

Original Contribution

Measures of Body Size and Composition and Risk of Incident Atrial Fibrillation in Older People

The Cardiovascular Health Study

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Various anthropometric measures, including height, have been associated with atrial fibrillation (AF). This raises questions about the appropriateness of using ratio measures such as body mass index (BMI), which contains height squared in its denominator, in the evaluation of AF risk. Among older adults, the optimal anthropometric approach to risk stratification of AF remains uncertain. Anthropometric and bioelectrical impedance measures were obtained from 4,276 participants (mean age = 72.4 years) free of cardiovascular disease in the Cardiovascular Health Study. During follow-up (1989–2008), 1,050 cases of AF occurred. BMI showed a U-shaped association, whereas height, weight, waist circumference, hip circumference, fat mass, and fat-free mass were linearly related to incident AF. The strongest adjusted association occurred for height (per each 1-standard-deviation increment, hazard ratio = 1.38, 95% confidence interval: 1.25, 1.51), which exceeded all other measures, including weight (hazard ratio = 1.21, 95% confidence interval: 1.13, 1.29). Combined assessment of log-transformed weight and height showed regression coefficients that departed from the 1 to –2 ratio inherent in BMI, indicating a loss of predictive information. Risk estimates for AF tended to be stronger for hip circumference than for waist circumference and for fat-free mass than for fat mass, which was explained largely by height. These findings highlight the prominent role of body size and the inadequacy of BMI as determinants of AF in older adults.

aging; atrial fibrillation; body size; obesity

Abbreviations: AF, atrial fibrillation; BMI, body mass index; CHS, Cardiovascular Health Study; HC, hip circumference; WC, waist circumference; WHR, waist-to-hip ratio.

Atrial fibrillation (AF), the most common sustained cardiac dysrhythmia (1), is a growing public health concern among aging populations worldwide (2). In addition to being an independent risk factor for stroke (3), AF has been linked to higher risks of heart failure (4), cognitive decline (5), and death (6). Together with aging trends, the global prevalence of obesity has registered a marked increase (7). It has been shown in multiple prior studies that excess adiposity, as defined by elevated body mass index (BMI) (8–11) or waist circumference (WC) (12), increases the risk of AF. Although the mechanisms linking obesity to AF are not well defined, proposed mediators include

hypertension, diabetes, chronic inflammation, and obstructive sleep apnea, along with left ventricular diastolic dysfunction and left atrial enlargement (13–17). Given the intersection of aging, obesity, and AF, a key question is the extent to which body composition in older adults might determine the higher incidence of AF later in life. Because aging is associated with an increase in adipose mass and its central redistribution (18), along with a decrease in skeletal muscle mass (19), the same relationships between adiposity and AF that have been documented in younger individuals may not apply equally in older people. Moreover, beyond adiposity measures, taller heights

(20–22) and larger hip circumferences (HCs) (21, 23) have been shown to be significantly associated with the risk of AF. These findings suggest that BMI, which includes height squared in its denominator, may not be the best anthropometric variable for assessing AF risk. They also raise questions about the suitability of waist-to-hip ratio (WHR) for capturing AF risk. In this regard, both fat mass and fat-free mass were recently associated with a higher risk of AF in a middle-aged cohort (21), but the corresponding associations of adipose and lean body mass in older adults have not been examined. We therefore investigated the relationships of various measures of body size and composition with incident AF in the Cardiovascular Health Study (CHS), a large cohort study of older adults with a high number of AF events.

METHODS

Study population

CHS is a prospective study of cardiovascular risk factors among community-dwelling people 65 years of age or older (24). Individuals were recruited from Medicare eligibility lists and examined at 4 field centers across the United States (24, 25). The original cohort consisted of 5,201 individuals who enrolled in 1989–1990, with a supplementary cohort of 687 black participants enrolled in 1992–1993. Health evaluations were conducted for all participants using standardized protocols (24, 25).

In the present study, subjects with prevalent AF ($n = 157$) were excluded, as were those with prevalent cardiovascular disease ($n = 1,410$), because the latter can alter the usual relations of adiposity measures with adverse outcomes. Prevalent cardiovascular disease comprised coronary heart disease, stroke, transient ischemic attack, heart failure, and peripheral arterial disease. These conditions were ascertained through the use of questionnaires, review of medical records, or adjudication of prior events by specialized committees. After additional exclusion of participants with missing data on anthropometric variables ($n = 45$), there were 4,276 participants eligible for evaluation.

