Risk of developing diabetes is inversely related to lung function: a population-based cohort study.

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Risk of developing diabetes is inversely related to lung function: a population-based cohort study

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Abstract

Aim To investigate whether reduced lung function is a risk factor for developing diabetes.

Methods Non-diabetic men (n = 382) from the population-based cohort 'Men Born in 1914' were examined with spirometry at age 55 years. The cohort was re-examined at 68 years. Diabetes and fasting plasma glucose at follow-up were studied in relation to vital capacity (VC) and forced expiratory volume ($FEV_{1.0}$) at baseline.

Results Fifteen men developed diabetes during the follow-up. The percentage with diabetes in the 1st, 2nd, 3rd and top quartile of vital capacity were 7%, 5%, 2%, and 1%, respectively (P for trend = 0.01). Fasting glucose (log transformed, mmol/l) at follow-up was 1.63 ± 0.16, 1.62 ± 0.18, 1.61 ± 0.11 and 1.60 ± 0.11, respectively (P for trend = 0.11). The longitudinal associations between VC and diabetes (P = 0.001) and log glucose (P = 0.036) were significant after adjustments for several potential confounders. $FEV_{1.0}$ at baseline showed similar associations with diabetes at follow-up.

Conclusions The risk of developing diabetes is inversely associated with pulmonary function among middle-aged men.

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Keywords diabetes mellitus, epidemiology, forced expiratory volume, vital capacity

Abbreviations $FEV_{1.0}$, forced expiratory volume in 1 s; VC, vital capacity; BMI, body mass index

Introduction

Clinical and population-based studies have shown that reduced lung function is common among diabetes patients [1–4]. The temporal relationship of this association is not fully understood. Reduced pulmonary function is often considered a complication following diabetes [1–3]. Others have suggested that pulmonary function could be a risk factor for insulin resistance [5] or non-insulin-dependent diabetes mellitus (NIDDM) [6].

'Men born in 1914' is a population-based study on the epidemiology of cardiovascular and pulmonary diseases. The cohort was established in 1969–70, and was invited to a follow-up examination 13 years later. This study reports on the relationships between lung function at 55 years of age and incidence of diabetes during 13 years.

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Subjects and methods

A random 50% of all men born in 1914, who in 1968 lived in Malmö, Sweden, were invited to participate in the study [7]. Seven hundred and three men (87%) participated, 679 of whom were free of diabetes. The cohort was invited to a re-examination at 68 years of age. During the follow-up, 146 men died and 75 moved out from the city. Of the remaining 458 men who initially were non-diabetic, 382 (83.4%) came to the follow-up. The Lund University Ethics Committee approved the study. The non-participants have been described elsewhere [8].

Table 1 Cardiovascular risk factors at 55 years and diabetes at 68 years in relation to vital capacity at 55 years

	Quartiles of vital capacity				
	Q1 *n* = 95	Q2 *n* = 95	Q3 *n* = 96	Q4 *n* = 96	*P* for trend
Vital capacity (l)	< 4.06	4.07–4.39	4.40–4.73	> 4.75	
Baseline characteristics (55 years)					
Smokers, *n* (%)	62 (65)	59 (62)	58 (60)	47 (49)	0.02
Systolic blood pressure (mmHg)	136 ± 21	137 ± 22	140 ± 21	138 ± 22	0.37
Vigorous physical activity, *n* (%)	9 (10)	14 (15)	16 (17)	18 (19)	0.07
Body mass index (kg/m^2)	24.4 ± 3.1	24.6 ± 3.0	24.4 ± 2.9	24.7 ± 2.4	0.64
Cholesterol (mmol/l)	6.4 ± 1.2	6.3 ± 1.1	6.5 ± 1.1	6.5 ± 1.2	0.28
History of CVD, *n* (%)	10 (11)	3 (3)	6 (6)	9 (9)	0.98
Family history of diabetes, *n* (%)	10 (11)	7 (7)	4 (4)	13 (14)	0.66
Weight increase between 55 and 68 years (kg)	0.8 ± 5.3	−0.1 ± 7.6	1.2 ± 6.1	0.8 ± 6.3	0.61
Diabetes and glucose at follow-up (at 68 years)					
Diabetes, *n* (%)	7 (7)	5 (5)	2 (2)	1 (1)	0.01
Mean glucose (mmol/l)	5.19 ± 0.99	5.15 ± 1.37	5.06 ± 0.60	4.98 ± 0.58	
Log transformed glucose	1.63 ± 0.16	1.62 ± 0.18	1.61 ± 0.11	1.60 ± 0.11	0.11
Follow-up (person-years)	1293	1299	1308	1307	

Examinations

The examinations have been described previously [7–11]. A structured interview and urine testing with enzyme strips (Clinistix; Miles Labs, Elkhart, IN, USA) were used to assess diabetes mellitus at 55 years. Oral glucose tolerance tests were performed in men with positive urine tests [7]. At 68 years of age diabetes was defined as fasting plasma glucose levels ≥ 6.7 mmol/l or history of diabetes. Cases with self-reported diabetes were validated by review of hospital records. Plasma glucose was determined with a colorimetric method at the laboratory of the University Hospital. Family history of diabetes was assessed in a questionnaire.

Leisure time physical activity was assessed in a questionnaire and dichotomized into non-vigorous and vigorous activity (heavy gardening, running, swimming, etc., at least 2–3 h per week) [9]. History of cardiovascular disease was defined history of angina pectoris, stroke or myocardial infarction (according to self-report, hospital records or ECG findings) [7–9].

