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Longitudinal association of anthropometric measures of adiposity with cardiometabolic risk factors in postmenopausal women

Geoffrey C. Kabat[a,*], **Moonseong Heo**[a], **Linda V. Van Horn**[b], **Rasa Kazlauskaite**[c], **Asqual Getaneh**[d], **Jamy Ard**[e], **Mara Z. Vitolins**[e], **Molly E. Waring**[f], **Oleg Zaslavsky**[g], **Sylvia Wassertheil Smoller**[a], and **Thomas E. Rohan**[a]

Geoffrey C. Kabat: Geoffrey.kabat@einstein.yu.edu; Moonseong Heo: Moonseong.heo@einstein.yu.edu; Linda V. Van Horn: lvanhorn@northwestern.edu; Rasa Kazlauskaite: rasa_kazlauskaite@rush.edu; Asqual Getaneh: asqual.getaneh@medstar.net; Jamy Ard: jard@wakehealth.edu; Mara Z. Vitolins: mvitolin@wakehealth.edu; Molly E. Waring: Molly.waring@umassmed.edu; Oleg Zaslavsky: oleg.zaslavsky@fulbrightmail.org; Sylvia Wassertheil Smoller: Sylvia.smoller@einstein.yu.edu; Thomas E. Rohan: Thomas.rohan@einstein.yu.edu

[a]Department of Epidemiology and Population Health, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY 10461, USA

[b]Department of Preventive Medicine, Fineberg School of Medicine, Northwest University, 680 N Lake Shore Drive, Suite 1400, Chicago IL 60611, USA

[c]Department of Preventive Medicine, Rush University Medical Center, 1700 W. Van Buren St., Suite 470, Chicago, IL 60612, USA

[d]MedStar Health Research Institute, MedStar Health, 6525 Belcrest Road, Suite 700, Hyattsville, MD 20782, USA

[e]Department of Epidemiology and Prevention, Wake Forest School of Medicine, Medical Center Blvd., Winston-Salem, NC 27157, USA

[*]Corresponding author: Geoffrey C. Kabat, Department of Epidemiology and Population Health, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY 10461; Tel. 718-430-3038; Fax: 718-430-8653., geoffrey.kabat@einstein.yu.edu.

The authors have no competing interests.

SHORT LIST OF WHI INVESTIGATORS

Program Office: (National Heart, Lung, and Blood Institute, Bethesda, Maryland) Jacques Rossouw, Shari Ludlam, Dale Burwen, Joan McGowan, Leslie Ford, and Nancy Geller

Clinical Coordinating Center: Clinical Coordinating Center: (Fred Hutchinson Cancer Research Center, Seattle, WA) Garnet Anderson, Ross Prentice, Andrea LaCroix, and Charles Kooperberg

Investigators and Academic Centers: (Brigham and Women's Hospital, Harvard Medical School, Boston, MA) JoAnn E. Manson; (MedStar Health Research Institute/Howard University, Washington, DC) Barbara V. Howard; (Stanford Prevention Research Center, Stanford, CA) Marcia L. Stefanick; (The Ohio State University, Columbus, OH) Rebecca Jackson; (University of Arizona, Tucson/ Phoenix, AZ) Cynthia A. Thomson; (University at Buffalo, Buffalo, NY) Jean Wactawski-Wende; (University of Florida, Gainesville/ Jacksonville, FL) Marian Limacher; (University of Iowa, Iowa City/Davenport, IA) Robert Wallace; (University of Pittsburgh, Pittsburgh, PA) Lewis Kuller; (Wake Forest University School of Medicine, Winston-Salem, NC) Sally Shumaker

Women's Health Initiative Memory Study: (Wake Forest University School of Medicine, Winston-Salem, NC) Sally Shumaker

For a list of all the investigators who have contributed to WHI science, please visit: https://cleo.whi.org/researchers/SitePages/Write%20a%20Paper.aspx

[f]Division of Epidemiology of Chronic Diseases and Vulnerable Populations, Department of Quantitative Health Sciences, University of Massachusetts Medical School, 55 Lake Avenue, North Worcester, MA 01655, USA

[g]The Cheryl Spencer Institute for Nursing Research, University of Haifa, Main Building, Fl. 500, room 570, Haifa 31905, Israel

Abstract

Purpose—Some studies suggest that anthropometric measures of abdominal obesity may be superior to body mass index for the prediction of cardiometabolic risk factors; however, most studies have been cross-sectional. Our aim was to prospectively examine the association of change in body mass index (BMI), waist-hip ratio (WHR), waist circumference (WC), and waist circumference-height ratio (WCHtR) with change in markers of cardiometabolic risk in a population of postmenopausal women.

