPWV was measured using a BP-203RPE II volume-plethysmography apparatus (Colin, Komaki, Japan), which simultaneously records baPWV and brachial and ankle blood pressure on the left and right sides. baPWV was calculated as the mean of the left and right baPWV values. Details of this method, including the validity and reproducibility, have been described in previous studies [11,12].

2.5. Statistical analyses

Each variable was assessed for a normal distribution. Data are expressed as a median (interquartile range [25–75%]). The data were described by menopausal status category, and differences between groups were tested using the Mann–Whitney *U*-test for continuous variables. Spearman correlation analysis was used to analyze the association of various anthropometric parameters including BMI, WC, and WHR with subclinical atherosclerosis represented as baPWV and CIMT for each group. The R package, CompOverlapCorr (developed by Li and Zhu, 2006; see R user's manual), was used to compare the correlation coefficients across various anthropometric parameters for predicting baPWV and CIMT values in pre- and postmenopausal women. The receiver operating characteristic (ROC) curve analysis was used to assess the accuracy of predictions for carotid atherosclerosis. The comparison of the area under the ROC curve (AUC) for two ROC curves was performed using the DeLong test. A *P*-value <0.05 was considered statistically significant in all analyses. We used the Kruskal–Wallis test and multiple comparison analysis for comparison of CIMT values in the subjects with normal BMI and overweight BMI according to the higher and lower WHR groups (cut off: median value within each group). All statistical results were based on two-sided tests. Data were analyzed using SPSS 20 for Windows