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Neck Circumference and Cardiovascular Outcomes: Insights From the Jackson Heart Study

Christopher A. Pumill, MD^{1,2}, Christopher G. Bush, MPH³, Melissa A. Greiner, MS³, Michael E. Hall, MD⁴, Shannon M. Dunlay, MD, MS⁵, Adolfo Correa, MD, PhD⁴, Lesley H. Curtis, PhD², Takeki Suzuki, MD, MPH, PhD⁴, N. Chantelle Hardy, MPH³, Chad T. Blackshear, MS⁶, Emily C. O'Brien, PhD³, and Robert J. Mentz, MD^{1,2}

¹Duke Clinical Research Institute, Duke University School of Medicine, Durham, NC;

²Department of Medicine, Duke University School of Medicine, Durham, NC;

³Department of Population Health Sciences, Duke University School of Medicine, Durham, NC;

⁴Department of Medicine, University of Mississippi Medical Center, Jackson, MS;

⁵Departments of Cardiovascular Medicine and Health Sciences Research, Mayo Clinic, Rochester, MN;

⁶Department of Data Science, University of Mississippi Medical Center, Jackson, MS.

Abstract

Background: Emerging data suggest that neck circumference (NC) is associated with cardiometabolic risk factors. Limited research is available regarding the association between NC and cardiovascular outcomes in African Americans.

Methods: Using data from the Jackson Heart Study, we included participants with recorded NC measurements at baseline (2000–2004). Baseline characteristics for the included population were summarized by tertiles of NC. We then calculated age- and sex-adjusted cumulative incidence of clinical cardiovascular outcomes and performed Cox proportional hazards with stepwise models.

Results: Overall, 5290 participants were categorized into tertiles of baseline NC defined as 37 cm (N=2179), 38–40 cm (N=1552), and >40 cm (N=1559). After adjusting for age and sex, increasing NC was associated with increased risk of heart failure (HF) hospitalization (cumulative incidence = 13.4% [99% CI, 10.7–16.7] in the largest NC tertile vs. 6.5% [99% CI, 4.7–8.8] in the smallest NC tertile), but not mortality, stroke, myocardial infarction or coronary heart disease (all *P* 0.1). Following full risk adjustment, there was a nominal increase in the risk of HF hospitalization with increasing NC, but this was not statistically significant (hazard ratio per 1-cm increase, 1.04 [99% CI, 0.99–1.10], *P*=0.06).

Address for correspondence: Robert J. Mentz, MD, PO Box 17969, Durham, NC 27715; telephone: 919-668-7121; fax: 919-668-7063; robert.mentz@duke.edu.

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Conclusions: In this large cohort of African American individuals, a larger NC was associated with increased risk for HF hospitalization following adjustment for age and sex, but this risk was not statistically significant after adjusting for other clinical variables. Although NC is not independently associated with increased risk for cardiovascular events, it may offer prognostic information particularly related to HF hospitalization.

INTRODUCTION

Features of anthropometry (i.e., body measurements and proportions) are routinely used in clinical practice to evaluate health status and predict risk on both an individual and population scale.^[1] Examples of anthropometry include waist circumference, which is a key component of the metabolic syndrome—a combination of clinical variables commonly used to predict risk for cardiovascular (CV) events.^[2, 3] While seemingly easy to perform, waist circumference measurements can vary between practitioners based on the fact that there is no uniformly accepted protocol.^[4] Furthermore, some patients may feel the process of measuring waist circumference distressing given the need to disrobe and have measuring instruments positioned around their central obesity. While we do not advocate for abandonment of useful maneuvers for the sake of patient modesty, the authors suggest that other measures such as neck circumference (NC) may be more consistently measured and entail less invasion of patients' privacy; however this has yet to be investigated in the literature. Emerging data suggest that not only is NC correlated with WC, but NC may support CV disease risk prediction given associations with other prognostic variables (e.g., body mass index [BMI], sleep apnea, insulin resistance, and lipid profiles).^[5–10] However, limited data exist regarding the association of NC and CV outcomes, and previous studies have not evaluated the associations in African Americans, who are disproportionately affected by CV disease.^[8, 11] We evaluated the association of NC with CV outcomes in the Jackson Heart Study (JHS), a large population-based cohort of African Americans.

