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ORIGINAL RESEARCH

Race, Body Mass Index, and the Risk of Atrial Fibrillation: The Multi-Ethnic Study of Atherosclerosis

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BACKGROUND: Higher body mass index (BMI) is associated with increased risk of incident atrial fibrillation (AF), but it is not known whether this relationship varies by race/ethnicity.

METHODS AND RESULTS: Eligible participants (6739) from MESA (Multi-Ethnic Study of Atherosclerosis) were surveilled for incident AF using MESA hospital surveillance, scheduled MESA study ECG, and Medicare claims data. After a median 13.8 years of follow-up, 970 participants (14.4%) had incident AF. With BMI modeled categorically in a Cox proportional hazards model, only those with grade II and grade III obesity had increased risks of AF (hazard ratio [HR], 1.50; 95% CI, 1.14–1.98, P=0.004 for grade II obesity and HR, 2.13; 95% CI, 1.48–3.05, P<0.0001 for grade III obesity). The relationship between BMI and AF risk was J-shaped. However, the risk of AF as a function of BMI varied substantially by race/ethnicity (P value for interaction=0.02), with Chinese-American participants having a much higher risk of AF with higher BMI and Black participants having minimal increased risk of AF with higher BMI.

CONCLUSIONS: Obesity is associated with an increased risk of incident AF, but the relationship between BMI and the risk of AF is J-shaped and this relationship differs by race/ethnicity, such that Chinese-American participants have a more pronounced increased risk of AF with higher BMI, while Black participants have minimal increased risk. Further exploration of the differential effects of BMI by race/ethnicity on cardiovascular outcomes is needed.

Key Words: atrial fibrillation ■ body mass index ■ ethnicity ■ race

Maintenance of a healthy body weight is one of the cornerstones of cardiovascular health,[1] and there is a growing body of literature suggesting that elevated body mass index (BMI) is associated with a heightened risk of atrial fibrillation (AF).[2–9] This relationship persists, even after adjusting for the comorbidities often present in those with overweight and obesity, including diabetes mellitus, hypertension, and dyslipidemia.[2,5,9–15] The increased risk of AF among the overweight is particularly interesting in light of the "obesity paradox," among those with AF, whereby the risk of stroke, cardiovascular death, and all-cause mortality appears lower among obese adults than among those of normal body weight.[16–26]

The prevalence of AF is higher in White participants as compared with Black participants, Chinese-American participants, or Hispanic participants,[27] but the reasons for this remain unclear.[28–30] Several risk factors for incident AF vary by race/ethnicity including pericardial fat volume,[31] hypertension,[32–34] left ventricular hypertrophy, cardiac surgery, and smoking.[29] Whether the relationship between BMI and AF varies by race/ethnicity has not previously been investigated in multiethnic cohort studies that include comprehensive phenotyping for other established risk factors for AF. Therefore, we aimed to characterize the relationship between BMI and incident AF and explore the effects of race/

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CLINICAL PERSPECTIVE

What Is New?

- Higher body mass index is associated with increased risk of incident atrial fibrillation, but it is not known whether this relationship varies by race/ethnicity.
- Evidence from MESA (Multi-Ethnic Study of Atherosclerosis) study suggests that the increased risk of atrial fibrillation associated with higher body mass index may differ depending on race/ethnicity.

What Are the Clinical Implications?

- Considering a patient's race/ethnicity may be important in understanding how their risk of cardiovascular disease relates to their body mass index and personalizing lifestyle and treatment recommendations.

Nonstandard Abbreviations and Acronyms

MESA	Multi-Ethnic Study of Atherosclerosis

ethnicity on this relationship in participants from MESA (Multi-Ethnic Study of Atherosclerosis), which is a prospective observational study designed to explore the prevalence, correlates, and progression of subclinical cardiovascular disease in a multi-ethnic US cohort.

METHODS

Study Population

Requests to access the data set from qualified researchers trained in human subject confidentiality protocols may be submitted at http://www.mesa-nhlbi.org. The design and conduct of the MESA study has been reported.[35] Briefly, MESA is a prospective cohort of 6814 participants, 45 to 84 years of age, initially free of clinical cardiovascular disease, recruited from 2000 to 2002. Participants were recruited from 6 United States communities: Baltimore, MD; Chicago, IL; Forsyth County, NC; Los Angeles County, CA; New York City, NY; and Saint Paul, MN. For the present analysis, we excluded 75 participants with either baseline AF or absent follow-up data (no interactions with study personnel after enrollment), leaving 6739 eligible participants. Study protocols were approved by the institutional review boards at participating institutions. All participants provided written informed consent.