Baseline assessment of body size and composition

Anthropometric measurements were obtained by trained personnel using standardized methods (26). Height was measured in centimeters using a stadiometer. Weight was measured in pounds using a balance beam scale while participants were wearing examination gowns and no shoes. WC and HC were measured at the level of the umbilicus and the maximal protrusion of the gluteal muscles, respectively. BMI was calculated as weight in kilograms divided by height in meters squared. WHR was calculated as WC divided by HC. Participants also underwent bioelectrical impedance analysis. Resistance was measured at 50 kHz in the supine position using a TVI-10 Body Composition Analyzer (Danninger Medical, Columbus, Ohio) attached to 4 adhesive electrocardiographic electrodes placed in the standard distal positions on the dorsum of the right hand and foot. Fat-free mass was calculated as $(6,710) \times (ht^2/R) + (3.1 \times S) + 3.9$, where ht^2 was standing height in meters squared, R was resistance in ohms, and S was

sex (0 = women, 1 = men) (27). Fat mass was calculated as body weight minus fat-free mass.

Definition of other covariates

Participants answered standard questionnaires regarding smoking, alcohol intake, and self-assessed health status. Recent smokers were defined as those who quit within the past 5 years. Physical activity level was determined using a validated questionnaire (28). Blood samples collected after a 12-hour overnight fast were processed for biochemical testing (29). Diabetes was defined as having a fasting glucose level of 126 mg/dL or higher or use of hypoglycemic therapy. Echocardiography performed at baseline on the original cohort, but not the supplementary cohort, included M-mode measurement of left atrial anteroposterior diameter (24).

AF events

Annual study clinic visits were conducted for all CHS participants for 10 years, with interim telephone contacts every 6 months. Thereafter, telephone contacts were made every 6 months. In addition, information on all hospitalizations was collected. Incident cases of AF were diagnosed through June 2008 from 12-lead electrocardiograms taken at the annual study clinic visits (30) or from discharge diagnosis codes, except when these accompanied coronary artery bypass or valve replacement surgery (31). Prior work in CHS has shown that the positive predictive value of hospital discharge codes for diagnosing AF was 98.6% compared with direct review of medical records (31).

Statistical analysis

Levels of baseline covariates were described across sex-specific quintiles of height. Spearman correlation coefficients among measures of body size and composition were computed. The functional forms of the associations of anthropometric and bioelectric impedance variables with AF were evaluated using penalized cubic splines (32).

Cox models were used to estimate the relative risk of AF associated with BMI, weight, height, WC, HC, WHR, fat mass, and fat-free mass. On the basis of assessment of penalized cubic splines, BMI was modeled using a linear plus quadratic term, whereas all other measures were modeled using linear terms. For each measure of body size/composition, 3 models were evaluated: 1) a model adjusted for demographic characteristics, including age, sex, and race; 2) a model additionally adjusted for the confounders smoking status, physical activity level, alcohol consumption, estrogen therapy use, and serum creatinine level; and 3) a model further adjusted for mediators, such as hypertension and dysglycemia measures, lipid fractions, and C-reactive protein concentration. The additional impact of adjustment of individual anthropometric and bioelectric impedance parameters for other such parameters was subsequently examined in these models. Assessment for interactions of body size/composition measures by age, sex, or race involved inclusion of cross-product terms. In sensitivity analyses, we restricted evaluation to 1) never smokers and smokers who quit less than 5 years earlier;

Table 1. Demographic and Clinical Characteristics of Study Participants by Sex-Specific Quintiles of Height, Cardiovascular Health Study, 1989–2008

