BMI and Coronary Heart Disease Risk Among Low-Income and Underinsured Diabetic Patients

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OBJECTIVE

The association between obesity and coronary heart disease (CHD) risk remains debatable, and no studies have assessed this association among diabetic patients. The aim of our study was to investigate the association between BMI and CHD risk among patients with type 2 diabetes.

RESEARCH DESIGN AND METHODS

The sample included 30,434 diabetic patients (10,955 men and 19,479 women) 30–95 years of age without a history of CHD or stroke in the Louisiana State University Hospital-Based Longitudinal Study.

RESULTS

During a mean follow-up period of 7.3 years, 7,414 subjects developed CHD. The multivariable-adjusted hazard ratios for CHD across levels of BMI at baseline (18.5–24.9, 25–29.9, 30–34.9, 35–39.9, and ≥40 kg/m^2) were 1.00, 1.14 (95% CI 1.00–1.29), 1.27 (1.12–1.45), 1.54 (1.34–1.78), and 1.42 (1.23–1.64) ($P_{trend} < 0.001$) in men and 1.00, 0.95 (0.85–1.07), 0.95 (0.84–1.06), 1.06 (0.94–1.20), and 1.09 (1.00–1.22) ($P_{trend} < 0.001$) in women, respectively. When we used an updated mean or last visit value of BMI, the positive association between BMI and CHD risk did not change in men. However, the positive association of BMI with CHD changed to a U-shaped association in women when we used the last visit value of BMI.

CONCLUSIONS

Our study suggests that there is a positive association between BMI at baseline and during follow-up with the risk of CHD among patients with type 2 diabetes. We indicate a U-shaped association between BMI at the last visit and the risk of CHD among women with type 2 diabetes.

Obesity and diabetes are two important public health problems in the U.S. (1). Two in three adults in the U.S. are currently classified as overweight or obese (BMI ≥25 kg/m^2), and one-third of them are frankly obese (BMI ≥30 kg/m^2) (1). The estimated number of adults with diabetes in the U.S. is 26.1 million in 2005–2010 or ~12% of the population (2). Among U.S. diabetic patients, the prevalence of overweight or obesity has increased to ≥80% (3). Obesity is associated with increased risks of several cardiometabolic diseases, including hypertension (4), diabetes (5), coronary heart disease (CHD) (6,7), heart failure (8), and stroke (9).

Cardiovascular diseases, especially CHD, are the leading causes of death worldwide. In recent years, several prospective studies have assessed the association

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between obesity and the risks of total and CVD mortality among diabetic patients, and the results are inconsistent. To date, many studies have reported positive associations (10,11), inverse associations (12–14), U-shaped associations (15–17), or no associations (18) between BMI and mortality among patients with diabetes. All of these studies were focused on the association between BMI and CVD mortality; however, no studies assessed the association between BMI and the risk of incident CHD among diabetic patients. In this study, we examined the association between BMI and the risk of CHD among patients with type 2 diabetes in the Louisiana State University Hospital-Based Longitudinal Study (LSUHLS).

RESEARCH DESIGN AND METHODS

Study Population

Between 1997 and 2012, the LSU Health Care Services Division (LSUHCSD) operated seven public hospitals and affiliated clinics in Louisiana providing quality medical care to the residents of Louisiana regardless of their income or insurance coverage (19–26). Overall, LSUHCSD facilities have served ~1.6 million patients (35% of the Louisiana population) since 1997. Administrative, anthropometric, laboratory, clinical diagnosis, and medication data collected at these facilities are available in electronic form for both inpatients and outpatients from 1997. Using these data, we have established the LSUHLS (19). A cohort of diabetic patients was established by using the ICD-9 (code 250) between 1 January 1999 and 31 December 2009. Both inpatients and outpatients were included, and all patients were under primary care. Confirmation of diabetes diagnoses was made by applying the American Diabetes Association criteria: a fasting plasma glucose level ≥126 mg/dL; 2-h glucose level ≥200 mg/dL after a 75-g 2-h oral glucose tolerance test; and one or more classic symptoms plus a random plasma glucose level ≥200 mg/dL (27,28). The first record of diabetes diagnosis was used to establish the baseline for each patient in the present analyses due to the design of the cohort study. Before diagnosis with diabetes, these patients have used the LSU system for an average 5.0 years. We have validated the diabetes diagnosis in LSUHCSD hospitals. The agreement of diabetes diagnosis was 97%: 20,919 of a sample of 21,566 hospital discharge diagnoses based on ICD codes also had physician-confirmed diabetes by using the American Diabetes Associates diabetes diagnosis criteria (27).

The current study included 30,434 newly diagnosed patients (10,955 men and 19,479 women) with type 2 diabetes who were 30–95 years of age without a history of CHD and stroke at the time of diabetes diagnosis and with complete repeated data on all risk factor variables. We only included African Americans and whites because the patient numbers of Hispanics, Asians, and Native Americans are very small in the LSUHCSD hospitals. Patients were excluded if they were underweight (BMI <18.5 kg/m^2) because of limited statistical power for this group. Compared with diabetic patients excluded from the present analyses due to missing data, those included in the analyses were younger (51.0 vs. 57.6 years old), had a higher frequency of African Americans (58.6 vs. 45.4%), and less males (37.2 vs. 47.1%). The study and analysis plan was approved by the Pennington Biomedical Research Center and LSU Health Sciences Center Institutional Review Boards, LSU System. We did not obtain informed consent from participants involved in our study because we used anonymized data compiled from electronic medical records.

