NIDDM, Impaired Glucose Tolerance, and Pulmonary Function in Older Adults

The Rancho Bernardo Study

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OBJECTIVE — To determine whether NIDDM or plasma glucose level in subjects without diabetes is associated with reduced pulmonary function in 525 men and 714 women, 51–95 years of age.

RESEARCH DESIGN AND METHODS — The analysis was based on data from a community-based study, the Rancho Bernardo Study. Between 1984 and 1987, 82% of community-dwelling residents had an oral glucose tolerance test. Between 1988 and 1991, 80% had lung function assessed by spirometry (forced expiratory volume in 1 s [FEV1] and forced vital capacity [FVC]).

RESULTS — In analyses adjusted for age, height, and cigarette smoking, pulmonary function was not associated with known or newly diagnosed NIDDM in men or women. However, FEV1 and FVC were each independently reduced in men with diabetes of 10 or more years' duration. Fasting plasma glucose (FPG) levels were correlated with FEV1 and FVC in men without diabetes. No associations were found in women.

CONCLUSIONS — The overall absence of an association of NIDDM with pulmonary function in these older adults may reflect survival bias and the small number of subjects with severe diabetes or diabetes of prolonged duration. The apparent relation of FPG levels to FEV1 and FVC suggests that any effect of glycemia precedes diabetes and contradicts any putative causal role for duration and severity of glycemia, however. More epidemiological studies are needed to provide further information about the relationship between NIDDM and lung function.

Diabetes is a multisystem disease with many complications suggestive of premature aging. The possibility that the lung is a target organ for diabetic complications was suggested by a 1976 study of 11 nonsmoking young men with IDDM who were found to have reduced elastic recoil and reduced total lung capacity compared with nonsmoking men without diabetes (1). Since that time, there have been many studies of pulmonary disease in diabetic patients; these have been well reviewed by Sandler (2). Most reports were based on small groups of highly selected young patients with IDDM: many used poorly characterized comparison groups and failed to control for cigarette smoking, which may explain the contradictory results. Nevertheless, the overall evidence points to reduced lung function in patients with IDDM (2,3).

Only one study has described pulmonary function in a large number of adults with NIDDM (4). That study reported impaired forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV1) in individuals who had diabetes identified by self-report or by raised plasma glucose; there were too few subjects in each age group to permit analysis of the impact of diabetes on pulmonary function in old age.

The present study was designed to determine whether NIDDM or plasma glucose levels in nondiabetic subjects are associated with reduced pulmonary function in older men and women in the community.

RESEARCH DESIGN AND METHODS

Population

From 1972 to 1974, 82% of the adult residents of Rancho Bernardo, a geographically defined Southern California community, participated in the Rancho Bernardo Heart and Chronic Disease Study. Between 1984 and 1987, 82% of surviving residents had a standard oral glucose tolerance test performed between 7:00 and 11:00 A.M. after a 12-h fast.

Between 1988 and 1991, 80% of the local surviving residents had pulmonary function assessed using a water-sealed spirometer (Warren E. Collins, Eagle models, Braintree, MA). FEV1 and FVC were measured by a specially trained technician, with quality control before and during the study in accordance with 1987 American Thoracic Society guidelines (ATS). Subjects were encouraged to perform from three to six tests until they satisfied the ATS standard for acceptability and reproducibility. Measured values were corrected for body temperature, air pressure, and water saturation.

NIDDM was defined by World Health Organization criteria (as a fasting plasma glucose [FPG] level of ≥140 mg/dl, a 2-h postchallenge glucose [2HPG] level of ≥200 mg/dl, or a history of physician-diagnosed diabetes not treated with insulin). Impaired glucose tolerance (IGT) was defined as an FPG level <140 mg/dl and a 2HPG level between 140 and 199 mg/dl and no history of diabetes. Severely limited joint mobility based on physical examination was defined as the inability to approximate the palmar surfaces because of Dupuytren's contractures or arthritis.

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ATS, American Thoracic Society; FEV1, forced expiratory volume in 1 second; FPG, fasting plasma glucose; FVC, forced vital capacity; 2HPG, 2-h postchallenge glucose; IGT, impaired glucose tolerance.

