Diagnosis of Type 2 Diabetes at an Older Age

Effect on mortality in men and women

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OBJECTIVE — To compare the mortality of people who were diagnosed with type 2 diabetes over 65 years of age with that of nondiabetic individuals.

RESEARCH DESIGN AND METHODS — Using a population-based diabetes information system for an observational cohort study in Tayside, Scotland, people who were diagnosed with type 2 diabetes over the age of 65 years between 1993 and 2002 were identified. Nondiabetic comparators, matched for age and sex, were identified from the nondiabetic population. The two cohorts were followed up for mortality and cardiovascular mortality according to death certification records.

RESULTS — There were 3,594 people with type 2 diabetes (48% male) and 7,188 matched comparators identified in the study. Over a mean follow-up period of 4.6 ± 2.9 years for 3,594 people with type 2 diabetes and 7,188 comparators, 909 (25.3%) patients in the diabetic cohort and 1,651 (23.0%) in the nondiabetic cohort died. The adjusted relative risk for mortality in the diabetic cohort compared with the nondiabetic cohort was 1.06 (95% CI 0.94–1.19) for men and 1.29 (1.15–1.45) for women. Cardiovascular deaths accounted for 49.4% of the deaths in people with and 45.2% in those without diabetes (adjusted relative risk 1.01 [0.93–1.10]).

CONCLUSIONS — Men diagnosed with type 2 diabetes over the age of 65 years have no excess mortality compared with their nondiabetic counterparts, a finding that was not replicated for women.

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Diabetes is known to reduce life expectancy in older people (1). However, older people with diabetes are a heterogeneous group, including newly diagnosed people and those whose diagnosis may have occurred up to 20 years previously (2–4). Some research suggests that the effect on mortality of a diagnosis of diabetes becomes progressively less as age at diagnosis increases (5). A group of older people whose diabetes was detected by screening had an increased risk of mortality (6), and even patients who were diagnosed with diabetes over the age of 80 years had a reduced life expectancy of ~1 year (7). However, two European studies found no difference in mortality between men diagnosed with diabetes over the age of 75 years and nondiabetic men (8,9). We compared all-cause and cardiovascular mortality in cohorts of people diagnosed with type 2 diabetes at an older age with that in nondiabetic individuals.

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A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

RESEARCH DESIGN AND METHODS

— The DARTS/MEMO (Diabetes Audit and Research in Tayside Scotland/Medicines Monitoring Unit) Collaboration (9) works on the record linkage of health care data to facilitate epidemiological and health services research in the population of Tayside, Scotland (estimated population of 389,800 in 1998). Record linkage is enabled by the widespread use of a unique health care identifier (community health index number) that is allocated to people when they register with a general practitioner in Scotland. This study was conducted in a defined population of general practitioner–registered people who were known to be residents of Tayside during the entire study period (unless they died).

DARTS is a validated population-based diabetes information system in Tayside that is compiled by record linking several independent data sources. It has 95% sensitivity at identifying people with diabetes (9). It was used to identify people aged >65 years who were diagnosed with type 2 diabetes between January 1993 and December 2002. For every diabetic individual, two nondiabetic comparators were identified from the general population, matched for age (within 1 year) and sex. The index date of a diabetic person was their date of diagnosis, as was the index dates of their matched comparators.

In a cohort study, the diabetic people and the nondiabetic comparators were followed for a maximum of 10 years for the primary outcomes of all-cause mortality and cardiovascular mortality. Mortality data were provided via death certification records, and the "underlying cause of death" was classified as a cardiovascular death according to ICD 9 codes 390–459 (10) and ICD 10 codes I00–99 (11). Kaplan-Meier survival curves were constructed. A Cox proportional hazards model with multiple covariates was fitted to the sample data. The covariates were population type (nondiabetic/diabetic), age at index date, sex, and Carstairs de-