Baseline Measurements

The patient's characteristics, including age at diabetes diagnosis, sex, race/ethnicity, family income, smoking status, types of health insurance, BMI, blood pressure, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, glycosylated hemoglobin (HbA_{1c}), estimated glomerular filtration rate (eGFR), and medication (antihypertensive drug, cholesterol-lowering drug, and antidiabetes drug) within a half year before the diabetes diagnosis (baseline), during follow-up after the diabetes diagnosis (follow-up), and the last visit were extracted from the computerized hospitalization records. Height and weight were measured without shoes and with light clothing according to a standardized protocol. BMI was calculated by dividing weight in kilograms by the square of height in meters. Values of BMI, blood pressure, HbA_{1c}, LDL cholesterol, and eGFR over time were measured firstly at baseline and secondly as an updated mean of annual measurements, calculated for each participant from baseline to each year of follow-up. For example, at 1 year, the updated mean is the average of the baseline and 1-year values, and at 3 years, it is the average of baseline, 1-year, 2-year, and 3-year values. In the case of an event during follow-up, the period for estimating updated mean values was from baseline to the year before this event occurred (29). The average number of BMI measurements during the follow-up period was 15.0.

Prospective Follow-up

Follow-up information was obtained from the LSUHLS inpatient and outpatient database by using the unique number assigned to every patient who visits the LSUHCSD hospitals. The diagnosis of CHD was the primary end point of interest of the study and defined according to the following ICD-9: CHD (ICD-codes 410–414). Follow-up of each cohort member continued until the date of the diagnosis of CHD, the date of the last visit if the subject stopped use of LSUHCSD hospitals, or the date of death, determined from linking to the Louisiana Office of Public Health Vital Records Registry, or 31 May 2012 (23,26).

Statistical Analyses

The association between BMI and the risk of CHD was analyzed by using Cox proportional hazards models. BMI was evaluated in the following two ways: *1*) as five weight categories (18.5–24.9 [reference group], 25–29.9, 30–34.9, 35–39.9, and ≥40 kg/m^2) and *2*) as a continuous variable. The trend over different categories of BMI was tested in models with the median of each category as a continuous variable. All analyses were adjusted for age (continuous variable) and race (African American and white) (model 1) and further for smoking (never, past, and current), income (continuous variable), and types of insurance (free, self-pay, Medicaid, Medicare, and commercial) (model 2), and additionally for systolic blood pressure (continuous variable), HbA_{1c} (continuous variable), LDL cholesterol

(continuous variable), HDL cholesterol (continuous variable), triglycerides (continuous variable), eGFR (≥90, 60–89, 30–59, 15–29, and <15 mL/min/1.73 m^2), use of antihypertensive drugs (no use, ACE inhibitor, angiotensin II receptor blockers, β-blockers, calcium channel blocker, diuretics, and other antihypertensive drugs), use of diabetes medications (no use, oral hypoglycemic agents, and insulin), and use of cholesterol-lowering agents (no use, statins, and other cholesterol-lowering agents) (model 3). We stratified the samples by sex because there was a significant interaction between sex and BMI on the risk of CHD. Since the interactions between race and BMI on the risk of CHD were not statistically significant, data for white and African Americans were combined in some analyses. Statistical significance was considered to be $P < 0.05$. All statistical analyses were performed with PASW for Windows, version 20.0 (IBM SPSS Inc., Chicago, IL).

RESULTS

General characteristics of the study population at baseline are presented in Table 1.

During a mean follow-up period of 7.3 years, 7,414 subjects (2,926 men and 4,488 women) developed CHD. Patients who developed CHD during follow-up were older and used more glucose-lowering, lipid-lowering, and antihypertensive medication compared with those who did not develop CHD.

The multivariable-adjusted (age, race, smoking, income, and types of insurance) (model 2) hazard ratios (HRs) for CHD at different levels of BMI at baseline (18.5–24.9 [reference group], 25–29.9, 30–34.9, 35–39.9, and ≥40 kg/m^2) were 1.00, 1.14 (95% CI 1.00–1.29), 1.27 (1.12–1.45), 1.54 (1.34–1.78), and 1.42 (1.23–1.64) ($P_{trend} < 0.001$) in men and 1.00, 0.95 (0.85–1.07), 0.95 (0.84–1.06), 1.06 (0.94–1.20), and 1.09 (1.00–1.22) ($P_{trend} < 0.001$) in women, respectively (Table 2). After further adjustment for other confounding factors (systolic blood pressure, HbA_{1c}, LDL cholesterol, HDL cholesterol, triglycerides, eGFR, use of antihypertensive drugs, use of diabetes medications, and use of cholesterol-lowering agents), this association remained significant among men ($P_{trend} < 0.001$) and women ($P_{trend} = 0.006$).

