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Ten-year mortality and glucose tolerance status in an elderly Finnish population

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Abstract

The aim of this study was to determine the 10-year mortality rate of an elderly population aged 70 years or over ($n = 379$) with reference to glucose tolerance status, taking into account other determinants of excess mortality. The baseline examination during 1991–1992 included a postal questionnaire, a physical examination and a 2 h OGTT, which was classified according to both the 1985 WHO criteria and the 1999 WHO criteria. Follow-up was continued until death or until 31 December 2001. 66% of men and 51% of women died within 10 years. In men, the cumulative mortalities were 84% for previously diagnosed diabetes, 67% for undiagnosed diabetes, 67% for impaired glucose tolerance (IGT) and 60% for normal glucose tolerance (NGT). The corresponding percentages for women were 76, 52, 49, and 40%. Male gender, poor self-rated health and previously diagnosed diabetes were the most powerful predictors of mortality. When adjustments were made for age, gender, BMI, cardiovascular disease, hypertension, physical exercise and self-rated health, the estimated relative mortality rate was 2.0 (95% CI 1.5–2.7) among previously diagnosed diabetic subjects, 1.3 (CI 0.8–2.2) among undiagnosed diabetic subjects and 1.1 (0.8–1.5) among IGT subjects compared to NGT subjects. These relative mortalities were higher in women than in men. When abnormal glucose tolerance was pooled into one category, the OR for excess mortality was 1.4 (95% CI 1.1–1.9).

Keywords: Mortality; Glucose; Finnish population

1. Introduction

Type 2 diabetes is associated with increased mortality due to cardiovascular diseases [1–4]. Previous findings suggest that relative excess mortality decreases with increasing age. Some research, mainly concerning middle-aged populations, suggests that undiagnosed diabetes and even IGT are also associated with increased mortality [4–6]. Studies concerning elderly people focusing on the association between mortality, undiagnosed diabetes and impaired glucose tolerance have not been extensively conducted. Higher levels of physical activity, avoidance of smoking and

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good self-rated health have also been associated with decreased mortality in middle-aged subjects and also in elderly subjects in [7–9]. The association of body mass index with mortality is inconsistent in all age groups in previous studies [8,10]. This might be due to methodological differences, e.g. failure to control for confounding factors such as smoking, biological intermediates of obesity-related mortality including diabetes, blood pressure and varying durations of follow-up in previous studies [10]. Results concerning gender differences in association with abnormal glucose tolerance and mortality are inconsistent. In addition, the amount of data on elderly subjects is limited [5,11].

The aim of this study was to describe the 10-year mortality rate of an elderly Finnish population with reference to glucose tolerance status, while taking into account other known determinants of excess mortality in elderly people.

2. Subjects and methods

The study population consisted of non-institutionalized persons born in 1920 or earlier residing in the municipalities of Kempele, Oulunsalo and Hailuoto in northern Finland. The ethical committee of the Oulu University Hospital approved the study protocol.

The study was conducted between 1 September 1991 and 29 February 1992 in two phases. The first phase consisted of a postal questionnaire and physical examination. The second phase in early 1992 included a 2 h oral glucose tolerance test (OGTT). At the beginning of the first phase on 1 September 1991, there were 501 eligible persons (190 men) participating in the study and 444 persons (163 men) took part in one or both examination days during the first phase. At the beginning of the second phase on 1 January 1992, there were 487 persons (183 men) eligible for the study. The change in subject number was because some subjects had died, some had been admitted to institutional care and some had moved. Four persons died before the second examination in 1992. The total number of non-institutionalized persons eligible for the second examination was 483 (180 men, 303 women). Of these people 83 (31 men) refused to take part and 21 (8 men) did not have their 2 h glucose values determined due to medical or other reasons.

The total number of participants in this study was thus 379 (141 men) and the participation rate was 78.5% (78.3% among men and 78.5% among women). Three hundred and thirty-six persons underwent the 2 h glucose tolerance test, while the remaining 43 had diabetes mellitus treated with oral hypoglycaemic drugs or insulin. Therefore, only fasting capillary whole blood glucose was determined for those patients.