Exposure Variables

Height and weight were measured at study enrollment using a balanced beam scale and a vertical ruler, with participants wearing light clothing and no shoes. Participant BMI was calculated as weight (kilograms) divided by height^2 (meters^2), with World Health Organization–defined categories for underweight (<18.5), normal weight (18.5–25.0), overweight (25.0–29.9), obese class I (30.0–34.9), obese class II (35.0–39.9), and obese class III (40.0+).[36] As prior literature has explored the associations between BMI and incident AF using either continuous or categorical modeling of BMI, we modeled BMI using both approaches in our analysis for comparison to the prior literature.

Outcome Variable

Incident AF was ascertained from a combination of MESA hospital surveillance, scheduled MESA study ECG at MESA visit 5 (2010–2012), and (for participants enrolled in fee-for-service Medicare) from inpatient, outpatient, and physician claims. Hospital surveillance was performed by contacting all participants every 9 to 12 months by telephone and specifically inquiring about interval hospitalizations and medical diagnoses, then requesting the relevant medical records and reviewing the discharge diagnoses for AF. Specifically, the presence of *International Classification of Disease, Ninth Revision, Clinical Modification* (*ICD-9 - CM*) codes 427.31 (AF) or 427.32 (atrial flutter) or I48.x in the *Tenth Revision* (*ICD-10 - CM*) in any position in a patient with no history of AF was defined as incident AF. Incident AF events occurring in the same hospitalization as open cardiac surgery were excluded. If the first AF-related claim occurred before the MESA baseline examination, the participant was considered to have prevalent AF and was excluded. For this analysis, cases of incident AF ascertained from enrollment through the end of 2015 were included.

Covariates

Baseline covariates were obtained at the initial MESA examination (2000–2002). Systolic blood pressure was measured using a Dinamap Pro 100 automated sphygmomanometer placed on the left upper arm and is the average of 2 readings performed with the participant in the seated position for at least 5 minutes. Smoking was modeled as a categorical variable, with current smoking being defined by having smoked any cigarettes in the preceding 30 days, prior smoking being defined as having smoked at least 100 cigarettes in the participant's lifetime, and never smoking being defined as having smoked <100 cigarettes in the participant's lifetime. Alcohol use was modeled continuously and based on self-reported alcoholic drinks per week. Diabetes mellitus was defined as

a fasting glucose concentration ≥126 mg/dL or the use of hypoglycemic medication.[37] Antihypertensive medication use was determined from review of prescription medications. Electrocardiographic left ventricular hypertrophy was assessed by Novacode criteria, which is a validated framework for describing electrocardiographic abnormalities.[38] Income was included as a marker of socioeconomic status and was based on self-reported gross family income over the preceding 12 months. Education was modeled as an ordinal variable and based on self-reported highest level completed (no schooling, grades 1 –8, grades 9 –11, high school graduate, some college, technical school certificate, associate degree, bachelor's degree, or graduate or professional school). Statin use was defined as current use of a hydroxymethyl glutaryl coenzyme A reductase inhibitor at the time of enrollment. Self-reported physical activity was modeled as a categorical variable with possible values of poor (none), intermediate (1–149 minutes per week of moderate-intensity or 1–74 minutes per week of vigorous-intensity activity or the sum of moderate- and vigorous-intensity activity 1–149 minutes per week) or ideal (150 + minutes per week of moderate-intensity activity or 75+minutes of vigorous-intensity activity or the sum of moderate- and vigorous-intensity activity 150+minutes per week).

Statistical Analysis

Baseline characteristics of the study population stratified by baseline BMI were compared using mean± SD for continuous variables and frequency (percentage) for categorical variables. Between-group differences were assessed using ANOVA for continuous variables and χ^2 tests for categorical variables. Cox proportional hazards modeling was used to compare the risk of incident AF as a function of BMI, generating hazard ratios (HRs) and 95% CI. In our main analysis, underweight and normal weight participants were considered as 1 category because of the small number (56) of underweight participants; a sensitivity analysis was performed in which underweight participants were excluded. The assumption of time-independent proportionality of hazards was assessed by examining the Martingale residual plots and by incorporating an interaction term between BMI and the natural logarithm of follow-up time as a time-dependent covariate: there was no evidence of substantial deviation from the assumed time-independent proportionality of hazards. Initial model was unadjusted, with subsequent models adjusted for covariates believed to be of clinical significance. Model 2 adjusted for age, sex, and race/ethnicity, with model 3 also adjusting for current smoking, diabetes mellitus, systolic blood pressure, antihypertensive medication use, left ventricular hypertrophy by ECG, income, education, and self-reported physical activity. Formal tests of interaction between BMI and sex, as well as BMI and race/ethnicity, separately, were conducted by including an interaction term in the model; there was evidence of a BMI*race/ethnicity interaction, so a secondary analysis was performed in which adjusted models included an interaction term. Nonlinear associations were explored nonparametrically using restricted cubic splines modeling with BMI modeled as a continuous variable, with 3 knots placed at the 10th, 50th, and 90th percentiles, as recommended by Harrell.[39] A *P* value for nonlinearity was computed by testing the null hypothesis that the estimated coefficient of the second spline is zero.[40] Two-sided *P* values <0.05 were considered to be statistically significant. All statistical analyses were conducted at Wake Forest University School of Medicine using SAS version 9.4 (Cary, NC).