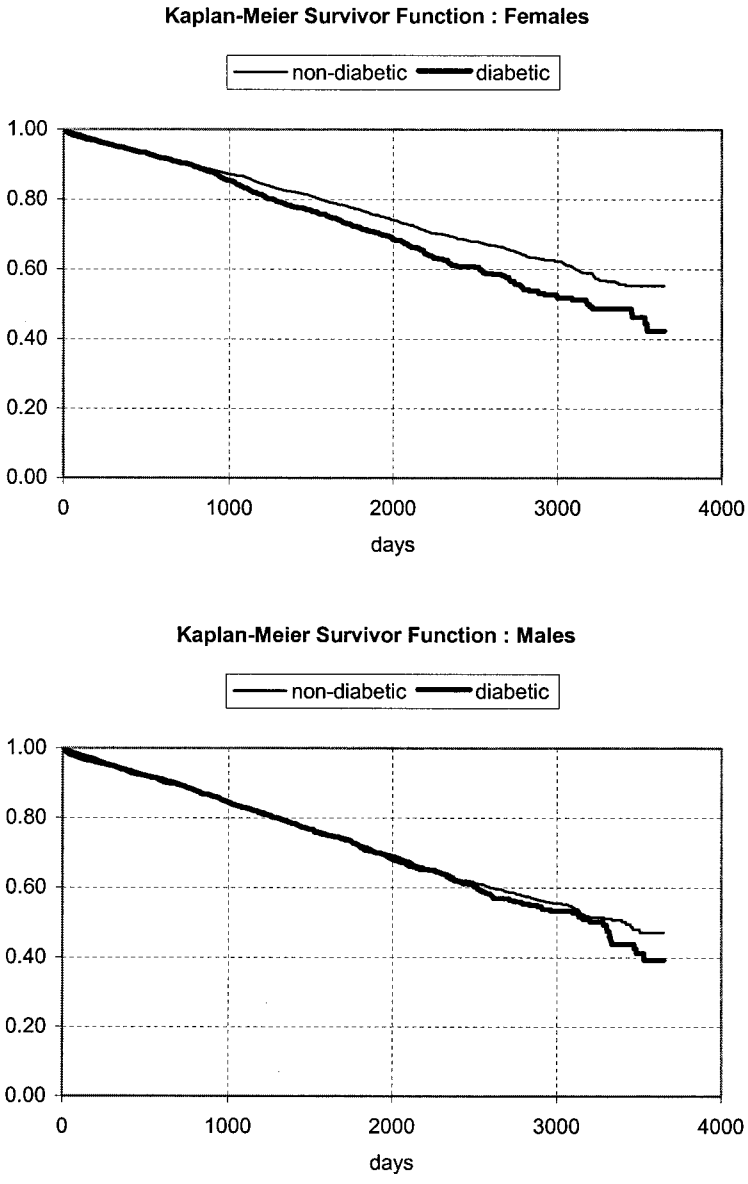

Figure 1—*Kaplan-Meier survival curves of older female* (top) *and male* (bottom) *individuals with type 2 diabetes and their nondiabetic comparators during 1993–2002.*

privation category (12) (an area-based measure of material deprivation).

RESULTS — There were 3,594 people with type 2 diabetes (48% male) and 7,188 matched comparators identified in the study. Subject survival is presented separately for men and women in Fig. 1. Over a mean follow-up period of 4.6 ± 2.9 years, 909 (25.3%) patients in the diabetic cohort and 1,651 (23.0%) in the nondiabetic cohort died. For men, the relative risk for mortality in the diabetic cohort compared with the nondiabetic cohort, adjusted for deprivation, was 1.06 (95% CI 0.94–1.19). There were no differences when patients were stratified by age at diagnosis. For women, the adjusted relative risk for mortality in the diabetic cohort compared with the nondiabetic cohort was 1.29 (1.15–1.45). The risks for those diagnosed with diabetes at 65–74 years, 75–84 years, and >85 years were 1.47 (1.21–1.78), 1.15 (0.97–1.38), and 1.36 (1.06–1.73), respectively. Cardiovascular deaths accounted for 49.4% of the deaths in people with diabetes and 45.2% in those without (adjusted relative risk 1.01 [0.93–1.10]).

CONCLUSIONS — In this study, men diagnosed with type 2 diabetes after 65 years of age had no increased risk of mortality compared with nondiabetic men of the same age. This result contrasts sharply with the significant effect of diabetes on mortality in a population of older diabetic people that included newly diagnosed individuals and those with a longer duration of disease (5). Studies that have found small differences in mortality, even in men diagnosed at a later age, have not adjusted for the confounding effect of deprivation (possibly independently associated with diabetes prevalence [13] and mortality).

Our data came from a validated diabetes system and are known to be reliable (9). The mean follow-up of almost 5 years was similar to that of an Italian study (7). It may be that mortality of diabetic and nondiabetic men diverges in later years after diagnosis, although this did not occur for at least 7 years following diagnosis in our study. A weakness of the study was that we were unable to adjust for cardiovascular risk factors at baseline. However, we might expect a poorer profile in the diabetic cohort (14,15), with adjustment resulting in even less of a difference between the two cohorts. The proportion of cardiovascular deaths was relatively low; however, we used "underlying cause of death" to determine whether a death had a cardiovascular cause, and this may underestimate cardiovascular mortality. We also acknowledge that there may be a degree of under-ascertainment of diabetes in the nondiabetic cohort.

