group may be an issue, demonstrating that smokers are less likely to participate in lung cancer screening programmes than ex-smokers.\textsuperscript{10} Patel \textit{et al}\textsuperscript{15} reported on the acceptance of annual CT scans, sputum cytometry and bronchoscopy surveillance in smokers and ex-smokers with mild to moderate chronic obstructive pulmonary disease (COPD) who had already consented to take part in the LungSEARCH trial. Although the majority of participants found the interventions acceptable, there was evidence of doubt about the value of early detection, particularly in older patients. They also found evidence to support the hypothesis that worry is a factor that deters people from participating in screening. Such considerations clearly need to be built in to cost-effectiveness analyses of any national screening programme.

While it is vital we continue to push for effective screening programmes, those that use current technology are likely to be of limited benefit, costly and not likely to be implemented in the near future, at least in the UK. Strenuous efforts are also needed to find better screening methods that can eventually supersede CT scanning. We simply cannot wait and have to trial—and carefully evaluate—a variety of approaches to promote earlier diagnosis in patients who already have symptoms of lung cancer.

### Competing interests

MJP is a co-author on the paper by Simon \textit{et al}, though his contribution was limited to advice on some elements of the text and the conclusions rather than the design or analysis of the study. He is also a participant in the LungSEARCH trial which is the subject of the paper by Patel \textit{et al}, though he is not a co-author and has not been directly involved in this sub-study or the preparation of the paper. He is the secondary care lead for the NAEDI programme.

**Provenance and peer review** Commissioned; internally peer reviewed.

**Published Online First** 17 March 2012


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**Airway disease and emphysema on CT: not just phenotypes of lung pathology**

Peter D Paré,\textsuperscript{1} Pat G Camp\textsuperscript{2}

In this issue of the journal, Martinez \textit{et al}\textsuperscript{1} examined the relationships between quantitative CT (QCT) parameters of emphysema, airway wall remodelling and airway narrowing and composite clinical and physiological indices of chronic obstructive pulmonary disease (COPD), the BODE index\textsuperscript{2} and the St George’s Respiratory Questionnaire (SGRQ).\textsuperscript{3} BODE stands for Body mass index (BMI), airflow Obstruction, Dyspnoea and Exercise capacity.

Not surprisingly, these QCT estimates of pathological changes were related to measures of clinical impact. More interestingly, the authors found that there were differences in the strength of the associations between measures of emphysema and airway disease and the composite indices. Measures of emphysema were more closely related with the BODE index while the airway wall abnormalities were better predictors of the SGRQ.

While it has long been recognised that there is a spectrum of changes in the airways and parenchyma in COPD,\textsuperscript{4} the separation of the airway predominant phenotype from the parenchymal predominant phenotype was largely limited to the autopsy room until the advent of CT CT has confirmed that some patients have airflow obstruction with little emphysema while others have predominant emphysema with little airway disease. Such individuals form the extremes while the majority of patients have various combinations of airway disease and emphysema.\textsuperscript{5} In addition, there is evidence that the predominant pattern is to some extent familial\textsuperscript{6} and is associated with different rates of decline of lung function.\textsuperscript{7} The presence of airway disease and emphysema on CT can be assessed qualitatively or quantitatively. The power

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of the quantitative indices, as used in the present study, is that they are completely reproducible provided that similar scanners, imaging parameters and software are used. The hope is that the separate mechanisms that lead to these pathological changes in COPD can be individually targeted by specific therapy and followed non-invasively with repeat imaging.

Since CT allows a measure of anatomic derangement, its validation has largely been by comparison with pathological estimates of emphysema and airway disease. Many studies have shown that CT provides an accurate estimate of the extent and severity of emphysema, although only a few have compared CT measures of airway lumen narrowing and wall remodelling with pathological changes.

