Smoking and the Risk of Diabetes in Elderly Finnish Men

Retrospective analysis of data from a 30-year follow-up study

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OBJECTIVE — To assess the association of smoking with the risk of glucose intolerance (diabetes plus impaired glucose tolerance).

RESEARCH DESIGN AND METHODS — A cohort consisting of 1,711 Finnish men born in 1900–1919 were followed up from 1959 to 1994. Smoking status was assessed in a similar way at each of the six surveys from 1959 to 1989, and subjects were classified as never, former, or current smokers. Diagnosis of diabetes and impaired glucose tolerance was made according to the oral glucose tolerance tests made in 1984 and 1989, and the 1985 World Health Organization criteria was applied.

RESULTS — Association between smoking and glucose intolerance was estimated separately for 420 participants and 243 nonparticipants in 1989. Multiple logistic regression analyses show that odds ratios of glucose intolerance in 1984 for current smokers in 1984 were 0.36 (0.19–0.70) and 1.20 (0.52–2.78), respectively, in the participants and the nonparticipants in 1989. Among the nonparticipants in 1989, the odds ratio for current smokers in 1969 was 2.23 (1.00–4.96). A reduced risk of glucose intolerance in 1989 associated with smoking in the participants in 1989 was found to be significant from the beginning of the follow-up. The participants in 1989 were generally healthier and had a longer life expectancy than the nonparticipants in 1989.

CONCLUSIONS — In a retrospective study of men, an increased risk of diabetes and impaired glucose tolerance in smokers was found among the nonparticipants, but a reduced risk was found among the participants in 1989. The difference observed might be attributed to the fact that the participants were constitutionally different from the nonparticipants.

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Obesity is by far the strongest modifiable risk factor for type 2 diabetes (1–3). Several other environmental determinants have also been identified (4). Epidemiological data relating smoking to diabetes are inconclusive. Cigarette smoking may increase the incidence of diabetes, and can thus be an independent modifiable risk factor for type 2 diabetes in some studies (5–9), but not in other prospective studies (10–12). Experimental evidence for the effect of smoking on insulin sensitivity and glucose tolerance is also inconsistent (13–16).

We analyzed the data collected from six examinations during a 30-year follow-up of a cohort of Finnish elderly men to study the association of smoking with the risk of diabetes and impaired glucose tolerance (IGT).

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Abbreviations: IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test.

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

RESEARCH DESIGN AND METHODS

— The original cohort consisted of 1,711 men born in 1900–1919 from two geographically defined areas, one in eastern and another in western Finland. They were recruited first in 1959 in connection with the Seven Countries Study (17,18), and were followed up until 1994. During the first 30 years of the follow-up, six examinations were performed in a similar way in 1959, 1964, 1969, 1974, 1984, and 1989. Information for smoking status was collected in each survey according to the same questionnaire, and men were grouped into three categories of smoking for each survey: never smokers, ex-smokers, and current smokers of cigarettes, cigars, or a pipe. Men who had quit smoking <1 year before each examination were regarded as current smokers.

At the 25th and the 30th year of the follow-up, in 1984 and 1989, 2-h 75-g oral glucose tolerance tests (OGTTs) were performed to study the prevalence of diabetes and glucose intolerance (19,20). In 1989, fasting and 2-h postload venous blood samples were taken, after overnight fast, in the morning between 700 and 1200. Plasma glucose concentrations were measured using the glucose dehydrogenase method with glucose Analyzer II (Beckmann, Brea, CA). Whereas in 1984 (20), a capillary blood glucose sample was obtained before and 2-h after the 75-g oral glucose load and was determined by reading Dextrostix sticks in a Glucometer refractometer (Miles Laboratories, Ames Division, Elkhart, IN). All men were asked to fast for at least 4 h, and the blood samples were taken between 0800 and 1630 in the 1984 examination. The classification of diabetes and IGT was made according to the 1985 World Health Organization criteria (21). Men with 2-h postload plasma or capillary blood glucose ≥11.1 mmol/l were considered to be diabetic. IGT was defined as 2-h postload blood glucose between 7.8 and 11.0 mmol/l. Men who were diagnosed as diabetic and on drug treatment before each of the two surveys were classified as having previously known diabetes and were not given OGTTs.