Methods—We used a subsample of participants in the Women's Health Initiative aged 50 to 79 at entry with available fasting blood samples and anthropometric measurements obtained at multiple time points over 12.8 years of follow-up (N = 2,672). The blood samples were used to measure blood glucose, insulin, total cholesterol, LDL-C, HDL-C, and triglycerides at baseline, and at years 1, 3, and 6. We conducted mixed-effects linear regression analyses to examine associations at baseline and longitudinal associations between change in anthropometric measures and change in cardiometabolic risk factors, adjusting for covariates.

Results—In longitudinal analyses, change in BMI, WC, and WCHtR robustly predicted change in cardiometabolic risk, whereas change in WHR did not. The strongest associations were seen for change in triglycerides, glucose, and HDL-C (inverse association).

Conclusion—Increase in BMI, WC, and WCHtR strongly predicted increases in serum triglycerides and glucose, and reduced HDL-C. WC and WCHtR were superior to BMI in predicting serum glucose, HDL-C, and triglycerides. WCHtR was superior to WC only in predicting serum glucose. BMI, WC, and WCHtR were all superior to WHR.

Keywords

obesity; anthropometric measures; cardiometabolic risk factors; insulin resistance

Introduction

Obesity and central adiposity are established risk factors for diabetes, coronary heart disease, certain cancers, and all-cause mortality [1–4]. In order to elucidate the mechanisms underlying these associations, numerous studies have examined the association between anthropometric measures of adiposity and levels of cardiometabolic risk factors [5–22]. Particular interest has focused on whether measures of central adiposity have greater discriminatory power in predicting metabolic risk compared to measures of overall adiposity, such as body mass index (BMI) [23–28]. The superiority of measures of central adiposity over BMI is suggested by studies indicating that, compared to BMI, waist circumference is more closely associated with metabolic risk (23) as well as by studies indicating the importance of visceral fat accumulation for cardiometabolic risk [29].

Among the studies that have compared various anthropometric measures of obesity (BMI, waist-to-hip ratio [WHR], waist circumference [WC], and/or waist circumference-to-height ratio [WCHtR]), some have found that measures of abdominal adiposity were superior to BMI [7–9, 14, 15, 19], whereas others have found no difference [5, 11, 13, 16, 18, 21, 23] or have found WHR to be superior to other anthropometric measures in predicting certain cardiometabolic factors [12, 17, 20]. The majority of these studies have been cross-sectional [6–10, 12, 13, 15, 17–20, 22]. Among the smaller number of prospective studies [5, 11, 14, 16, 21], few have examined change in different measures of adiposity in relation to change in serum levels of cardiometabolic markers [16]. Furthermore, some studies did not control for potential confounding factors other than age and sex [7, 8, 9, 12, 15, 18]. Several meta-analyses have compared different anthropometric indices in relation to cardiometabolic risk [24–28]; however, these have relied mainly on cross-sectional studies, and their conclusions are somewhat discrepant.

Use of repeated measurements of both anthropometric measures of adiposity and of metabolic factors over time allows us to capture changes over time, and therefore may provide a clearer picture of associations between these variables. We used data from a sub-cohort of the Women's Health Initiative (WHI) to compare the association of change in different anthropometric measures and changes in cardiometabolic risk factors over time among postmenopausal women. We hypothesized that measures of central obesity would show stronger associations with cardiometabolic risk than measures of overall obesity. Because the metabolic syndrome assesses the clustering of cardiometabolic risk factors, we also examined the association of different anthropometric measures with a "metabolic score" based on the number of risk factors exhibited by each subject.

Material and Methods

Study population

The WHI is a large, multi-center prospective study designed to identify the causes of major chronic diseases in postmenopausal women [30]. Women between the ages of 50 and 79 and representing major racial/ethnic groups were recruited from the general population at 40 clinical centers throughout the US between 1993 and 1998. In total, 68,132 and 93,676 women were enrolled in the clinical trial (CT) and the observational study (OS) of the WHI, respectively. Details of the study design and reliability of the baseline measures of demographic and health characteristics have been published [30, 31].

The study population for the present analysis was derived from the 6% random sample of women in the CT [N = 4,544] who provided fasting blood samples at baseline and years 1, 3, and 6 during follow-up and a 1% sample of women in the OS [N= 1,062] who provided a fasting blood sample at baseline and at year 3. The 6% random sample was stratified by age, clinical center, and hysterectomy status, with over-sampling of minority groups to increase the numbers of Black, Hispanic and Asian-Pacific women. Of the 5,606 women with measured analytes, we restricted our analysis to the subcohort of 2,672 women who were in the OS or in the control arms of the CT, in order to eliminate the effects of interventions.

Data collection and variable definition

At study entry, self-administered questionnaires were used to collect information on demographics, medical, reproductive, and family history, and on dietary and lifestyle factors, including smoking history, alcohol consumption, and recreational physical activity. Questions about physical activity at baseline referred to a woman's usual pattern of activity, including walking and recreational physical activity. From these data, current total leisure-time physical activity (MET-hours/week) was computed by multiplying the number of hours per week of specific leisure-time physical activities by the metabolic equivalent (MET) value of the activities and summing over all types of activities [32].