The first phase of the study consisted of a postal questionnaire, including questions about the participant's previously diagnosed diabetes. The physical examination comprised measurements of body height and weight and an evaluation of signs of previous stroke. The physical examinations were preformed by a nurse and a physician, respectively. Height and weight were measured in light indoor clothing without shoes. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). Cardiovascular disease (CVD) was considered to be present if the participant took medication for coronary heart disease and/or had signs of a previous stroke. Information about the medication for coronary heart disease was derived from the codes printed on the subject's medication (including long-acting nitrates, sublingual nitrates and beta blockers). The diagnosis of hypertension was derived from health insurance records and from questionnaire information identifying subjects who did not receive medication free of charge or subjects who were not on medication. The frequency and strenuousness of physical exercise were measured by a question with seven alternative answers. These were dichotomized into two categories in the analysis. The two categories were described as follows: 1: 'inactive' ('no exercise' or 'no more exercise than going shopping or participating in other light activity once or twice a week); 2: 'active' ('walking or corresponding exercise many times a week' to 'exercising many times a week causing much sweating and breathlessness during the exercise'). Smoking was assessed using one question: 1: no, 2: yes. Self-perceived health was assessed by one question with five alternatives: 1: very good, 2: rather good, 3: moderate, 4: rather poor, 5: very poor. In the analysis, the alternatives were classified into three categories as follows: 1: good, 2: average, 3: poor.

The second phase of the study in early 1992 included a 2 h oral glucose tolerance test (OGTT) which was classified according to both the WHO 1985 and WHO 1999 criteria [11,12]. All the participants, except the diabetic patients on insulin or oral hypoglycaemic drug treatment, underwent an OGTT.

According to the 1985 WHO criteria, a person has diabetes if fasting capillary whole blood glucose values are $\geq$6.7 mmol/l or 2 h OGTT values are $\geq$11.1 mmol/l [12]. In epidemiological studies the diagnosis may be restricted to 2 h values only. The corresponding WHO 1999 criteria for diabetes are as follows: fasting whole blood glucose values $\geq$6.1 mmol/l and/or 2 h OGTT values $\geq$11.1 mmol/l. Impaired glucose tolerance (IGT) is defined by 2 h OGTT values from 7.8 to 11.0 mmol/l according to both criteria and persons with 2 h OGTT values $<$7.8 mmol/l are classified as having normal glucose tolerance [13]. The WHO 1999 criteria additionally include the category of impaired fasting glycemia (IFG), which is defined as fasting blood glucose values of 5.6–6.0 mmol/l. In this study a person was classified as having previously diagnosed diabetes if he/she took an oral drug or insulin treatment, or if he/she was on a diabetes diet and additionally had a new OGTT 2 h value $\geq$11.1 mmol/l. The latter was done because after checking medical records, patient-reported diagnosis of diet-treated diabetes was found to include some persons who actually had nearnormal fasting values or IGT, so called ‘pre-diabetes’, which was a term in general use and was easily confused with diabetes in the 1980s. A person without previously diagnosed diabetes was classified as having previously undiagnosed diabetes if the 2 h OGTT showed a value of $\geq$11.1 mmol/l and impaired glucose tolerance if the 2 h value was 7.8–11.0 mmol/l. Those with 2 h OGTT values $<$7.8 mmol/l and not on an oral diabetes treatment drug or insulin treatment were classified as having normal glucose tolerance (NGT). At baseline, subjects who had IFG based on the 1999 WHO criteria were also included in the analysis.

The mortality follow-up was started on the date of the OGTT in 1992 and continued until the death of the subject or until 31 December 2001. Information on deaths during the follow-up period was obtained regularly from official death certificates (lists of names). Because death certificates in this age group usually do not include autopsy information, causes of death were not collected from death certificates.

2.1. Statistical methods

The Kaplan–Meier method for males and females was used to describe cumulative survival in the four glucose tolerance groups. To assess the impact of glucose tolerance status on all causes of mortality in relation to other selected variables, the Cox Proportional Hazards Model was used. The following covariates were used in the basic model: gender, age (continuous variable), presence of CVD (dichotomized variable), hypertension (dichotomized variable), body mass index (continuous variable), smoking, physical activity (dichotomized variables) and self-perceived health (three categories). Smoking was excluded from the final model due to the very small number of smokers in the population (15 men, 7 women) SPSS for Windows was used for the statistical calculations.