More recently, there have been a number of studies in which quantitative estimates of CT phenotypes have been compared with clinical phenotypes, measures of lung function and symptoms. The reasoning is that, in the absence of a structural gold standard, lung function and symptoms can act as surrogates for test validity. If CT can accurately assess anatomic derangement of lung structure and if structural damage correlates with lung function and symptoms, then there should be good relationships between the CT measures and these clinical features. In general, the results of these studies have been reasonably robust, supporting the idea that CT can be used to grade the clinical as well as the pathological severity of emphysema. Only a few have compared CT measures of airway lumen narrowing and wall remodelling with pathological changes.

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The SGRQ (http://www.healthstatus.sgul.ac.uk/sgrq-downloads/sgrq-c-downloads) is a 50-item questionnaire that assesses respiratory symptoms, physical activity such as cough, dyspnoea, and airway remodelling (Pi10). Diaz et al have examined the relationship between 6MWD and OCT-defined measures of emphysema and airway disease and found that emphysema was better correlated with the 6MWD than airway remodelling parameters. In the present study, the strength of the association, as assessed by r values, was slightly stronger for Pi10 (r = -0.53, p<0.001) than for emphysema (r = -0.24, p<0.001). Interestingly, the factor that may contribute to the weaker relationship between the BODE index and airway scores is the completely opposite, but significant, relationship between BMI and airway remodelling (Pi10). Individuals who have thicker airways have significantly greater BMI (r = 0.17, p<0.001). This positive relationship between measures of airway wall remodelling and BMI (or body weight) has been previously reported by Lee et al and Camp et al, but its cause and significance is unknown.

More surprising to us was the closer relationship of airway wall parameters to respiratory health status as measured by the SGRQ. Why would respiratory health status measures be more closely related to airway pathology than emphysema? Previous studies have reported an association of measures of altered airway dimensions with symptoms such as cough, sputum, wheeze and dyspnoea. For example, Lee et al reported that CT-measured wall area and wall area per cent correlated with dyspnoea as measured with the MMRC, whereas the CT measure of emphysema did not. In supplementary table 2 Martinez et al used multivariate analysis to determine the independent contribution of the three SGRQ domains to the relationships with airway remodelling and emphysema. All three domains—symptoms, impacts and activity—were significantly associated with airway wall remodelling (Pi10). On the other hand, quantitative emphysema was only associated with the activity score and unrelated to symptoms and impacts. It is understandable that the symptoms of cough, sputum and wheeze are more closely related to airway morphology than to emphysema. The relationship of emphysema to activity is also logical since dynamic hyperinflation during exercise is an expected consequence of the loss of lung recoil that is characteristic of emphysema. What is unclear is why the impacts domain, which measures psychosocial impacts of COPD (including questions on panic during symptoms, or feeling one is a burden to friends or family), relates to airway disease measures but not to emphysema. We are unaware of any study that has probed the relationships between phenotypes of COPD and psychosocial functioning, but if the relationship between the airway measurements and the SGRQ impacts component can be confirmed, this could lead to an intriguing area of investigation.

It is especially impressive that airway measurements correlated so well with the SGRQ since the airways that are assessed using high resolution CT are relatively large airways which are not the site of major airway resistance in COPD. The fact that large airway dimensions are related to respiratory health status as measured by the SGRQ supports the suggestion that airway wall remodelling in large airways is a reflection of generalised airway narrowing and/or obliteration as has been suggested by Nakano et al. McDonough et al have recently shown that an early lesion in COPD is the loss of terminal bronchioles. Perhaps there is a relationship between this...
The history of CF treatment has been by any standards a major success story. Median survival has risen from less than a year in 1938 to a predicted value for current newborns of around 50 years.\(^1\) This has arisen from advances in the multidisciplinary treatment of the condition, and latterly with earlier diagnosis through genetic tests, particularly in newborns.\(^1\) As a consequence of the CF transmembrane conductance regulator (CFTR) gene dysfunction, such as mutations that arise in about 5% of the population in the UK, some patients born with severe disease now survive into their adult years.\(^1\)

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Thorax 2012 67: 380-382
doi: 10.1136/thoraxjnl-2012-201769

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