Table 1—*Characteristics of participants in 1989 and nonparticipants who were alive in 1989 and those who died between 1984 and 1989 according to data collected before 1984*

Characteristics	Participants in 1989	Nonparticipants in 1989		*P* value
		Alive in 1989	Died before 1989	
n	420	102	177	—
Age at baseline (years)	46.3 ± 4.6	48.7 ± 4.7	50.2 ± 5.2	<0.001
BMI (kg/m²)	24.9 ± 3.2	24.4 ± 3.2	24.9 ± 3.3	0.39
Systolic blood pressure (mmHg)	143 ± 15.4	144 ± 15.1	145 ± 15.4	0.31
Diastolic blood pressure (mmHg)	83 ± 8.0	84 ± 7.8	84 ± 8.1	0.24
Total cholesterol (mmol/l)	6.6 ± 1.02	6.7 ± 1.00	6.7 ± 1.06	0.65
Current smokers at baseline	55.3	60.6	64.8	0.12
Current smokers in 1984	17.7	24.4	25.7	0.06
Medication of any kind, age-standardized				
At baseline	1.3	1.6	3.8	0.16
In 1964	14.7	32.3	27.9	<0.001
In 1969	26.8	34.2	45.2	<0.001
In 1974	43.0	62.3	65.3	<0.001
Age-standardized 5-year mortality	34.1	54.7	—	<0.001

Data are means ± SD or %. For BMI, blood pressure, and cholesterol data, the age-adjusted mean of the values was collected in the first five examinations from 1959 to 1984.

In 1989, 522 men were still alive and 469 (90%) attended one or more stages of the survey. Some 420 could be classified as diabetic, IGT, or normal according to the OGTTs given in 1989. Among the rest of the 102 men alive but unclassified in 1989, glucose tolerance status could be classified according to the 1984 OGTTs in 66 (65%) men. These men (n = 66) and those who participated in the OGTTs in 1984 but died before 1989 (n = 177) were similar with regard to baseline smoking status, BMI, blood pressure, and serum cholesterol levels (Table 1). They were thus pooled together and defined as nonparticipants in 1989 in the analyses to assess whether these nonparticipants were different from the participants in 1989. The effect of smoking on glucose intolerance in the nonparticipants (n = 243) was analyzed according to the glucose tolerance status in 1984 in the same way as were the participants in 1989.

Blood pressure was measured twice to the nearest 2 mmHg with a mercury sphygmomanometer in supine position. The mean of the two readings was used in the analysis. BMI was calculated by dividing the weight (kilograms) by height (meters) squared. A change in weight between two consecutive examinations was computed by subtracting the weight at previous examination from the weight at follow-up. Mean BMI was computed by taking the BMI data obtained in the five surveys from 1959 to 1984 into account. The same method has been used for calculating mean blood pressure and mean cholesterol. Age-standardized 5-year mortality from 1989 to 1994 and proportion of men taking medication of any kind during the follow-up was also calculated, separately, for men participating and not participating in 1989, to compare whether they were different constitutionally (Table 1). The procedures for measurements carried out in the surveys have been described in detail elsewhere (17,18,22,23).