When BMI was examined as a continuous variable, the multivariable-adjusted (model 2) HRs of CHD for each one-unit increase in BMI at baseline were 1.015 (95% CI 1.011–1.020) in men and 1.004 (95% CI 1.001–1.008) in women (Table 2). There was a significant interaction between sex and BMI on CHD risk ($\chi^2 = 9.86$; 1df, $P < 0.005$), which indicated that this positive

Table 1—Baseline characteristics of patients with type 2 diabetes by the outcome during follow-up[a]

	Men			Women		
	No CHD	CHD	*P* value	No CHD	CHD	*P* value
Number of participants	8,029	2,926		14,991	4,488	
Age, mean (SE) (years)	50.2 (0.11)	54.1 (0.18)	<0.001	51.1 (0.08)	53.9 (0.15)	<0.001
Income, mean (SE) ($/family)	18,935 (319)	22,207 (521)	<0.001	18,850 (203)	20,273 (371)	<0.001
BMI at baseline, mean (SE) (kg/m^2)	32.5 (0.09)	33.3 (0.14)	<0.001	35.6 (0.07)	35.7 (0.12)	0.36
BMI during follow-up, mean (SE) (kg/m^2)	32.3 (0.08)	33.2 (0.13)	<0.001	35.5 (0.07)	35.7 (0.12)	0.18
BMI at last visit, mean (SE) (kg/m^2)	32.2 (0.09)	33.0 (0.14)	<0.001	35.3 (0.07)	35.4 (0.13)	0.42
Race, *N* (%)			<0.001			<0.001
African American	4,731 (58.9)	1,369 (46.8)		9,168 (61.2)	2,380 (53.0)	
White	3,298 (41.1)	1,557 (53.2)		5,823 (38.8)	2,108 (47.0)	
HbA_{1c}, mean [% (mmol/mol)]	8.02 (64)	7.99 (64)	0.59	7.51 (59)	7.71 (61)	<0.001
HDL cholesterol, mean (SE) (mg/dL)	39.5 (0.1)	38.8 (0.2)	0.006	46.0 (0.1)	45.0 (0.2)	<0.001
LDL cholesterol, mean (SE) (mg/dL)	109 (0.5)	105 (0.8)	<0.001	116 (0.3)	113 (0.6)	<0.001
Triglycerides, mean (SE) (mg/dL)	151 (1.0)	160 (1.7)	<0.001	140 (0.6)	149 (1.2)	<0.001
GFR, *N* (%) (mL/min/1.73 m^2)			<0.001			<0.001
≥90	4,261 (53.1)	1,215 (41.5)		7,256 (48.4)	1,824 (40.7)	
60–89	2,977 (37.1)	1,208 (41.3)		6,027 (40.2)	1,820 (40.5)	
30–59	656 (8.2)	430 (14.7)		1,539 (10.3)	752 (16.8)	
15–29	84 (1.0)	52 (1.8)		113 (0.7)	73 (1.6)	
<15	51 (0.6)	21 (0.7)		56 (0.4)	19 (0.4)	
Current smoker, *N* (%)	2,930 (36.5)	987 (33.7)	0.014	3,808 (25.4)	1,178 (26.3)	0.46
Types of insurance, *N* (%)			<0.001			<0.001
Free	5,999 (74.7)	1,969 (67.3)		12,559 (83.8)	3,399 (75.7)	
Self-pay	698 (8.7)	141 (4.8)		601 (4.0)	125 (2.8)	
Medicaid	368 (4.6)	150 (5.1)		692 (4.6)	325 (7.3)	
Medicare	732 (9.1)	591 (20.2)		844 (5.6)	561 (12.5)	
Commercial	232 (2.9)	75 (2.6)		295 (2.0)	78 (1.7)	
Uses of medications, *N* %						
Glucose-lowering medication	5,196 (64.7)	1,989 (68.0)	<0.001	9,730 (64.9)	3,085 (68.7)	<0.001
Lipid-lowering medication	3,852 (48.0)	1,879 (64.2)	<0.001	8,188 (54.6)	2,994 (66.7)	<0.001
Antihypertensive medication	5,495 (68.4)	2,183 (74.6)	<0.001	11,017 (73.5)	3,484 (77.6)	<0.001

[a]Data represent means or percentages. All data except age are adjusted for age and race.

Table 2—HRs of CHD according to different levels of BMI at baseline, during follow-up, and at last visit among patients with type 2 diabetes