Covariate	Quintile of Height														
	1 ^a (n = 918)			2 ^b (n = 833)			3 ^c (n = 859)			4 ^d (n = 850)			5 ^e (n = 816)		
	Mean (SD)	No.	%	Mean (SD)	No.	%	Mean (SD)	No.	%	Mean (SD)	No.	%	Mean (SD)	No.	%
Age, years	74.2 (6.0)			73.0 (5.7)			72.2 (5.2)			71.4 (4.8)			70.9 (4.6)		
Male sex		360	39.2		313	37.6		349	40.6		291	34.2		327	40.1
Black race		129	14.1		119	14.3		134	15.6		136	16.0		135	16.5
Systolic blood pressure, mm Hg	140 (22)			137 (21)			137 (21)			133 (21)			134 (21)		
Diastolic blood pressure, mm Hg	71 (11)			71 (11)			71 (11)			71 (11)			73 (12)		
Antihypertensive medication use		368	40.1		340	40.8		323	37.6		325	38.2		299	36.6
Impaired fasting glucose level		109	13.8		105	14.3		106	14.2		96	13.3		98	14.1
Diabetes		128	13.9		99	11.9		111	12.9		128	15.1		120	14.7
Smoking status															
Never		481	52.4		416	49.9		411	47.8		378	44.5		366	44.9
Former		351	38.2		303	36.4		342	39.8		350	41.2		351	43.0
Current		86	9.4		114	13.7		106	12.3		122	14.4		99	12.1
No. of alcoholic drinks per week															
0		500	54.5		416	49.9		396	46.1		391	46.0		384	47.1
<7		307	33.4		315	37.8		332	38.6		320	37.6		298	36.5
7–13		50	5.4		48	5.8		51	5.9		61	7.2		60	7.4
≥14		61	6.6		54	6.5		80	9.3		78	9.2		74	9.1
Estrogen replacement (women)		185	33.2		187	36.0		212	41.6		251	44.9		199	40.7
Self-reported health															
Excellent/very good		353	38.5		381	45.7		361	42.0		384	45.2		393	48.2
Good		371	40.4		285	34.2		333	38.8		317	37.3		290	35.5
Fair/poor		194	21.1		167	20.0		165	19.2		149	17.5		133	16.3
Physical activity, kcal ^f	1,065 (324, 2,288)			1,076 (431, 2,266)			1,098 (406, 2,382)			1,166 (508, 2,480)			1,226 (480, 2,660)		
LDL, mg/dL	132 (38)			131 (36)			130 (36)			128 (36)			128 (36)		
HDL, mg/dL	56 (16)			56 (16)			56 (16)			57 (16)			54 (16)		
Triglycerides, mg/dL ^f	117 (91, 159)			117 (90, 166)			118 (91, 162)			116 (89, 154)			122 (93, 159)		

Table continues

Table 1. Continued

Covariate	Quintile of Height									
	1 ^a (n = 918)		2 ^b (n = 833)		3 ^c (n = 859)		4 ^d (n = 850)		5 ^e (n = 816)	
	Mean (SD)	No. %	Mean (SD)	No. %	Mean (SD)	No. %	Mean (SD)	No. %	Mean (SD)	No. %
Creatinine, mg/dL	1.0 (0.3)		1.0 (0.3)		1.0 (0.3)		1.0 (0.3)		1.0 (0.2)	
C-reactive protein, mg/L ^f	1.9 (1.0, 3.4)		1.8 (0.9, 3.3)		1.7 (0.9, 3.2)		1.7 (0.9, 2.9)		1.8 (0.9, 3.2)	

Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein; SD, standard deviation.
 a For women, height = 124.0–154.0 cm; for men, height = 152.0–168.0 cm.
 b For women, height = 154.1–157.5 cm; for men, height = 168.3–171.5 cm.
 c For women, height = 157.6–160.4 cm; for men, height = 171.6–175.0 cm.
 d For women, height = 160.5–164.5 cm; for men, height = 175.1–178.5 cm.
 e For women, height = 164.6–186.5 cm; for men, height = 178.6–193.1 cm.
 f Value presented as median (interquartile range).

2) participants with good or better self-reported health; and 3) events that occurred after 3 years of follow-up. Additional secondary analyses were adjusted for echocardiographic left atrial diameter or incident myocardial infarction and heart failure as time-dependent covariates.

The proportion of missing data for demographic and clinical variables was low (<3%). Such missing values were imputed as described previously (33). Models were checked for violation of proportional hazards using Schoenfeld residual tests; none were found.

Last, we evaluated the adequacy of ratio measures (BMI, WHR) relative to their component body size measures in relation to incident AF. Specifically, we log-transformed body size variables to construct multiplicative Cox models, because body size variables tend to be multiplicatively related, providing a means to determine whether these ratio measures capture most of the predictive information expressed by their numerator and denominator variables modeled separately. Because BMI is given by the regression of ln(weight) on ln(height), which yields the result that 2 × ln(height) is the linear predictor of ln(weight) (and thus weight/height² is on average a constant), if inclusion of both ln(height) and ln(weight) in a Cox model yields coefficients for AF that are not in the ratio of 1 to −2, then use of ln(BMI) results in a loss information. The same holds for WHR if the Cox model coefficients for ln(WC) and ln(HC) are not in the ratio of 1 to −1. We examined these coefficients to gain insight into the associations of the corresponding ratio measures BMI and WHR with AF.

