



ORIGINAL ARTICLE

Excess Mortality among Persons with Type 2 Diabetes

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Abstract

The excess risks of death from any cause and death from cardiovascular causes among persons with type 2 diabetes and various levels of glycemic control and renal complications are unknown. In this registry-based study, we assessed these risks according to glycemic control and renal complications among persons with type 2 diabetes.

We included patients with type 2 diabetes who were registered in the Swedish National Diabetes Register on or after January 1, 1998. For each patient, five controls were randomly selected from the general population and matched according to age, sex, and county. All the participants were followed until December 31, 2011, in the Swedish Registry for Cause-Specific Mortality.

The mean follow-up was 4.6 years in the diabetes group and 4.8 years in the control group. Overall, 77,117 of 435,369 patients with diabetes (17.7%) died, as compared with 306,097 of 2,117,483 controls (14.5%) (adjusted hazard ratio, 1.15; 95% confidence interval [CI], 1.14 to 1.16). The rate of cardiovascular death was 7.9% among patients versus 6.1% among controls (adjusted hazard ratio, 1.14; 95% CI, 1.13 to 1.15). The excess risks of death from any cause and cardiovascular death increased with younger age, worse glycemic control, and greater severity of renal complications. As compared with controls, the hazard ratio for death from any cause among patients younger than 55 years of age who had a glycated hemoglobin level of 6.9% or less (≤ 52 mmol per mole of nonglycated hemoglobin) was 1.92 (95% CI, 1.75 to 2.11); the corresponding hazard ratio among patients 75 years of age or older was 0.95 (95% CI, 0.94 to 0.96). Among patients with normoalbuminuria, the hazard ratio for death among those younger than 55 years of age with a glycated hemoglobin level of 6.9% or less, as compared with controls, was 1.60 (95% CI, 1.40 to 1.82); the corresponding hazard ratio among patients 75 years of age or older was 0.76 (95% CI, 0.75 to 0.78), and patients 65 to 74 years of age also had a significantly lower risk of death (hazard ratio, 0.87; 95% CI, 0.84 to 0.91).

Mortality among persons with type 2 diabetes, as compared with that in the general population, varied greatly, from substantial excess risks in large patient groups to lower risks of death depending on age, glycemic control, and renal complications. (Funded by the Swedish government and others.)

2型糖尿病患者における超過死亡 Excess Mortality among Persons with Type 2 Diabetes M. Tancredi and Others

●背景 血糖コントロールと腎合併症の状態が異なる2型糖尿病患者における、全死因死亡、心血管系の原因による死亡の超過リスクは明らかにされていない。われわれは2型糖尿病患者において、血糖コントロールと腎合併症とによるリスクを評価することを目的として、登録に基づく調査を行った。
●方法 スウェーデン全国糖尿病登録に1998年1月1日以降に登録された2型糖尿病患者を対象とした。患者1例につき対照5例を一般集団から無作為に選択し、年齢、性別、県をマッチさせた。対象全例を、スウェーデン死因別死亡登録を用いて2011年12月31日まで追跡した。
●結果 平均追跡期間は糖尿病患者群4.6年、対照群4.8年であった。全体で、糖尿病患者435,369例中77,117例(17.7%)が死亡したのに対し、対照2,117,483例中306,097例(14.5%)が死亡した(補正ハザード比1.15、95%信頼区間[CI]1.14~1.16)。心血管系死亡率は、糖尿病

患者群7.9%に対し、対照群6.1%であった(補正ハザード比1.14、95%CI1.13~1.15)。全死因死亡および心血管系死亡の超過リスクは、年齢がより低いこと、血糖コントロールがより不良であること、腎合併症がより重症であることに伴い増加した。対照群と比較して、糖化ヘモグロビン値6.9%以下(非糖化ヘモグロビン52 mmol/mole以下)の糖尿病患者の全死因死亡のハザード比は、55歳未満の患者群で1.92(95%CI1.75~2.11)、75歳以上の患者群で0.95(95%CI0.94~0.96)であった。正常アルブミン尿の患者において、対照群に対する死亡のハザード比は、糖化ヘモグロビン値6.9%以下の55歳未満の患者群で1.60(95%CI1.40~1.82)であったが、75歳以上の患者群では0.76(95%CI0.75~0.78)であり、65~74歳の患者群でも死亡リスクは有意に低かった(ハザード比0.87、95%CI0.84~0.91)。