Assessment of anthropometric measures

Trained staff measured weight, height, and waist and hip circumferences according to a standard protocol. A balance beam scale that measures in kilograms was used for all weight measurements. Weight was measured to the nearest 0.1 kg. Height was measured using a wall-mounted stadiometer that measures in centimeters. Participants were asked to remove their shoes and to stand erect, facing straight ahead, with arms hanging loosely at their sides. Height was measured to the nearest 0.1 cm. Waist circumference at the natural waist or narrowest part of the torso, and hip circumference at the maximal circumference, were recorded to the nearest 0.1 cm. Anthropometric measurements were also taken during follow-up (in years 1, 3, and 6). BMI was computed as weight in kilograms divided by the square of height in meters. In addition to WC and WHR, we created the variable WCHtR, which in some studies has been shown to be superior to BMI or WC in predicting mortality [33, 34] and cardiometabolic risk [23–28]. WCHtR may be superior to WC in predicting individual metabolic risk, since the height adjustment standardizes adipose tissue distribution for body size [34].

Assessment of cardiometabolic risk factors

Cardiometabolic risk factors studied here included serum glucose, insulin, Homeostasis Model Assessment Insulin Resistance (HOMA-IR) ([fasting insulin (μIU/mL) X fasting glucose (mg/dL)]/22.5) [35], serum HDL-C, LDL-C, total cholesterol, triglycerides, and systolic and diastolic blood pressure. At each visit, two blood pressure measurements were obtained ≥30 seconds apart while subjects were seated, and the average of the two measurements was used in the analysis. Values for anthropometric measures and blood pressure in the years corresponding to the blood analytes were used in the analysis. Fasting blood samples were collected with minimal stasis and maintained at 4° C until plasma/serum was separated. Plasma/serum aliquots were then frozen at −70° C and sent on dry ice to the central repository (Fisher BioServices, Rockville, MD), where storage at −70° C was maintained.

Serum glucose was measured using the hexokinase method on a Hitachi 747 analyzer (Boehringer Mannheim Diagnostics, Indianapolis, Indiana) [36, 37]. An ongoing monthly quality assurance program was maintained with the Diabetes Diagnostic Laboratory (DDL) at the University of Missouri. Monthly inter-assay coefficients of variation (CV) were <2% for mean concentrations of 84 and 301 mg/dL. Serum insulin was measured in a step-wise sandwich ELISA procedure following the manufacturer's instruction (BMD, Indianapolis,

Indiana) [38]. The bound insulin is then quantitated using a second monoclonal antibody labeled with peroxidase, which then reacts with a chromogenic substrate to generate a photometrically monitored chromogen. Monthly inter-assay CVs were 4.7–9.5% and 3.2–7.9% at mean concentrations of 26.6 and 80.6 microIU/ml, respectively. Total cholesterol and triglycerides were analyzed by enzymatic methods on a Hitachi 747 analyzer [39]. High-density lipoprotein (HDL-C) was isolated using heparin manganese chloride [40]. Coefficients of variation for total cholesterol, triglycerides, and HDL-C were all ≤2.0.

Assessment of diabetes and the metabolic syndrome

A history of diabetes was based on self-report of taking diabetes medication or having a fasting glucose of ≥126 mg/dL at baseline. Diabetes occurring during follow-up was based on self-report of diabetes medication use or a fasting glucose ≥126 mg/dL during the follow-up period. We used the definition of the metabolic syndrome proposed by the Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program (NCEP) [41, 42]. An indicator variable was created for presence of the metabolic syndrome (yes/no), defined as having 3 or more of the following characteristics: waist circumference ≥88 cm, fasting glucose ≥110 mg/dL or diabetes medication, fasting HDL-C <50 mg/dL, fasting triglycerides ≥150 mg/dL, and blood pressure ≥130/85 mmHg or anti-hypertension medication. In addition, we created an ordinal variable for metabolic score, ranging from 0 to 4 depending on the number of metabolic factors above/below the cutoffs, with “0” representing no cardiometabolic risk factors and “4” representing 4 or 5 risk factors.