RESULTS

Baseline characteristics

The mean age of participants in the cohort was 72.4 (standard deviation, 5.4) years; 61.7% were men and 15.3% were black. The distribution of baseline covariates by sex-specific quintiles of height is shown in Table 1. Increasing sex-specific quintiles of height were associated with younger age; a higher prevalence of blacks; lower systolic blood pressure and anti-hypertensive therapy; less frequent fair/poor health status; more physical activity; and lower low-density lipoprotein levels.

Table 2 presents the correlations among different measures of body size and composition stratified by sex. In both men and women, weight was highly correlated with BMI, WC, HC, and fat mass; moderately correlated with fat-free mass; and mild-moderately correlated with height and WHR. Findings were similar for BMI, except for its lack of correlation with height and its more modest correlations with fat-free mass. The correlations of height with WC, HC, and WHR in men and women were modest or nonexistent, but those with fat-free mass were moderately strong. In turn, WC and HC were highly correlated with each other and with fat mass, whereas correlations with fat-free mass were moderate.

Relationship with AF

During a median follow-up of 13 years, 1,050 cases of incident AF occurred. Using cubic spline analysis, we

Table 2. Correlations Between Measures of Body Size and Composition, Cardiovascular Health Study, 1989–2008

Sex and Measure	Height	BMI	Waist Circumference	Hip Circumference	WHR	Fat Mass	Fat-Free Mass
Women (<i>n</i> = 2,636)							
Weight	0.35	0.91	0.77	0.90	0.30	0.95	0.68
Height		-0.03	0.08	0.19	-0.05	0.24	0.47
BMI			0.80	0.88	0.35	0.90	0.52
Waist circumference				0.74	0.76	0.77	0.45
Hip circumference					0.18	0.89	0.54
WHR						0.30	0.15
Fat mass							0.43
Fat-free mass							
Men (<i>n</i> = 1,640)							
Weight	0.44	0.86	0.84	0.86	0.42	0.86	0.67
Height		-0.02	0.17	0.28	-0.03	0.29	0.47
BMI			0.84	0.81	0.49	0.79	0.48
Waist circumference				0.83	0.73	0.82	0.42
Hip circumference					0.26	0.78	0.51
WHR						0.47	0.12
Fat mass							0.24
Fat-free mass							

Abbreviations: BMI, body mass index; WHR, waist-to-hip ratio.

demonstrated that the association of BMI with incident AF was U-shaped in nature ($P = 0.020$ for nonlinearity) (Figure 1). This U-shaped relationship, which persisted in

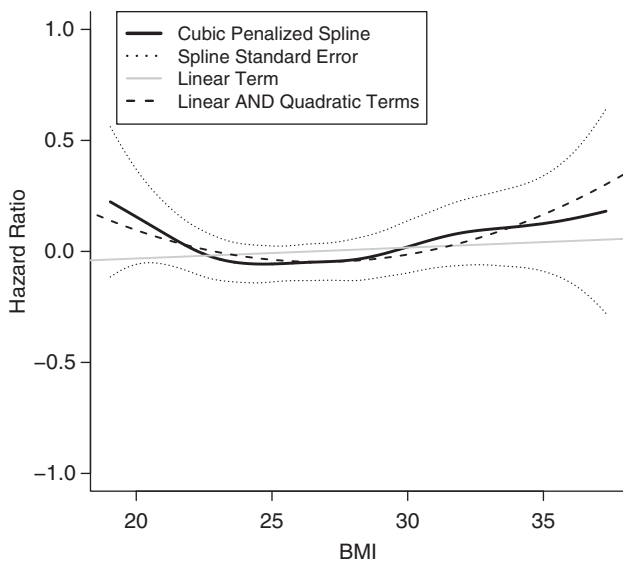


Figure 1. Plot of logarithm of the hazard ratio for atrial fibrillation versus body mass index (BMI), Cardiovascular Health Study, 1989–2008. The y-axis gives the logarithm of the hazard ratio; the x-axis gives BMI as weight in kilograms divided by height in meters squared. The plot shows the unadjusted linear term, linear and quadratic terms, and penalized cubic spline for BMI.

the model that was adjusted for demographic and clinical confounders, had its nadir at a BMI of 23.8, with risk of AF increasing at higher and lower values. By contrast, none of the other measures of adiposity—weight, WC, HC, WHR, fat mass, and fat-free mass—showed significant departure from a linear relationship with incident AF.