Table 1—*Descriptive characteristics of subjects according to NIDDM, Rancho Bernardo, California*

	Men			Women		
	NIDDM	Others	*P* value	NIDDM	Others	*P* value
n	71	454		68	646	
Age (years)	76.1 ± 8.5	72.2 ± 9.3	0.0009	75.7 ± 8.4	72.3 ± 9.0	0.003
Height (m)	1.73 ± 0.05	1.74 ± 0.06	0.57	1.58 ± 0.05	1.60 ± 0.06	0.03
Smoking habits						
Never	38.0	29.3		45.6	51.7	
Past	57.7	61.2	0.17	47.0	38.4	0.36
Current	4.3	9.5		7.4	9.9	
FEV1 (liters)	2.90 ± 0.60	2.89 ± 0.70	0.89	1.98 ± 0.52	2.01 ± 0.53	0.63
FVC (liters)	3.84 ± 0.77	3.95 ± 0.83	0.32	2.56 ± 0.61	2.64 ± 0.61	0.29
BMI (kg/m^2)	26.3 ± 3.1	26.1 ± 3.5	0.57	26.4 ± 4.9	24.4 ± 3.7	0.002
CHD	26.8	17.8	0.07	25.0	16.1	0.06
Limited joint mobility	5.6	4.2	0.53	7.4	2.0	0.05
FPG (mg/dl)	130.3 ± 42.9	99.4 ± 11.3	0.0001	120.6 ± 51.5	95.3 ± 10.4	0.0001
2HPG (mg/dl)	242.6 ± 76.5	117.2 ± 33.6	0.0001	232.7 ± 81.6	123.6 ± 31.9	0.0001

Data are means ± SD or % except where indicated. Data for FEV1 and FVC are adjusted for age and height.

Smoking history was collected using standard questionnaires. Subjects were considered never to have smoked if they had smoked <100 cigarettes in their lifetime. Cigarette consumption was expressed in cigarettes smoked per day. Other questions asked were: Has a doctor ever told you that you had asthma? Do you get short of breath walking with other people at an ordinary pace on level ground? Does your chest ever sound wheezy or whistling? Do you usually bring up any phlegm from your chest? Subjects were also asked about physician-diagnosed emphysema, bronchitis, and heart disease.

There were 525 men and 714 women who had both known diabetes status and complete spirometric data meeting ATS criteria. (ATS criteria were met by 86% of men and 84% of women; the proportion was similar in subjects with and without diabetes.) The association of categorical variables was evaluated using χ^2 tests. For continuous variables, analysis of variance, multiple linear regression, and correlation were used. Spearman correlation coefficients were used to study the association of pulmonary function with the duration of diabetes. The skewed FPG and 2HPG values were transformed to logarithms (log 10) of measured values for statistical comparisons.

RESULTS — The 68 men and 71 women with diabetes determined by history or glucose tolerance test criteria were significantly older than those without diabetes (76 vs. 72 years, $P < 0.001$). As shown in Table 1, both men and women with diabetes had smoking habits similar to those without diabetes (<10% were current smokers), but had more chronic heart disease. Women with diabetes had limited joint mobility more often than did women without diabetes, and diabetic men tended to have higher FPG and 2HPG levels than did diabetic women. NIDDM was not associated with asthma, wheezing, phlegm, emphysema, or chronic bronchitis in men or women. Twice as many women with diabetes as those without reported shortness of breath, $P = 0.008$; no such association was seen in men, $P = 0.67$.

Age- and height-adjusted FEV1s and FVCs in men and women are presented in Fig. 1 (FEV1) and Fig. 2 (FVC) according to five categories of glucose tolerance: normal, high normal, impaired (IGT), newly diagnosed NIDDM, and known NIDDM. Lung function assessed by FEV1 or FVC was not associated with any category of glucose tolerance in men or women.

Table 2 shows that age, height, cigarette smoking, and heart disease were each independently associated with FEV1 and FVC in both sexes. Diabetes was not associated with FEV1 or FVC in men or women.

We considered the possibility that the absence of an association reflected the short duration of diabetes; only 26 of the 71 men (38%) and 15 of the 68 women (22%) with NIDDM had known diabetes diagnosed before the 1984–1987 oral glucose tolerance tests. Among these subjects, the duration of diabetes was 14.1 ± 13.7 years in men and 9.7 ± 7.4 years in women. In an analysis restricted to those with known diabetes, there was no overall association between the duration of NIDDM and FEV1 or FVC (not shown). However, when analyses were restricted to the 15 men and 7 women with NIDDM of 10 or more years' duration, pulmonary function tests were significantly associated with duration of diabetes in men ($r = 0.73$; $P = 0.002$) but not in women ($P = 0.60$).