Statistical analysis

Baseline characteristics of the subcohort were summarized in terms of means (± standard deviations) and frequencies. Means and standard deviations were computed for measurements of cardiometabolic factors and anthropometric measures at each time point. The association of a given anthropometric factor with each cardiometabolic factor at baseline was estimated first using Pearson correlation coefficients followed by partial correlations adjusted for multiple covariates: age (continuous), smoking status (never, former, current smoker), alcoholic drinks per week (continuous), MET hrs per week (continuous), education (less than high school, high school grad, some college, post-college, and race/ethnicity (White, Black, other). Mixed-effects linear models were used to assess the association of anthropometric factors and cardiometabolic factors at baseline and longitudinally, with anthropometric measures as the independent variables and cardiometabolic factors as the dependent variables. To permit comparison of regression coefficients across different anthropometric measures, we converted the repeatedly-measured anthropometric measures to their corresponding z-scores, which center the measures on their means and then divide by their standard deviations. Therefore, the estimated regression coefficients represent the increase in a metabolic factor associated with a 1 SD-unit increase in an anthropometric factor for both baseline/cross-sectional and repeatedly-measured longitudinal analyses. In the longitudinal analysis, change in anthropometric factors measured at different time points was regressed on change in contemporaneously measured cardiometabolic risk factors. Age-adjusted- and multivariable-adjusted models with baseline and time-varying covariates were run for each metabolic factor. Covariates included in the multivariable models were the same as those included in

the partial correlation analysis (see above). In alternative models, we additionally included ever use of oral contraceptives (yes, no) and ever use of hormone therapy (yes, no). However, the results were unchanged, and we present the model without these two covariates. To compare differences in the associations with different predictors, we tested the equality of the regression coefficients of the longitudinal z-scores between pairs of predictors of the metabolic factors using mixed-effects models in which the z-score difference was the primary predictor controlling for the covariates. Because of the large number of possible comparisons, we limited statistical testing to the cardiometabolic risk factors that showed the strongest associations with anthropometric measures (i.e., glucose, triglycerides, and HDL-C) and are, therefore, likely to be most clinically meaningful. We further carried out two sensitivity analyses: 1) excluding women with a history of cardiovascular disease (CVD), cancer (other than squamous or basal cell skin cancer), or diabetes prior to baseline (N of remaining sample: 2,166 women) and 2) excluding women who developed CVD, cancer, or diabetes during follow-up (N of the remaining sample = 1,667). All significance tests were 2-tailed. Analyses were done with SAS v9.3 (SAS Institute, Cary, North Carolina).

Results

Baseline characteristics of the study population are shown in Table 1. Women in the present study had a mean BMI of 28.5 kg/m^2. The proportions of women with a history of diabetes, cardiovascular disease, hypertension, and cancer were: 7.8, 9.8, 37.9, and 6 percent, respectively. Thirty-three percent of women met the definition of the metabolic syndrome.

Mean levels of anthropometric variables and cardiometabolic risk factors at 4 time points are shown in Table 2. There was a slight increase in anthropometric measures from baseline to year 6. Mean levels of several cardiometabolic factors declined modestly (HDL-C, LDL-C, total cholesterol, systolic blood pressure, diastolic blood pressure), whereas there was no clear trend in other variables. With the exception of triglycerides, the means of all other variables over the 4 time points were statistically different. (Results were similar when the sample was restricted to women with all 4 measurements for each factor).

In the baseline data, the strongest partial Pearson correlations of anthropometric measures with cardiometabolic factors were seen for HDL-C, insulin, glucose, and triglycerides (Table 3). Compared to BMI and WHR, WC and WCHtR showed stronger partial correlations with the following metabolic factors: glucose (r for WC = 0.26 and for WCHtR = 0.25), insulin (r = 0.30 for both), HOMA-IR (r = 0.22 for both), HDL-C (r = −0.32 for both), and metabolic score (0.40 for both). WC, WCHtR, and WHR showed comparable correlations with triglycerides (0.26–0.28). BMI and WCHtR had the strongest correlations with systolic blood pressure, whereas BMI had the strongest correlation with diastolic blood pressure. Correlations between personal characteristics and cardiometabolic risk factors were generally weak, with the exception of a positive correlation between HDL-C and alcohol intake (r = 0.18) and an inverse association between HDL-C and physical activity (r = −0.16) (data not shown).

Table 4 shows the beta-coefficients for change in the mean level of cardiometabolic risk factors associated with a 1-unit (SD) increase in the z-score for anthropometric measures at baseline, with adjustment for multiple covariates. For example, a 1-SD unit increase in WC was associated with an increase in triglyceride level of 20.8 mg/dL. With the exception of the association of BMI, WC, and WCHtR with total cholesterol, all 4 anthropometric factors had statistically significant positive associations with all cardiometabolic factors. The strongest associations (based on comparing the β-coefficients) were seen between anthropometric factors and triglycerides, HDL-C (inverse), and glucose. WC and WCHtR appeared to be slightly better predictors of change in glucose, insulin, HOMA-IR, and HDL-C compared to BMI, but the differences were not large. Coefficients for the associations of anthropometric factors with triglycerides were 14.8 for BMI, 20.8 for WC, 20.6 for WCHtR, and 24.1 for WHR. WHR showed associations with HDL-C (inverse), LDL-C, total cholesterol, and triglycerides, which were stronger or comparable to those of the other anthropometric factors. Diastolic blood pressure was most strongly associated with BMI.