Table 3 presents the risk estimates for the various measures of body size and composition considered in relation to incident AF. For BMI, risk increases modeled using linear plus quadratic terms are presented for levels 1 standard deviation above and below the mean value, whereas risk estimates for the remaining measures modeled linearly correspond to 1-standard-deviation increments throughout their distribution. All measures except for WHR exhibited significant associations with AF after adjustment for potential confounders. In the case of weight, height, WC, HC, fat mass, and fat-free mass, these associations were positive and, though not directly comparable to the standardized risk estimates around the mean BMI value, tended to be stronger in magnitude. Height exhibited the largest standardized risk estimate for AF of all measures, and its lower 95% confidence bound exceeded the upper 95% confidence bounds for WC, HC, and fat mass. Like height relative to weight, fat-free mass also had a numerically higher risk estimate than did fat mass, but there was broad overlap of the corresponding 95% confidence intervals. After additional adjustment for putative mediators, the relationship between BMI and AF ceased to be significant, whereas those for weight, height, WC, HC, fat mass, and fat-free mass persisted. For all of the latter measures, associations were attenuated after such adjustment, with the exception of height.

Table 3. Relationships of Measures of Body Size and Composition With Incident Atrial Fibrillation, Cardiovascular Health Study 1989–2008

Measure	Model 1 ^a		Model 2 ^b		Model 3 ^c	
	HR ^d	95% CI	HR ^d	95% CI	HR ^d	95% CI
Body mass index	1.10	1.03, 1.16	1.08	1.02, 1.15	1.03	0.96, 1.10
Weight	1.21	1.13, 1.30	1.21	1.13, 1.29	1.17	1.08, 1.26
Height	1.37	1.25, 1.50	1.38	1.25, 1.51	1.40	1.28, 1.54
Waist circumference	1.15	1.08, 1.23	1.14	1.07, 1.22	1.10	1.02, 1.18
Hip circumference	1.17	1.10, 1.25	1.17	1.10, 1.24	1.13	1.06, 1.21
Waist-to-hip ratio	1.04	0.97, 1.11	1.02	0.96, 1.10	1.00	0.93, 1.07
Fat mass	1.17	1.10, 1.25	1.16	1.09, 1.24	1.12	1.04, 1.20
Fat-free mass	1.26	1.13, 1.39	1.26	1.13, 1.40	1.23	1.11, 1.37

Abbreviations: CI, confidence interval; HR, hazard ratio.

^a Adjusted for age, sex, and race.

^b Adjusted for age, sex, race, smoking status, physical activity level, alcohol consumption, estrogen therapy use, and serum creatinine level.

^c Adjusted for age, sex, race, smoking status, physical activity level, alcohol consumption, estrogen therapy use, serum creatinine level, systolic blood pressure, antihypertensive medication use, impaired fasting glucose level, diabetes, low-density lipoprotein level, high-density lipoprotein level, triglyceride level, and C-reactive protein concentration.

^d All measures were modeled linearly, except for body mass index (weight (kg)/height (m)²), which was modeled with linear and quadratic terms. For body mass index, risk estimates are per 1–standard-deviation increment (4.7) from the mean (26.6). For other measures, risk estimates are per 1–standard-deviation increments across the range: for weight, 14.6 kg; height, 9.4 cm; waist circumference, 13.2 cm; hip circumference, 10.0 cm; waist-to-hip ratio, 0.09 units; fat mass, 10.8 kg; and fat-free mass, 9.2 kg.

We next examined whether the individual associations of BMI, weight, WC, and HC with AF remained significant after we accounted for each of the others or for height, as appropriate, in addition to other potential confounders. As shown in Table 4, BMI ceased to be significantly associated with AF after adjustment for WC and became instead inversely associated after adjustment for HC. For weight, adjustment for height substantially attenuated the association with AF, but there was little if any change after adjustment for WC or HC. Conversely, adjustment for weight abolished the associations of WC and HC with the outcome. The relationship between height and AF was minimally affected after adjustment for weight, WC, or HC, whereas risk estimates for WC and HC were modestly attenuated after adjustment for height. Of note, the association with weight became nonsignificant with concurrent adjustment for height, WC, and HC, but that for height was not meaningfully changed by concurrent adjustment for weight, WC, and HC (data not shown). In turn, mutual adjustment of WC and HC abolished the association of WC with AF but only negligibly affected the association of HC with AF. In addition, the relations of fat mass and fat-free mass with AF were attenuated after adjustment for each other. In contrast to fat mass, however, the association for fat-free mass was strongly attenuated after adjustment for height (but not vice versa; data not shown).