METHODS

Data Sources

The JHS is a prospective, observational cohort study that began in 2000 to investigate risk factors for CV health outcomes in a population of African Americans from Jackson, MS. A total of 5306 participants were recruited from the Jackson metropolitan area and included volunteers (25%), randomly selected residents of the area (17%), eligible residents from Jackson who participated in the Atherosclerosis Risk in Communities (ARIC) cohort study (31%), and relatives of JHS (22%) or ARIC (5%) participants. Participants completed 3 study visits from September 2000 through December 2013. Visit and data collection procedures have been previously reported.^[12–14] The institutional review board of the Duke University Health System approved the study.

Neck Circumference

The exposure of interest for this analysis was baseline NC, which was measured to the nearest centimeter using tape wrapped snugly around the neck, just below the participant's thyroid cartilage. This technique was consistent with that used in previous investigations and

National Health and Nutrition Examination Survey data.^[5, 7] We modeled NC on a continuous scale with 1-cm increments and present descriptive information and incidence rates according to tertiles of NC: 37 cm, 38–40 cm, and >40 cm.

Study Population

We included JHS participants who completed Exam 1 and had complete information on NC, BMI, and waist circumference measurements. For the heart failure (HF) hospitalization outcome analysis, we restricted the cohort to those who survived to January 1, 2005, when surveillance for HF hospitalization began.^[15] Participants with histories of myocardial infarction (MI), stroke, and coronary heart disease (CHD) were excluded from incident MI, stroke, and CHD models, respectively.

Outcomes

Outcomes of interest included all-cause mortality, incident stroke, incident CHD, incident MI, and HF hospitalization. All-cause mortality, incident stroke, CHD, and incident MI were assessed within 11 years after the exam 1 visit date, which fell between the median study follow-up time of 11 years and the 75th percentile of 12 years. HF hospitalization was assessed within 9 years of the exam 1 visit date between 2005 and 2013 among those surviving to the beginning of HF hospitalization surveillance (median and 75th percentile HF follow-up was 9 years starting in 2005). Incident CHD was defined as the first occurrence of fatal CHD, MI, or cardiac procedure determined through annual telephone follow-up interviews, hospitalization surveillance with medical abstraction and death certificate review. Computer-generated lists derived from hospital discharges were further reviewed by a committee of trained medical personnel resulting in final, disease-specific event classification.^[16] Methods for identifying both all-cause mortality and HF hospitalizations in the cohort have been described previously.^[16]

Covariates

We included baseline clinical exam variables for demographic information, medical history, medications, and measures taken from the physical examination. Medical histories were derived from clinical examination, self-reported disease history, or health behaviors. To determine the presence of HF at baseline, we applied modified Gothenburg criteria as developed and validated in the ARIC study.^[17] Variables that had less than 5% missingness were imputed to the overall median value for continuous variables, dichotomous variables to “no,” and multichotomous variables to the most frequent categorical value.^[18] For variables that had greater than 5% missing, specifically medications, a separate category was created for missing values.

Statistical Analysis

We summarized baseline characteristics for the included population by tertiles of NC with frequencies and percentages presented for categorical variables, and medians with interquartile ranges or means with standard deviations presented for continuous variables. Differences between groups were evaluated via chi-square tests for categorical variables and Kruskal-Wallis tests for continuous variables. We calculated age and sex weights per

participant standardized to the overall study population. We then calculated age- and sex-adjusted cumulative incidence rates from weighted Kaplan-Meier estimates and tested for differences using log-rank tests. For all-cause mortality, participants were censored at the time of loss to follow-up or the end of study event surveillance follow-up (December 31, 2013). For all other outcomes, participants were additionally censored at the time of death.