	BMI (kg/m^2)						
	<25.0	25.0–29.9	30–34.9	35–39.9	≥40	*P* for trend	Each 1-kg/m^2 increase
Baseline							
Men	1,561	3,008	2,948	1,789	1,649		
Number of cases	350	774	811	540	451		
Person-years	11,085	21,192	19,990	11,382	10,889		
Adjustment							
HR (95% CI)							
Model 1[a]	1.00	1.12 (0.98–1.27)	1.24 (1.09–1.41)	1.50 (1.31–1.72)	1.39 (1.20–1.61)	<0.001	1.015 (1.010–1.020)
Model 2[b]	1.00	1.14 (1.00–1.29)	1.27 (1.12–1.45)	1.54 (1.34–1.78)	1.42 (1.23–1.64)	<0.001	1.015 (1.011–1.020)
Model 3[c]	1.00	1.16 (1.00–1.33)	1.24 (1.07–1.43)	1.47 (1.26–1.72)	1.45 (1.24–1.70)	<0.001	1.015 (1.009–1.020)
Women	1,681	3,873	4,719	3,968	5,238		
Number of cases	420	904	1,054	938	1,172		
Person-years	12,664	30,032	36,548	30,102	39,538		
Adjustment							
HR (95% CI)							
Model 1[a]	1.00	0.93 (0.83–1.05)	0.92 (0.82–1.03)	1.03 (0.91–1.16)	1.05 (0.94–1.18)	0.010	1.004 (1.000–1.007)
Model 2[b]	1.00	0.95 (0.85–1.07)	0.95 (0.84–1.06)	1.06 (0.94–1.20)	1.09 (1.00–1.22)	<0.001	1.004 (1.001–1.008)
Model 3[c]	1.00	0.93 (0.82–1.06)	0.92 (0.82–1.05)	1.02 (0.90–1.16)	1.07 (0.95–1.22)	0.006	1.005 (1.001–1.009)
Follow-up							
Men	1,494	3,108	3,028	1,797	1,528		
Number of cases	335	814	813	529	435		
Person-years	10,691	21,876	20,542	11,629	9,806		
Adjustment							
HR (95% CI)							
Model 1[a]	1.00	1.14 (1.00–1.30)	1.22 (1.07–1.39)	1.49 (1.30–1.72)	1.50 (1.29–1.74)	<0.001	1.017 (1.012–1.023)
Model 2[b]	1.00	1.16 (1.02–1.32)	1.26 (1.11–1.44)	1.53 (1.33–1.77)	1.55 (1.33–1.80)	<0.001	1.018 (1.013–1.023)
Model 3[c]	1.00	1.18 (1.02–1.36)	1.24 (1.07–1.44)	1.45 (1.24–1.69)	1.55 (1.31–1.82)	<0.001	1.017 (1.011–1.023)
Women	1,579	3,897	4,874	3,965	5,164		
Number of cases	388	905	1,086	948	1,161		
Person-years	12,098	30,034	37,749	29,862	39,139		
Adjustment							
HR (95% CI)							
Model 1[a]	1.00	0.97 (0.86–1.10)	0.95 (0.84–1.07)	1.10 (0.98–1.25)	1.10 (0.98–1.24)	<0.001	1.004 (1.001–1.008)
Model 2[b]	1.00	0.99 (0.88–1.12)	0.98 (0.87–1.11)	1.14 (1.01–1.29)	1.14 (1.01–1.29)	<0.001	1.006 (1.002–1.009)
Model 3[c]	1.00	1.00 (0.88–1.15)	1.00 (0.88–1.14)	1.12 (0.98–1.28)	1.12 (0.99–1.28)	0.003	1.005 (1.000–1.009)
Last visit							
Men	1,715	3,064	2,892	1,713	1,571		
Number of cases	406	794	782	494	450		
Person-years	12,241	21,431	19,682	11,108	10,076		
Adjustment							
HR (95% CI)							
Model 1[a]	1.00	1.12 (0.99–1.27)	1.20 (1.06–1.36)	1.44 (1.25–1.64)	1.48 (1.28–1.70)	<0.001	1.016 (1.011–1.020)
Model 2[b]	1.00	1.15 (1.01–1.30)	1.25 (1.10–1.41)	1.49 (1.30–1.70)	1.53 (1.32–1.76)	<0.001	1.016 (1.011–1.021)
Model 3[c]	1.00	1.11 (0.97–1.26)	1.19 (1.04–1.37)	1.33 (1.15–1.54)	1.46 (1.25–1.70)	<0.001	1.015 (1.009–1.020)
Women	1,891	3,989	4,708	3,837	5,054		
Number of cases	502	907	1,039	913	1,127		
Person-years	14,259	30,874	36,346	28,962	38,442		
Adjustment							
HR (95% CI)							
Model 1[a]	1.00	0.87 (0.78–0.97)	0.87 (0.78–0.97)	1.01 (0.90–1.13)	1.00 (0.90–1.12)	0.022	1.004 (1.000–1.007)
Model 2[b]	1.00	0.89 (0.80–1.00)	0.90 (0.81–1.00)	1.05 (0.93–1.17)	1.04 (0.93–1.17)	0.003	1.004 (1.001–1.008)
Model 3[c]	1.00	0.90 (0.80–1.02)	0.91 (0.81–1.03)	1.03 (0.92–1.17)	1.00 (0.89–1.13)	0.085	1.003 (0.999–1.006)

[a]Adjusted for age and race. [b]Adjusted for age, race, types of insurance, income, and smoking. [c]Adjusted for age, race, types of insurance, income, smoking, systolic blood pressure, LDL cholesterol, HDL cholesterol, triglycerides, HbA_{1c}, eGFR, use of antihypertensive drugs (none, ACE inhibitor, angiotensin II receptor blockers, β-blockers, calcium channel blocker, diuretics, other antihypertensive drugs, and any two or more of above treatments), glucose-lowering agents (none, oral hypoglycemic agents, and insulin), and cholesterol-lowering agents (none, statins, and other cholesterol-lowering agents).

association was stronger in men than in women.

When we did an additional analysis by using an updated mean value of BMI, we found the same positive association between BMI and CHD risk among both men ($P_{trend} < 0.001$) and women ($P_{trend} < 0.001$) (Table 2). When we did another additional analysis by using the last visit value of BMI, we found a positive association between BMI and CHD risk among men ($P_{trend} < 0.001$) and a

U-shaped association between BMI and CHD risk among women (P_{trend} = 0.003) (Table 2). Women who were overweight and had class I obesity (BMI 25–34.9 kg/m^2) at last visit had a lower risk of CHD compared with normal-weight women (BMI <25 kg/m^2).

After excluding subjects who were diagnosed with CHD during the first 2 years of follow-up (n = 3,207), the multivariable-adjusted HRs (model 2) of CHD for each one-unit increase in BMI at baseline, during follow-up, and at the last visit were 1.014 (95% CI 1.010–1.019), 1.017 (1.012–1.022), and 1.015 (1.009–1.019) in men and 1.005 (1.001–1.009), 1.006 (1.002–1.010), and 1.005 (1.000–1.008) in women (data not shown), respectively.

