Cross-Sectional and Prospective Study of Lung Function in Adults With Type 2 Diabetes

The Atherosclerosis Risk in Communities (ARIC) Study

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OBJECTIVE — The aim of this study was to test the hypothesis that diabetes is independently associated with reduced lung function, both cross-sectionally and longitudinally.

RESEARCH DESIGN AND METHODS — We conducted cross-sectional and prospective analyses of diabetes status and lung function decline using baseline and 3-year follow-up data on 1,100 diabetic and 10,162 nondiabetic middle-aged adults from the Atherosclerosis Risk in Communities (ARIC) Study. Forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV_1) were measured at baseline and at the 3-year follow-up using standard spirometry.

RESULTS — At baseline, adults with diabetes had significantly lower predicted FVC (96 vs. 103%, $P < 0.001$) and predicted FEV_1 (92 vs. 96%, $P < 0.001$) than those without diabetes. These differences remained significant after adjustment for demographic characteristics, adiposity, smoking, physical activity index, education, and ARIC field center. Graded, inverse associations were observed between hyperglycemia, diabetes severity (i.e., duration of diabetes and types of antidiabetes medications), and FVC and FEV_1 (all $P_{trend} < 0.001$). In prospective analyses, FVC declined faster in diabetic adults than in their nondiabetic counterparts (64 vs. 58 ml/year, $P = 0.01$). Diabetes severity as indicated by intensity of antidiabetic treatment also showed graded relationships with the rate of FVC decline ($P < 0.01$).

CONCLUSIONS — These data support the notion that the lung is a target organ for diabetic injury. Additional research is required to identify pathophysiologic mechanisms and to determine clinical significance.

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Impaired lung function has attracted growing interest as a potential complication of diabetes (1–10). Cross-sectional studies have consistently shown that adults with diabetes have lower vital capacity than their nondiabetic counterparts (1–5,7), but such studies cannot establish the temporal sequence of events. We therefore analyzed longitudinal data from the Atherosclerosis Risk in Communities (ARIC) Study, a biracial, community-based cohort of adults aged 45–64, to test the hypothesis that diabetes is associated with reduced lung function independently of known risk factors.

RESEARCH DESIGN AND METHODS

— The ARIC Study is a prospective cohort study of 15,792 adults from the following four U.S. communities: Forsyth County, North Carolina; Jackson, Mississippi; the northwest suburbs of Minneapolis, Minnesota; and Washington County, Maryland. The design and conduct of the ARIC Study have been described previously (11). The present analysis was based on ~3 years of follow-up, which included the baseline examination (1987 through 1989), and a follow-up clinic visit at year 3 (1990–1992). The rate of follow-up for individuals still alive at the time of the second visit was 93%.

For the current analysis, the following criteria were used for excluding individuals: ethnicity other than black or white American ($n = 48$), missing data on spirometry or diabetes status at baseline ($n = 2,014$), self-reported asthma or chronic lung disease or use of medications for the conditions at baseline ($n = 1,233$), use of heart failure medications ($n = 101$), and missing data on relevant covariates ($n = 250$). We also excluded individuals in the upper or lower 1% of forced vital capacity (FVC), forced expiratory volume in 1 s (FEV_1), or FEV_1-to-FVC ratio at baseline or 3-year follow-up visit, as they were presumed to represent outliers ($n = 884$). The final study sample consisted of 11,262 individuals including 1,100 adults with diabetes at baseline and 10,162 adults who were free of diabetes at baseline.

Spirometry

At the baseline and 3-year follow-up visits, measurement of FEV_1 and FVC were performed on the basis of recommendations from the Epidemiology Standardization Project (12) and the American Thoracic Society (13). The methodology was standardized across the four field centers. Quality control and reproducibil-

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Abbreviations: ARIC, Atherosclerosis Risk in Communities; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity.

See accompanying editorial, p. 828.