RESULTS

Among 6739 eligible MESA participants (age 62.0±10.2 years, 52.8% female), 28.6% had normal BMI, 39.0% were overweight, 21.1% had grade I obesity, 7.6% had grade II obesity, and 3.7% had grade III obesity. Baseline characteristics of the study population stratified by BMI category are provided in Table 1. The distribution of BMI by race/ethnicity is provided in Figure S1.

Over a combined 79 959 person-years of follow-up (median 13.8 years), 970 participants (14.4%) had incident AF. The overall incidence rate in events per 1000 person-years was 12.1, with race-specific incidence rates of 14.5 (White participants), 12.5 (Chinese-American participants), 10.1 (Black participants), and 10.1 (Hispanic participants), and BMI-specific incidence rates of 12.4, 12.0, 11.5, 12.7, and 13.6 for those with BMI <25, 25.0 to 29.9, 30.0 to 34.9, 35.0 to 39.9, and ≥40.0, respectively. The multivariable-adjusted HRs for incident AF by BMI are provided in Table 2. When BMI was modeled as a categorical variable, only those with grade II and grade III obesity had a significantly increased risk of AF (HR, 1.53; 95% CI, 1.16–2.00, *P*=0.002 for grade II obesity and HR, 2.16; 95% CI, 1.51–3.10, *P*<0.0001 for grade III obesity). There was evidence of interaction between BMI and race/ethnicity, so a secondary analysis was performed. Table S1 provides the race/ethnicity-specific HRs for elevated BMI when modeled as a continuous variable.

Given prior literature suggesting a curvilinear relationship between BMI and the risk of AF, we then utilized restricted cubic splines models. The *P* value for nonlinearity was 0.001, confirming a substantial

Table 1. Characteristics of MESA Study Participants by BMI (n=6739)

	BMI Category				
	<25.0 n=1930 (28.6%)	25.0–29.9 n=2630 (39.0%)	30.0–34.9 n=1420 (21.1%)	35.0–39.9 n=510 (7.6%)	40.0 + n=249 (3.7%)
Age, y	62.6±10.6	62.6±10.2	61.6±9.9	60.3±9.0	58.1±9.0
Sex (% male)	855 (44.3%)	1432 (54.4%)	688 (48.5%)	155 (30.4%)	49 (19.7%)
Race/Ethnicity					
White	831 (43.1%)	1034 (39.3%)	489 (34.4%)	165 (32.4%)	63 (25.3%)
Chinese-American	517 (26.8%)	247 (9.4%)	32 (2.3%)	1 (0.2%)	1 (0.4%)
Black	332 (17.2%)	687 (26.1%)	505 (35.6%)	227 (44.5%)	122 (49.0%)
Hispanic	250 (13.0%)	662 (25.2%)	394 (27.7%)	117 (22.9%)	63 (25.3%)
Cholesterol, mg/dL					
Total	194.1±34.7	194.8±35.9	193.4±37.0	194.3±34.6	191.7±36.8
HDL	56.8±17.1	49.5±13.3	47.1±12.9	48.3±12.6	48.3±11.8
LDL	114.7±30.8	118.9±31.7	117.2±31.5	119.2±30.8	117.0±33.4
Triglycerides	113.4±82.8	135.1±89.3	146.4±88.9	140.1±106.1	132.4±66.7
Blood pressure, mm Hg					
Systolic	121.7±22.2	127.0±20.8	129.4±20.6	131.5±20.3	132.0±21.8
Diastolic	69.9±10.3	72.8±9.9	73.2±10.3	72.3±10.3	70.6±10.7
Cigarette smoking					
Never	1048 (54.5%)	1275 (48.6%)	696 (49.2%)	242 (47.7%)	122 (49.2%)
Former	618 (32.1%)	991 (37.8%)	536 (37.9%)	209 (41.2%)	100 (40.3%)
Current	258 (13.4%)	358 (13.6%)	182 (12.9%)	56 (11.0%)	26 (10.5%)
Alcohol (drinks/wk)	3.9±5.8	4.0±6.3	3.9±7.1	2.4±4.9	2.2±5.6
Physical activity					
Poor	380 (19.7%)	543 (20.7%)	371 (26.2%)	156 (30.6%)	98 (39.8%)
Intermediate	320 (16.6%)	453 (17.3%)	264 (18.7%)	105 (20.6%)	48 (19.5%)
Ideal	1225 (63.6%)	1629 (62.1%)	780 (55.1%)	248 (48.7%)	100 (40.7%)
Diabetes mellitus					
Normal	1644 (85.5%)	1942 (74.0%)	930 (65.8%)	290 (57.0%)	131 (53.3%)
Impaired fasting glucose	146 (7.6%)	387 (14.7%)	240 (17.0%)	109 (21.4%)	53 (21.5%)
Untreated diabetes mellitus	29 (1.5%)	67 (2.6%)	42 (3.0%)	30 (5.9%)	9 (3.7%)
Treated diabetes mellitus	104 (5.4%)	228 (8.7%)	201 (14.2%)	80 (15.7%)	53 (21.5%)
Statin use	205 (10.6%)	428 (16.3%)	237 (16.7%)	81 (16.0%)	40 (16.1%)
Antihypertensive use	480 (24.9%)	960 (36.5%)	645 (45.5%)	262 (51.5%)	139 (55.8%)
Annual income (in $1000s)	48.4±32.5	48.5±31.3	45.4±29.8	44.6±28.8	41.0±26.3
High school graduate	1623 (84.4%)	2107 (80.3%)	1138 (80.5%)	419 (82.6%)	214 (86.3%)
LVH by ECG	12 (0.6%)	33 (1.3%)	16 (1.1%)	5 (1.0%)	1 (0.4%)
Incident AF	289 (15.0%)	373 (14.2%)	192 (13.5%)	76 (14.9%)	40 (16.1%)