Statistical analysis

The statistical analyses were performed with the SPSS for Windows program, version 8.0 (SPSS, Chicago). The χ^2 test was used to analyze differences between the groups for categorical data. The differences between the group means of continuous variables were tested for significance by one-way analysis of variance or by general factorial model when adjusted for age. Age-standardized rates were calculated by using direct standardization and a European standard population as standard (24). Multiple logistic regression analyses were performed to study the association of smoking with the risk of diabetes or IGT adjusted for factors related to diabetes. Data on smoking status collected in each of the six surveys were analyzed separately. BMI, blood pressure, and total cholesterol were available for all of the six examinations and were adjusted, therefore, for all of the occasions. Fasting blood glucose concentration was also adjusted for the 1984 and 1989 surveys in which they were determined. Because the effect of smoking on the risk of IGT was as strong as that on diabetes, men with diabetes or IGT were combined together and defined as "glucose intolerant" in the analy-

Table 2—*Characteristics of the study population in relation to glucose tolerance status in 1989*

Variable	Type 2 diabetes	IGT	Normal glucose tolerance	*P* value
n	137	83	200	
Age (years)	76.9 ± 5.0	75.7 ± 4.5	75.6 ± 4.3	0.03
BMI (kg/m²)	26.2 ± 3.7	27.1 ± 3.9	26.0 ± 3.7	0.07
Weight increase (kg)				
<0	67.4	50.6	50.8	0.03
0–2.0	12.1	23.5	19.8	—
>2.0	20.5	25.9	29.4	—
Smoking status				
Never smoker	34.1	37.3	21.5	0.02
Ex-smoker	56.3	51.8	61.5	—
Current smoker	9.6	10.8	17.0	—
Systolic blood pressure (mmHg)	158 ± 25	161 ± 24	153 ± 20	0.03
Diastolic blood pressure (mmHg)	84 ± 12	87 ± 11	84 ± 11	0.09
Fasting insulin (mU/l)	12.7 ± 2.1	11.5 ± 2.3	8.1 ± 2.1	<0.001
Fasting blood glucose (mmol/l)	7.2 ± 2.9	6.0 ± 0.7	5.5 ± 0.6	<0.001
HDL cholesterol (mmol/l)	1.1 ± 0.3	1.1 ± 0.3	1.2 ± 0.4	0.13
Total cholesterol (mmol/l)	5.5 ± 1.2	5.6 ± 1.0	5.9 ± 1.2	0.02
Antihypertensive medication	29.6	30.1	19.1	0.04

Data are means ± SD or %. Data for fasting insulin are based on geometric means. Weight increase was calculated as 1989 weight minus 1984 weight.

Table 3—*Adjusted odds ratios (95% CI) of glucose intolerance in 1989 (diabetes plus impaired glucose tolerance) in relation to smoking status from 1959 to 1989 in subjects participating in the 1989 examination*

	Nonsmoker		Ex-smoker		Current smoker	
Survey	*n*	OR (95% CI)	*n*	OR (95% CI)	*n*	OR (95% CI)
1959	101	1	83	0.62 (0.34–1.13)	228	0.57 (0.34–0.95)
1964	105	1	110	0.76 (0.43–1.34)	201	0.54 (0.33–0.90)
1969	101	1	142	0.68 (0.40–1.18)	171	0.53 (0.31–0.89)
1974	95	1	181	0.72 (0.42–1.23)	128	0.41 (0.23–0.73)
1984	112	1	227	0.55 (0.33–0.91)	73	0.33 (0.17–0.64)
1989	118	1	241	0.45 (0.27–0.75)	55	0.32 (0.15–0.68)

Data have been adjusted for age, BMI, weight change between two examinations, blood pressure, and total cholesterol on all six occasions. Fasting blood glucose was also adjusted for the 1984 and 1989 surveys.

ses. Odds ratios and their 95% CIs of smoking for glucose intolerance in 1989 and 1984 were estimated and reported separately for the participants in 1989. Odds ratio for the glucose intolerance in 1984 was also estimated and presented for the nonparticipants in 1989 to examine whether the risk of smoking was different between these two groups of the men.