Our result may be due to a survivor effect, with men with more severe diabetes having presented and died before the age of 65 years. However, this does not detract from the important clinical point: that the effects of diabetes (in this case, mortality) in those diagnosed at an older age clearly differs markedly from those diagnosed when younger.

In contrast to men, women diagnosed with type 2 diabetes at an older age had an increased risk of mortality compared with older nondiabetic women. This was evident 3 years after diagnosis, particularly for women aged 65–74 years. Diabetes may be a stronger risk factor for women compared with men (as our results suggest), although whether this can be accounted for by a higher prevalence of classic cardiovascular risk factors in diabetic women compared with diabetic men is still controversial (16). We were unable to adjust for cardiovascular risk

factors, but our study suggests that the effects of diabetes may vary according to sex, even in older individuals.

This study therefore highlights the importance of recognizing the heterogeneity of the older diabetic population.

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References

1. Waugh NR, Dallas JH, Jung RT, Newton RW: Mortality in a cohort of diabetic patients: causes and relative risks. *Diabetologia* 32:103–104, 1989
2. Stengard JH, Tuomilehto J, Pekkanen J, Kivinen P, Kaarsalo E, Nissinen A, Karvonen MJ: Diabetes mellitus, impaired glucose tolerance and mortality among elderly men: the Finnish cohorts of the Seven Countries Study. *Diabetologia* 35: 760–765, 1992
3. Katakura M, Naka M, Kondo T, Nishii N, Komatsu M, Sato Y, Yamauchi K, Hiramatsu K, Ikeda M, Aizawa T, Hashizume K: Prospective analysis of mortality, morbidity, and risk factors in elderly diabetic subjects: Nagano Study. *Diabetes Care* 26: 638–644, 2003
4. Panzram G: Mortality and survival in type 2 (non-insulin-dependent) diabetes mellitus. *Diabetologia* 30:123–131, 1987
5. Croxson SCM, Price DE, Burden M, Jagger C, Burden AC: The mortality of elderly people with diabetes. *Diabet Med* 11:250–252, 1994
6. Roper NA, Bilous RW, Kelly WF, Unwin NC, Connolly VM: Excess mortality in a population with diabetes and the impact of material deprivation: longitudinal, population based study. *BMJ* 322:1389–1393, 2001
7. Muggeo M, Verlato G, Bonora E, Bressan F, Girotto S, Corbellini M, Gemma ML, Moghetti P, Zenere M, Cacciatori V, et al: The Verona diabetes study: a population-based survey on known diabetes mellitus prevalence and 5-year all-cause mortality. *Diabetologia* 38:318–325, 1995
8. Panzram G, Zabel-Langhennig: Prognosis of diabetes mellitus in a geographically defined population. *Diabetologia* 20:587–591, 1981
9. Morris AD, Boyle DI, MacAlpine R, Emslie-Smith A, Jung RT, Newton RW, MacDonald TM: The diabetes audit and research in Tayside Scotland (DARTS) study: electronic record-linkage to create a diabetes register. *BMJ* 315:524–528, 1997
10. World Health Organization: *Manual of the International Statistical Classification of Disease, Injuries and Causes of Death: Ninth Revision*. Geneva, World Health Org., 1978
11. World Health Organization: *International Statistical Classification of Diseases and Related Health Problems: Tenth Revision*. Geneva, World Health Org.,1994
12. Carstairs V: Deprivation and health in Scotland. *Health Bull (Edinb)* 48:162–175, 1990
13. Evans JMM, Newton RW, Ruta DA, MacDonald TM, Morris AD: Socio-economic status, obesity and prevalence of type 1 and type 2 diabetes mellitus. *Diabet Med* 17:478–480, 2000
14. Laakso M, Rönnemaa T, Pyörälä K, Kallio V, Puukka P, Penttila I: Atherosclerotic vascular disease and its risk factors in non-insulin-dependent diabetic and non-diabetic subjects in Finland. *Diabetes Care* 11:449–463, 1988
15. Serrano Rios M, Martinez Larrad MT: Hypertension in type 2 diabetes mellitus. In *Cardiovascular Risk in Type 2 Diabetes*. Hancu N, Ed. Berlin, Springer-Verlag, 2003, p. 63–84
16. Kanaya AM, Grady D, Barrett-Connor E: Explaining the sex difference in coronary heart disease mortality among patients with type 2 diabetes mellitus. *Arch Intern Med* 162:1737–1745, 2002