Imaging

Is limited computed tomography the future for imaging the lungs of children with cystic fibrosis?

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Perspective on the paper by Jiménez *et al* (see page 388)

In this issue of the Journal, Jiménez *et al* describe a new technique in high resolution computed tomography (HRCT) of the chest in children with cystic fibrosis (CF).[1] HRCT is widely available to clinicians who care for children with CF; it has some advantages over plain chest radiography but exposes the child to more radiation. The HRCT technique described by Jiménez *et al* reduces the radiation exposure by limiting the number of slices to six. Will six slices be sufficient to provide the information that the clinician seeks?

Pulmonary disease in children with CF is characterised by impaired clearance of pathogens, resulting in intermittent and later permanent infection of the lower respiratory tract, with bacterial and fungal pathogens causing progressive mucous impaction and bronchiectasis. Asymptomatic infants with CF have been shown to have abnormalities in pulmonary function[2 3] and to have airway inflammation on lavage studies.[4 5] Plain chest radiographs traditionally have been the mainstay of radiological assessment to detect collapse, consolidation, peribronchial thickening, patches of fibrosis, and cystic change. Several scoring systems based on these changes have been developed and are used for annual data collection and within national databases,[6–10] and show low interobserver variability and good correlation with lung function and infective exacerbation rate in older children.[11] The current North American Cystic Fibrosis Foundation guideline[12] and the European Consensus on CF standards of care recommend an annual plain chest radiograph, the latter recommending use of the Northern score (to limit the radiograph to a single posterior–anterior view).[10 13]

High resolution computed tomography of the chest has the ability to detect abnormalities in the airway and lung parenchyma including air trapping, mucoid impaction, and bronchiectasis that are often too subtle to detect on a plain radiograph.[14 15] Long *et al* have recently shown that half of the 34 asymptomatic children with CF studied (aged 10 weeks to 5.5 years) had evidence of bronchiectasis and more than half had abnormal airway wall thickening seen on HRCT.[16] The degree to which airways were dilated increased with increasing age, suggesting to the authors that structural airway changes that lead to bronchiectasis begin very early in life. They were able to make accurate and reproducible measurements of airway wall thickness, airway lumen diameter, and accompanying vessel diameter on all children using a sedated and controlled positive pressure ventilation protocol and taking computed tomography (CT) slices at four anatomical levels. Brody and colleagues have reported the HRCT scores of 60 children with CF aged 6–10 years that participated in the Pulmozyme Early Intervention Trial.[17] All had a forced vital capacity (FVC) of greater than 85% although their forced expiratory volume in 1 second (FEV_1) ranged from 51.8% to 136.7% of predicted values. Thirty five children (58%) had evidence of bronchiectasis and 11 of the 37 children (30%) who had normal spirometry (FEV_1 and FVC greater than 85% predicted) had evidence of bronchiectasis in at least one lobe. A quarter of the group had normal HRCTs. There was moderately good correlation between pulmonary function tests and HRCT scores, but spirometry and HRCT are clearly not measuring the same thing: the CT scan may show extensive changes despite normal or near-normal spirometry. De Jong *et al* reached similar conclusions: HRCT is more sensitive than pulmonary function tests in the detection of early and progressive lung disease and may worsen over a two year follow up period despite no worsening of lung function.[15] One problem with these scoring systems is that they are time consuming to conduct, although de Jong and colleagues have recently described a semi-automated system for measuring airway wall area, airway lumen area and perimeter, and accompanying arterial area; they found that these quantitative measurements show progressive changes over a two year interval despite stable pulmonary function tests.[18]