In stratified analyses, the multivariable-adjusted positive association between BMI and CHD risk was present among men with different smoking status (Tables 3 and 4). When stratified by age, race, and use of antidiabetic drugs, this positive association of BMI at baseline, during follow-up, and at the last visit with CHD risk was still present among men in all subgroups and among women in some of the subgroups (Tables 3 and 4).

CONCLUSIONS

Our study found a positive association of BMI at baseline and during follow-up with the risk of CHD among both men and women with type 2 diabetes, and this association was stronger among men than among women. In addition, we found that a positive association between BMI and the risk of CHD was present in both African Americans and whites with type 2 diabetes and in nonsmokers and smokers. The positive association did not change among men but changed to a U-shaped association among women with type 2 diabetes when we assessed BMI of the last visit with CHD risk.

Only a few prospective studies have evaluated the association between obesity and total and CVD mortality among diabetic patients, and the results are controversial including inverse associations (12–14), positive associations (10,11), U-shaped associations (15–17), or no association (18). The current study was the first, to our knowledge, to assess the association between BMI and the risk of incident CHD among diabetic patients. The results of our study indicated a positive association between BMI and the risk of CHD among patients with type 2 diabetes. We found this positive association of CHD risk by

Table 3—HRs (95% CIs) of CHD according to different levels of BMI at baseline among various subpopulations[a]

	BMI (kg/m^2)						
	<25.0	25.0–29.9	30–34.9	35–39.9	≥40	*P* for trend	*P* for interaction
Men							
Age groups (years)							>0.50
<50	1.00	1.07 (0.86–1.33)	1.19 (0.96–1.48)	1.47 (1.19–1.85)	1.44 (1.15–1.80)	<0.001	
50–59	1.00	1.28 (1.01–1.60)	1.48 (1.17–0.85)	1.57 (1.23–2.00)	1.56 (1.22–2.01)	<0.001	
≥60	1.00	1.01 (0.8–1.27)	1.07 (0.84–1.35)	1.42 (1.10–1.85)	0.83 (0.59–1.15)	0.38	
Race							>0.10
African American	1.00	1.18 (0.99–1.40)	1.26 (1.05–1.51)	1.54 (1.26–1.88)	1.53 (1.24–1.89)	<0.001	
White	1.00	1.08 (0.89–1.32)	1.27 (1.05–1.54)	1.54 (1.26–1.88)	1.35 (1.10–1.66)	<0.001	
Smoking status							<0.05
Never	1.00	1.17 (0.95–1.44)	1.35 (1.10–1.67)	1.68 (1.35–2.09)	1.70 (1.36–2.12)	<0.001	
Ever or current	1.00	1.33 (1.09–1.62)	1.41 (1.15–1.73)	1.61 (1.28–2.03)	1.38 (1.08–1.76)	<0.001	
Glucose-lowering medication							>0.25
No use	1.00	1.56 (1.19–2.06)	1.40 (1.05–1.88)	1.66 (1.20–2.29)	1.85 (1.33–2.56)	0.001	
Oral hypoglycemic agents	1.00	1.25 (0.95–1.65)	1.46 (1.11–1.92)	1.66 (1.23–2.23)	1.57 (1.15–2.14)	<0.001	
Metformin	1.00	1.08 (0.87–1.34)	1.31 (1.06–1.62)	1.56 (1.24–1.95)	1.47 (1.16–1.85)	<0.001	
Sulfonylureas	1.00	1.04 (0.83–1.32)	1.24 (0.98–1.56)	1.47 (1.15–1.88)	1.32 (1.02–1.71)	<0.001	
Other oral agents	1.00	1.13 (0.78–1.66)	1.35 (0.93–1.95)	1.52 (1.03–2.22)	1.76 (1.20–2.59)	<0.001	
Insulin	1.00	1.09 (0.88–1.34)	1.29 (1.05–1.58)	1.56 (1.26–1.94)	1.49 (1.19–1.86)	<0.001	
Women							
Age groups (years)							>0.05
<50	1.00	1.10 (0.89–1.37)	1.04 (0.84–1.29)	1.09 (0.88–1.35)	1.06 (0.86–1.30)	0.70	
50–59	1.00	0.89 (0.73–1.08)	0.88 (0.73–1.07)	1.02 (0.84–1.24)	1.06 (0.87–1.28)	0.048	
≥60	1.00	0.89 (0.72–1.09)	0.89 (0.73–1.09)	0.99 (0.79–1.23)	1.06 (0.85–1.33)	0.46	
Race							>0.20
African American	1.00	0.90 (0.77–1.05)	0.85 (0.72–0.99)	1.06 (0.90–1.24)	1.07 (0.92–1.26)	0.005	
White	1.00	1.03 (0.86–1.23)	1.09 (0.91–1.30)	1.08 (0.90–1.29)	1.13 (0.95–1.35)	0.17	
Smoking status							>0.75
Never	1.00	0.92 (0.77–1.08)	0.96 (0.82–1.13)	1.06 (0.90–1.26)	1.11 (0.94–1.31)	0.005	
Ever or current	1.00	1.05 (0.85–1.29)	1.04 (0.85–1.28)	1.11 (0.89–1.37)	1.10 (0.89–1.37)	0.21	
Glucose-lowering medication							>0.05
No use	1.00	1.05 (0.82–1.34)	1.08 (0.84–1.38)	1.08 (0.83–1.40)	1.30 (1.01–1.67)	0.029	
Oral hypoglycemic agents	1.00	0.94 (0.75–1.17)	0.87 (0.70–1.08)	0.93 (0.74–1.16)	0.89 (0.71–1.12)	0.43	
Metformin	1.00	1.04 (0.86–1.26)	1.04 (0.86–1.26)	1.16 (0.95–1.40)	1.12 (0.93–1.36)	0.073	
Sulfonylureas	1.00	0.85 (0.69–1.05)	0.92 (0.75–1.12)	0.99 (0.80–1.22)	0.99 (0.81–1.22)	0.17	
Other oral agents	1.00	0.79 (0.60–1.03)	0.77 (0.59–0.99)	0.83 (0.64–1.09)	0.83 (0.64–1.07)	0.80	
Insulin	1.00	0.90 (0.74–1.10)	0.97 (0.80–1.18)	1.12 (0.92–1.36)	1.14 (0.94–1.38)	0.001	