3. Results

Of the participants, 37% (141) were men and 63% (238) were women. The median age of the men in the study was 75 years (range from 71 to 93). The median age of women was 77 years (range from 71 to 94). The median age of the male and female subject groups was calculated on the date of the OGTT. The OGTT-corrected prevalence figures from the beginning of the follow-up period have been presented in detail previously [14]. For previously diagnosed diabetes the values were 14% ($n = 19$) for the men and 19% ($n = 46$) for the women. The prevalence of previously undiagnosed diabetes was 9% ($n = 12$ for men, $n = 21$ for women) in both genders. 32% ($n = 45$) of the men and 35% ($n = 84$) of the women took IGT. When glucose tolerance was defined using the WHO 1999 criteria, 39 (10%) of the subjects took impaired fasting glycemia and 113 (30%) NGT. Some selected background variables of the study population have also been presented earlier and are presented in Table 1.

The mean follow-up time for the survivors was 9.8 years, the maximum being 10 years. The mean follow-up time for the men who died during the follow-up was 4.8 years and for women 5.4 years. In all, 57% ($n = 215$) of the study population had died by the end of 2001: 66% ($n = 93$) of the men and 51% ($n = 122$) of women (Table 2). Impaired fasting glycemia was not associated with increased mortality (data not

Table 1
Some selected characteristics of the study groups at baseline examination by gender

	Prev. DM (19M, 46W)	Undg. DM (12M, 21W)	IGT (45M, 84W)	NGT (65M, 86WF)
Age (median) (years)				
M	73	74	76	74
W	78	78	76	75
M + W	76	77	76	75
BMI (median) (kg/m^2)				
M	28.5	29.3	26.5	26.0
W	28.8	29.3	28.2	28.4
M + W	28.6	29.3	27.4	27.2
Syst. BP (median) (mmHg)				
M	158	152	148	144
W	160	158	158	160
M + W	159	157	155	156
Diast. BP (median) (mmHg)				
M	88	85	84	82
W	76	78	84	84
M + W	78	81	84	82
CVD present (%)				
M	47	58	40	43
W	59	71	50	36
M + W	55	67	47	39
Physical inactivity (%)				
M	39	58	50	35
W	70	71	58	49
M + W	61	67	55	43

Prev. DM: previously diagnosed diabetes; Undg. DM: previously undiagnosed diabetes; IGT: impaired glucose tolerance; NGT: normal glucose tolerance; BMI: body mass index; Syst. BP: systolic blood pressure; Diast. BP: diastolic blood pressure; CVD: cardiovascular disease; M: men; W: women.

shown) and in further analyses these subjects were included in the NGT group. In both men and women, cumulative mortality increased along with the deterioration in glucose tolerance status (Table 2). The gender difference was largest in the NGT group (20%) and smallest in the previously diagnosed diabetes group (8%). The Kaplan–Meier survival curves of each study group by gender are presented in Figs. 1 and 2.

Table 2
Proportions of subjects who died during 10 years of follow-up according to glucose tolerance status and gender

	Prev. DM% (n)	Undg. DM% (n)	IGT% (n)	NGT% (n)	Total% (n)
Men	84 (16)*	67 (8)	67 (30)	60 (39)	66 (93)
Women	76 (35)**	52 (11)	49 (41)	40 (35)	51 (122)
M + W	79 (51)**	58 (19)	55 (71)	49 (74)	57 (215)

M: men; W: women.
** $p < 0.001$ compared to NGT.
* $p < 0.05$ compared to NGT.

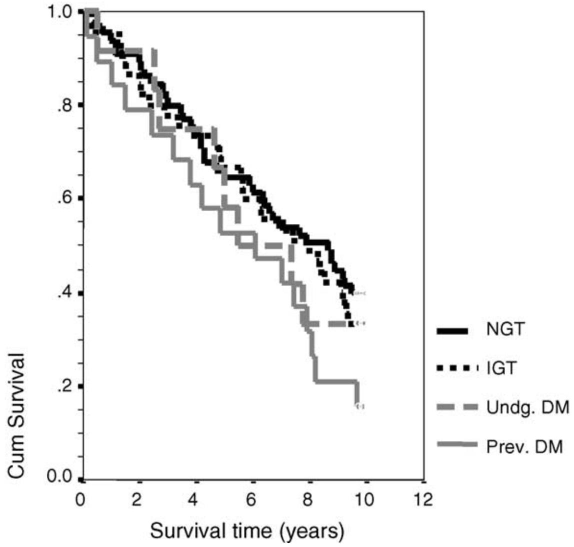

Fig. 1. Survival curves for the elderly male study subjects according to glucose tolerance category.