We examined the association between continuous NC and each outcome via Cox proportional hazards models using a stepped model approach as follows: NC only (Model 1); NC with age and sex (Model 2); Model 2 covariates plus BMI (Model 3); Model 3 plus adjustments for clinical exam variables including medical history and medications (Model 4). Candidate variables for model adjustment were preselected based on clinical judgment, prior literature, and estimated events per variable for each outcome. Covariates included in the final adjusted models were prior stroke (except for incident stroke models), prior MI (except for incident MI and CHD models), baseline HF, chronic kidney disease, hypertension (HTN), diabetes, and ejection fraction, as well as medication use indicator variables for beta blockers, statins, oral antihyperglycemics, and angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker (ACE-I/ARB). For all-cause mortality and HF hospitalizations, we also adjusted for physical activity, modeled as an ordinal covariate. For each outcome, we first evaluated multicollinearity for all variables included in the models and removed those with variance inflation factor > 3 . We excluded waist circumference as a covariate in our models due to evidence of collinearity with BMI, a decision that was made *a priori*. We used Box–Tidwell and supremum tests to examine appropriate functional form for NC in each outcome model, and if indicated, we explored nonlinear functional forms including restricted cubic splines and linear splines. Lastly, we tested the interaction between gender and NC for the presence of effect modification, which was not present.

Due to the number of outcomes and comparisons, we prespecified a 2-tailed alpha of 0.01 to establish statistical significance and report 99% confidence intervals. All analyses were performed with SAS version 9.4 (SAS Institute Inc., Cary, NC).

RESULTS

Of the original 5306 JHS participants, 16 were excluded due to missing data for BMI, waist circumference, and NC. The remaining 5290 participants were further categorized into tertiles of NC defined as < 37 cm (N=2179), 38–40 cm (N=1552), and > 40 cm (N=1559) (Figure 1).

Table 1 includes the baseline characteristics within each tertile. The overall mean population age at baseline was 55.4 years and did not vary by NC category. Of the 5290 participants, 36.5% were male, with significantly ($p<0.001$) higher proportion of men in the largest NC tertile. More than half of the overall population had HTN, with nearly two thirds of the largest NC tertile having baseline HTN. Additionally, $> 20\%$ of the overall cohort had diabetes mellitus. A higher percentage of those in the largest NC tertile did not exercise when compared to the smallest one. There was a significant difference (all $p<0.001$) between NC groups for weight, BMI, and waist circumference. The largest tertile had lower high-

density lipoprotein (HDL) values compared to the lowest tertile. Lastly, there was a stepwise increase in use of beta-blockers, statins, oral antihyperglycemics, and ACE-I/ARB by NC tertile.

Table 2 reports the cumulative incidence of all-cause mortality, HF hospitalization, and incident stroke, MI, and CHD by tertiles of NC adjusted for age and sex. There was no difference between the NC tertiles for all-cause mortality, incident stroke, MI, or CHD. However, there was a significant difference in cumulative incidence of HF hospitalization between NC groups: 13.4% in the largest NC tertile vs. 6.5% in the smallest (Table 2). Supplemental Figure 1 presents the unadjusted cumulative incidence curves of all-cause mortality, incident MI, HF hospitalization, incident stroke, and CHD. In the unadjusted analysis, there was a significant difference in the cumulative incidence of all-cause mortality, HF hospitalization, and CHD. However, after age- and sex adjustment, only HF hospitalization remained statistically significant (Figure 2).

