Lifetime Risk of Cardiovascular Disease Among Individuals With and Without Diabetes Stratified by Obesity Status in the Framingham Heart Study

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OBJECTIVE — We assessed the lifetime risk of cardiovascular disease (CVD) among individuals with and without obesity and diabetes.

RESEARCH DESIGN AND METHODS — Participants were drawn from the original and offspring cohorts of the Framingham Heart Study. Lifetime (30-year) risk of CVD was assessed using a modified Kaplan-Meier approach adjusting for the competing risk of death, beginning from age 50 years.

RESULTS — Over 30 years, the lifetime risk of CVD among women with diabetes was 54.8% among normal-weight women and 78.8% among obese women. Among normal-weight men with diabetes, the lifetime risk of CVD was 78.6%, whereas it was 86.9% among obese men.

CONCLUSIONS — The lifetime risk of CVD among individuals with diabetes is high, and this relationship is further accentuated with increasing adiposity.

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The prevalence of obesity among individuals with diabetes continues to rise (1). The lifetime risk of coronary heart disease is 42% among men and 25% among women (2) and is higher among individuals with diabetes (3). However, given the close relationship between obesity and diabetes, it is important to evaluate the joint impact of the presence of obesity and diabetes on the lifetime risk of cardiovascular disease (CVD). The purpose of this study is to quantify the lifetime risk of CVD among individuals with and without diabetes and obesity in the Framingham Heart Study.

RESEARCH DESIGN AND METHODS

Study design

Participants were drawn from the Framingham Heart Study. For details regarding the study sample, outcome ascertainment, and diabetes diagnosis, please see an online appendix available at http://dx.doi.org/10.2337/dc08-0025.

All participants gave written informed consent, and the study was approved by the institutional review board of the Boston Medical Center.

Statistical analysis

All analyses were sex specific. Participants who developed diabetes during follow-up were allowed to contribute information to both nondiabetic and diabetic categories (transition in this direction was permitted). Short- (10-year), medium- (20-year) and long-term (30-year) risks of developing CVD were calculated for participants with and without diabetes. The 30-year risk estimate approximates the lifetime risk in individuals aged 50 years or older. The original cohort was further stratified by BMI category; this was not done on the offspring cohort due to fewer numbers of events. The inclusion of the offspring cohort allows for the analysis of more contemporary data. For computing the 10-, 20-, and 30-year risks, we used the Practical Incidence Estimators macro approach developed by Beiser et al. (4) based on a method proposed by Gaynor et al. (5) as previously described (6). This approach uses age as a time scale of analysis and adjusts for the competing risk of death to avoid risk inflation introduced in standard survival methods that do not fully account for individuals who die during follow-up (and, therefore, can no longer develop the event of interest).

RESULTS — Table 1 presents the number of individuals, BMI categories, and CVD cases over the duration of follow-up stratified by diabetes status. Overall, in the original cohort, the lifetime risk of CVD was 38.7% in women and 55.4% in men. In the offspring cohort, the lifetime risk of CVD in women was 27.2% and 39.8% in men.

The 10-, 20-, and 30-year risk of CVD by diabetes status

Over 30 years, the lifetime risk of developing CVD in the original cohort was 38.0% among women without diabetes, whereas it was 67.1% among women with diabetes (Table 1, *middle panel*). Among men, the lifetime risk of CVD without diabetes was 54.8% and with diabetes 78.0%. Similar patterns were observed in

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C.F. had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Table 1—*Characteristics of study participants aged 50–89 years and the 10-, 20-, and 30-year risk of CVD by diabetes status†*