[a]Adjusted for age, race, types of insurance, income, and smoking, other than the variable for stratification.

Table 4—HRs (95% CIs) of CHD according to different levels of BMI during follow-up and at last visit among various subpopulations[a]

	BMI (kg/m^2)						
	<25.0	25.0–29.9	30–34.9	35–39.9	≥40	*P* for trend	*P* for interaction
Follow-up							
Men							
Age groups (years)							>0.25
<50	1.00	1.07 (0.86–1.34)	1.21 (0.97–1.51)	1.43 (1.13–1.81)	1.58 (1.25–2.00)	<0.001	
50–59	1.00	1.21 (0.90–1.52)	1.36 (1.08–1.71)	1.59 (1.25–2.02)	1.52 (1.18–1.95)	<0.001	
≥60	1.00	1.12 (0.89–1.41)	1.10 (0.86–1.39)	1.34 (1.02–1.77)	1.07 (0.76–1.49)	0.22	
Race							>0.10
African American	1.00	1.08 (0.91–1.29)	1.14 (0.95–1.36)	1.50 (1.23–1.82)	1.62 (1.31–2.01)	<0.001	
White	1.00	1.25 (1.03–1.53)	1.41 (1.16–1.72)	1.62 (1.31–1.99)	1.56 (1.26–1.94)	<0.001	
Smoking status							<0.05
Never	1.00	1.23 (0.99–1.53)	1.40 (1.12–1.73)	1.73 (1.38–2.17)	1.93 (1.53–2.43)	<0.001	
Ever or current	1.00	1.27 (1.04–1.55)	1.34 (1.09–1.64)	1.61 (1.29–2.03)	1.36 (1.05–1.76)	<0.001	
Glucose-lowering medication							>0.25
No use	1.00	1.55 (1.18–2.05)	1.46 (1.08–1.96)	1.71 (1.24–2.37)	1.86 (1.32–2.62)	0.001	
Oral hypoglycemic agents	1.00	1.11 (0.85–1.45)	1.33 (1.02–1.73)	1.44 (1.07–1.93)	1.60 (1.18–2.18)	<0.001	
Metformin	1.00	1.18 (0.95–1.48)	1.36 (1.09–1.70)	1.62 (1.28–2.05)	1.64 (1.29–2.10)	<0.001	
Sulfonylureas	1.00	0.98 (0.77–1.24)	1.13 (0.90–1.43)	1.37 (1.07–1.75)	1.35 (1.04–1.76)	<0.001	
Other oral agents	1.00	1.18 (0.78–1.78)	1.41 (0.94–2.09)	1.56 (1.03–2.35)	1.79 (1.18–2.71)	<0.001	
Insulin	1.00	1.18 (0.95–1.46)	1.32 (1.06–1.64)	1.64 (1.31–2.05)	1.63 (1.29–2.07)	<0.001	
Women							
Age groups (years)							>0.25
<50	1.00	1.11 (0.87–1.40)	1.16 (0.92–1.45)	1.21 (0.97–1.52)	1.14 (0.92–1.42)	0.18	
50–59	1.00	1.01 (0.82–1.24)	0.93 (0.76–1.14)	1.11 (0.90–1.36)	1.15 (0.94–1.40)	0.030	
≥60	1.00	0.87 (0.71–1.07)	0.84 (0.69–1.03)	1.04 (0.84–1.29)	1.01 (0.81–1.27)	0.42	
Race							>0.25
African American	1.00	0.94 (0.80–1.10)	0.97 (0.83–1.14)	1.11 (0.95–1.31)	1.15 (0.98–1.36)	<0.001	
White	1.00	1.06 (0.89–1.28)	1.01 (0.84–1.20)	1.19 (1.00–1.43)	1.15 (0.96–1.38)	0.044	
Smoking status							>0.90
Never	1.00	0.99 (0.83–1.18)	1.01 (0.86–1.20)	1.15 (0.96–1.36)	1.19 (1.01–1.42)	<0.001	
Ever or current	1.00	1.14 (0.92–1.41)	1.15 (0.93–1.42)	1.31 (1.06–1.64)	1.20 (0.96–1.49)	0.036	
Glucose-lowering medication							>0.10
No use	1.00	1.08 (0.84–1.40)	1.06 (0.82–1.37)	1.33 (1.02–1.73)	1.38 (1.06–1.79)	0.002	
Oral hypoglycemic agents	1.00	0.96 (0.77–1.20)	0.94 (0.76–1.17)	0.94 (0.75–1.18)	0.90 (0.72–1.13)	0.35	
Metformin	1.00	1.11 (0.91–1.35)	1.13 (0.93–1.37)	1.21 (0.99–1.47)	1.21 (0.99–1.47)	0.035	
Sulfonylureas	1.00	0.99 (0.79–1.24)	1.01 (0.82–1.25)	1.08 (0.87–1.35)	1.08 (0.87–1.35)	0.17	
Other oral agents	1.00	0.96 (0.71–1.31)	0.82 (0.61–1.11)	0.88 (0.64–1.20)	0.92 (0.68–1.25)	0.76	
Insulin	1.00	1.05 (0.85–1.31)	1.10 (0.89–1.35)	1.26 (1.02–1.56)	1.29 (1.05–1.59)	<0.001	
Last visit							
Men							
Age groups (years)							>0.25
<50	1.00	1.03 (0.83–1.28)	1.14 (0.92–1.41)	1.45 (1.16–1.81)	1.50 (1.20–1.87)	<0.001	
50–59	1.00	1.25 (1.01–1.55)	1.37 (1.10–1.69)	1.56 (1.24–1.96)	1.50 (1.19–1.91)	<0.001	
≥60	1.00	1.10 (0.89–1.36)	1.13 (0.90–1.41)	1.24 (0.95–1.63)	1.17 (0.86–1.60)	0.09	