Sensitivity analyses revealed that the associations of BMI, height, weight, WC, HC, fat mass, and fat-free mass with incident AF were similar after excluding current and recent smokers, participants with self-reported fair/poor health, or subjects who experienced AF in the first 3 years of follow-up.

In additional analyses, adjustment for incident myocardial infarction and heart failure as time-varying covariates minimally attenuated the observed associations. Among participants in the original cohort, further adjustment for echocardiographic left atrial diameter resulted in mild-moderate attenuations of the associations for weight, WC and HC, and fat mass and fat-free mass but did not meaningfully affect that for height (Appendix Table 1). In addition, there was no evidence of effect modification by age, sex, or race for any of the body size and composition measures examined.

Last, the relationships of log-transformed height and weight with AF and of log-transformed WC and HC with AF were assessed. In the confounder-adjusted model, the regression coefficients of ln(weight) and ln(height) were 0.49 (95% confidence interval: 0.10, 0.89) and 4.81 (95% confidence interval: 3.02, 6.59), showing that the relationship of these individual components of BMI with AF is inconsistent with the expected 1 to –2 given by the ratio measure, such that use of BMI in lieu of height and weight individually leads to a loss of information in predicting AF. Similarly, the regression coefficients for ln(WC) and ln(HC) were 0.01 (95% confidence interval: –0.73, 0.76) and 1.62 (95% confidence interval: 0.55, 2.70), which were also incompatible with the expected 1 to –1 for WHR.

DISCUSSION

The present study of a large population-based cohort of older adults reveals several important findings. First, most measures of body size and composition were positively

Table 4. Relationship of Measures of Body Size and Composition With Incident Atrial Fibrillation After Adjustment, Cardiovascular Health Study, 1989–2008

Measure	Model 2 ^a	
	HR ^b	95% CI
Body mass index adjusted for waist circumference	0.92	0.82, 1.03
Body mass index adjusted for hip circumference	0.80	0.70, 0.91
Weight adjusted for height	1.12	1.03, 1.21
Weight adjusted for waist circumference	1.24	1.10, 1.40
Weight adjusted for hip circumference	1.18	1.02, 1.36
Height adjusted for weight	1.30	1.18, 1.44
Height adjusted for waist circumference	1.35	1.23, 1.48
Height adjusted for hip circumference	1.33	1.21, 1.47
Waist circumference adjusted for hip circumference	1.02	0.91, 1.13
Waist circumference adjusted for height	1.11	1.04, 1.19
Waist circumference adjusted for weight	0.96	0.86, 1.08
Hip circumference adjusted for waist circumference	1.15	1.04, 1.28
Hip circumference adjusted for height	1.13	1.06, 1.20
Hip circumference adjusted for weight	1.03	0.90, 1.17
Fat mass adjusted for fat-free mass	1.12	1.05, 1.20
Fat mass adjusted for height	1.11	1.03, 1.18
Fat-free mass adjusted for fat mass	1.19	1.06, 1.33
Fat-free mass adjusted for height	1.08	0.96, 1.22

Abbreviations: CI, confidence interval; HR, hazard ratio.

^a Adjusted for age, sex, race, smoking status, physical activity level, alcohol consumption, estrogen therapy use, and serum creatinine level.

^b All measures were modeled linearly, except for body mass index (weight (kg)/height (m)²), which was modeled with linear and quadratic terms. For body mass index, risk estimates are per 1–standard-deviation increment (4.7) from the mean (26.6). For other measures, risk estimates are per 1–standard-deviation increments across the range: for weight, 14.6 kg; height, 9.4 cm; waist circumference, 13.2 cm; hip circumference, 10.0 cm; waist-to-hip ratio, 0.09 units; fat mass, 10.8 kg; and fat-free mass, 9.2 kg.

associated with incident AF in older persons, with the exception of BMI, which had a U-shaped association. Second, among all measures, height proved to be most strongly associated with incident AF, an association that was minimally altered by adjustment for other markers of body composition or cardiovascular risk factors. Third, assessment of logarithmically transformed weight and height yielded regression coefficients that differed from the expected 1 to –2 ratio given by the equation for BMI, indicating that inclusion of BMI in lieu of height and weight in AF risk models leads to a loss of predictive information.