Table 3 presents the association of a 1-cm increase in NC with the risk of each outcome. For every 1-cm increase in NC, there was a significant increase in the unadjusted hazard for all-cause mortality (HR=1.03; $P=0.001$) and HF hospitalization (HR=1.08; $P<0.001$). NC was also significantly associated with HF hospitalization and incident stroke after adjustment for age, sex, and BMI (HR=1.09, $P<0.001$; HR=1.09, $P=0.006$, respectively). NC was not associated with incident CHD or incident MI in any of the adjustment models. Lastly, there were no statistically significant associations with any outcomes after full adjustment (Model 4).

Based on the results of the aforementioned significance tests, we explored modeling the relationship between NC and all-cause mortality with non-linear functional forms. We first evaluated the association via restricted cubic splines with knots at 35, 43 and 47 cm (Supplemental Figure 2) and median (38 cm) as reference; the Wald chi-square non-linear association $p=0.0012$. For ease of interpretation and using Akaike information to guide optimal model fit, we ultimately chose to model the association as linear spline terms with 1 knot at the NC median (38 cm) (Supplemental Figure 2). In the fully adjusted multivariable Model 4, there was a 9% decrease in risk of death for each 1-cm increase in NC up to 38 cm. However, the association with death was not statistically significant for NC > 38 cm ($P=0.53$) (Supplemental Table 2). The interaction term between NC and gender was not statistically significant in any model.

DISCUSSION

In the present analysis, we found that NC was associated with previously mentioned cardiometabolic risk factors including BMI, HTN, HDL, and low-density lipoproteins (LDL). Additionally, on unadjusted analysis, we found that for each 1-cm increase in NC, there was a significant increase in the risk of all-cause mortality, and HF hospitalization. The association between increasing NC and HF hospitalization remained after partial adjustment (age, sex, and BMI); however, this association was not statistically significant after full adjustment.

Similar to previously published data, we observed associations between traditional CV risk factors and increasing NC.[5, 6, 8] Participants with NC > 40 cm had significantly higher weight, BMI, and waist circumference. Additionally, HDL measurements were significantly lower. Those in the largest NC cohort were also more sedentary, and more of them had a history of smoking. Lastly, various medical comorbidities were more prevalent in the largest NC tertile. There was an increased percentage of participants who had a history of MI, stroke, CHD, HTN, diabetes, and HF in the highest NC tertile. Although the aforementioned studies demonstrated this association in various populations, to date, there has not been an investigation specifically in African Americans. Thus, in addition to reinforcing previously demonstrated associations between NC and patient characteristics and medical comorbidities, we are the first to study this association in an African American population.

After a follow-up period of 9 years, there was a significant difference in the cumulative incidence of HF hospitalization between the NC tertiles (13.4% in largest tertile vs. 6.5% in the smallest). This difference was evident after only 2 years of follow-up. However, as NC increased, there was not a statistically significant difference in all-cause mortality, incident stroke, incident MI, or incident CHD between NC groups.

We also analyzed the association between continuous NC and adverse outcomes via a stepwise model building approach. After adjusting for age, sex, and BMI, continuous NC was associated with increased risk for HF hospitalization, but this association was attenuated after full adjustment for comorbidities (HR=1.09 [99% CI, 1.04–1.14] vs. HR=1.04 [99% CI, 0.99–1.10]). This is consistent with previous literature investigating clinical outcomes with regard to waist circumference. Waist circumference is strongly associated with various cardiometabolic risk factors and the development of DM, but after full adjustment for baseline comorbidities, waist circumference is not independently associated with adverse clinical outcomes.^[19] Therefore, while we are unable to conclude that NC is independently associated with adverse CV outcomes such as HF hospitalization, it may still have clinical relevance as a surrogate measure of risk in the context of established prognostic variables.