Continued on p. 3210

Table 4—Continued

	BMI (kg/m^2)						
	<25.0	25.0–29.9	30–34.9	35–39.9	≥40	*P* for trend	*P* for interaction
Race							>0.10
African American	1.00	1.06 (0.89–1.25)	1.15 (0.97–1.36)	1.42 (1.17–1.72)	1.61 (1.32–1.97)	<0.001	
White	1.00	1.26 (1.04–1.51)	1.36 (1.13–1.64)	1.58 (1.30–1.93)	1.53 (1.25–1.87)	<0.001	
Smoking status							>0.05
Never	1.00	1.25 (1.02–1.52)	1.44 (1.19–1.76)	1.66 (1.35–2.05)	1.95 (1.58–2.41)	<0.001	
Ever or current	1.00	1.15 (0.95–1.38)	1.19 (0.98–1.44)	1.50 (1.20–1.88)	1.25 (0.98–1.59)	0.003	
Glucose-lowering medication							>0.10
No use	1.00	1.54 (1.19–2.00)	1.41 (1.06–1.86)	1.69 (1.25–2.30)	1.65 (1.18–2.32)	0.004	
Oral hypoglycemic agents	1.00	1.06 (0.83–1.36)	1.32 (1.03–1.69)	1.42 (1.08–1.88)	1.61 (1.21–2.14)	<0.001	
Metformin	1.00	0.99 (0.82–1.21)	1.23 (1.01–1.49)	1.40 (1.13–1.73)	1.48 (1.19–1.83)	<0.001	
Sulfonylureas	1.00	0.97 (0.78–1.21)	1.19 (0.96–1.47)	1.40 (1.11–1.78)	1.34 (1.06–1.71)	<0.001	
Other oral agents	1.00	0.97 (0.66–1.41)	1.26 (0.88–1.81)	1.38 (0.94–2.02)	1.46 (1.00–2.14)	<0.001	
Insulin	1.00	1.04 (0.85–1.26)	1.22 (1.00–1.48)	1.38 (1.12–1.70)	1.47 (1.19–1.82)	<0.001	
Women							
Age groups (years)							>0.25
<50	1.00	0.93 (0.75–1.14)	0.97 (0.79–1.19)	1.04 (0.85–1.28)	0.96 (0.79–1.16)	0.75	
50–59	1.00	0.86 (0.72–1.04)	0.86 (0.72–1.03)	0.99 (0.83–1.20)	1.05 (0.87–1.25)	0.055	
≥60	1.00	0.87 (0.72–1.05)	0.80 (0.66–0.97)	0.99 (0.81–1.22)	1.02 (0.82–1.27)	0.66	
Race							>0.25
African American	1.00	0.83 (0.72–0.97)	0.88 (0.76–1.02)	1.02 (0.88–1.19)	1.04 (0.90–1.21)	0.001	
White	1.00	0.97 (0.82–1.15)	0.93 (0.79–1.09)	1.08 (0.91–1.28)	1.06 (0.90–1.25)	0.14	
Smoking status							>0.90
Never	1.00	0.88 (0.75–1.03)	0.92 (0.79–1.07)	1.05 (0.90–1.23)	1.07 (0.92–1.25)	0.005	
Ever or current	1.00	1.03 (0.84–1.26)	1.06 (0.87–1.29)	1.18 (0.96–1.45)	1.08 (0.88–1.33)	0.26	
Glucose-lowering medication							0.262
No use	1.00	0.93 (0.73–1.19)	1.15 (0.91–1.45)	1.13 (0.88–1.45)	1.23 (0.96–1.58)	0.016	
Oral hypoglycemic agents	1.00	0.94 (0.77–1.14)	0.87 (0.71–1.06)	0.95 (0.77–1.17)	0.85 (0.69–1.05)	0.23	
Metformin	1.00	1.02 (0.86–1.22)	0.97 (0.82–1.16)	1.14 (0.96–1.36)	1.08 (0.91–1.29)	0.11	
Sulfonylureas	1.00	0.91 (0.74–1.11)	0.88 (0.72–1.07)	1.05 (0.86–1.28)	0.97 (0.79–1.18)	0.39	
Other oral agents	1.00	0.83 (0.63–1.08)	0.74 (0.57–0.96)	0.81 (0.62–1.06)	0.80 (0.62–1.04)	0.40	
Insulin	1.00	0.85 (0.70–1.03)	0.88 (0.73–1.05)	1.07 (0.89–1.30)	1.03 (0.86–1.24)	0.013	

[a]Adjusted for age, race, types of insurance, income, and smoking, other than the variable for stratification.