Table 1—*Baseline characteristics of 11,262 middle-aged adults according to diabetes status*

	Diabetes	No diabetes	*P* value
n	1,100	10,162	
Male sex (%)	48	44	0.01
African American (%)	37	21	<0.001
Age (years)	55 ± 5.6	54 ± 5.6	<0.001
Education <12 years (%)	32	19	<0.001
Smoking status (%)			0.03
Current	19	23	
Former	33	33	
Never	48	44	
Pack-years in ever smokers	28 ± 21	25 ± 20	0.0004
Sport index	2.3 ± 0.74	2.5 ± 0.80	<0.001
BMI (kg/m^2)	30.9 ± 5.7	27.2 ± 4.8	<0.001
Waist circumference (cm)	105.7 ± 13.6	95.4 ± 12.9	<0.001
White blood count ($\times 10^9$/l)	6.5 ± 1.0	6.0 ± 1.9	<0.001
Fibrinogen(g/l)	3.2 ± 0.7	3.0 ± 0.6	<0.001
Hypertension (%)	65	37	<0.001
FVC (l)			
Men	4.2 ± 0.8	4.6 ± 0.7	<0.001
Women	3.0 ± 0.5	3.3 ± 0.6	<0.001
FEV_1 (l)			
Men	3.2 ± 0.6	3.4 ± 0.7	<0.001
Women	2.3 ± 0.5	2.5 ± 0.5	<0.001
FEV_1-to-FVC ratio (%)	76.7 ± 6.3	75.1 ± 6.6	<0.001
FVC % predicted	96.5 ± 13.2	103.1 ± 13.6	<0.001
FEV_1 % predicted	92.5 ± 14.1	96.4 ± 14.6	<0.001

Data are means ± SD unless indicated otherwise.

ity were coordinated by a centralized pulmonary function reading center (The Johns Hopkins School of Public Health, Baltimore, MD).

Type 2 diabetes

Individuals were classified as having diabetes if any of the following criteria, adapted from 1997 American Diabetes Association criteria, were met: fasting glucose level of at least 7.0 mmol/l (126 mg/dl); nonfasting glucose level of at least 11.1 mmol/l (200 mg/dl); current use of antidiabetes medication; or a positive response to the question "Has a doctor ever told you that you had diabetes (sugar in the blood)?"

Other variables

The definitions and methods used for other baseline measurements (age, race, education level, cigarette smoking status and pack-years, height, BMI, waist and hip circumferences, sport activity index, glucose, hypertension, white blood cell count, and fibrinogen) have been reported previously (14). A1C was measured as part of a previous study (15) and was only available for all 1,637 participants with prevalent cases of type 2 diabetes at the second ARIC visit and a subgroup of 598 randomly selected (stratified by age, sex, and ethnic origin) nondiabetic individuals from the ARIC visit 2 cohort (excluding those with prevalent and incident cases of coronary heart disease, diabetes, and transient ischemic attack/stroke), which was used as a comparison group in our analysis of the A1C data.

Data analysis

Predicted FVC and FEV_1 were calculated by the ARIC Data Coordinating Center using the equations developed by Crapo et al. (16) for nonsmokers that included age, sex, height, and race. Baseline differences between characteristics of diabetic and nondiabetic individuals were compared using *t* tests for continuous variables and χ^2 tests for categorical variables.

Multiple linear regression models were fitted to describe the cross-sectional association between lung function and fasting glucose levels, duration of diabetes, and type of antidiabetes medications at baseline (1987–1989) after adjustment for potential confounding variables. Additional multivariable analyses were performed to investigate the roles of the inflammatory markers as potential confounders.

Weighted univariate and multivariable analyses were used to assess the cross-sectional relationship between A1C and lung function in the diabetic patients and the subgroup of individuals without diabetes for whom A1C measurements were available at ARIC visit 2 (1990–1992), accounting for the stratified random sampling design.

In the prospective analyses, multiple linear regressions were used to model the changes of FVC, FEV_1, FVC % predicted, FEV_1 % predicted, and the FEV_1-to-FVC ratio per year from baseline to ARIC visit 2 (3-year follow-up) in relation to baseline diabetes status, fasting glucose level, diabetes duration, and use of antidiabetes medications after adjustment for covariates.