As far as we are aware, this is the largest study focused on older adults to report on a wide range of anthropometric variables, along with measures of fat mass and fat-free mass, in relation to incidence of AF. In previous studies largely comprising younger, middle-aged populations, investigators have

documented that greater adiposity, as assessed principally by BMI (although also WC (12)), is associated with a higher risk of future AF. In these studies, BMI has often been assessed based on World Health Organization categories (10, 11), which may have obscured nonlinear associations. More recently, nonlinear associations with incident AF were detailed for BMI, WHR, and fat mass in a large cohort of middle-aged Danish adults (21), wherein values between 1 standard deviation and 2 standard deviations below the mean exhibited a horizontal slope. The more marked U-shaped association observed here occurred despite exclusion of prevalent cardiovascular disease, and it was not affected by sensitivity analyses in which we excluded participants with fair/poor self-reported health or AF during the initial 3 years of follow-up. Nonetheless, these differences likely relate to the fact that a lower BMI represents a marker of underlying illness in older adults rather than of health and fitness, as is typical of middle-aged individuals (34). It is possible that failure to detect nonlinear associations for WHR and fat mass here is due to the smaller sample size relative to the Danish study.

That use of BMI instead of height and weight separately for AF prediction leads to a loss of information is important because BMI has traditionally been relied upon as the anthropometric variable of choice for risk-adjustment or risk-prediction equations (9). Lately, a new multicohort AF prediction model has been developed that uses height and weight, instead of BMI, as predictors (35). It was noted that replacement of weight by BMI or WC therein led to similar model discrimination, but the question of whether BMI or WC remains the more pathophysiologically relevant measure remains unresolved.

Although BMI represents a useful measure of adiposity because it captures the component of weight that is independent of body height, this surrogate has notable limitations. Specifically, the relationship between BMI and body fat changes with age, such that older individuals have an increased ratio of fat mass to fat-free mass despite a constant BMI over time (36). Additionally, racial and ethnic differences in the relationship between BMI and body fat have been documented (37). Beyond these considerations, and perhaps of greatest importance to AF, inclusion of the square of height in the denominator of BMI dissipates height's very considerable contribution to the risk of this dysrhythmia.

In fact, our findings in older adults provide evidence that body size, rather than adiposity, may be the more dominant risk factor for AF incidence. This premise is supported by the stronger risk estimate observed for height than for weight upon mutual adjustment, as well as by a risk estimate for fat-free mass that was comparable to, if not stronger than, that for fat mass. It is also suggested by the persistence of a significant association with AF of HC but not WC upon mutual adjustment, although HC showed a stronger correlation than did WC with not just fat-free mass but also with fat mass.

Although these findings do not entirely agree with those from the only other previous study in which body size/composition measures in relation to AF were assessed (21), there are notable similarities. In the Danish cohort, the strength of the association between weight and AF was greater than that for height, but weight was also more strongly associated with AF than was BMI. Moreover, fat-free mass was more strongly

associated with AF than was fat mass and, with mutual adjustment, the association was far more substantially attenuated for fat mass than for fat-free mass. These previous findings from a younger population (50–64 years of age) are consistent with the concept underscored here that BMI is a weaker determinant of AF than are height and weight assessed separately. The greater association for weight than for height, however, could reflect greater lean mass per unit of body weight in this age group than in our older participants. Interestingly, the strong association of fat-free mass with AF in the Danish cohort persisted after adjustment for height, which was not the case in our older population, perhaps again reflecting the lower lean body mass in elders and its closer dependence on height. The findings from the earlier report suggest that, compared with fat mass, lean body mass could be a stronger determinant of left atrial size, as it is for left ventricular mass (38), possibly because of its greater metabolic activity and oxygen delivery needs; however, the relationship in elders appears more largely driven by the relationship to body height than lean mass content per se.