RESULTS — Age-standardized prevalence of glucose intolerance (diabetes plus IGT) in 1984 was 63.8 and 67.5% (P = 0.013), respectively, for men participating and not participating in the 1989 survey' it was 53.0% in 1989 for the participants. Nonparticipants were more prone to medication of any kind during the follow-up than the participants, and the difference in taking medicine of any kind was significant after adjustment for the difference in age. Age-standardized 5-year mortality (from 1989 to 1994) was also higher in the nonparticipants who were alive in 1989 (54.7%) than in the participants in 1989 (34.1%) (Table 1). Among the nonparticipants, the men alive in 1989 did not significantly differ from the men who died before 1989 in terms of BMI, blood pressure, or serum total cholesterol levels when adjusted for age (Table 1).

The characteristics of the participants in 1989 in relation to diabetes and IGT are shown in Table 2. Men with diabetes or IGT had higher systolic blood pressure and fasting insulin and fasting glucose concentrations, and were taking more antihypertensive drugs than men with normal glucose tolerance. Subjects with normal glucose tolerance tended to have more weight gain. The proportion of current and ex-smokers was also higher in men with normal glucose tolerance than in men with diabetes or IGT.

According to the smoking status in 1984, the age-adjusted mean BMI was lowest in the current smokers (23.5 ± 3.3 kg/m^2) for all men. BMI for the former smokers (24.7 ± 3.5 kg/m^2) was in between current and nonsmokers (26.1 ± 3.5 kg/m^2). Such a relationship between smoking and BMI did not change when the analysis was further stratified by participants and nonparticipants in the 1989 survey.

In 1989, a negative association between smoking and glucose intolerance among the participants in 1989 was detectable from the very beginning of the follow-up of the cohort (Table 3). The odds ratios were lower in current smokers than in ex-smokers and lower in men who were smoking recently than in men who were smoking at the baseline. The lowest odds ratio was found in current smokers in 1989.

According to the glucose tolerance status determined in 1984, a reduced risk of glucose intolerance in current smokers was also observed in the participants in 1989 (Table 4). In the nonparticipants in 1989, however, a significantly increased risk of glucose intolerance in current smokers in 1964 and 1969 was detected (Table 4). An increased trend in the nonparticipants in 1989 was also observed in smokers, both ex- and current, in 1959, 1974, and 1984, but failed to reach statistical significance.

Association between glucose intolerance and risk factors other than smoking were also tested and reported in Table 5, separately, for men participating and not participating in the 1989 survey. Glucose intolerance defined in 1989 for the participants and in 1984 for the nonparticipants was assessed. Fasting blood glucose was associated with the deterioration to glu-

Table 4—*Adjusted odds ratios (95% CI) of glucose intolerance in 1984 (diabetes plus impaired glucose tolerance) in relation to smoking status from 1959 to 1984 for men participating and not participating in the 1989 examination*

Smoking status	*n*	Participants in 1989	*n*	Nonparticipants in 1989
1959	395		241	
Nonsmoker	96	1	48	1
Ex-smoker	79	0.66 (0.34–1.29)	38	2.48 (0.87–7.05)
Current smoker	220	0.69 (0.39–1.21)	155	1.83 (0.87–3.83)
1964	400		240	
Nonsmoker	100	1	47	1
Ex-smoker	106	0.81 (0.43–1.52)	54	1.81 (0.75–4.40)
Current smoker	194	0.55 (0.32–0.95)	139	2.44 (1.11–5.38)
1969	398		237	
Nonsmoker	96	1	42	1
Ex-smoker	138	0.71 (0.39–1.28)	62	2.26 (0.93–5.49)
Current smoker	164	0.57 (0.33–1.01)	133	2.23 (1.00–4.96)
1974	392		229	
Nonsmoker	91	1	41	1
Ex-smoker	176	0.73 (0.41–1.29)	92	2.20 (0.96–5.05)
Current smoker	125	0.54 (0.30–0.99)	96	2.06 (0.88–4.79)
1984	402		240	
Nonsmoker	109	1	52	1
Ex-smoker	221	0.71 (0.42–1.22)	126	1.82 (0.86–3.86)
Current smoker	72	0.36 (0.19–0.70)	62	1.20 (0.52–2.78)

Nonparticipants include men alive in 1989 and those who died between 1984 and 1989. Data have been adjusted for age, BMI, weight change between two examinations, blood pressure, and total cholesterol on all six occasions. Fasting blood glucose was also adjusted for the 1984 survey.