The pattern of associations with BMI, WC, and WCHtR in the longitudinal analysis using all values for the predictor and dependent variables at all time points (Table 5) was generally similar to that of the baseline analysis. As in the baseline analysis, the strongest associations overall were those with triglycerides, glucose, and HDL-C. The association of WCHtR with glucose was significantly stronger than that of WC, and the associations of WC with glucose, HDL-C, and triglycerides was significantly stronger than those of BMI. In contrast to the baseline analysis, the association of change in WHR with changes in cardiometabolic factors was greatly attenuated, and its associations with change in LDL-C, total cholesterol, and diastolic blood pressure were no longer statistically significant. Change in BMI showed the strongest association with both change in systolic and diastolic blood pressure.

In the sensitivity analysis repeating the fully-adjusted longitudinal analysis after excluding women with a prior history of cancer, CVD, or diabetes, the pattern of associations was unchanged (N remaining = 2,166; data not shown). In the sensitivity analysis excluding women who developed CVD, cancer, or diabetes during follow-up (N remaining = 1,667; data not shown), several associations were attenuated. For all anthropometric factors, the association of all anthropometric measures with glucose was reduced by half; however, the associations were still highly statistically significant ($p < 0.0001$). Smaller attenuations were seen for HDL-C and triglycerides. Overall, however, the pattern of associations was similar to that in the main analysis.

Discussion

Few studies have examined the longitudinal association of change in anthropometric measures of obesity and change in levels of cardiometabolic risk factors [16]. We found significant associations between change in anthropometric measures and change in cardiometabolic factors over a 7-year period. In the baseline analysis all 4 anthropometric variables showed robust associations with cardiometabolic factors. In the longitudinal analysis WHR showed greatly attenuated associations. In contrast, BMI, WC, and WCHtR all showed stronger associations with most cardiometabolic risk factors. Compared to BMI,

WC and WCHtR appeared to be superior predictors of change in triglycerides, glucose, and HDL-C (inverse association).

Previous studies that have examined the association of different anthropometric measures of obesity with metabolic factors have been mostly cross-sectional [5–22]. Some had small numbers [7, 12, 18] or selected subjects in specific weight categories [7, 10, 18]. Many of these studies did not adjust for basic sociodemographic or behavioral characteristics [6–10, 12, 15, 18–20]. A number of these studies suggested that WC or WCHtR are stronger predictors of cardiometabolic risk than BMI [6–9, 14, 15, 17, 19, 20], and some suggested that WCHtR may be superior to WC [9, 15, 17]. However, other studies found no difference between indices of overall and central obesity in prediction of cardiometabolic risk [5, 8, 10, 13, 16, 18].

Recently, several meta-analyses have been published comparing WC and WCHtR with BMI with respect to their associations with cardiometabolic factors [24–28]. These meta-analyses included both 1) cross-sectional studies with measurements of anthropometric variables and cardiometabolic factors, and 2) prospective studies which examined diabetes and CVD as outcomes. In several meta-analyses WCHtR appeared to be a better discriminator of cardiometabolic risk than BMI [24, 25, 27, 28]. However, the meta-analysis by van Dijk et al. [26] reported that WC was superior to other measures, including WCHtR. In most studies, differences between WC and WCHtR were modest, and in some meta-analyses were not statistically significant [24]. The studies included in these meta-analyses all appear to have used a single baseline measurement for both anthropometric factors and metabolic factors. Savva et al. [28] found substantial heterogeneity among studies, which was not explained by meta-regression evaluating sex, Asian/non-Asian population, and optimal BMI or WCHtR cutoffs. They concluded that further research is needed to assess the relative merits of WCHtR and BMI in predicting metabolic risk in different populations.

Our results suggest that adjustment for confounding variables and, to a greater extent, use of repeated measurements, may influence the results obtained. For example, in the baseline analysis WHR showed the strongest association with triglyceride levels, whereas in the repeated measures analysis, WHR was the weakest predictor. Additionally, in the baseline analysis, WHR was the strongest predictor of LDL-C; however, in the longitudinal analysis, WHR was no longer significantly associated with LDL-C. Similarly, the baseline associations of WHR with HDL-C and total cholesterol were markedly attenuated in the longitudinal analysis.

Several previous studies which examined cross-sectional associations reported that WHR was superior or comparable to other anthropometric measures in predicting glucose [12], LDL-C [20], triglycerides [12, 20], reduced HDL-C [12, 20], and development of the metabolic syndrome [17]. Our findings suggest these cross-sectional associations with WHR might be overestimates of the effect of change in WHR on change in these cardiometabolic risk factors.

In contrast with WHR, in our longitudinal analysis BMI, WC, and WCHtR were all stronger predictors of cardiometabolic risk. Our results add to the evidence that measures of

abdominal adiposity (WC and WCHtR) may be superior to BMI for the prediction of cardiometabolic risk. While WCHtR showed a marginally stronger association with several risk factors compared to WC, the difference was statistically significant only for serum glucose.