●結論 2型糖尿病患者における死亡率は、一般集団と比較して、大規模な患者群としては相当な超過リスクがあるが、年齢、血糖コントロール、腎合併症別にみると死亡リスクは低くなり、多様であった。(スウェーデン政府ほかから研究助成を受けた。)
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Table 1. Baseline Characteristics of Patients with Type 2 Diabetes and Matched Controls from the General Population.*

| Characteristic | Patients with Type 2 Diabetes (N=435,369) | Controls (N=2,117,483) |
|------------------------------------------------------------------|-------------------------------------------|--------------------------|
| Age—yr | 65.8±12.6 | 65.5±12.5 |
| Women—no. (%) | 193,540 (44.5) | 953,960 (45.1) |
| Born in Sweden—no. (%) | 360,856 (82.9) | 1,855,675 (87.6) |
| Educational level—no./total no. (%) | | |
| Low | 189,808/425,706 (44.6) | 781,319/2,080,022 (37.6) |
| Intermediate | 169,159/425,706 (39.7) | 812,340/2,080,022 (39.1) |
| High | 66,739/425,706 (15.7) | 486,363/2,080,022 (23.4) |
| Information from National Diabetes Register | | |
| Glycated hemoglobin | | |
| No. of persons with data | 388,643 | — |
| Mean—mmol/mole of nonglycated hemoglobin | 54.3±14.5 | — |
| Diabetes treatment—no. (%) | | |
| Diet | 165,144 (37.9) | — |
| Tablets | 184,002 (42.3) | — |
| Insulin | 46,037 (10.8) | — |
| Insulin and tablets | 40,186 (9.2) | — |
| Diabetes duration | | |
| No. of persons with data | 386,621 | — |
| Mean—yr | 5.66±7.02 | — |
| Body-mass index | | |
| No. of persons with data | 326,586 | — |
| Mean | 29.6±5.3 | — |
| Low-density lipoprotein cholesterol | | |
| No. of persons with data | 210,262 | — |
| Mean—mmol/liter | 2.94±0.95 | — |
| Blood pressure | | |
| No. of persons with data | 375,133 | — |
| Systolic—mm Hg | 140.4±18.4 | — |
| Diastolic—mm Hg | 78.5±9.3 | — |
| Smoking—no./total no. (%) | 53,796/151,842 (35.5) | — |
| Blood-pressure-lowering medication—no./total no. (%) | 265,846/409,442 (64.9) | — |
| Lipid-lowering medication—no./total no. (%) | 168,431/407,357 (41.3) | — |
| Registration in the In-Patient Register before baseline—no. (%)† | | |
| Acute myocardial infarction | 39,115 (9.0) | 90,933 (4.3) |
| Coronary heart disease | 68,945 (15.8) | 168,292 (7.9) |
| Atrial fibrillation | 38,164 (8.8) | 117,844 (5.6) |
| Heart failure | 30,249 (6.9) | 69,844 (3.3) |
| Stroke | 27,293 (6.3) | 81,976 (3.9) |
| Cancer | 45,907 (10.5) | 208,394 (9.9) |

* Plus-minus values are means ±SD. Educational level was categorized as low (compulsory only), intermediate, or high (university level or similar). Percentages for the glycated hemoglobin level were based on values from the National Glycohemoglobin Standardization Program, and concentrations were based on values from the International Federation of Clinical Chemistry. The body-mass index is the weight in kilograms divided by the square of the height in meters. † The following codes from the International Classification of Diseases, 10th Revision, were used: I21 for acute myocardial infarction; I20 through I25 for coronary heart disease; I48 for atrial fibrillation; I50 for heart failure; I61, I62.9, I63, I64, and I67.9 for stroke; and C00 through C97 for cancer.

Table 1. Baseline Characteristics of Patients with Type 2 Diabetes and Matched Controls from the General Population.

Table 2. Mortality, According to Cause of Death, among Patients with Type 2 Diabetes and Matched Controls from the General Population, According to Age at Baseline.*

