**CT in COPD: just a pretty picture or really worth a thousand words (or dollars)?**

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We like pretty pictures and, in pulmonary medicine, we use computed axial tomography (CT) to generate pretty pictures to help us diagnose and manage patients with respiratory complaints. In 2007 more than 10 million chest CT scans were performed across the USA, representing an astounding 11,000% increase in the CT rate since 1980.1 CT scans rely on ionising radiation to generate images, and recent estimates suggest that CT scans may be responsible for 24% of the total ‘background’ radiation to which the population is exposed in a given year.2 Thankfully, there are several large-scale efforts to reduce the radiation exposure related to CT scans and to mitigate the health risks imposed by ionising radiation.3 What is not being adequately addressed is the issue of economic costs (and benefits) of CT scans. CT scans are expensive for patients and to the healthcare system, with prices ranging from $500 to $1500 per scan.4 Recently, the cost-effectiveness ratio of lung cancer screening with CT scans was reported to be $2.5 million dollars per quality-adjusted life years,5 providing us with a sobering reminder that these ‘pretty pictures’ are not without significant costs.

Chronic obstructive pulmonary disease (COPD) is a condition that lends itself to anatomical medical imaging. For practical reasons, COPD is largely defined based on spirometric criteria. However, there is general discontent with this approach because spirometric measurements are relatively insensitive and correlate only very loosely with histological abnormalities or with patient symptoms or outcomes.6 Furthermore, spirometric measurements are poorly responsive to medical interventions (even those that are known to improve morbidity and mortality) and cannot discriminate the major pathological subphenotypes of COPD—emphysema and small airways disease.6 More complete and elaborate lung function measurements provide more information but they are expensive, time-consuming, difficult to standardise and relatively inaccessible beyond large hospitals, making them non-user friendly for many practising physicians. On the other hand, high-resolution CT (HRCT) provides the clinicians with excellent anatomical detail and takes away the veil and mystery of lung function measurements. With continued evolution and refinement of this technology, the hope is that HRCT will one day complement (or even replace) lung function measurements in diagnosing and managing patients with COPD in routine clinical practice. However, is this notion realistic?

It is now well established that some current and former smokers with no or minimal pulmonary symptoms can have normal forced expiratory volume in 1 s (FEV₁) and ratio of FEV₁ to forced vital capacity (FVC) but still harbour significant emphysematous changes in their lungs.7 The clinical relevance of this observation, however, was unknown. The study by Hoesein et al8 offers an answer to this clinical conundrum. Using data from 2085 current and former heavy smokers who enrolled in the Dutch—Belgian Lung Cancer Screening Trial (NELSON), Hoesein and colleagues showed that individuals with the largest burden of CT-based ‘emphysema’ experienced the fastest decline in lung function over 3 years of follow-up. This effect was independent of age, smoking status or baseline lung function of these individuals.9 These data are in keeping with those of Yuan et al who showed that lung ‘overinflation’ was associated with a rapid decline in FEV₁. However, owing to the small sample study (n=143), Yuan et al could not show a relationship with more traditional CT-based measures of emphysema.7 The physiological rationale for the relationship between CT-based emphysema, lung ‘overinflation’ and rapid decline in lung function is obscure, but several possibilities exist. Although, in general, mild degrees of lung emphysema do not result in airflow limitation, they can lead to air trapping and lung ‘overinflation’.9 However, with emphysema progression, airflow limitation ensues owing to reductions in elastic recoil pressure and loss of alveolar attachments10 which leads to narrowing and premature closure of airways. Alternatively, it is possible that CT-based measures of emphysema may just be a marker of pathological changes in the small airways (eg, remodelling and fibrosis) that may be the more salient drivers of COPD progression but cannot be well visualised on HRCT scans.

The study by Hoesein et al has several limitations that deserve emphasis. First, emphysema is a pathological (and not a radiological) diagnosis and in this study, there was no histological confirmation of CT-based assessment of emphysema. Furthermore, the study used only one metric to evaluate emphysema—the extent of low attenuation areas on the CT scan. While this is commonly used, inclusion of other salient radiographic features of emphysema such as low attenuation cluster analysis, the presence of gas trapping and the regional distribution of the low attenuation areas across the lobes would have enhanced the accuracy of the definition.11 Second, only men were studied so these data cannot be generalised to the female COPD population. Third, only one follow-up spirometric value was obtained, making it possible that ‘regression to the mean’ could have confounded the results.

The NELSON trial is a lung cancer screening study which uses low-dose CT scans for early detection of malignant tumours. The final results from this trial are not expected until 2015.12 Thus, the current study by Hoesein et al could not provide any data on the relationship between CT measures of emphysema and the subsequent risk of lung cancer, which is the leading cause of mortality in patients with mild COPD.13 However, a previous study by Wilson et al14 which used CT scans collected in a different lung cancer screening programme suggests that smokers with emphysema on CT scans have a significantly increased risk of lung cancer, independent of their lung function. Together, the data by Hoesein et al and Wilson et al indicate that CT-based measurements of emphysema in smokers...
with normal or near normal lung function are not just pretty pictures but are clinically important because they identify individuals at high risk of COPD progression and lung cancer. In such individuals it may be highly cost-effective to intervene with aggressive tobacco treatment programmes and with close observation and follow-up.

On 4 November 2010 the US National Cancer Institute (NCI) released the initial results from the National Lung Screening Trial (NSLT), showing a reduction of 20% in lung cancer mortality and a reduction of 7% in total mortality among ex-smokers and current smokers screened with low-dose CT compared with those screened with chest x-rays. Notwithstanding the costs associated with HRCT scans, these and other data on screening CT for lung cancer will probably lead to an exponential increase in the number of thoracic HRCT scans that will be performed over the next few years. This will present new opportunities for clinical care and research for the respiratory community. In addition to using these CT scans as tools for lung cancer screening, the data by Hoesein et al suggest that chest physicians can also use them to identify high-risk patients who are likely to experience rapid COPD progression and to aggressively treat them for tobacco addiction (if they are current smokers) and to institute therapies for their COPD when clinically appropriate. With agreed protocols to acquire and analyse the images, the widespread use of thoracic CT scans may also provide a tremendous opportunity for researchers to understand the natural history of COPD in individuals with ‘subclinical’ COPD (based on CT only) and its associated comorbidities such as lung cancer, cardiovascular disease and osteoporosis. Perhaps, by doing so, we can maximise the value of screening lung CT scans and make these pretty pictures worth a thousand words (or dollars)!

Acknowledgements DDS is the holder of a Canada Research Chair in COPD and a senior scholar with the Michael Smith Foundation for Health Research.

Competing interests None.

Patient consent Obtained.

Contributors All of the authors were involved in the drafting and revising of the editorial.

Provenance and peer review Commissioned; externally peer reviewed.


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*Thorax* published online May 14, 2011

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