In all multivariable models, tests for interactions with diabetes status were performed with sex, race, waist circumference, and smoking status. No interactions were detected (all $P > 0.05$), and therefore only pooled results were presented. Diabetes status–specific categories were included as an ordinal variable in the linear model to test for linear trend. All tests of significance were two-tailed, with an α level of 0.05. All analyses were performed using SAS statistical software (version 9.1; SAS Institute, Cary, NC).

RESULTS

Baseline characteristics

Table 1 presents baseline characteristics of the sample by diabetes status. Compared with their nondiabetic counterparts, adults with diabetic were significantly more likely to be male, African American, older, and less educated; furthermore, among ever smokers, diabetic subjects smoked more cigarettes, were less physically active, had higher BMI and a higher waist-to-hip ratio, and were noted to have a higher prevalence of hypertension and higher white blood cell counts and fibrinogen levels. Adults with diabetes also had significantly lower FVC, FEV_1, FVC % predicted, and FEV_1 % predicted at baseline compared with adults without diabetes. In contrast, the ratio of FEV_1 to FVC was significantly higher in adults with diabetes than in those without diabetes.

Table 2—*Baseline spirometry by diabetes status and adjusted differences in adults with diabetes versus without diabetes at baseline*

	FVC (ml)	FEV_1 (ml)	FVC % predicted	FEV_1 % predicted	FEV_1-to-FVC ratio (%)
No diabetes	3,873 (3,863 to 3,882)	2,911 (2,904 to 2,919)	102.8 (102.6 to 103.1)	96.5 (96.3 to 96.8)	75.4 (75.3 to 75.5)
Diabetes	3,740 (3,711 to 3,769)	2,839 (2,856 to 2,863)	98.3 (98.5 to 100.1)	94.1 (93.3 to 94.9)	76.2 (75.8 to 76.5)
Diabetes vs. no diabetes	−133 (−163 to −103)	−72 (−97 to −47)	−3.6 (−4.4 to −2.7)	−2.4 (−3.2 to −1.6)	0.8 (0.4 to 1.1)
P value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Diabetes, by fasting glucose					
<140 mg/dl vs. no diabetes	−109 (−155 to −63)	−66 (−105 to −29)	−2.9 (−4.1 to −1.7)	−2.3 (−3.5 to −1.0)	0.4 (−0.1 to 0.9)
140–199 mg/dl vs. no diabetes	−147 (−202 to −93)	−81 (−127 to −36)	−3.8 (−5.3 to −2.4)	−2.6 (−4.1 to −1.1)	0.9 (−0.2 to 0.1)
200 + vs. no diabetes	−155 (−216 to −94)	−69 (−120 to −19)	−4.2 (−5.7 to −2.6)	−2.4 (−4.1 to −0.8)	1.3 (0.6 to 1.9)
P_{trend}*	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Diabetes, by duration					
≤5 years vs. no diabetes	−105 (−166 to −43)	−27 (−78 to 24)	−2.8 (−4.5 to −1.2)	−1.1 (−2.7 to 0.6)	1.3 (0.7 to 2.0)
6–9 years vs. no diabetes	−153 (−249 to −56)	−77 (−158 to 3)	−3.9 (−6.4 to −1.4)	−2.5 (−5.1 to 0.1)	1.0 (−0.02 to 2.1)
≥10 years vs. no diabetes	−155 (−224 to −86)	−86 (−144 to −29)	−4.0 (−5.8 to −2.2)	−2.8 (−4.7 to −0.9)	0.8 (0.01 to 1.5)
Unknown vs. no diabetes	−135 (−175 to −95)	−84 (−118 to −51)	−3.7 (−4.7 to −2.6)	−2.8 (−3.9 to −1.8)	0.5 (0.05 to 0.94)
P_{trend} in known duration*	<0.0001	0.0005	<0.0001	0.0005	0.0002
Diabetes, by medications					
No medication vs. no diabetes	−112 (−154 to −77)	−70 (−100 to −36)	−3.0 (−4.0 to −2.0)	−2.2 (−3.2 to −1.1)	0.5 (0.1 to 1.0)
Oral agents vs. no diabetes	−141 (−198 to −84)	−56 (−103 to −9)	−3.7 (−5.2 to −2.2)	−2.0 (−3.5 to −0.4)	1.3 (0.7 to 1.9)
Insulin (alone or with oral) vs. no diabetes	−187 (−257 to −117)	−112 (−170 to −53)	−5.3 (−7.1 to −3.4)	−4.0 (−5.9 to −2.1)	0.9 (0.1 to 1.6)
P_{trend}*	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