Continuous variables are described as mean±SD deviation. Categorical variables are described as frequency (percentage).
Race/ethnicity rows describe the fraction of participants in each BMI category of each race.
AF indicates atrial fibrillation; BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LVH, left ventricular hypertrophy; and MESA, Multi-Ethnic Study of Atherosclerosis.

departure from the assumption of linearity. The relationship between BMI and incident AF among all MESA participants is graphically depicted in Figure 1, confirming the J-shaped curve.

Because MESA included 4 racial/ethnic groups, we explored how the BMI–AF relationship varied by race/ethnicity after finding evidence of interaction between BMI and race/ethnicity (*P* value for interaction of 0.02). The risk of AF as a function of BMI differed substantially by race/ethnicity, with increased BMI conferring a much higher risk of AF among Chinese-American participants, minimal additive risk in Black participants, and a graded increased risk in White and Hispanic participants (Figure 2).

As a sensitivity analysis, the underweight participants were excluded, with no significant impact on

Table 2. BMI and Incident AF

BMI	Incidence Rate (per 1000 Person-Years)	Model 1 Unadjusted Hazard Ratio (95% CI; *P* value)	Model 2 Demographic-Adjusted Hazard Ratio (95% CI; *P* value)	Model 3 Fully Adjusted Hazard Ratio (95% CI; *P* value)
<25.0	12.4	Reference	Reference	Reference
25.0–29.9	12.0	0.97 (0.83–1.13) 0.67	0.98 (0.84–1.15) 0.83	0.96 (0.82–1.13) 0.65
30.0–34.9	11.5	0.93 (0.77–1.11) 0.41	1.09 (0.90–1.32) 0.38	1.07 (0.88–1.30) 0.49
35.0–39.9	12.7	1.03 (0.80–1.32) 0.85	1.56 (1.19–2.04) 0.001	1.53 (1.16–2.00) 0.002
40.0 +	13.6	1.10 (0.79–1.53) 0.58	2.30 (1.62–3.25) < 0.0001	2.16 (1.51–3.10) < 0.0001

AF indicates atrial fibrillation; and BMI, body mass index.
Model 1 is unadjusted.
Model 2 adjusts for age, sex, and race/ethnicity.
Model 3 adjusts for the covariates in Model 2, plus smoking, alcohol use, diabetes mellitus, systolic blood pressure, antihypertensive medication use, income, education, left ventricular hypertrophy by ECG, and self-reported physical activity.

the study findings. To explore the possibility of differential ascertainment of incident AF by Medicare fee-for-service enrollment status, an additional sensitivity analysis was conducted to explore how the risk of AF varied by BMI when only considering those participants who were diagnosed with incident AF on study ECG, rather than from Medicare discharge diagnoses. However, only 2% of the incident AF events were from study ECG, with 98% being from Medicare discharge diagnoses, so we did not have a sufficient number of events to answer this question.

