Lung function, diabetes and the metabolic syndrome

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An association between abnormal lung function and diabetes has been recognised since the mid-1990s. A variety of spirometric studies have shown that diabetes is associated with a restrictive lung defect that persists after adjustment for body mass index and smoking, and which reflects glycaemic exposure in longitudinal studies. Although diabetes-associated reductions in forced expiratory volume in the first second (FEV1) and in forced vital capacity (FVC) are relatively modest, they equate to changes observed in smokers. In addition, and as seen in the general population, FEV1 is an independent predictor of mortality in patients with type 2 diabetes.

Degrees of glucose intolerance short of diabetes are also associated with impaired lung function, as is the metabolic syndrome. Indeed, a recent cross-sectional study has shown a stepwise reduction in spirometric measures as the number of components of the metabolic syndrome increases. There is evidence that lung damage starts several years before the diagnosis of type 2 diabetes, given this and the finding that fasting plasma glucose and HbA1c increased with the number of metabolic syndrome components in this latter study, an association between glycaemia and the graded reduction in pulmonary function might have been expected but was not seen, the authors postulating that a limited sample size may have obscured such a relationship. However, other mechanisms independent of glycaemia and specific to individual metabolic syndrome criteria – namely central obesity, hypertension and dyslipidaemia (low serum high-density lipoprotein cholesterol and high serum triglyceride concentrations) – may be more influential, especially abdominal fat accumulation. The finding that the restrictive lung defect was most marked in the patients with type 2 diabetes relative to those with varying severity of the metabolic syndrome suggests that the combination of glycaemia and central obesity is particularly adverse.

Putative mechanisms linking dysglycaemia with impaired lung function

Structures within the thorax are relatively abundant in collagen and elastin which are vulnerable to non-enzymatic glycation. This chronic and eventually irreversible process could lead to rigidity of the chest wall, bronchial tree and lung parenchyma, and thus cause or contribute to a restrictive defect. Hyperglycaemia-related pulmonary microvascular changes may include damage to alveolar epithelial and pulmonary capillary basal laminae, and autonomic and/or phrenic neuropathy that alters bronchial reactivity and respiratory muscle function, factors that could promote the changes in spirometric measures observed in clinical studies. Diabetes is associated with chronic inflammation and there is epidemiological evidence of an association between restrictive lung disease and elevated circulating inflammatory markers such as C-reactive protein. There is also evidence that patients with diabetes exhibit increased susceptibility to the adverse respiratory effects of airborne particles and perhaps tobacco smoke.

Lastly, there is the possibility that an increased propensity to, and severity of, respiratory infections in diabetic patients may augment lung damage over time.

Non-glycaemic features of the metabolic syndrome and abnormal lung function

There is evidence that abdominal obesity assessed by waist circumference is the feature of the metabolic syndrome with the strongest relationship of any of the components to impaired lung function. This association may reflect mechanical effects of truncal obesity that attenuate diaphragmatic function and chest wall compliance, thus decreasing lung volumes, and/or the systemic proinflammatory effects of adipocytokines secreted by increased visceral fat. Although there is an association between hypertension and reduced pulmonary function, it is relatively weak, as is also the case for dyslipidaemia.

Clinical implications

Spirometry is relatively inexpensive and easy to perform at all levels of the health care system, especially with digital devices that have pre-programmed criteria for acceptability and repeatability. Periodic monitoring of lung function (FEV1 and FVC) has been advocated as an index of overall health status in the general population, as well as a prognostic indicator of premature all-cause mortality and cardiovascular death. It has also been suggested as part of usual diabetes care. Impaired lung function detected in a patient with type 2 diabetes or the metabolic syndrome may indicate restrictive pulmonary disease unrelated to glycaemia or obesity, but it might also be a marker of chronic suboptimal glycaemic control and/or the local or systemic effects of central adiposity. Its presence could justify a review of weight reduction strategies, as well as blood glucose-lowering, antihypertensive and lipid-modifying therapies, and steps to achieve smoking cessation if appropriate.

Attempts to deliver prandial insulin therapy by inhalation have stalled, in part because of the possibility of augmentation of diabetes-associated lung damage. In future, however, it may be possible to deliver other peptides relevant to the treatment of diabetes and components of the metabolic syndrome (such as incretin analogues) by the pulmonary route as a safe alternative to subcutaneous injections.

Summary

Diabetes, impaired glucose tolerance and the metabolic syndrome are all associated with a modest restrictive lung defect. There appears to be a dose-response relationship between increasing numbers of components of the metabolic syndrome and the degree of impairment of pulmonary function. Possible underlying mechanisms include glycation of structural proteins within the
Thorax, the mechanical effects of visceral adiposity, and chronic inflammation. Spirometry as part of usual care may be an inexpensive and efficient way of identifying patients at increased cardiopulmonary risk and as a prognostic marker of all-cause mortality.

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Acknowledgements
The author is supported by a National Health and Medical Research Council (NHMRC) of Australia Practitioner Fellowship.

Declaration of interests
There are no conflicts of interest declared.

References

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- Complete institutional data collection form
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- Return the 6 completed forms to ketan.dhatariya@nhs.net

If you have any questions about the project contact Dr Ketan Dhatariya who is steering the audit as lead author on the upcoming JBDS Guidelines on the management of DKA