Data are means (95% CI) adjusted for baseline age, sex, race, height, BMI, waist circumference, pack-years of smoking, sport activity index, education level, and ARIC center. *P values correspond to tests for linear trend across categories.

Cross-sectional analyses

As shown in Table 2, compared with their nondiabetic counterparts, in the models adjusting for age, sex, race, BMI, waist circumference, height, pack-years of smoking, sport activity index, educational level, and ARIC field center, adults with diabetes had FVC, FEV_1, FVC % predicted, and FEV_1 % predicted lowered by 133 ml, 72 ml, 3.6%, and 2.4%, respectively (all $P < 0.001$). In the subsequent analysis, we stratified individuals with diabetes according to the level of fasting glucose (Table 2). In diabetic adults, higher fasting glucose was significantly associated with further reductions in FVC and FVC % predicted (all $P_{trend} < 0.001$). A similar, but less pronounced, graded inverse relationship was observed between fasting glucose and FEV_1 ($P_{trend} < 0.001$), resulting in a graded increase in the ratio of FEV_1 to FVC with increasing hyperglycemia.

To further explore the relationship between diabetes severity and lung function at baseline, we performed two additional analyses: one stratified by diabetes duration and the other by type of antidiabetes medication currently used. Compared with their nondiabetic counterparts, diabetic adults who reported a longer duration of diabetes had further reductions in FVC, FEV_1, FVC % predicted, and FEV_1 % predicted (all $P_{trend} < 0.0001$). Likewise, there was a significant, graded, and inverse relationship between lung function and antidiabetes medication use (Table 2) ($P_{trend} < 0.001$). A similar pattern of results but in smaller magnitude was observed for FEV_1, leading in all cases to an inversion of the ratio of FEV_1 to FVC.

Subsidiary analyses

To determine whether diabetes-related differences in inflammatory markers might help explain the relationship of diabetes to lung function, we performed additional analyses after introducing white blood cell count and plasma fibrinogen concentration into fully adjusted multivariable models. Additional adjustment for these markers attenuated the observed relationships only slightly (data not shown).

Finally, to confirm the association between glycemia and FVC, we performed an additional analysis in diabetic individuals and a subgroup of individuals without diabetes for whom A1C levels were available at ARIC visit 2 (1990–1992). As shown in Fig. 1, the relationships be-