Forced expiratory volume during 1 s ($FEV_{1.0}$) and vital capacity (VC) were determined with a Bernstein type of spirometer [10–12] and corrected to body temperature, atmospheric pressure and water saturation. The best of two, or more if not congruent, measurements was used. $FEV_{1.0}$ was height-adjusted using 0.039 l/cm and VC was adjusted using 0.057 l/cm [10,11]. The presented volumes are adjusted to the mean height in the present study (175.0 cm).

Statistical analysis

One-way ANOVA and the Mantel–Haenszel test were used to test the linear trends of diabetes, glucose (log transformed) and cardiovascular risk factors over the quartiles of VC. The association between baseline VC (in litres) and log glucose was adjusted for potential confounders in a multiple linear regression. Due to the limited number of cases, a backward stepwise logistic regression was used to assess the association between VC (in litres) and diabetes at follow-up (*P* for removal: 0.20).

Results

Fifteen men (3.9%) developed diabetes mellitus between 55 and 68 years. Nine of them had known diabetes and six had glucose levels > 6.7 mmol/l (range 7.2–13.5 mmol/l). VC at baseline showed inverse associations with diabetes ($P = 0.01$) and log glucose at follow-up ($P = 0.11$) (Table 1). Decline in VC or $FEV_{1.0}$ between 55 and 68 years showed no significant difference between men with and without diabetes at 68 (VC decline: 0.23 ± 0.37 vs. 0.30 ± 0.40 l, respectively; $P = 0.50$).

Low VC was associated with a higher prevalence of smoking and a smaller proportion performing vigorous physical activity (Table 1). There was no association between smoking at baseline and future diabetes (non-smokers vs. smokers 3.2% vs. 4.4%, $\chi^2 = 0.36$, $P = 0.55$) or log glucose at follow-up (mean log glucose 1.62 ± 0.14 vs. 1.62 ± 0.15, $P = 0.85$; mean glucose was 5.1 mmol/l in both groups).

After adjustments for smoking (at 55 years), physical activity (at 55 and 68 years), body mass index (BMI) (at 55 years) and weight increase, VC was significantly associated with log glucose at follow-up (b = −0.028, SE = 0.013, $P = 0.036$). BMI (b = 0.013, SE = 0.003, $P < 0.001$), weight increase (b = 0.003, SE = 0.001, $P = 0.007$) and physical activity at 68 years (b = −0.056, SE = 0.019, $P = 0.003$) were also significantly associated with log glucose in this model.

In a backward stepwise logistic regression model, diabetes at follow-up was significantly associated with VC at baseline (b = −1.7, SE = 0.54, $P = 0.0014$) and BMI (b = 0.27, SE = 0.10, $P = 0.008$). Weight increase was also in the equation (b = −0.06, SE = 0.04, $P = 0.12$), while smoking and physical activity (at 55 and 68 years) were removed from the model. After

adjustments in the same models, baseline $FEV_{1.0}$ showed similar association with diabetes (b = –0.89, SE = 0.45, $P < 0.05$) at 68 years. The association between $FEV_{1.0}$ and log glucose was not significant (b = –0.023, SE = 0.013, $P = 0.075$).

Discussion

Several cross-sectional studies have shown that diabetes is associated with impaired lung function [1–3]. Whether lung function could be a risk factor for future diabetes has, however, not been studied extensively. This population-based study shows that lung function is inversely related to the risk of developing diabetes. The results are in accordance with two previous studies in which low lung function was associated with future insulin resistance [5] or incidence of NIDDM [6].

The study has some important limitations. Diabetes at baseline was assessed in a semistructured interview by urine testing with enzyme strips. Oral glucose tolerance tests were performed for men with positive urine tests. Although the specificity of this method is high in an unselected population, the sensitivity of urine tests is lower than that of blood glucose [13]. Whether misclassification of diabetes was related to lung function is not known. However, the previously reported associations between lung function and insulin resistance [5] or NIDDM [6] were unaffected by adjustments for oral glucose tolerance or fasting glucose levels at baseline.

A second limitation is the small number that developed diabetes. Nevertheless, baseline lung function was also associated with follow-up glucose levels, and this association was based on 382 individuals.

Adiposity and physical inactivity are both associated with reduced lung function and risk of diabetes. BMI, weight increase during follow-up and physical activity were, however, taken into account in the analysis. The assessment of physical activity has shown high validity in several previous studies from the cohort [9], and it seems unlikely that physical activity confounded the results.

Non-participation and mortality during follow-up are other potential causes of bias. The participation rate was high in this study. A study of the non-participants showed that the cohort was fairly representative with respect to, for example, smoking habits [8]. The mortality rates during follow-up were increased among men with low lung function [11] and may also have been increased among men who developed diabetes. Mortality during follow-up would therefore, if anything, bias the results towards negative findings.

The causal associations between lung function and future diabetes remain to be evaluated. Inflammatory processes often play key roles in the development of reduced lung function [14,15]. There is also a growing recognition of associations between the immune system and metabolism of glucose and insulin [16,17]. It is possible that susceptible individuals have a greater tendency to react with inflammation, which could cause reduced lung function, insulin resistance and Type 2 diabetes. Another possibility is that reduced lung function and risk of diabetes are both partially determined by early growth. Low birth weight has been associated both with Type 2 diabetes [18] and reduced adult lung function [19].

The conclusion of this population-based study of middle-aged men is that lung function is inversely associated with risk of future diabetes.

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