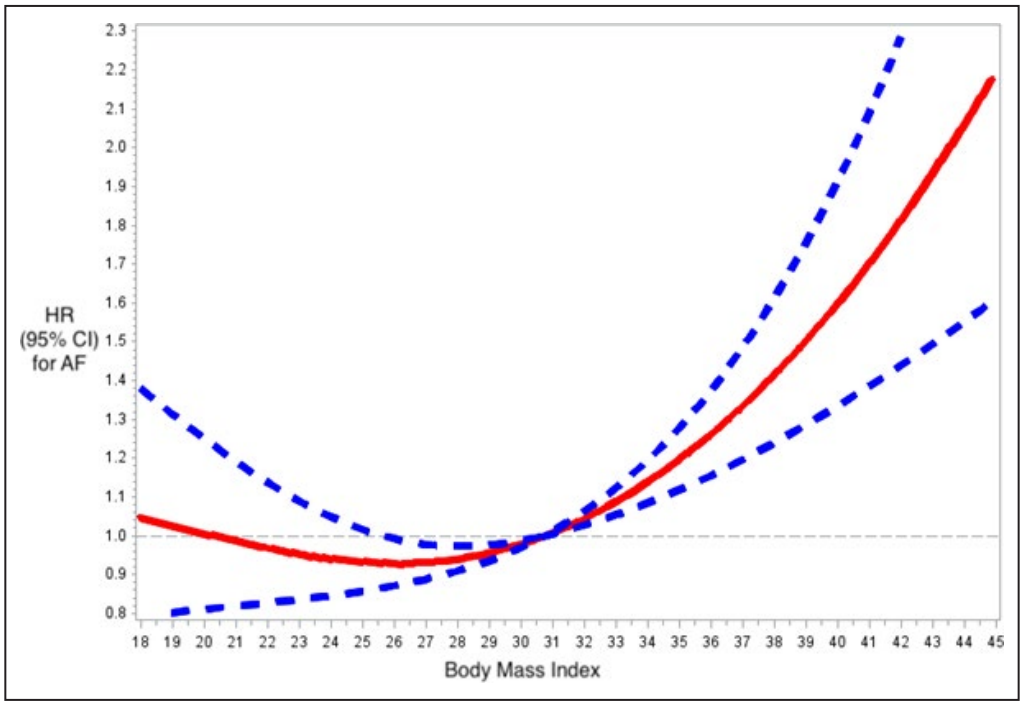

Figure 1. Risk of incident AF by BMI.
The relationship between BMI and incident AF is J-shaped. Both normal and overweight participants have the lowest risk of AF, with significantly increased risk seen in the obese and severely obese participants. Restricted cubic splines model with knots at the 10th, 50th, and 90th percentiles is adjusted for age, sex, race/ethnicity, race/ethnicity*BMI, smoking, alcohol use, diabetes mellitus, systolic blood pressure, antihypertensive medication use, income, education, left ventricular hypertrophy by ECG, and self-reported physical activity. AF indicates atrial fibrillation; BMI, body mass index; and HR, hazard ratio.