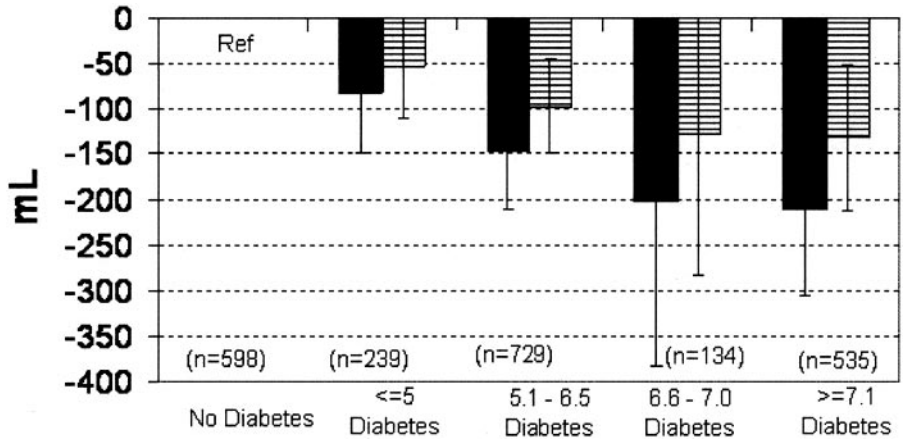

Figure 1—*Adjusted weighted mean differences in baseline FVC and FEV_1 by diabetes status and A1C level in a subset of 1,637 diabetes case (incident and prevalent) and 598 noncase (stratified random sample) subjects at ARIC visit 2 (1990–1992) in whom A1C was measured. All differences are simultaneously adjusted for age, sex, race, BMI, waist circumference, height, pack-years of smoking, sport activity index, educational level, and ARIC field center. Both* P *values <0.001 for linear trends.* Error bars *are 95% CIs.*

tween poor glycemic control (as indicated by higher percent A1C) and reduced FVC and FEV_1 were significant and graded. In addition, compared with their nondiabetic counterparts, diabetic adults with A1C ≤5, 5.1–6.5, 6.6–7.0, and >7.1% had FVC % predicted values that were lower by 2.7% (95% CI 0.9–4.5), 3.7% (2.0–5.4), 5.5% (0.5–10.4), and 5.8% (3.2–8.4), respectively ($P_{trend} < 0.0001$). The corresponding decreases in FEV_1 % predicted were 2.3% (0.3–4.2), 3.0% (1.2–4.8), 4.5% (0.8–9.8), and 4.7% (1.9–7.5) ($P_{trend} < 0.0001$). Again, differences in the degree of impairment with increasing glycemia led to an increase in the ratio of FEV_1 to FVC ($P = 0.06$).

Prospective analysis from baseline to visit 2

To reduce the potential confounding effect from weight gain, we further excluded individuals in the top 1% of increase in BMI or waist circumference from baseline to the 3-year follow-up visit ($n = 164$). During 3 years of follow-up, FVC and FVC % predicted declined more rapidly in diabetic adults than in those without diabetes (Table 3). The differences were small (about 6 ml/year) but consistent and significant. Use of antidiabetes medications showed faster declines in absolute FVC and FVC % predicted with graded relationships ($P_{trend} < 0.01$). In contrast, a lesser decline in the FEV_1-to-FVC ratio was noted in diabetes.

To address the observation that lung function loss in the nondiabetes comparisons was greater than that in the previous report (17), we limited the analysis to nondiabetic adults with baseline age <55 years, who had BMI <25 kg/m^2, who never smoked, who did not have lung diseases nor asthma, and who were in professional, technical, or service occupations ($n = 681$). In this subgroup analysis, the adjusted annual FVC and FEV_1 decreases were still 50 ml (95% CI 45–54) and 45 ml (41–48), respectively.

Additional cross-sectional and prospective analyses were performed among lifetime nonsmokers only. All results and patterns observed in never smokers were similar and were comparable to those for the total study population.

Table 3—*Adjusted changes in FVC, FEV_1, and FEV_1-to-FVC ratio over 3 years of follow-up by diabetes status at baseline*