| Cause of Death | Patients (N=435,369) | Controls (N=2,117,483) | <55 Yr | | 55–64 Yr | | 65–74 Yr | | ≥75 Yr | |
|-------------------------------------------|----------------------|------------------------|---------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
| | | | Patients (N=78,086) | Controls (N=389,657) | Patients (N=115,451) | Controls (N=574,492) | Patients (N=126,530) | Controls (N=619,517) | Patients (N=115,302) | Controls (N=533,817) |
| Any cause | | | | | | | | | | |
| No. of persons (%) | 77,117 (17.7) | 306,097 (14.5) | 2603 (3.3) | 5691 (1.5) | 9203 (8.0) | 27,302 (4.8) | 20,647 (16.3) | 74,594 (12.0) | 44,664 (38.7) | 198,510 (37.2) |
| No. of deaths per 1000 person-yr (95% CI) | 38.64 (38.37–38.91) | 30.30 (30.19–30.41) | 6.89 (6.63–7.18) | 2.97 (2.90–3.05) | 16.20 (15.87–16.54) | 9.42 (9.31–9.54) | 35.19 (34.71–35.67) | 24.79 (24.61–24.97) | 96.41 (95.52–97.31) | 87.00 (86.62–87.39) |
| Cardiovascular cause | | | | | | | | | | |
| No. of persons (%) | 34,238 (7.9) | 129,917 (6.1) | 831 (1.1) | 1374 (0.4) | 3254 (2.8) | 7,633 (1.3) | 8,287 (6.5) | 26,579 (4.3) | 21,866 (19.0) | 94,111 (17.7) |
| No. of deaths per 1000 person-yr (95% CI) | 17.15 (16.97–17.34) | 12.86 (12.79–12.93) | 2.20 (2.05–2.35) | 0.72 (0.68–0.76) | 5.73 (5.53–5.93) | 2.64 (2.58–2.70) | 14.12 (13.82–14.43) | 8.83 (8.73–8.94) | 47.20 (46.58–47.83) | 41.33 (41.07–41.60) |
| Cancer | | | | | | | | | | |
| No. of persons (%) | 16,873 (3.9) | 77,149 (3.6) | 622 (0.8) | 2098 (0.5) | 2021 (2.5) | 11,759 (2.0) | 5,735 (4.5) | 26,742 (4.3) | 7,595 (6.6) | 36,550 (6.8) |
| No. of deaths per 1000 person-yr (95% CI) | 8.45 (8.33–8.58) | 7.64 (7.58–7.69) | 1.65 (1.52–1.78) | 1.10 (1.05–1.14) | 5.14 (4.96–5.33) | 4.06 (3.99–4.13) | 9.77 (9.52–10.03) | 8.89 (8.78–9.00) | 16.39 (16.03–16.77) | 16.02 (15.86–16.18) |
| Diabetes-related cause | | | | | | | | | | |
| No. of persons (%) | 8,024 (1.8) | 3,893 (0.2) | 273 (0.3) | 89 (<0.1) | 884 (0.8) | 357 (0.1) | 2,127 (1.7) | 931 (0.2) | 4,740 (4.1) | 2,516 (0.5) |
| No. of deaths per 1000 person-yr (95% CI) | 4.02 (3.93–4.11) | 0.39 (0.37–0.40) | 0.72 (0.64–0.81) | 0.05 (0.04–0.06) | 1.56 (1.46–1.66) | 0.12 (0.11–0.14) | 3.62 (3.47–3.78) | 0.31 (0.29–0.33) | 10.23 (9.94–10.53) | 1.10 (1.06–1.15) |
| External cause | | | | | | | | | | |
| No. of persons (%) | 2,462 (0.6) | 11,088 (0.5) | 287 (0.4) | 883 (0.2) | 390 (0.3) | 1,696 (0.3) | 568 (0.4) | 2,379 (0.4) | 1,217 (1.1) | 6,130 (1.1) |
| No. of deaths per 1000 person-yr (95% CI) | 1.23 (1.19–1.28) | 1.10 (1.08–1.12) | 0.76 (0.67–0.85) | 0.46 (0.43–0.49) | 0.69 (0.62–0.76) | 0.59 (0.56–0.61) | 0.97 (0.89–1.05) | 0.79 (0.76–0.82) | 2.63 (2.48–2.78) | 2.69 (2.62–2.75) |
| Other | | | | | | | | | | |
| No. of persons (%) | 15,520 (3.6) | 84,050 (4.0) | 590 (0.8) | 1247 (0.3) | 1754 (1.5) | 5,837 (1.0) | 3,930 (3.1) | 17,963 (2.9) | 9,246 (8.0) | 59,001 (11.1) |
| No. of deaths per 1000 person-yr (95% CI) | 7.78 (7.65–7.90) | 8.32 (8.26–8.38) | 1.56 (1.44–1.69) | 0.65 (0.62–0.69) | 3.09 (2.95–3.24) | 2.01 (1.96–2.07) | 6.70 (6.49–6.91) | 5.97 (5.88–6.06) | 19.96 (19.55–20.37) | 25.86 (25.62–26.07) |

* CI denotes confidence interval.

Table 2. Mortality, According to Cause of Death, among Patients with Type 2 Diabetes and Matched Controls from the General Population, According to Age at Baseline.