Table 5—*Adjusted odds ratios (95% CI) of glucose intolerance (diabetes plus impaired glucose tolerance) in relation to risk factors other than smoking from 1959 to 1989 in men participating and not participating in the 1989 examination*

Factors	*n*	Participants in 1989	Factors	*n*	Nonparticipants in 1989
1959	412			241	
BMI (kg/m²)		1.08 (1.00–1.16)	Age (years)		1.07 (1.01–1.13)
Systolic blood pressure (mmHg)		1.01 (1.00–1.02)	Systolic blood pressure (mmHg)		1.02 (1.00–1.04)
1964	416			240	
BMI (kg/m²)		1.06 (0.99–1.14)	Age (years)		1.07 (1.01–1.14)
Systolic blood pressure (mmHg)		1.02 (1.00–1.03)			
1969	414			237	
BMI (kg/m²)		1.10 (1.03–1.18)	Age (years)		1.07 (1.01–1.14)
Systolic blood pressure (mmHg)		1.01 (1.00–1.02)			
1974	404			229	
BMI (kg/m²)		1.10 (1.03–1.18)	Age (years)		1.07 (1.01–1.14)
Systolic blood pressure (mmHg)		1.01 (1.00–1.02)			
1984	412			240	
BMI (kg/m²)		1.10 (1.03–1.18)	Age (years)		1.06 (1.00–1.13)
Systolic blood pressure (mmHg)		1.02 (1.01–1.03)			
Fasting blood glucose (mmol/l)		1.53 (1.26–1.87)	Fasting blood glucose (mmol/l)		1.33 (1.07–1.64)
Cholesterol (mmol/l)		0.70 (0.58–0.85)			
1989	414				
BMI (kg/m²)		1.00 (0.94–1.07)			
Systolic blood pressure (mmHg)		1.01 (1.00–1.02)			
Fasting blood glucose (mmol/l)		2.92 (2.10–4.08)			
Cholesterol (mmol/l)		0.78 (0.63–0.95)			
1989 weight minus 1984 weight (kg)		0.94 (0.90–0.99)			

Glucose intolerance defined in 1989 or in 1984 was used as a dependent variable, respectively, for the participants and for the nonparticipants in 1989. The nonparticipants include the men alive in 1989 and the men who died between 1984 and 1989. In the same model are smoking status, age, BMI, weight change between two examinations, blood pressure, and total cholesterol on all six occasions. Fasting blood glucose was also adjusted for the 1984 and 1989 surveys. Only the factors with a P value <0.05 in each model were presented.

cose intolerance in both the participants and the nonparticipants. BMI and systolic blood pressure measured in all six examinations increased the risk of glucose intolerance, and serum cholesterol tested in the 1984 and the 1989 surveys decreased the risk of glucose intolerance in the participants in 1989. Age was a strong risk factor for glucose intolerance in the nonparticipants in 1989.

CONCLUSIONS — We found that the effect of smoking on the risk of diabetes and IGT was different in the different groups of men with the same ethnic origin and living in the same areas. Apparently, a decreased risk of diabetes and IGT in smokers was found in men who, on average, had a long and healthy life. On the contrary, an increased risk was found in men who died earlier. Men who participated in the OGTTs in 1989 seem to be constitutionally different from the men who did not participate. The age-adjusted prevalence of diabetes and IGT and the age-adjusted all-cause mortality were significantly lower in the participants than in the nonparticipants in 1989. When we check the history of medication of any kind, we found that the nonparticipants in 1989 had taken more medicine of any kind since the beginning of the study, when they were in the middle ages of their life, than did the participants in 1989. The difference in taking medication was significant even though the age was adjusted. All these factors indicate that the nonparticipants were weaker in various ways than were the participants in 1989. This may partly explain why smoking had affected the participants and the nonparticipants differently by 1989.

