2011-12-29

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

Fox, Caroline S.
American Diabetes Association

Fox, Caroline S., Michael J. Pencina, Peter W.F. Wilson, Nina P. Paynter, Ramachandran S. Vasan, Ralph B. D'Agostino. "Lifetime Risk of Cardiovascular Disease Among Individuals With and Without Diabetes Stratified by Obesity Status in the Framingham Heart Study" Diabetes Care 31(8): 1582-1584. (2008)
https://hdl.handle.net/2144/2547

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

CAROLINE S. FOX, MD, MPH1,2,3
MICHAEL J. PENCINA, PhD1,4
PETER W.F. WILSON, MD5
NINA P. PAYNTER, PhD1,4
RAMACHANDRAN S. VASAN, MD1,6
RALPH B. D’AGOSTINO, SR, PhD1,4

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.

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 the offspring cohort.
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

---

**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 |
|------------------|-------------|----------|
|                  | Women       | Men      |
|                  |             |          |
| Baseline         |             |          |
| characteristics  |             |          |
| and follow-up    |             |          |
| information      |             |          |
| Original cohort  |             |          |
| Normal weight    | 1225 (48.0) | 694 (35.6) |
| Overweight       | 880 (34.5)  | 998 (51.3) |
| Obese            | 448 (17.6)  | 256 (13.1) |
| New CVD events   | 1424        | 1267     |
| Person-years     | 63765       | 39685    |
| follow-up        |             |          |
| Offspring        |             |          |
| Normal weight    | 931 (49.6)  | 399 (24.5) |
| Overweight       | 593 (31.6)  | 858 (52.6) |
| Obese            | 353 (18.8)  | 373 (22.9) |
| New CVD events   | 244         | 387      |
| Person-years     | 28229       | 23408    |
| follow-up        |             |          |
| Lifetime risk    |             |          |
| CVD*             |             |          |
| Original cohort  |             |          |
| 10-year          | 6.9 (5.8–7.9) | 15.0 (13.3–16.8) |
| 20-year          | 21.7 (20.1–23.4) | 36.0 (33.8–38.2) |
| 30-year          | 38.0 (36.1–39.9) | 54.8 (52.5–57.0) |
| Offspring        |             |          |
| 10-year          | 3.9 (3.0–4.9) | 8.7 (7.1–10.2) |
| 20-year          | 11.0 (9.2–12.7) | 23.7 (21.3–26.2) |
| 30-year          | 26.0 (22.6–29.4) | 37.8 (34.3–41.3) |
| Lifetime risk of |             |          |
| CVD stratified   |             |          |
| by BMI category*|             |          |
| Original cohort  |             |          |
| 10-year          | 6.2 (4.7–7.6) | 9.4 (0.0–22.1) |
| Overweight       | 6.8 (5.0–8.6) | 16.5 (0.0–34.1) |
| Obese            | 9.3 (6.3–12.3) | 41.9 (14.2–69.6) |
| 20-year          | 18.8 (16.2–21.1) | 30.9 (27.4–34.4) |
| Overweight       | 21.6 (18.9–24.4) | 37.3 (34.2–40.3) |
| Obese            | 30.0 (25.6–34.3) | 44.4 (37.9–50.8) |
| 30-year          | 34.3 (31.6–37.0) | 49.2 (45.4–52.9) |
| Overweight       | 38.7 (35.5–41.9) | 55.5 (52.4–58.6) |
| Obese            | 46.7 (42.1–51.4) | 66.8 (60.7–73.0) |

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.
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.

Acknowledgments—This work was supported by the National Heart, Lung and Blood Institute’s Framingham Heart Study (grant N01-HC-25195). R.S.V. was supported in part by grant K24 HL04334.

References
1. Leibson CL, Williamson DF, Melton LJ 3rd, Palumbo PJ, Smith SA, Ransom JE, Schilling PL, Narayan KM: Temporal trends in BMI among adults with diabetes. Diabetes Care 24:1584–1589, 2001
2. Lloyd-Jones DM, Larson MG, Beiser A, Levy D: Lifetime risk of developing coronary heart disease. Lancet 353:89–92, 1999
3. Lloyd-Jones DM, Leip EP, Larson MG, D’Agostino RB, Beiser A, Wilson PW, Wolf PA, Levy D: Prediction of lifetime risk for cardiovascular disease by risk factor burden at 50 years of age. Circulation 113:791–798, 2006
4. Beiser A, D’Agostino RB Sr, Seshadri S, Sullivan LM, Wolf PA: Computing estimates of incidence, including lifetime risk: Alzheimer’s disease in the Framingham Study: the Practical Incidence Estimators (PIE) macro. Stat Med 19:1495–1522, 2000
5. Gaynor JJ, Feuer EJ, Tan CC, Wu DH, Little CR, Straus DJ, Clarkson BD, Brennan MF: On the use of cause-specific failure and conditional failure probabilities—examples from clinical oncology data. J Am Stat Assoc 88:400–409, 1993
6. Vasan RS, Pencina MJ, Cobain M, Freiberg MS, D’Agostino RB: Estimated risks for developing obesity in the Framingham Heart Study. Ann Intern Med 143:473–480, 2005
7. Narayan KM, Boyle JP, Thompson TJ, Sorensen SW, Williamson DF: Lifetime risk for diabetes mellitus in the United States. JAMA 290:1884–1890, 2003
8. Narayan KM, Boyle JP, Thompson TJ, Gregg EW, Williamson DF: Effect of BMI on lifetime risk for diabetes in the U.S. Diabetes Care 30:1562–1566, 2007
9. Narayan KM, Boyle JP, Geiss LS, Saadidine JB, Thompson TJ: Impact of recent increase in incidence on future diabetes burden in the U.S., 2005–2050. Diabetes Care 29:2114–2116, 2006
10. Fox CS, Coady S, Sorel PC, D’Agostino RB Sr, Pencina MJ, Vasan RS, Meigs JB, Levy D, Savage PJ: Increasing cardiovascular disease burden due to diabetes mellitus: the Framingham Heart Study. Circulation 115:1544–1550, 2007