To our knowledge, the present analysis is the first to evaluate the association between NC and CV outcomes in an African American population including those without known CV disease. These results are consistent with a prospective Chinese cohort that demonstrated association between NC and the development of CV disease and overall mortality. However, that cohort included only patients with 2 or more CAD risk factors.^[11] Additionally, there was a secondary analysis of incident CV disease with participants in the Framingham data, but they did not find a significant association between NC and CV disease after multivariable adjustment.^[7]

One possible explanation for the lack of association between NC and MI is the distribution of participant characteristics at baseline. The average age of the study population was 55.4 years of age; however, recent data from the American Heart Association demonstrates that the average age of MI is 65 years for men and 72 years for women.^[20] Based on the average age of 55 years with 11 years of follow-up, the JHS cohort is just now approaching this average age. This hypothesis is supported by our data, which demonstrated an increasing

difference between NC tertiles as time elapsed. Analyses based on additional years of follow-up may better represent the long-term association between NC and incident MI.

Lastly, this is the first study to our knowledge reporting an association between increasing NC and HF hospitalization risk after adjustment for age, sex, and BMI. One proposed hypothesis is the physiological association between NC, obstructive sleep apnea (OSA), and HF. The association between increasing NC and increased risk of developing obstructive sleep apnea has been well documented in the literature.[21–23] Additionally, OSA has been associated with increased risk of incident HF.[24] Additional research on potential mechanisms of the association between NC and HF is needed.

Clinical Application

As clinical medicine continues to evolve, there is an increased emphasis on the prevention of disease in addition to its management. A powerful way to prevent disease is to accurately identify individuals at risk and implement additional surveillance and management. In everyday practice, clinicians have an increasing number of patient variables to support outcome prognostication. As part of the metabolic syndrome, the measurement of waist circumference is often difficult to perform, as it can be difficult to measure above a pannus. It can also be embarrassing and uncomfortable for the patient. We report the first investigation of NC and CV outcomes in an African American population. While we were unable to conclude that NC is independently associated with adverse CV outcomes, NC was strongly associated with HF hospitalization after adjustment for age, sex, and BMI. This is consistent with previous investigations of waist circumference. Therefore, when used with other patient data values, NC may be an important part of the routine risk assessment as it is 1) associated with cardiometabolic risk factors, 2) associated with adverse clinical outcomes, and 3) is less intrusive to measure than waist circumference. While not the focus of the present study, the authors feel that a potential future direction includes further investigation into the utility of NC as a proxy for cardiometabolic risk factors.

Limitations

A common criticism of BMI is that it does not take lean muscle mass into consideration. There is the possibility that NC can carry similar limitations. Further investigation will be needed to better understand the limitations of NC with regards to lean muscle mass. NC was only measured at baseline, which prevented us from evaluating the associations of change in NC over time with CV outcomes. Since heart failure surveillance did not begin until 2005 and there was no retrospective adjudication of events, we excluded 86 subjects who died prior to 2005 and 21 who were lost to administrative follow-up. Our estimation of association between NC and HF may have been biased if patients who died prior to 2005 were more likely to have HF events in the unobserved period. As in all statistical analyses, there is the possibility of residual and unmeasured confounding in the adjusted analyses. Finally, we performed our statistical analysis with a more rigorous $\alpha=0.01$ with 99% confidence intervals in order to minimize the risk of a Type I error in light of the many associations we were testing. However, in doing so, we could have inflated the risk of a Type II error, thus leading to our insignificant associations.

Conclusions

This is the first report that NC is associated with all-cause mortality and HF hospitalization in analyses of an African American population. NC is associated with HF hospitalization after partial adjustment for age, sex, and BMI. More research is needed to further delineate the clinical utility of NC as a risk marker for HF hospitalization risk and its predictive power of other common clinical measures.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Study Cohort from the Jackson Heart Study.

Figure 2.
Age- and Sex-Adjusted Cumulative Incidence

Table 1.