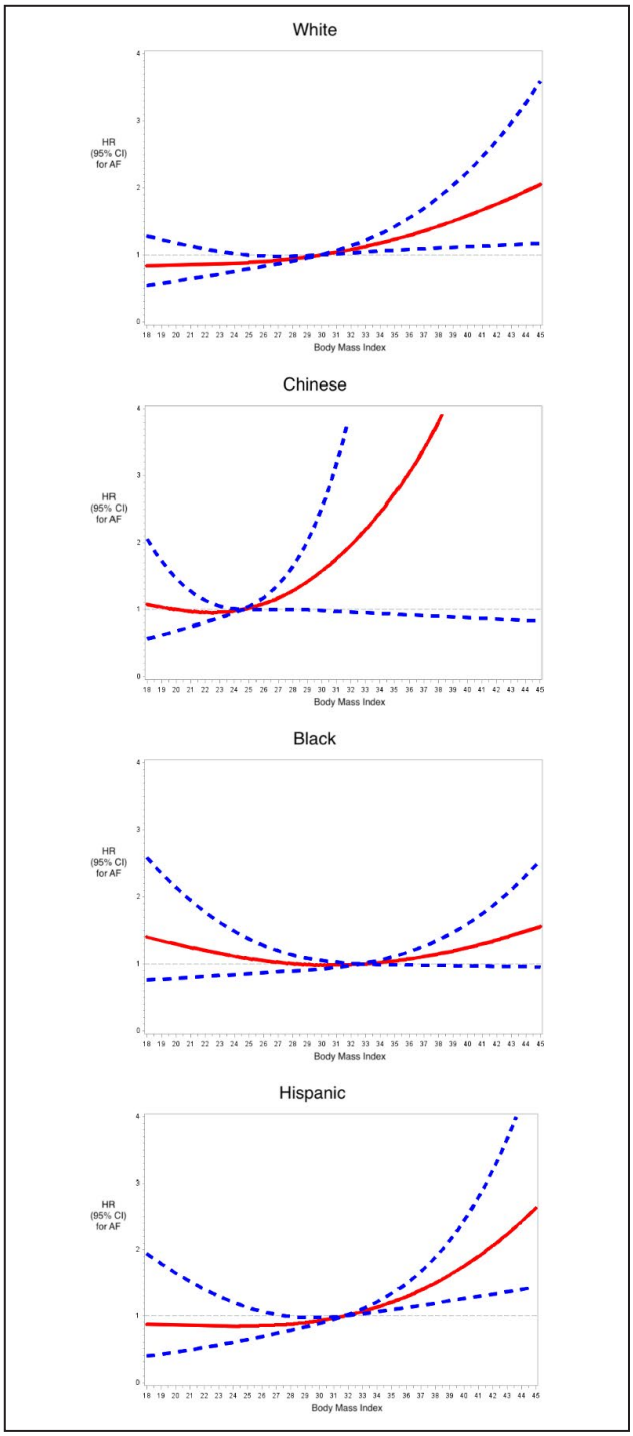

Figure 2. Risk of incident AF by BMI, stratified by race/ethnicity
The relationship between BMI and incident AF varies by participant race/ethnicity (*P* value for race/ethnicity*BMI interaction=0.02). Chinese-American participants have the greatest increase in risk associated with elevated BMI, while Black participants have a negligible increased risk with elevated BMI. Restricted cubic splines models with knots at the 10th, 50th, and 90th percentiles are adjusted for age, sex, smoking, alcohol use, diabetes mellitus, systolic blood pressure, antihypertensive medication use, income, education, left ventricular hypertrophy by ECG, and self-reported physical activity. AF indicates atrial fibrillation; BMI, body mass index; and HR, hazard ratio.

DISCUSSION

Principal Findings

In this analysis of the MESA study, we found that BMI is independently associated with incident AF. This relationship is best characterized as J-shaped, whereby the risk of AF increases substantially in those with grade II and grade III obesity. There is an interaction between BMI and race/ethnicity, with Chinese-American participants having a much more pronounced increased risk of AF with higher BMI and Black participants having minimal increased risk of AF at higher BMI.

Results in Context

Though the preponderance of evidence suggests that there is an association between elevated BMI and increased risk of AF, the effect of race/ethnicity on this association is still being elucidated. The only prior study to explore the interaction between race/ethnicity and BMI in the risk of AF reported that, though Black participants and Hispanic participants had a lower risk of AF in every category of BMI, there was no differential effect of BMI by race/ethnicity.[11] In contrast, we found that the BMI–AF relationship was modified by race/ethnicity. This novel finding may be explained by our use of a prospective cohort with formal assessment of covariates, all of our participants being initially free of AF by both ECG and self-report, and the long duration of follow-up, which may have enhanced our ability to find a between-group difference that is present.

Interaction Between Race/Ethnicity and BMI

The association between BMI and incident AF may be mediated through visceral adiposity, which is associated with alterations in cellular signaling in adipocytes[41] and systemic inflammation,[42] both of which are implicated in the pathogenesis of AF.[43] While our analysis was focused on BMI as a proxy for adiposity, it is possible that increased body mass, whether fat-mass or lean-mass, may be the key factor, because there is evidence that elevated body mass is independently associated with increased risk of AF, so adiposity may not be the key mediator of the BMI–AF relationship.[44,45] Our findings of an interaction in the relationship of BMI with incident AF by race/ethnicity is consistent with prior literature suggesting that BMI may not reflect visceral adiposity equally by race/ethnicity.[46] For instance, Black participants have substantially lower subcutaneous adipose tissue and total-body fat mass at a given BMI when objectively quantified by computed tomography.[47] Similarly, White participants have a higher burden of visceral adipose tissue than Black participants at the same BMI.[48] Variability in the relationship between visceral

BMI and adiposity by race/ethnicity is the most plausible explanation for our findings.

The idea that Black race/ethnicity modifies the relationship between BMI and adverse health outcomes has been documented outside of the cardiovascular literature as well. While elevated BMI is associated with increased incidence of adult-onset asthma, this association was greatly attenuated in Black participants, suggesting that elevated BMI may not confer as much additional risk among Black participants.[49] While obese patients of all races have higher markers of chronic inflammation, overweight is only associated with elevated markers of inflammation in European-American participants, but not Black participants,[50] and overweight was only associated with adverse outcomes among European-American participants, but not Black participants. In aggregate, the literature suggests that the ideal BMI for health may be higher in Black participants than among other races.