HRCT may be of particular interest in the clinical assessment of children under 5 years of age because it is much more difficult or impossible for them to perform spirometry. HRCT scoring systems have been used as an outcome measure within intervention studies. Nasr *et al* evaluated the efficacy of aerosolised recombinant human DNase (rhDNase) in CF children younger than 5 years of age.[19 20] In this randomised double blind, placebo controlled pilot study, children aged less than 5 years had plain chest *x* ray (CXR) examinations and HRCTs performed before and after 100 days of treatment. As expected, most of the 12 children studied had mild respiratory disease as assessed by the CXR and the HRCT score. A significant change in CXR score between the two groups was not found, but there was a significant improvement in HRCT score despite a high interobserver variation in these scores (49.1%).[20] These HRCT scans were performed without sedation or anaesthesia and were all of sufficient quality to be scored despite some motion artefact. The HRCT scans were limited to five evenly spaced slices per child, resulting in radiation doses claimed by the authors to be similar to those of the CXR. The importance of this study is that it shows the potential for HRCT as an outcome measure to assess efficacy of an intervention when compared with placebo and is not dependent on the voluntary effort of the patient. Furthermore, it suggests that some of the morphological changes seen on the HRCT in a young child may be reversible.

ROUTINE CT SCANS FOR ALL?

When should a clinician request a CT scan of the chest in a child with CF? Should it be a part of the annual review and used as a means of monitoring progress? CT scans will show abnormalities not suspected on clinical grounds and will usually appear worse than the clinician and family expect, but how are changes of early bronchiectasis, peribronchial thickening, and mucoid impaction to be interpreted? These changes will be seen in many children with near normal chest radiographs and in whom clinical progress is considered to be good. The finding of abnormalities on the CT is likely to cause anxiety, at least for the family, even if not for the clinical team. If these findings cannot be linked to an intervention or a change in the course of treatment, the information is unlikely to be of benefit to the child

and the family. There will be instances where the clinician wishes to gain the additional radiological information available from an HRCT scan, including assessment of:

- Allergic bronchopulmonary aspergillosis[21]
- Atypical mycobacterial infection[22–24]
- Unexplained clinical deterioration
- Pulmonary embolism
- Severe haemoptysis[13]
- Sinus disease.

What are the disadvantages of performing HRCT scans in children with CF? Firstly, these tests are expensive in terms of equipment and radiologist time. Secondly, low dose scanning protocols are not routinely used and there is no standardisation between centres so there will be wide variation in the amount of radiation exposure. There is likely to be a radiation dose related increased risk of future cancers, though the magnitude of this relationship is difficult to assess. The overall excess mortality associated with regular HRCT scanning in CF is unknown. de Jong *et al* have performed computational modelling and estimated that survival reduction associated with annual scans from age 2 years until death was approximately 1 month and 2 years for CF cohorts, with a median survival of 26 and 50 years, respectively.[25] Younger patients will be at greater excess risk because of their increased cumulative time available to develop cancers.[26]

An HRCT score will be useful and powerful within a longitudinal clinical study because the same CT technique and scoring system can be used across all participating children, allowing their scores to be compared and interpreted alongside other outcome measures. Similarly, scores can be used within CF centres and for regional and national databases as a means of monitoring and comparing groups of patients outside of clinical studies, but this requires a unified approach to the HRCT technique used, with a scoring system that is acceptable to radiologists across centres and has high interobserver agreement. The scoring systems and techniques described recently show great potential. It is very encouraging to read that Jiménez and colleagues confirm that limiting the number of slices on an HRCT to six appears to be acceptable for adequate scoring of the CT.[1] However, the child is still being exposed to radiation. A limited HRCT scan may be adequate for providing a score but will it be adequate for detecting focal changes? If the request for the HRCT scan is generated by clinical concern, then more information than that generated by a limited scan may be required and deserves further evaluation.

In conclusion, the benefit of performing a CT scan of the lungs of a child with CF must be balanced against the risk. In longitudinal clinical trials, CT used with a standardised scoring system offers a powerful quantifiable outcome measure that is more sensitive to change than CXR. Outside of clinical trials there are a limited number of indications that are listed above where a CT will be helpful. However, CT scans are expensive to perform and carry a small but cumulative risk of future cancer development. Strategies to minimise radiation dosage can be used and will continue to be developed; they will reduce this risk further. No author has yet shown an advantage to the patient in performing routine CT scans. Until this can be shown the CT should be reserved for limited indications and for clinical trials.

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