BMI at baseline and during follow-up. In addition, this positive association was present in different race, antidiabetes medication, and smoking groups. It is noteworthy that there was a U-shaped association between BMI at the last visit and the risk of CHD among women with type 2 diabetes in the current study. Our study found that diabetic women who were overweight and had class I obesity (BMI 25–34.9 kg/m^2) at the last visit had a lower risk of CHD compared with normal-weight women (BMI $<$25 kg/m^2).

It is well known that women with diabetes have a greater or equal relative risk of CHD than men with diabetes (30,31). The current study found a significant positive association of BMI and CHD risk among both men and women with type 2 diabetes, and this association is stronger among men than among women. The finding from our study is noteworthy for us to prevent CHD among patients with type 2 diabetes. In addition, more studies are needed to confirm the different effect size of BMI with CHD risk among men and women with type 2 diabetes.

It has been suggested that three potential methodological concerns should be considered when assessing the associations between obesity and health outcomes (32). The most serious concern is reverse causation associated with CHD and death risk. People with a history of CVD and several other chronic diseases frequently lose weight, and thus, people with a lower weight might increase the estimated risk of death. A recent analysis pooling five longitudinal studies has found that patients who have normal weight at the time of diabetes diagnosis have a higher mortality risk than those who are overweight or obese (12). They suggest that diabetic individuals with metabolically obese normal-weight may reflect underlying illness that predisposes to mortality (33). Despite having a normal BMI, these diabetic individuals have hyperinsulinemia, insulin resistance, and dyslipidemia, and all of these factors predispose individuals to death (33). In the current study, we excluded patients with a history of CHD and stroke at time of diabetes diagnosis, which can minimize the influence of reverse causation. Moreover, we performed another sensitivity analysis by excluding the subjects who were diagnosed with CHD during the first 2 years of follow-up (n = 3,207), and the positive association of BMI at baseline and during follow-up with CHD risk was still present. The second major concern is that confounding factors may distort the association between body weight and CHD. Smoking is a particularly important factor because smokers tend to weigh less and have much higher CHD risk than nonsmokers. In the current study, smoking status was considered as a confounding factor in the multivariable model, and the positive association between BMI and the risk of CHD was found in both never-smokers and smokers. The third methodological concern in some analyses between weight and CHD risk is that the physiologic effects of excess fatness, such as hypertension, diabetes, and dyslipidemia, were controlled for statistically, thus artificially removing some of the effects of being overweight. Obesity has been found as a strong risk factor for hypertension (4), high levels of HbA_{1c} (5), and high serum cholesterol among diabetic patients (34) and has also been the key or important component of the metabolic syndrome (35). All of these factors are associated with an increased risk of CHD (35–37) and considered as mediating factors for the physiologic effects of obesity on the CHD risk. In the current study, the adjustment for systolic blood pressure, LDL cholesterol, HDL cholesterol, triglycerides, HbA_{1c}, eGFR, and treatment attenuated the association between BMI and CHD risk, but BMI as a continuous variable remained a statistically significant predictor of CHD in the multivariable model.

There are several strengths in our study, including the large sample size, high proportion of African Americans, and the use of administrative databases to avoid differential recall biases. We have used baseline BMI levels, updated mean values of BMI during follow-up, and the last visit value of BMI in the analyses, which can avoid potential bias from a single baseline measurement. In addition, participants in this study used the same public health care system that minimizes the influence of accessibility to health care, particularly in comparing men and women. One limitation of our study is that our analysis was not performed on a representative sample of the population, which limits the generalizability of this study; however, LSUHCSD hospitals are public hospitals and cover $>$1.6 million patients, most of whom are low-income persons in Louisiana. The results of the current study will have wide applicability for the population with low income and without health insurance in the U.S. Another limitation of our study is that we did not have data on other obesity indicators, such as waist, hip, and thigh circumferences, and did not assess abdominal height, although these adiposity predictors have been shown to be associated with CVD risk (6,38,39). Third, while body weight was measured at each clinic visit, clinically measured BMI might not be as accurate as BMI measured in carefully conducted laboratory studies (40). Fourth, even though our analyses adjusted for an extensive set of confounding factors, residual confounding due to the measurement error in the assessment of confounding factors, unmeasured factors such as heart rates, physical activity, education, and dietary factors, cannot be excluded.

In summary, we found a positive association between BMI at baseline and during follow-up with the risk of CHD among men and women with type 2 diabetes, and this association was stronger among men than among women. We also found a positive association between BMI at the last visit and the risk of CHD among men with type 2 diabetes and a U-shaped association between BMI at the last visit and the risk of CHD among women with type 2 diabetes.

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