It should also be mentioned that most studies have assessed the association of anthropometric factors and metabolic risk factors measured in mid-life. However, as suggested by a recent study [43] that examined the association of BMI at 3 time points, including early adulthood, with total mortality and cause-specific mortality, the onset of weight gain at an early age in adulthood appears to carry a greater risk than onset in middle age or later. Thus, there is a need for prospective studies with a variety of anthropometric measurements made at different times throughout the life course to assess the full impact of different anthropometric measures on cardiometabolic risk in later life.

Strengths of the present study include the large number of women with measurements of a wide range of cardiovascular risk factors and clinical variables and the availability of repeated measurements of anthropometric variables and cardiometabolic factors over follow-up, which may provide a clearer picture of associations between these variables than has been provided by cross-sectional studies. In addition, we adjusted for a number of covariates, including markers of socioeconomic status that could affect the associations under study.

Our study has a number of limitations. First, our population is limited to postmenopausal women, and, thus, the observed associations may not apply to premenopausal women or to men. A number of studies [8, 11, 21] indicate that the association of anthropometric factors with cardiometabolic risk factors may differ between men and women. In addition, the number of non-Whites in this small subsample of the WHI was too small to permit separate analyses among other ethnic groups.

In conclusion, longitudinal analyses indicated that, after adjustment for covariates, change in BMI, WC, and WCHtR robustly predicted change in cardiometabolic risk, whereas WHR did not. The strongest associations were seen for change in triglycerides, glucose, and HDL-C. Compared to BMI, WC and WCHtR were statistically superior predictors of glucose, HDL-C, and triglycerides. WCHtR was superior to WC only in predicting change in glucose. BMI, WC, and WCHtR were all superior to WHR.

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Highlights

- We used repeated measures of anthropometric measures and cardiometabolic risk factors to examine the association of change in the former with change in the latter
- Change in waist circumference, waist-to-height ratio, and body mass index (but not waist-hip ratio) showed robust associations with change in triglycerides, insulin, and HDL-cholesterol
- Waist circumference and waist-to-height ratio were superior to body mass index for the prediction of serum glucose, HDL-C, and triglycerides.

Table 1

Baseline characteristics of women in the subcohort of the Women's Health Initiative.

Characteristic	N = 2,672
Age (yrs)[a]	63.1 (± 7.2)
Body mass index (kg/m^2) [a]	28.5 (± 6.0)
Parity [a]	2.6 (± 1.7)
Age at menopause (yrs)[a]	46.9 (± 6.8)
Alcohol (servings/week)[a]	1.8 (± 4.2)
Physical activity (METs/week[b])[a]	10.9 (± 13.4)
Oral contraceptive use (% ever)	40.7
Hormone therapy use (% ever)	50.9
Age at menarche (% ≤12 yrs)	47.6
Age at first birth (% ≥30 yrs)	10.1
Education (%)	
Less than high school grad	8.3
High school grad – some college	57.2
College grad	9.5
Post-college	25.0
Ethnicity (%)	
White	55.0
Black	21.9
Other	23.1
Smoking (%)	
Never	52.5
Former	39.7
Current	7.8
History of diabetes (%)	7.8
History of CVD (%)	9.8
History of hypertension (%)	37.9
History of cancer	6.0
Presence of the metabolic syndrome (%)	32.7

[a] Mean (± SD)

[b] MET, metabolic equivalent tasks (defined as the caloric need per kilogram of body weight per hour of activity divided by the caloric need per kilogram of body weight per hour at rest) per hour per week.

Table 2

Baseline and subsequent levels (mean ± SD) of anthropometric and cardiometabolic factors in the subcohort of the Women's Health Initiative.*