	Nondiabetic	Diabetic	Nondiabetic	Diabetic
	Women		Men	
Baseline characteristics and follow-up information				
Original cohort				
Normal weight	1225 (48.0)	73 (33.2)	694 (35.6)	35 (17.5)
Overweight	880 (34.5)	69 (31.4)	998 (51.3)	113 (56.5)
Obese	448 (17.6)	78 (35.5)	256 (13.1)	52 (26.0)
New CVD events	1424	159	1267	146
Person-years follow-up	63765	2778	39685	2248
Offspring				
Normal weight	931 (49.6)	40 (19.8)	399 (24.5)	39 (15.2)
Overweight	593 (31.6)	63 (31.2)	858 (52.6)	121 (47.3)
Obese	353 (18.8)	99 (49.0)	373 (22.9)	96 (37.5)
New CVD events	244	52	387	102
Person-years follow-up	28229	2027	23408	2573
Lifetime risk CVD*				
Original cohort				
10-year	6.9 (5.8–7.9)	21.6 (9.5–33.6)	15.0 (13.3–16.8)	28.2 (15.4–41.1)
20-year	21.7 (20.1–23.4)	50.0 (39.2–60.9)	36.0 (33.8–38.2)	57.7 (47.7–67.7)
30-year	38.0 (36.1–39.9)	67.1 (58.3–76.0)	54.8 (52.5–57.0)	78.0 (71.5–84.4)
Offspring				
10-year	3.9 (3.0–4.9)	15.9 (7.2–24.6)	8.7 (7.1–10.2)	13.3 (7.1–19.5)
20-year	11.0 (9.2–12.7)	29.3 (19.8–38.7)	23.7 (21.3–26.2)	43.8 (36.1–51.6)
30-year	26.0 (22.6–29.4)	48.6 (38.5–58.7)	37.8 (34.3–41.3)	61.6 (53.9–69.3)
Lifetime risk of CVD stratified by BMI category*				
10-year				
Normal weight	6.2 (4.7–7.6)	9.4 (0.0–22.1)	11.9 (9.3–14.5)	33.2 (6.3–60.0)
Overweight	6.8 (5.0–8.6)	16.5 (0.0–34.1)	15.1 (12.7–17.5)	21.5 (5.9–37.0)
Obese	9.3 (6.3–12.3)	41.9 (14.2–69.6)	22.8 (17.0–28.5)	47.6 (12.1–83.2)
20-year				
Normal weight	18.8 (16.6–21.1)	33.7 (16.2–51.2)	30.9 (27.4–34.4)	54.0 (30.1–77.9)
Overweight	21.6 (18.9–24.4)	52.2 (34.6–69.9)	37.3 (34.2–40.3)	57.9 (45.4–70.4)
Obese	30.0 (25.6–34.3)	65.6 (47.1–84.1)	44.4 (37.9–50.8)	65.4 (40.2–90.6)
30-year				
Normal weight	34.3 (31.6–37.0)	54.8 (39.0–70.5)	49.2 (45.4–52.9)	78.6 (63.7–93.4)
Overweight	38.7 (35.5–41.9)	69.3 (55.9–82.7)	55.5 (52.4–58.6)	74.0 (64.8–83.3)
Obese	46.7 (42.1–51.4)	78.8 (66.4–91.2)	66.8 (60.7–73.0)	86.9 (75.8–97.9)

Data are *n*, *n* (%), and odds ratio (95% CI). *Expressed as percent developing CVD, adjusted for the competing risk of death. For original cohort and offspring among participants aged 50–89 years, 95% CIs are stratified by BMI category for the offspring cohort only. †In the original cohort, 0.08% of participants were lost to follow-up, and in the offspring cohort, 0.5% of participants were lost to follow-up. In the original cohort, 10.3% of CVD events were fatal and in the offspring cohort, 5.4% were fatal.

the offspring cohort and with 10- or 20-year risk data (Table 1, *middle panel*).

The 10-, 20-, and 30-year risk of CVD by diabetes and BMI status

Over 30 years, the lifetime risk of CVD among normal-weight women without diabetes was 34.3% (Table 1, *lower panel*), whereas it was 46.7% among obese women without diabetes. Among women with diabetes, the 30-year risk was 54.8% among normal weight women and 78.8% among obese women with diabetes. Similar patterns were observed among men, and the lifetime risk of CVD approached 90% among men with both obesity and diabetes. Results are displayed graphically in the Online Supplemental Figure.

CONCLUSIONS — The lifetime (i.e., 30-year) incidence of CVD adjusted for mortality among participants with diabetes was two-thirds to three-quarters in the original cohort, and roughly one-half to two-thirds in the offspring cohort. Lifetime risk varied according to BMI category, with participants with obesity and diabetes having the highest risk of developing CVD.

The lifetime risk of diabetes has been estimated at 32.8% for men and 38.5% for women (7). The lifetime risk of diabetes increases in proportion to BMI, ranging from 7.6% among underweight individuals to as high as 74.4% among individuals with stage 2 obesity (8). Similarly, our findings demonstrate that the lifetime risk of CVD is higher among individuals with both obesity and diabetes, with the lifetime risk of CVD approaching nearly 80% in obese women and nearly 90% in obese men.

Given the recent increases in both the

prevalence and incidence of diabetes, projections for the burden of diabetes in the U.S. by 2050 have increased to 48.3 million cases (9). We have already demonstrated that the attributable risk of CVD due to diabetes has increased (10); this trend may continue to worsen if current trajectories do not change.

Limitations of our study include the selection of all white individuals, which potentially limits generalizability. We did not exclude individuals with type 1 diabetes; however, there are less than 10 individuals in our sample and, therefore, this is unlikely to have affected the results. Lastly, given the shorter follow-up time in the offspring, we note that these are more long-term than lifetime risk estimates.

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