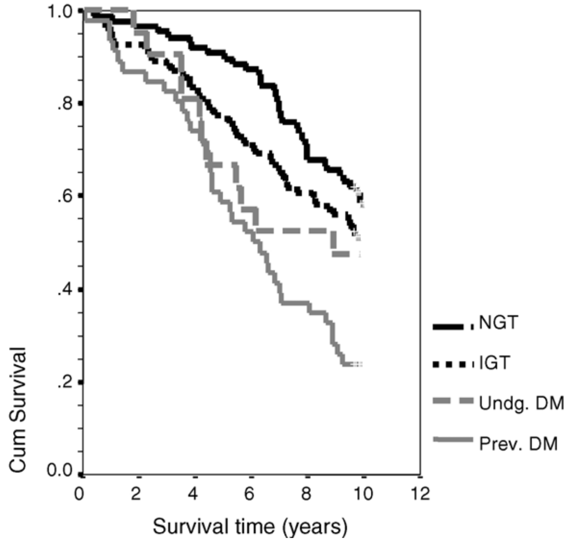

Fig. 2. Survival curves for the elderly female study subjects according to glucose tolerance category.

The results of the Cox Proportional Hazards Model (Table 3) revealed that male gender (OR 2.0, 95% CI 1.5–2.7), poor self-rated health (OR 1.9, 95% CI 1.2–3.1) and previously diagnosed diabetes (OR 1.9, 95% CI 1.3–2.8) were the most powerful predictors independently associated with mortality. In addition, previously diagnosed diabetes was positively associated with mortality after adjustments for age, body mass index, presence of CVD, hypertension, physical activity and self-perceived health were made. A model applied separately by gender indicated that previously diagnosed diabetes was positively associated with mortality in women (OR 2.3, 95% CI 1.4–3.7), but not in men (OR 1.5, 95% CI 0.7–3.0). Physical inactivity and the presence of cardiovascular disease had greater impacts on mortality among men than among women, whereas hypertension predicted mortality better among women than among men.

When all diabetes factors were included in the analyses, the odds ratio for mortality in the total population for diabetes was 1.8 (95% CI 1.3–2.6) and 1.2 for IGT (95% CI 0.8–1.6). As for gender, the

Table 3
Cox regression analysis on 10 years mortality of 379 elderly persons with known baseline glucose tolerance status

	Men + women		Men		Women	
	Relative risk	95% CI	Relative risk	95% CI	Relative risk	95% CI
Age (per 5 years)	1.6	1.4–1.9	1.7	1.3–2.0	1.6	1.3–1.9
BMI (per 5 kg/m^2)	0.8	0.7–1.0	1.2	0.8–1.7	0.7	0.6–0.9
Prev. DM	1.9	1.3–2.8	1.5	0.7–3.0	2.3	1.4–3.7
Undg. DM	1.3	0.8–2.2	1.2	0.5–2.8	1.4	0.7–2.7
IGT	1.1	0.8–1.5	1.0	0.6–1.6	1.2	0.7–2.1
Physical activity (inactive vs. active)	1.5	1.1–2.0	2.0	1.3–3.3	1.2	0.8–1.7
Self-rated health (poor vs. good)	1.9	1.2–3.1	2.2	1.0–4.9	1.9	1.0–3.6
Self-rated health (average vs. good)	1.3	0.8–1.9	1.0	0.5–2.0	1.4	0.8–2.5
CVD	1.1	0.8–1.5	1.5	1.0–2.4	1.0	0.6–1.4
Hypertension	1.2	0.9–1.6	1.0	0.6–1.7	1.4	1.0–2.0
Male gender	2.0	1.5–2.7				

Estimated relative mortalities with 95% confidence intervals (95% CI). BMI: body mass index; NGT: normal glucose tolerance; Prev. DM: previously diagnosed diabetes; Undg. DM: previously undiagnosed diabetes; IGT: impaired glucose tolerance; CVD: cardiovascular disease.

corresponding figures for the men were 1.5 (0.8–2.6) and 1.0 (0.6–1.6) and for the women 2.1 (1.3–3.2) and 1.3 (0.8–2.1). Finally, when diabetes and IGT were pooled in the analysis, the odds ratio of mortality for abnormal glucose tolerance was 1.4 (1.1–1.9) among the total population: 1.1 (0.7–1.8) among men and 1.6 (1.1–2.5) among women.

