Spirometry and Diabetes

Implications of reduced lung function

The association of reduced lung function and diabetes has been described for many years (1). Although the clinical significance of this association is not known, it is intriguing to think of the lung as another end organ adversely affected by diabetes. It is also interesting to consider that reduced lung function may be present before the clinical recognition of diabetes (2) or insulin resistance (3,4), suggesting that the lung may be involved in the pathogenesis of diabetes.

The issue of lung function and diabetes is addressed in the current study by Davis et al. (5). Taking advantage of an extensive population database in western Australia, this group has conducted the largest prospective longitudinal survey to date of the pulmonary function of a cohort of patients with type 2 diabetes who had no history of lung disease. A total of 125 patients had spirometry measured at baseline and then again 7 years later. The key finding was that the average rate of decline of lung function as measured by forced expiratory volume in 1 s (FEV_1) was 71 ml/year compared with an expected decline in healthy nonsmokers of 25–30 ml/year. This change in lung function was similar whether or not smokers were included in the analysis, indicating its independence from smoking status. Although the follow-up group clearly represented healthy survivors, their lung function decline was still greater than expected, which would likely only underestimate the true rate of decline among all diabetic subjects. When explored by linear regression, the only predictor of reduced lung function was the level of glycemic control. An increase of 1% in mean HbA_{1c} was associated with a decrease of 4% in predicted forced vital capacity (FVC). Extrapolating back to 100% predicted (i.e., normal) lung function revealed that normal lung function predated the diagnosis of diabetes by 1 to 2 years. In addition, of all factors identified, only reduced lung function was an independent predictor of all-cause mortality with a 10% reduction in FEV_1 associated with a 12% increase in all-cause mortality.

A potential concern about this study is the use of spirometry as a primary outcome measure. Performing reproducible, good quality spirometry is difficult to do in the primary care setting (6). However, the authors have convincingly demonstrated the validity of their results. The measurements were made in a research setting, adhered to the standardized guidelines of the American Thoracic Society (7), and were in accord with other similar studies (8). Although two different spirometers were used, each met American Thoracic Society standards and used the same predicted equations that were validated for the local population. In addition, in an analysis not included in the published study, the authors found no change in their results when they assumed a hypothetical difference in performance of the two spirometers. Since spirometry may be insensitive to subtle changes in pulmonary function (1), the large decline in pulmonary function and its profound relation to glycemic state and all-cause mortality substantiate the results of this important study.

This study adds to the growing body of literature that supports an association between reduced lung function and diabetes recently reviewed in *Diabetes Care* (1). That glycemic control may be a key factor in this association is highlighted not only by the current study, but also by the recent report on the Framingham Offspring Cohort, which examined the cross-sectional relationship of diabetes and the level of fasting glucose to pulmonary function among 3,200 subjects (9). The association of reduced lung function with other end-organ damage, such as retinopathy and renal vasculopathy (1), and the improvement in lung function following intensive insulin therapy (10) further support the concept that the lung may be a target organ for damage in diabetes.

The current study also speculates that abnormal lung function may precede the diagnosis of diabetes, suggesting that the lung may contribute to, or at least be commonly affected by, the factors involved in the pathogenesis of diabetes. In support of this idea are data from the Malmo Preventative Study (3) and the Normative Aging Study (4). These studies found that nondiabetic subjects with reduced lung function were at higher risk of developing insulin resistance and hyperinsulinemia. One explanation for this may be that inflammatory markers such as fibrinogen, which have been associated with reduced lung function in healthy individuals (11), have also been associated with the development of diabetes (12).

Subjects with diabetes may also be at increased risk for reduced lung function, possibly as a result of increased effects from inhaled exposures. For example, subjects with diabetes may be more susceptible to the adverse health effects of airborne particles (13), perhaps including tobacco smoke (9). Diabetes has also been associated with asthma at the population level (14), suggesting that despite their immunological differences, susceptibility to diabetes and asthma may be influenced by common environmental factors. As pointed out by Davis et al. (5), the potential adverse effects of inhaled environmental exposures in diabetic subjects is important to consider when interpreting the pulmonary effects of the new inhaled insulin regimens currently under investigation.

The findings of the current study add to the large body of literature that demonstrates that lung function is an independent risk factor of cardiovascular, pulmonary, and all-cause mortality (15). How lung function relates to such important disease outcomes and whether the lung is a cause or simply a marker of underlying disease is unknown. The lung is one of the first organs to interact with the environment, so it is reasonable to expect that environmental toxins may first impinge on lung function before resulting in more widespread effects. The link between reduced lung function and cardiovascular disease may be the elevation of serum markers of inflammation and increased insulin resistance as already de-

scribed (3,4,11,12). How reduced lung function relates to insulin resistance is unknown, but may be due to underlying defects in skeletal muscle function (16) or to the mechanical effects of centripetal obesity (17), both of which can affect ventilatory function.

Whatever the cause, the findings of Davis et al. (5) support the notion that lung function is an important marker of increased risk of death in patients with diabetes. Monitoring periodic lung function (FEV_1 and FVC) has been advocated as a general measure of overall health status as well as a prognostic indicator of premature death from all causes, including cardiovascular disease, chronic obstructive pulmonary disease, and lung cancer (15). If a low FEV_1 is a marker of diabetes or poor glycemic control, then efforts should be focused on identifying and modifying known risk factors for cardiopulmonary disease and diabetes, such as smoking, lipid status, blood pressure, body weight, exercise, and periodontal disease. Glycemic control should also be improved, perhaps by including use of insulin sensitizers that have been shown to reduce markers of subclinical inflammation (12). If a low FEV_1 reflects a causative role played by the lungs in the development of diabetes, then optimizing lung health through smoking cessation, avoidance of irritant and toxic exposures, control of underlying airway inflammation, and promotion of physical activity seems warranted. Indeed, it's time to add the spirometer to the tools available for monitoring diabetes and its important sequelae.

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