Baseline Characteristics by Neck Circumference

	Total Cohort	<37cm	38–40 cm	>40cm	p-value
N	5290	2179	1552	1559	
Demographics					
Age, mean (SD)	55.4 (12.8)	55.5 (13.3)	55.8 (12.7)	54.6 (12.3)	0.02
Male sex, no. (%)	1930 (36.5)	201 (9.2)	611 (39.4)	1118 (71.7)	<0.001
Medical History, no. (%)					
Myocardial infarction	408 (7.7)	130 (6.0)	119 (7.7)	159 (10.2)	<0.001
Heart failure	396 (7.5)	129 (5.9)	123 (7.9)	144 (9.2)	<0.001
Stroke	236 (4.5)	82 (3.8)	65 (4.2)	89 (5.7)	0.01
CHD	422 (8.0)	137 (6.3)	124 (8.0)	161 (10.3)	<0.001
Hypertension	2989 (56.5)	1118 (51.3)	893 (57.5)	978 (62.7)	<0.001
Diabetes	1141 (21.6)	291 (13.4)	366 (23.6)	484 (31.0)	<0.001
Behavioral factors					
Average number of hours of physical activity per week, no. (%)	1.5 (1.8)	1.5 (1.8)	1.5 (1.8)	1.4 (1.7)	0.01
None	2531 (47.8)	985 (45.2)	764 (49.2)	782 (50.2)	0.005
<1 hour	551 (10.4)	240 (11.0)	144 (9.3)	167 (10.7)	0.21
1 - <2 hours	866 (16.4)	378 (17.3)	247 (15.9)	241 (15.5)	0.26
2 - <3 hours	426 (8.1)	183 (8.4)	125 (8.1)	118 (7.6)	0.66
3 - <4 hours	328 (6.2)	141 (6.5)	91 (5.9)	96 (6.2)	0.75
4 hours	588 (11.1)	252 (11.6)	181 (11.7)	155 (9.9)	0.21
Current smoker, no. (%)	690 (13.0)	276 (12.7)	201 (13.0)	213 (13.7)	0.67
Prior smoker, no. (%)	1018 (19.2)	321 (14.7)	301 (19.4)	396 (25.4)	<0.001
Physical examination measures, median (IQR)					
Weight, kg	87.7 (75.7, 102.0)	75.8 (67.5, 86.0)	89.1 (80.4, 99.7)	102.8 (92.0, 116.5)	<0.001
BMI, kg/m ²	30.5 (26.9, 35.4)	28.3 (24.9, 32.1)	31.2 (27.1, 36.0)	33.3 (29.8, 38.5)	<0.001
Waist circumference, cm	99.0 (90.0, 109.0)	90.0 (83.0, 99.0)	100.0 (93.0, 109.0)	109.0 (101.0, 119.0)	<0.001
Neck circumference, cm	38.0 (36.0, 41.0)	35.0 (34.0, 36.0)	39.0 (38.0, 40.0)	42.0 (41.0, 44.0)	<0.001
Systolic blood pressure, mmHg	125.7 (115.6, 136.7)	123.8 (113.7, 134.8)	125.7 (116.5, 136.7)	127.5 (118.3, 138.5)	<0.001

	Total Cohort	Neck Circumference		p-value
		<37cm	38–40 cm	
Pulse, beats per minute	63.0 (57.0, 71.0)	63.0 (57.0, 70.0)	65.0 (57.0, 72.0)	<0.001
Laboratory values, median (IQR) eGFR, %	85.9 (75.8, 96.9)	85.9 (75.7, 97.1)	85.9 (75.8, 96.9)	0.97
Hemoglobin A1c, %	5.7 (5.3, 6.1)	5.6 (5.2, 5.9)	5.8 (5.5, 6.5)	<0.001
HDL-cholesterol, mg/dL	49.0 (41.0, 59.0)	55.0 (47.0, 65.0)	43.0 (37.0, 51.0)	<0.001
LDL-cholesterol, mg/dL	124.0 (101.0, 147.0)	122.0 (99.0, 144.0)	125.0 (104.0, 151.0)	<0.001
Medications, no. (%)				
Beta-blocker	531 (10.0)	178 (8.2)	183 (11.7)	<0.001
Calcium channel blocker	857 (16.2)	335 (15.4)	280 (18.0)	0.08
Statin	600 (11.3)	206 (9.5)	217 (13.9)	<0.001
Oral diabetic medication	573 (10.8)	163 (7.5)	238 (15.3)	<0.001
ACE-inhibitor/ARB	882 (16.7)	278 (12.8)	336 (21.6)	<0.001

Included *P*-value is between neck circumference groups.