	BMI (kg/m^2)	WC (cm)	WCHtR	WHR	Glucose (mg/dL)	Insulin (mg/dL)	HOMA-IR
Baseline (N= 2,672)	28.5 ± 6.0	87.5 ± 13.8	0.54 ± 0.09	0.82 ± 0.08	100.2 ± 29.0	11.6 ± 10.7	3.1 ± 5.4
Year 1 (N= 1,412)	29.2 ± 5.9	88.8 ± 13.5	0.55 ± 0.08	0.82 ± 0.08	103.1 ± 30.9	12.4 ± 10.3	3.5 ± 5.9
Year 3 (N= 1,274)	28.7 ± 5.9	88.1 ± 14.2	0.55 ± 0.09	0.82 ± 0.10	101.7 ± 28.8	13.3 ± 10.2	3.6 ± 4.0
Year 6 (N= 1,150)	29.4 ± 6.1	90.8 ± 13.9	0.57 ± 0.09	0.83 ± 0.09	104.2 ± 28.1	11.4 ± 19.1	3.1 ± 5.0
	HDL-C (mg/dL)	**LDL-C (mg/dL)**	**Total cholesterol (mg/dL)**	**Triglycerides (mg/dL)**	**Systolic BP (mm Hg)**	**Diastolic BP (mm Hg)**	**Metabolic score**
Baseline	60.0 ± 16.1	131.8 ± 36.3	221.8 ± 39.3	150.8 ± 84.3	128.8 ± 18.0	76.0 ± 9.3	1.5 ± 1.2
Year 1	58.4 ± 15.1	132.5 ± 35.5	220.9 ± 38.5	150.0 ± 79.4	126.6 ± 16.7	74.8 ± 9.4	1.5 ± 1.2
Year 3	57.0 ± 14.9	131.2 ± 35.9	218.1 ± 38.2	152.2 ± 77.5	127.1 ± 16.9	74.1 ± 9.4	1.5 ± 1.0
Year 6	57.2 ± 14.5	125.6 ± 35.1	212.4 ± 38.9	149.9 ± 80.1	125.7 ± 16.8	71.9 ± 9.5	1.6 ± 1.2

* Except for triglycerides, the means of all the other variables over the four time points are significantly different.

Abbreviations: BMI – body mass index; WC – waist circumference; WCHtR – waist circumference/height; WHR – waist-to-hip ratio; HOMA-IR—homeostasis assessment model – insulin resistance; HDL-C – high-density lipoprotein; LDL-C – low-density lipoprotein.

Table 3

Partial correlations of anthropometric variables and cardiometabolic factors at baseline in the subcohort of the Women's Health Initiative (N = 2,672).[*†]

Metabolic factor / anthropometric factor	BMI	WC	WCHtR	WHR
	r	r	r	r
Glucose	0.21	0.26	0.25	0.21
Insulin	0.26	0.30	0.30	0.22
HOMA-IR	0.19	0.22	0.22	0.17
HDL-C	−0.26	−0.32	−0.32	−0.30
LDL-C	0.03	0.05	0.06	0.08
Total cholesterol	−0.01	0.01	0.01	0.05
Triglycerides	0.19	0.26	0.26	0.28
Systolic BP	0.16	0.14	0.16	0.10
Diastolic BP	0.12	0.11	0.11	0.004
Metabolic score	0.34	0.40	0.40	0.35

[*] Adjusted for age (continuous), servings of alcohol per week (continuous), smoking status (never, former, current), MET-hrs/wk of physical activity (continuous), education (less than high school grad, high school grad/some college, college grad, post-college), ethnicity (white, black, other).

[†] All associations were statistically significant at p <0.0001, with the exception of the associations of LDL-C with BMI, WC, and WCHtR (p = 0.16, 0.01, and 0.01, respectively) and of total cholesterol with BMI, WC, WCHtR, and WHR (p = 0.52, 0.67, 0.49, and 0.01, respectively).

Abbreviations: BMI – body mass index; WC – waist circumference; WCHtR – waist circumference/height; WHR – waist-to-hip ratio; HOMA-IR—homeostasis assessment model – insulin resistance; HDL-C - high-density lipoprotein cholesterol; LDL-C - low-density lipoprotein cholesterol; BP – blood pressure.

Table 4

Baseline association cardiometabolic factors with a 1-unit increase in the z-score for anthropometric measures in the subcohort of the Women's Health Initiative (N = 2,672).[*†]

Metabolic factor/ anthropometric factor	BMI		WC		WCHtR		WHR	
	β-coeff	95% CI	β-coeff	95% CI	β-coeff	95% CI	β-coeff	95% CI
Glucose	6.6	(5.5 – 7.7)	7.7	(6.6 – 8.8)	7.5	(6.4 – 8.6)	6.2	(5.2 – 7.3)
Insulin	3.0	(2.6 – 3.4)	3.4	(3.0 – 3.8)	3.4	(2.9 – 3.8)	2.4	(2.0 – 2.9)
HOMA-IR	1.1	(0.9 – 1.4)	1.3	(1.1 – 1.5)	1.3	(1.1 – 1.5)	1.0	(0.8 – 1.2)
HDL-C	−4.4	(−5.0 – −3.8)	−5.4	(−6.0 – −4.8)	−5.3	(−5.9 – −4.7)	−5.0	(−5.6 – −4.4)
LDL-C	1.3	(−0.2 – 2.8)	2.3	(0.9 – 3.8)	2.3	(0.8 – 3.8)	3.3	(1.8 – 4.7)
Total cholesterol	−0.06	(−1.7 – 1.6)	1.1	(−0.5 – 2.7)	1.1	(−0.5 – 2.7)	2.9	(1.3 – 4.4)
Triglycerides	14.8	(11.5 – 18.2)	20.8	(17.6 – 24.0)	20.6	(17.4 – 23.8)	24.1	(21.0 – 27.2)
Systolic BP	2.9	(2.2 – 3.5)	2.7	(2.0 – 3.3)	2.9	(2.3 – 3.6)	1.7	(1.0 – 2.3)
Diastolic BP	1.2	(0.8 – 1.6)	1.0	(0.6 – 1.4)	1.0	(0.7 – 1.4)	0.5	(0.1 – 0.9)
Metabolic score	0.4	(0.4 – 0.5)	0.5	(0.4 – 0.5)	0.5	(0.4 – 0.5)	0.4	(0.4 – 0.5)