	ΔFVC (ml/year)	Δ FEV_1 (ml/year)	Δ FVC % predicted (%/year)	Δ FEV_1 % predicted (%/year)	Δ FEV_1-to-FVC ratio (%/year)
No diabetes	↓ 58 (56–59)	↓ 47 (45–48)	↓ 0.96 (0.9–1.0)	↓ 0.7 (0.7–0.8)	↓ 0.1 (0.07–0.1)
Diabetes	↓ 64 (59–69)	↓ 49 (46–53)	↓ 1.1 (1.0–1.3)	↓ 0.9 (0.7–1.0)	↓ 0.05 (−0.02–0.1)
P value	0.01	0.13	0.009	0.08	0.22
Diabetes by fasting glucose					
<140 mg/dl	↓ 63 (53–72)	↓ 49 (42–56)	↓ 1.1 (0.8–1.3)	↓ 0.8 (0.6–1.0)	↓ 0.1 (−0.03–0.2)
140–199 mg/dl	↓ 61 (52–69)	↓ 47 (40–53)	↓ 1.1 (0.9–1.3)	↓ 0.8 (0.6–1.0)	↓ 0.1 (−0.1–0.2)
200+ mg/dl	↓ 56 (46–65)	↓ 47 (40–54)	↓ 0.9 (0.7–1.2)	↓ 0.8 (0.5–1.0)	↓ 0.2 (0.01–0.3)
P_{trend}*	0.59	0.89	0.65	0.88	0.83
Diabetes by duration					
≤5 years	↓ 57 (48–67)	↓ 45 (38–52)	↓ 1.0 (0.7–1.3)	↓ .7 (0.5–1.0)	↓ 0.1 (−0.1–0.1)
6–9 years	↓ 63 (47–79)	↓ 52 (40–63)	↓ 1.1 (0.7–1.5)	↓ 0.9 (0.5–1.3)	↓ 0.1 (−0.3–0.1)
≥10 years	↓ 68 (57–79)	↓ 50 (41–58)	↓ 1.3 (1.0–1.6)	↓ 0.9 (0.6–1.2)	↑ 0.03 (−0.1–0.2)
Unknown	↓ 65 (59–72)	↓ 51 (46–56)	↓ 1.2 (1.0–1.3)	↓ 0.9 (0.7–1.1)	↓ 0.1 (−0.2–0.0)
P_{trend} in known duration*	0.07	0.42	0.05	0.31	0.11
Diabetes by medications					
No medication	↓ 63 (57–69)	↓ 48 (44–53)	↓ 1.1 (0.9–1.3)	↓ 0.8 (0.7–1.0)	↓ 0.1 (−0.02–0.1)
Oral agents	↓ 57 (48–66)	↓ 50 (43–57)	↓ 1.0 (0.7–1.2)	↓ 0.9 (0.6–1.1)	↓ 0.2 (0.1–0.3)
Insulin (alone or with oral)	↓ 79 (68–90)	↓ 52 (44–61)	↓ 1.5 (1.2–1.9)	↓ 0.9 (0.6–1.2)	↑ 0.2 (−0.4 −0.1)
P_{trend}*	0.001	0.40	0.001	0.33	0.0003

Data are means (95% CI) adjusted for baseline age, sex, race, height, BMI, waist circumference, pack-years of smoking, sport activity index, education level, baseline lung function, BMI change from baseline to year 3, waist change from baseline to year 3, incident asthma or chronic lung disease or use of medications for the conditions at 3-year follow-up, and ARIC center. **P* values correspond to tests for linear trend across categories.

CONCLUSIONS — In cross-sectional analyses, middle-aged adults with type 2 diabetes had significantly lower FVC, FEV_1, FVC % predicted, and FEV % predicted compared with their nondiabetic counterparts. These relationships were graded (by fasting glucose, A1C, diabetes duration, and intensity of antidiabetic treatment) and were independent of traditional risk factors. In prospective analyses, FVC declined faster in diabetic adults than in their nondiabetic counterparts. Again, these associations were independent of known risk factors (i.e., age, smoking, and central obesity) for lung function decline and showed graded associations with indicators of diabetes severity.

In this study, the nondiabetic group had an annual FVC decrease of 58 ml/year, which was higher than the 25–35 ml/year from a previous report (17). Further research is needed to explain the possible differences. On the other hand, an absolute difference of 6 ml more decline per year due to diabetes (64 vs. 58 ml/year) deserves clinical attention.

Our results are generally consistent with those of prior cross-sectional studies, which demonstrated lower FVC and FEV_1 in adults with prevalent diabetes compared with their nondiabetic counterparts (1–5,7), especially when diabetes was of longer duration (2,3) and required insulin treatment (1) and when diabetic individuals had existing complications of the disease (3,7). Furthermore, in nondiabetic adults, lower FVC and FEV_1 were associated with higher fasting glucose (1,2) and with hyperinsulinemia and estimated insulin resistance (4,5,9).