Except for the different effect of smoking, the other factors that were independently associated with the development of diabetes and IGT were also different between participants and nonparticipants in 1989. This may also be attributed to the fact that the participants were constitutionally different from the nonparticipants in 1989.

Smoking associated with a lower body weight has been previously reported (25–27) and was also observed in this study. Current smokers in this study had the lowest BMI of either participants or nonparticipants in 1989. Obesity and abdominal obesity is by far the strongest modifiable risk factor for type 2 diabetes (1–3,28,29). BMI associated with increased risk of diabetes and IGT in the participants in 1989 was also found in this study. Therefore, it would be logical to speculate that the reduced risk of smoking for diabetes and IGT in the participants in 1989 might have been attributed to the reduction of BMI related to smoking. But, the speculation does not explain the fact that smoking-related weight reduction did not protect smokers from suffering diabetes and IGT in the nonparticipants in 1989. No matter the reduction in BMI, smoking nonparticipants still had an increased risk of diabetes and IGT in 1989. BMI and weight change that was related to smoking did not differ between these two groups of men. Therefore, the different effect of smoking on glucose intolerance between the participants and the nonparticipants could not have resulted from the difference in BMI and weight change related to smoking.

In this study, ~70% of the original cohort died before the 30-year follow-up examination in 1989, when an OGTT was

performed. More than 70% of the deaths occurred among current smokers at baseline, whereas only 15% occurred among never smokers. It is clear that smoking increased the risk of premature death, and the smoking men who had survived into old age must have a special ability to struggle against the noxious effect of smoking on health. Therefore, the observation of the relationship between smoking and the risk of diabetes and IGT among the elderly survivors may be different from that among younger populations. To our knowledge, few previous studies have prospectively evaluated the effect of smoking on the risk of diabetes in an elderly population, particularly in men, who are more likely to be smokers than are women. Some prospective epidemiological studies have shown a positive relationship between smoking and incidence of type 2 diabetes in middle-aged subjects (5–9). In the Nurses' Health Study (6), a relative risk of 1.42 (1.18–1.72) for diabetes was found among women who smoked ≥25 cigarettes per day compared with nonsmokers. In the health professionals' follow-up study, the relative risk of diabetes was 1.94 (1.25–3.03) among middle-aged men who smoked ≥25 cigarettes per day compared with nonsmokers in a 6-year follow-up (5). In addition, some studies have shown that smoking may reduce insulin action in healthy subjects (13,14,30,31), and quitting smoking may increase insulin sensitivity (32). Nevertheless, there are studies that have failed to show any relationship between smoking and the risk of diabetes (10–12) or insulin resistance (15). So far, most of the evidence showing that smoking increases the risk of diabetes comes from studies among middle-aged or even younger populations (5–9). More studies among elderly populations are therefore needed to clarify the association of smoking with the risk of diabetes in the elderly.

When the first glucose tolerance test was administrated to the cohort in 1984, all men were aged >65 years, and 56% of the original cohort had died. The relationship between smoking and glucose intolerance was not known among the men who died before 1984. In the analysis in which all the men participating and not participating in 1989 were combined together, a negative association between smoking and glucose intolerance defined in 1984 was found (results are not shown). This result was expected because the participants in 1989 constituted about two-thirds of the study population. On the other hand, the results would have been obscured by including the nonparticipants in 1989 into the analysis because smoking increased the risk of glucose intolerance in the nonparticipants. Therefore, we would like to assume that if men who were similar constitutionally to the nonparticipants in 1989 constituted a major part of a study population, a positive association between smoking and glucose intolerance might have been observed.

In conclusion, smoking increased the risk of diabetes and IGT among men who were subsequently prone to premature death but was associated with a reduced risk among men who survived to a much older age. The constitutional difference between the men may explain the different observations. More studies in the very old men are therefore required to clarify the relationship between smoking and glucose intolerance.

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