The sex-specific correlation coefficients of glucose levels to age- and height-adjusted FEV1 and FVC levels in individuals without diabetes are presented in Table 3. There was an inverse relation of FPG to FVC ($P = 0.01$) and FEV1 ($P = 0.04$) only in men, which remained significant after adjusting for BMI and smoking habit. The 347 men with IGT had significantly worse age- and height-adjusted FEV1s (2.77 ± 0.60 liters) than men with normal glucose tolerance (2.93 ± 0.71 l, $P = 0.04$) and FVC (3.77 ± 0.77 vs. 4.00 ± 0.84 l, $P = 0.01$); no difference by IGT status was observed in women.

Limited joint mobility was not associated with FEV1 or FVC in men or women without diabetes or in men with diabetes. The five diabetic women with limited joint mobility showed a lower FEV1 (but not FVC) than did the 63 diabetic women with normal mobility (adjusted FEV1, 1.52 ± 0.60 vs. 2.01 ± 0.50 liters, $P = 0.04$).

CONCLUSIONS — In the only previous study of pulmonary function in older

adults who were not taking insulin (4), diabetes was associated with reduced pulmonary function independent of age and cigarette smoking. In contrast, in the Rancho Bernardo cohort, pulmonary function decreased with age (5), but was not associated with known or newly diagnosed NIDDM in men or women.

There are several possible reasons for the overall absence of an association between pulmonary function and diabetes in this cohort. First, the population was elderly, and men and women who had both pulmonary disease and diabetes may have been selectively lost because of illness or death. This possibility is compatible with results from the Copenhagen Heart Study (6), in which those who developed diabetes during a 5-year follow-up had the steepest declines in ventilatory function, while the decline in lung function in those who had diabetes at the baseline evaluation was similar to that observed in subjects without diabetes.

It is also possible that only severe hyperglycemia alters pulmonary function and that only those with less severe diabetes survive to old age. Thus the absence of an association in this relatively healthy community-dwelling cohort could reflect the fact that only 30% of men and 15% of women with new and known diabetes had fasting hyperglycemia (FPG ≥140 mg/dl). The high frequency of disease unrecognized before the glucose tolerance test in this cohort is compatible with U.S. national data showing that about half of older adults with NIDDM have clinically unrecognized disease (7), but in this relatively affluent population with good access to medical care, it may suggest diabetes of relatively recent onset. Only in men with diabetes of at least 10 years' duration was there an inverse correlation between age- and height-adjusted FEV1. It is important not to overinterpret this diabetes–pulmonary function association in men, which was found in a post hoc analysis; but, men with categorically defined IGT also had significantly poorer pulmonary function than those with normal glucose tolerance. There was no association in women. This unexpected sex difference could be due to chance, but the results are also compatible with a Japanese study of middle-aged subjects, in which diabetes was associated with reduced pulmonary function in men but not women. In both studies, differences persisted after adjusting for sex differences in cigarette smoking (8).

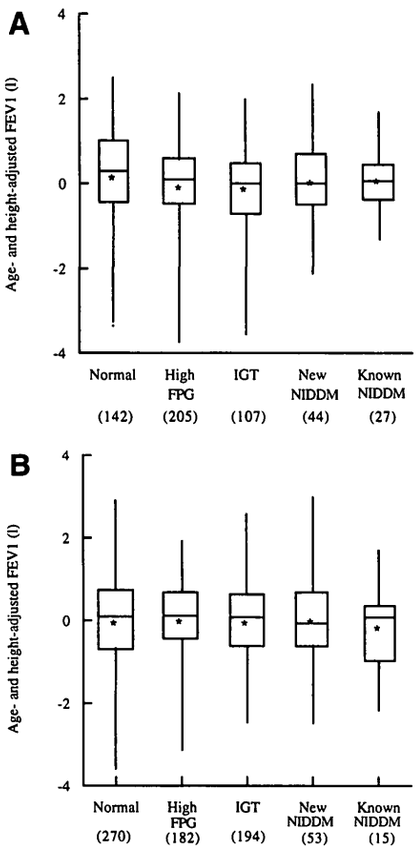

Figure 1—*Box plots of age- and height-adjusted FEV1 for five categories of glucose tolerance in men (A) and women (B). Box: top, 3rd quartile (Q3); bottom, 1st quartile (Q1); *, mean; horizontal line within box, median. Vertical axis: top, maximum; bottom, minimum.*