[*] Adjusted for age (continuous), servings of alcohol per week (continuous), smoking status (never, former, current), MET-hrs/wk of physical activity (continuous), education (less than high school grad, high school grad/some college, college grad, post-college), ethnicity (white, black, other).

[†] All associations were statistically significant at p <0.0001, with the exception of the association of BMI with LDL-C (p = 0.09) and the associations of BMI, WC, and WCHtR with total cholesterol (p = 0.95, 0.18, and 0.16, respectively).

Abbreviations: BMI – body mass index; WC – waist circumference; WCHtR – waist circumference/height; WHR – waist-to-hip ratio; HOMA-IR— homeostasis assessment model – insulin resistance; HDL-C - high-density lipoprotein cholesterol; LDL-C - low-density lipoprotein cholesterol; BP – blood pressure.

Table 5

Longitudinal association of cardiometabolic factors with a 1-unit increase in the z-score for anthropometric measures in the subcohort of the Women's Health Initiative (N = 2,672).[*†]

Metabolic factor/ anthropometric factor	BMI		WC		WCHtR		WHR	
	β-coeff	95% CI	β-coeff	95% CI	β-coeff	95% CI	β-coeff	95% CI
Glucose	5.3[b,c]	(4.4 – 6.2)	6.5[a,b]	(5.6 – 7.4)	7.2[a,c]	(6.3 – 8.2)	3.0	(2.4 – 3.7)
Insulin	2.8	(2.4 – 3.2)	3.0	(2.6 – 3.3)	3.3	(2.9 – 3.7)	1.4	(1.1 – 1.7)
HOMA-IR	1.1	(0.9 – 1.2)	1.2	(1.0 – 1.4)	1.2	(1.1 – 1.4)	0.6	(0.5 – 0.8)
HDL-C	−3.1[d,e]	(−3.6 – −2.7)	−3.7[d]	(−4.1 – −3.3)	−4.6[e]	(−5.2 – −4.1)	−1.1	(−1.4 – −0.9)
LDL-C	0.9	(−0.2 – 2.1)	1.0	(−0.1 –2.2)	1.6	(0.3 – 2.9)	0.5	(−0.4 – 1.3)
Total cholesterol	−0.1	(−1.4 – 1.1)	0.1	(−1.1 – 1.3)	0.3	(−1.1 – 1.7)	0.4	(−0.5 – 1.3)
Triglycerides	13.0[f,g]	(10.5 – 15.5)	17.4[f]	(15.0 – 19.9)	18.1[g]	(15.3 – 20.9)	9.6	(7.8 – 11.4)
Systolic BP	2.6	(2.1 – 3.1)	2.3	(1.8 – 2.8)	2.4	(1.9 – 2.9)	0.9	(0.5 – 1.3)
Diastolic BP	1.2	(0.9 – 1.5)	0.7	(0.5 – 1.0)	0.6	(0.3 – 0.9)	0.1	(−0.1 – 0.4)
Metabolic score	0.3	(0.3 – 0.3)	0.4	(0.3 – 0.4)	0.4	(0.3 – 0.4)	0.2	(0.2 – 0.2)

[*] Adjusted for age (continuous), servings of alcohol per week (continuous), smoking status (never, former, current), MET-hrs/wk of physical activity (continuous), education (less than high school grad, high school grad/some college, college grad, post-college), ethnicity (white, black, other).

[†] All associations were statistically significant at p <0.0001, with the exception of the associations of BMI, WC, and WCHtR with LDL-C (p = 0.1, 0.08, and 0.3, respectively); BMI, WC, WCHtR, and WHR with total cholesterol (p = 0.8, 0.9, 0.7, and 0.3, respectively); and WHR with diastolic blood pressure (0.2).

a – g Denotes statistically significant pair-wise differences between coefficients – all <0.01. All differences between coefficients for WHR and the other anthropometric variables with glucose, HDL-C, and triglycerides were statistically significant – p <0.01.

Abbreviations: BMI – body mass index; WC – waist circumference; WCHtR – waist circumference/height; WHR – waist-to-hip ratio; HOMA-IR—homeostasis assessment model – insulin resistance; HDL-C - high-density lipoprotein cholesterol; LDL-C - low-density lipoprotein cholesterol; BP – blood pressure.