Three previous studies offer prospective data on diabetes and subsequent lung function (6,8,10). Lange et al. (6) followed 17,506 Danish adults in the Copenhagen City Heart Study for 15 years. At baseline, FVC and FEV_1 were consistently lower in diabetic individuals, with an ~8% difference in FVC between diabetes and nondiabetes (similar to what we found in ARIC: 96 vs. 103%). However, longitudinal analyses showed no influence of diabetes on subsequent declines. FVC declined ~24 ml/year in women and 39 ml/year in men in diabetic individuals. Davis et al. (8) followed 125 Australian patients with type 2 diabetes for a mean of 7 years. FVC and FEV_1 continued to decline at annual rates of 68 and 71 ml/year, respectively. Declines in FVC and FEV_1 were more rapid in patients with higher baseline A1C. Nevertheless, no nondiabetic control group was assembled for comparison. Litonjua et al. (10) performed a nested case-control analysis in 352 men who developed diabetes and 352 nondiabetic men in the Normative Aging Study. The study showed that although individuals with diabetes had lower FEV_1 and FVC at all time points, they had only 5.4 ml/year greater declines compared with control subjects after diagnosis of diabetes ($P = 0.2$; median follow-up 11.9 years). Like other case-control studies, it was possible that only healthy subjects who were at risk for diabetes completed the lung function tests.

Although the underlying mechanism relating diabetes to reduced lung function remains unclear, previous studies suggest several possible explanations including glycosylation of chest wall and bronchial tree proteins (19), thickening of basal lamina (18), and perhaps increased susceptibility to respiratory infections (20). Additionally, hyperglycemia, inflammation, and diabetes-related oxidative stress have been shown to induce muscle dysfunction (21).

Other studies of lung function in the prediabetic individual complicate causal inferences. In particular, several recent prospective studies, including the ARIC Study, have demonstrated that reduced lung function is an independent predictor of incident type 2 diabetes (4,22,23). In the present study, the associations between diabetes status and lung function were more significant cross-sectionally than prospectively. These results suggested the notion that abnormalities in lung function precede diabetes and then continue after diabetes onset.

Furthermore, it is possible that our findings in ARIC fit into the broadening picture of mild organ dysfunction associated with altered gene expression found in the common conditions underlying diabetes. The effects could be mediated by proinflammatory master regulator molecules such as the mediators of the nuclear factor-κB and activator protein-1 pathways, which themselves might be subject to further inflammation by hyperglycemia (24,25). In this study, however, addition of inflammatory markers to the models, although slightly reducing the size of the decline associated with diabetes, did not provide clear evidence of a role for inflammatory markers.

Attention to the lung as a possible target organ of diabetes-related injury has been highlighted recently by the approval of delivery of insulin by inhalation (26). A recent meta-analysis of randomized controlled trials of at least 12 weeks' duration (27) reported a greater decrease in FEV_1 from baseline among those taking inhaled insulin than did those in the comparison group (weighted mean difference, −0.31 l [95% CI −0.043 to −0.020 l]).

Strengths of the present study included a community-based population, standardized spirometric techniques, extensive data on potential confounders, and the large, biracial, community-based sample, which increased precision of our estimates and permitted multivariable statistical adjustments. Nonetheless, several limitations should be kept in mind. First, although the availability of standardized follow-up data on lung function was a definite strength, the interval was short (only 3 years). Second, A1C was measured only at year 3 of follow-up, limiting its usefulness in longitudinal analyses. Finally, given the strong relation between type 2 diabetes and central adiposity, even the most meticulous adjustment for BMI and waist circumference leaves some concern about the possibility of residual confounding.

In summary, this study supports the notion that lower lung function, particularly decreased vital capacity, not only precedes the onset of diabetes but also continues, at an accelerated pace, with the onset of the disease. Additional research is required to identify pathophysiologic mechanisms and to determine clinical significance of this association. In the meantime, clinicians should pay heightened attention to pulmonary function in their patients with type 2 diabetes.

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