In contrast to Black participants, prior literature has shown that, for Asian participants, elevated BMI confers a much higher risk of adverse outcomes. Despite having lower BMI on average, Asian participants have a higher risk of developing the metabolic syndrome, and this risk increases more rapidly with increasing BMI among Asian participants[51] than among non-Hispanic White participants.[52] In the Nurses Health Study, both increased BMI and weight gain were more strongly associated with incident diabetes mellitus in Asian participants compared with White, Black, and Hispanic participants.[53] This is likely explained by the fact that compared with White participants, Asian participants have a higher body fat percentage at any given BMI,[54] with Asian participants having an average body fat percentage 3% to 5% higher than White participants for any given BMI.[55] Since visceral adiposity is linked to the risk of AF, our findings of rapidly increasing risk of AF with increasing BMI among Chinese is in agreement with the prior literature on the relationship between BMI and metabolic syndrome in Asian participants.

Race/Ethnicity-Specific BMI

Since race/ethnicity appears to modify both the BMI-adiposity and BMI-outcomes relationships, there have been increasing calls for race/ethnicity-specific BMI cut points, though these have not been widely implemented.[56–58] The World Health Organization recommends BMI thresholds of 23.5 and 27.5 for defining overweight and obesity in Asians,[58] as the optimal anthropometric cut points for discrimination of diabetes mellitus may be 4 BMI units lower in Asian participants than in White participants.[59] However, BMI is a continuous variable and the additive risk associated with a 1-unit increase in BMI varies by both race/ethnicity (which affects the shape of the curve) and the patient's BMI (since the slope differs depending on where along the curve the reference lies), so conceptualizing BMI as a threshold value above which there is an increased risk may be overly simplistic.

Importance

Understanding the relationship between BMI and risk of incident AF has important implications for motivating behavioral change in those at risk of AF, as well as those with AF. In those who had prevalent AF and who were enrolled in a targeted weight management program, participants who lost ≥10% of their body weight had a 6-fold increased probability of arrhythmia-free survival.[60] However, this effect has not been explored by race/ethnicity, so it is possible that only certain races/ethnicities receive the salutary effects of weight loss in the setting of overweight or stage I obesity. Though the Look AHEAD (Action for Health in Diabetes) trial found no association between intensive lifestyle interventions and incident AF, the mean BMI at enrollment was only 36.[61] Based on our study, the greatest increase in risk of AF occurs in those with BMI >35, so this population of those with grade II and grade III obesity might be a more appropriate target for targeted weight loss interventions if the goal is to reduce incident AF. If our findings are replicated in additional studies, confirming that race/ethnicity modifies the BMI–AF relationship, then guidance regarding a patient's ideal BMI and the risks associated with elevated BMI may be able to be personalized, taking into account the patient's race/ethnicity.

Limitations and Strengths

Our findings should be interpreted in the context of their limitations. Although follow-up for incident AF was periodically performed that resulted in little missing data, we probably missed some cases of asymptomatic AF, which would not be clinically recognized or reported. We did not have continuous outpatient electrocardiographic monitoring, which may have led to residual confounding because of differential ascertainment of AF by race/ethnicity.[62] In addition, the fact that only a subset of MESA participants was eligible for fee-for-service Medicare, which was one of the methods of outcome ascertainment, makes differential ascertainment by participant age a possibility. The threshold values for BMI categories that define underweight, normal, overweight, and the grades of obesity are arbitrary, and the risk of incident AF likely varies continuously with BMI, which is why both categorical and continuous modeling approaches were used.

Though we adjusted for covariates believed to be associated with the risk of incident AF, residual confounding remains a possibility. The low prevalence of severe obesity among Chinese participants led to relatively wide CIs in the upper range of our models. Our analysis does not account for longitudinal variability in BMI, which may confer additive risk beyond that explained by baseline BMI alone. Since MESA recruited adults initially free of cardiovascular disease, our findings may not be generalizable to those with prevalent cardiovascular disease, in which the relationship between BMI and the risk of AF may differ. The strengths of our study include a thoroughly phenotyped study population, long follow-up time, inclusion of multiple races/ethnicities, and the use of an exposure outcome (BMI) that is already available and in widespread clinical use.

CONCLUSIONS

In conclusion, elevated BMI is associated with an increased risk of incident AF in this multiethnic cohort of participants initially free of cardiovascular disease, and the curve relating BMI and AF is best characterized as J-shaped. Our hypothesis-generating secondary analysis suggests that there is an interaction between race/ethnicity and BMI with regard to the risk of incident AF, such that Chinese-American participants may have a greater increased risk with increased BMI and Blacks have minimal increased risk. With the steadily increasing societal burden of AF, the widespread implementation of lifestyle modification strategies to curb obesity is necessary.

ARTICLE INFORMATION

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Author contributions: MS and JY conceived and designed the analysis. MS performed the analysis. MS, CG, ES, MC, and JY interpreted the results. MS drafted the manuscript. CG, ES, MC, and JY revised for critical intellectual content. All authors approved of the final manuscript for submission.