Both larger body size and greater lean mass may therefore confer larger left atrial size, which is recognized as an important risk factor for AF (39). Such greater chamber size may foster greater ectopic activity as a trigger of the dysrhythmia while at the same time serving as a larger substrate to allow development of multiple re-entrant wavelets for its propagation (40, 41). Interestingly, however, the risk estimate for only fat-free mass, but not height, exhibited moderate attenuation upon adjustment for left atrial diameter here. Determining whether adjustment for left atrial volume, a more accurate measure of left atrial size that was not routinely obtained herein, dampens the association for height—as hypothesized—will require further investigation. Nonetheless, the association of AF with greater body proportions has implications for clinical practice, where indexation of left atrial volume to body surface area is recommended in order to differentiate pathophysiological processes from large body size alone (42). However, this practice may not be useful if body size in itself is a risk factor for the disease process, as our data suggest.

The more pronounced association for height observed here does not negate the role of adiposity as a risk factor for AF in this population. Apart from BMI, weight, and fat mass, both WC and HC were significantly associated with AF. Indeed, excess adiposity and AF have many shared risk factors, including diabetes, hypertension, and obstructive sleep apnea (12, 35, 43). Unlike height and lean-body mass, these and other (44–46) obesity-related factors can foster inflammation and fibrosis as underlying substrates for the dysrhythmia (40). Obesity-related factors can also promote left atrial enlargement (39), but this influence does not tend to be as sustained through the lifespan as it is for height and fat-free mass. The pathophysiological changes associated with obesity, however, are difficult to capture using generalized body size and composition measures and will require further evaluation by examining specific fat depots and their respective contributions.

Our study has several limitations. The present results come from predominantly white older adults free of major comorbid conditions after the additional exclusion of overt cardiovascular disease, and the findings are not generalizable

to less healthy or more ethnically distinct older populations. Furthermore, despite exploring the relationships of fat mass and fat-free mass with incident AF, we did not explore specific anatomical fat depots, which may be important for pathophysiologic mechanisms linking obesity and AF. In addition, these findings are based on annual electrocardiogram and discharge diagnoses of AF, and associations may have been attenuated by underdetection of paroxysmal AF. Notwithstanding these limitations, the validity of the documented associations is bolstered by our study's prospective, population-based nature, its standardized assessment of exposures and outcome, and a large number of incident AF events during long-term follow-up.

The predominance of height as an anthropometric risk factor for AF in elders documented here, and the demonstrated loss of information content for BMI relative to height and weight considered separately, have implications not only for epidemiologic studies but also for clinical practice. These findings indicate that the use of BMI should be abandoned in favor of height and weight in order to optimally incorporate body size, and not just adiposity, into risk assessment of AF in older populations and suggest that the recommendation of indexation of left atrial volume by body size requires re-evaluation as relates to the prognostic value of left atrial size for this dysrhythmia.

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Appendix Table 1. Sensitivity Analysis of the Impact of Additional Adjustment for Echocardiographic Left Atrial Anteroposterior Diameter on the Relationship Between Measures of Body Size and Composition and Incident Atrial Fibrillation (Original Cohort Only, $n = 3,789$), Cardiovascular Health Study, 1989–2008

Measure	Model 2 ^a		Model 2 ^a and Left Atrial Diameter	
	HR ^b	95% CI	HR ^b	95% CI
Body mass index	1.00	0.93, 1.08	0.93	0.87, 1.02
Height	1.41	1.28, 1.55	1.40	1.27, 1.54
Weight	1.19	1.11, 1.29	1.12	1.04, 1.22
Waist circumference	1.07	0.99, 1.16	1.02	0.94, 1.10
Hip circumference	1.15	1.08, 1.23	1.10	1.02, 1.18
Fat mass	1.16	1.08, 1.24	1.09	1.01, 1.18
Fat free mass	1.25	1.10, 1.40	1.16	1.03, 1.31

Abbreviations: CI, confidence interval; HR, hazard ratio.

^a Adjusted for age, sex, race, smoking status, physical activity level, alcohol consumption, estrogen therapy use, and serum creatinine concentration.

^b All measures were modeled linearly, except for body mass index (weight (kg)/height (m)²), which was modeled with linear and quadratic terms. For body mass index, risk estimates are per 1–standard-deviation increment (4.7) from the mean (26.6). For other measures, risk estimates are per 1–standard-deviation increments across the range: for weight, 14.6 kg; height, 9.4 cm; waist circumference, 13.2 cm; hip circumference, 10.0 cm; waist-to-hip ratio, 0.09 units; fat mass, 10.8 kg; and fat-free mass, 9.2 kg.