Abbreviations: CHD indicates coronary heart disease; BMI, body mass index; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker.

Table 2.

Age and Sex-Adjusted Cumulative Incidence of All-Cause Mortality, Heart Failure Hospitalization, Incident Stroke, Incident Myocardial Infarction, and Incident Coronary Heart Disease by Tertiles of Neck Circumference

End point	Neck Circumference			p-value
	37cm	38–40 cm	>40cm	
Mortality	238 (13.6) [11.0–16.6]	195 (13.3) [11.1–15.9]	227 (14.9) [12.1–18.4]	0.47
Heart failure hospitalization	119 (6.5) [4.7–8.8]	126 (9.0) [7.2–11.2]	160 (13.4) [10.7–16.7]	<0.001
Incident stroke	56 (3.5) [2.2–5.4]	61 (4.5) [3.2–6.2]	57 (4.8) [3.2–7.2]	0.23
Incident myocardial infarction	62 (3.3) [2.1–5.1]	51 (4.0) [2.8–5.8]	57 (5.0) [3.2–7.6]	0.41
Incident coronary heart disease	74 (3.9) [2.6–5.9]	76 (6.0) [4.4–8.1]	76 (6.4) [4.4–9.3]	0.10

Data shown as n (cumulative incidence %) [99% CI].

Table 3.

Hazard Ratios and 99% CI for the Association Between Neck Circumference (per 1 cm) and All-Cause Mortality, Incident Stroke, Incident Coronary Heart Disease (CHD), Incident Myocardial Infarction (MI), and Incident Heart Failure Hospitalization

Model	All-cause mortality*		Incident stroke		CHD		Incident MI		Heart failure hospitalization*	
	HR (99% CI)	P-value	HR (99% CI)	P-value	HR (99% CI)	P-value	HR (99% CI)	P-value	HR (99% CI)	P-value
1	1.03 (1.01–1.06)	0.001	1.03 (0.98–1.09)	0.09	1.04 (1.00–1.09)	0.02	1.03 (0.98–1.08)	0.16	1.08 (1.04–1.11)	<0.001
2	1.02 (0.99–1.06)	0.07	1.05 (0.98–1.11)	0.06	1.04 (0.99–1.10)	0.049	1.02 (0.96–1.09)	0.32	1.12 (1.08–1.17)	<0.001
3	1.01 (0.97–1.05)	0.60	1.09 (1.01–1.18)	0.006	1.07 (0.99–1.15)	0.02	1.05 (0.96–1.14)	0.15	1.09 (1.04–1.14)	<0.001
4	0.98 (0.94–1.02)	0.18	1.05 (0.96–1.14)	0.16	1.01 (0.94–1.09)	0.70	0.99 (0.91–1.08)	0.81	1.04 (0.99–1.10)	0.06

Model 1: Only neck circumference. Model 2: Model 1 + adjusted for age and sex. Model 3: Model 2 + BMI. Model 4: Model 3 + prior MI, prior stroke, heart failure history, chronic kidney disease history, hypertension, diabetes, current smoker, systolic blood pressure, ejection fraction, medications including angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker, beta-blocker, statin, diuretics, and indicator for missing medications.

* Mortality and heart failure model 4 is additionally adjusted for physical activity (n=5290).

1: Excludes prior stroke (remaining n=5054).

2: Excludes prior CHD (remaining n=4868).

3: Excludes prior MI (remaining n=4482)

4: Among those who survived to 2005 (remaining n=5183)