4. Discussion

In the 10 years follow-up study focusing on all causes of mortality among a Finnish community population aged 70 years or over, men had higher mortality rate values than women. Previously diagnosed diabetes predicted increased mortality and the relative risk was clearly higher among women. As in some earlier studies, mainly conducted on middle-aged populations, the gender difference in mortality diminished with impairment of glucose tolerance among these elderly subjects [5]. Previously diagnosed diabetes predicted higher mortality rates than IGT and NGT among the total population and among elderly women, but not among elderly men. This is probably because of the larger proportion of female participants. All types of diabetes also predicted increased mortality in the total population. When diabetes and IGT were pooled in the analyses, the present results also suggest, as do some other earlier studies concerning middle-aged subjects, that abnormal glucose tolerance may have a relatively greater impact on mortality in elderly women than in elderly men [15,16]. This is also in accordance with results obtained in the 1980s by Pan et al. focusing on the early stages of diabetes and asymptomatic hyperglycemia. These assumptions are also in accordance with relatively recent data on newly diagnosed diabetes among middle-aged subjects in the DECODE Study [4,5]. The current results also confirm the findings of the previous, shorter follow-up study of the present population for 3.5 years [17]. In combining earlier data, derived mainly from younger populations, and the present data, it could be suggested that diabetes and IGT in elderly women increases mortality in all age groups. Even after adjustment for age, presence of cardiovascular disease and BMI, the results of the present study are not in line with those of the meta-analysis of Kanaya et al. who concluded that the gender difference found in some studies is due to a failure to adjust results for classic risk factors of coronary heart disease [11]. However, direct comparison of the present results with earlier studies is complicated because of methodological differences including variable durations of follow-up and differences in the age distributions of the study populations.

In the ‘‘Seven Countries Study’’, diabetes was associated with a 2.1-fold and IGT with a 1.17-fold mortality risk in a Finnish population aged 65–84 years. These results are very close to those of the present study when the age differences among study populations are taken into account [18]. Present results also parallel those obtained by Swerdlow and Jones considering previously diagnosed diabetes and women. The results of the study by Swerdlow and Jones found a 1.45-fold relative risk of death among previously diagnosed elderly diabetic men and a 2.15 fold risk among diabetic women aged 60–84 years in a 25-year follow-up study [19].

High BMI was inversely and independently associated with increased mortality among women (OR 0.7, 95% CI 0.6–0.9), but not among men (OR 1.2, 95% CI 0.8–1.7) in this elderly population. Because of the smaller number of male participants ($n = 141$), the OR of 0.8 for the total population was similar to that for the women ($n = 238$). The small numbers of male participants limit the interpretation of the present results. However, it seems that in women, the contribution of obesity to increased mortality is diminished with advancing age. This relationship is opposite to that seen in younger people.

It is worth noting that poor self-rated health was one of the best independent predictors of mortality in both genders in these elderly subjects even when adjustments were made for age, gender, BMI, presence of cardiovascular disease and glucose status. There are several similar earlier findings concerning this topic, including those of Pijls et al. in 1993 and Mossey and Shapiro in 1982. These studies found self-rated health to be an independent predictor of survival as well as one of the best predictors of the use of the health care services [20,21]. Based on similar findings in a large middle-aged Finnish population, Miilunpalo et al. concluded that self-rated health is a valid health status indicator and can be used in population health monitoring [7]. In elderly subjects who often have multiple diseases and symptoms, self-rated health status might offer a simple and easily administered tool for health status assessment in primary health care.

The main limitation of the findings of the present results is the relatively small size of the study population. The final classification of the diet-treated subjects was done according to the OGTT rather than reported diet-treated diabetes. Many of them, according to medical records, actually had nearnormal fasting values or IGT which were both generally labeled 'pre-diabetes' at that time. However, will successful life-style modification, a person on a diet treatment may have had normal or IGT values for the subsequent OGTT. Thus, the extent to which these factors have influenced the final results is not clear.

In conclusion, previously diagnosed diabetes increased mortality rates in these elderly persons and the impact was more significant in women. In pooled data analyses of both previous and undiagnosed diabetes, diabetes was also associated with increased mortality rates even when known risk factors for death related to cardiovascular problems were adjusted for. Self-rated health also represents one of the best predictors of mortality among elderly subjects.

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