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Disclosures

None.

Supplementary Material

Table S1
Figure S1

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Supplemental Material

Table S1. BMI (continuous) and Incident AF (by race/ethnicity).

Race/Ethnicity	Participants (n)	Cases (%)	Incidence Rate (per 1,000 person-years)	Model 1 Unadjusted Hazard Ratio (95% CI; p-value)	Model 2 Demographic-Adjusted Hazard Ratio (95% CI; p-value)	Model 3 Fully Adjusted Hazard Ratio (95% CI; p-value)
White	2,582	456 (17.7%)	14.5	1.05 (0.95 – 1.15) 0.37	1.19 (1.07 – 1.32) 0.002	1.17 (1.04 – 1.32) 0.008
Chinese-American	798	120 (15.0%)	12.5	1.24 (0.92 – 1.67) 0.16	1.33 (0.99 – 1.80) 0.06	1.24 (0.91 – 1.70) 0.18
African-American	1,873	219 (11.7%)	10.1	0.96 (0.85 – 1.09) 0.51	1.11 (0.97 – 1.27) 0.12	1.12 (0.97 – 1.29) 0.12
Hispanic	1,486	175 (11.8%)	10.1	1.20 (1.04 – 1.38) 0.01	1.44 (1.23 – 1.68) < 0.0001	1.39 (1.18 – 1.64) < 0.0001

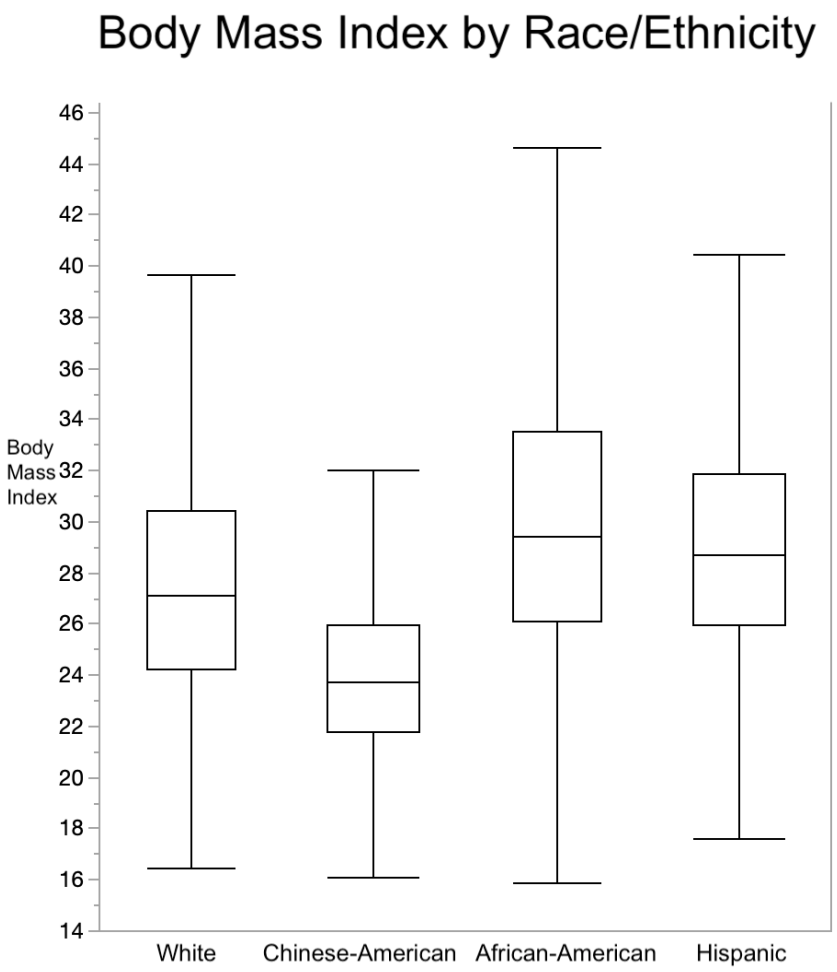
BMI is modeled continuously, with results provided as the hazard ratio per one standard-deviation (5.5 units) increase in BMI.

Model 1 is unadjusted

Model 2 adjusts for age and sex.

Model 3 adjusts for the covariates in Model 2, plus smoking, alcohol use, diabetes, systolic blood pressure, antihypertensive medication use, income, education, left ventricular hypertrophy by electrocardiogram, and self-reported physical activity.

Figure S1. Body Mass Index by Race/Ethnicity.



The distributions of body mass index by race/ethnicity is provided in a box-and-whiskers plot, demonstrating the lower average body mass index among Chinese-American participants and higher average body mass index among African-Americans.