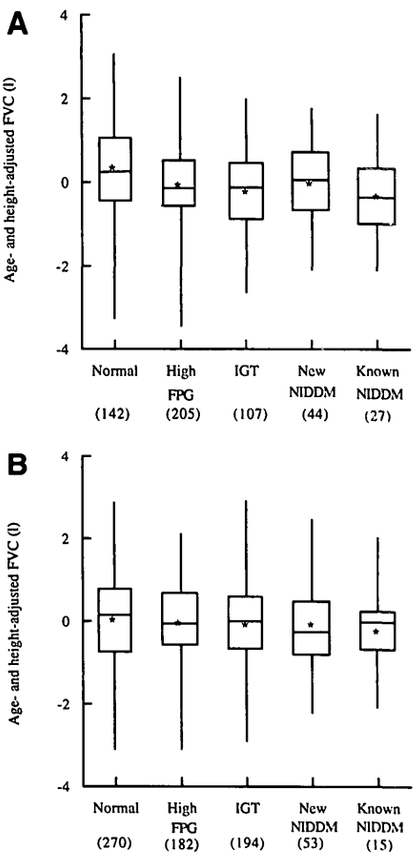

Figure 2—*Box plots of age- and height-adjusted FVC for five categories of glucose tolerance in men (A) and women (B). Box: top, 3rd quartile (Q3); bottom, 1st quartile (Q1); *, mean; horizontal line within box, median. Vertical axis: top, maximum; bottom, minimum.*

Table 2—*Regression of FEV1 and FVC on age, height, BMI, smoking, and diabetes in elderly men and women, Rancho Bernardo, California, 1988-1991*

	Men (n = 525)			Women (n = 714)		
	β	SE	*P* value	β	SE	*P* value
Independent variable: FEV1 (liters)						
Age (years)	−0.042	0.003	0.0001	−0.031	0.002	0.0001
Height (m)	2.208	0.382	0.0001	2.821	0.257	0.0001
BMI (kg/m²)	−0.011	0.007	0.09	0.001	0.004	0.89
Smoking (cigarettes/day)	−0.007	0.002	0.0001	−0.011	0.001	0.0001
CHD	−0.070	0.058	0.23	−0.086	0.038	0.02
Diabetic subjects vs.others	0.019	0.067	0.78	−0.004	0.050	0.93
Dependent variable: FVC (liters)						
Age (years)	−0.043	0.003	0.0001	−0.033	0.002	0.0001
Height (m)	4.337	0.447	0.0001	3.927	0.285	0.0001
BMI (kg/m²)	−0.040	0.008	0.0001	−0.010	0.004	0.01
Smoking (cigarettes/day)	−0.002	0.002	0.35	−0.007	0.002	0.0001
CHD	−0.043	0.068	0.53	−0.090	0.042	0.03
Diabetic subjects vs. others	−0.054	0.078	0.49	−0.021	0.055	0.70

Table 3—*Correlation coefficients (r) between FPG and 2HPG and lung function, assessed by FEV1 and FVC, in elderly nondiabetic men and women*

			Men (n = 454)		Women (n = 646)	
			r	P value	r	P value
log	FPG	FEV1	−0.095	0.04	−0.009	0.82
log	2HPG	FEV1	−0.017	0.72	0.015	0.70
log	FPG	FVC	−0.117	0.01	−0.062	0.11
log	2HPG	FVC	−0.080	0.09	−0.021	0.60

FEV1 and FVC were adjusted for age and height.

One mechanism whereby diabetes might be expected to worsen pulmonary function is atherosclerosis (9). Although coronary heart disease was more common in Rancho Bernardo men and women with diabetes than in those without, heart disease did not affect pulmonary function in adjusted models.

Glycosylation of collagen (10) could reduce chest-wall mobility (11,12), which could co-vary with limited joint mobility (13). Although reduced joint mobility was observed in only five women with diabetes in this cohort, they showed a significantly reduced FEV1. Pulmonary function was not associated with joint mobility in nondiabetic subjects, suggesting that any association with diabetes reflects a noxious effect of glycemia or its covariate, rather than a musculoskeletal etiology.

In summary, the overall absence of an association of NIDDM with pulmonary function may reflect the relatively small number of surviving older diabetic subjects who had had severe diabetes for at least 10 years. The finding that a diabetes–pulmonary function association was limited to men who had had diabetes for more than 10 years parallels the observation that the diabetic men in this cohort had higher glycemia levels than the diabetic women. This explanation for the sex-specific association is compatible with observations in other complications of diabetes, which appear to reflect both degree and duration of hyperglycemia. On the other hand, the pulmonary-glycemia association in nondiabetic subjects, again only in men, suggests that any effect of glycemia precedes diabetes and contradicts the putative causal role for duration and severity of glycemia. More studies are needed to elucidate the frequency and etiology of pulmonary dysfunction in older adults with NIDDM.

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