

REPLY

High-resolution computed tomography in pediatric common variable immunodeficiency: risks and benefits

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Editor,

We recently reviewed the literature on pulmonary complications in children with common variable immunodeficiency (CVID) and concluded that these complications are common, that they may be severe, and that high-resolution computed tomography (HRCT) is the most sensitive method to detect pulmonary complications in these patients (1). Recent findings in our pediatric CVID cohort confirm that HRCT abnormalities are common (2) and can be identified even in children with normal chest X-rays or spirometry (Van de Ven et al. submitted). In response, Turner et al. stated their concerns regarding radiation exposure with chest HRCT in children with CVID. We agree that one should be careful with roentgen techniques, particularly in patients with CVID, as they are more prone to develop hematological malignancies and more sensitive to radiation (3). Roentgen tests must be obtained at a dose as low as reasonably achievable, and when this is adhered to, we believe that risks are generally small and the decision to scan mainly concerns the patient benefit side of the risk-benefit balance.

First, for HRCT to be beneficial, it should demonstrate CVID-related pulmonary complications reliably and reproducibly. Second, it must be accurate and show additional value to easier and safer tests, and third it should lead to changes in management and improvement in quality-adjusted life-years at reasonable costs.

First, we recently showed that even at low-dose HRCT can demonstrate CVID-related pulmonary complications in children by using a simple end-inspiratory and end-expiratory breathhold technique. The CVID-related abnormalities could be evaluated reproducibly by observers with moderate levels of chest CT interpretation experience.

Second, pulmonary complications contribute significantly to the morbidity (and in some cases mortality) of a large part of the pediatric and of the majority of the adult CVID population, and we believe that evidence of the extra diagnostic value of HRCT is accumulating (1, 4–7). Our experiences differ from those by Turner et al. who question whether the supplementary value of HRCT outweighs the risk of radiation, as complications such as bronchiectasis can easily be diagnosed using alternative techniques. For example, persistent sputum production with positive microscopy was reported to correlate well with HRCT evidence of bronchiectasis in patients with CVID. However, in the referred retrospective study, sputum was only available from 25 of the 47 patients (53%), and the incidence of bronchiectasis was not

described in the patient population without productive cough (8). The majority of studies on pulmonary complications in CVID are retrospective and relate to selected patients with CVID undergoing HRCT for clinical purposes, thus carrying a high risk of selection bias. Also, Turner et al. do not mention parenchymal and interstitial lung disease (9, 10), which is common in CVID, even in childhood (2). It is important to distinguish interstitial lung disease from airway disease, as interstitial lung disease is associated with decreased survival (11) and requires a different, immunosuppressive treatment regimen (12). In conclusion, HRCT is indispensable for accurate detection of pulmonary complications in (pediatric) patients with CVID and in our experience adds value to other tests.

Third, for HRCT to be able to improve outcome, effective treatment is needed. Turner et al. are correct in pointing out that optimal treatment has not been defined. The relatively high incidence of chronic lung disease in adult CVID, however, underlines that improved prevention and treatment of pulmonary complications is urgently needed. To prevent progression of structural lung changes, literature suggests that prophylactic antibiotics and high through levels of immunoglobulin are beneficial (9, 13), although robust randomized-controlled trials defining optimal therapy are not available. Interstitial lung disease (ILD) requires different therapy and usually responds well to immunosuppression. In our cohort, nodules on HRCT disappeared after steroid treatment, suggesting that ILD is still reversible at an early stage. It remains unclear whether treatment of asymptomatic lesions is advisable to prevent further progression. Additionally, ILD appears to be initially asymptomatic, which implies that screening of patients at risk (shown by the presence of other autoimmune phenomena and severely affected lymphocyte subsets; own unpublished observations) could facilitate early detection and henceforth prevent progression of CVID-related ILD.

In conclusion, HRCT performed by using low-dose HRCT can vividly and reproducibly demonstrate CVID-related airway and interstitial complications, even in asymptomatic patients with normal chest radiograph and lung function. To develop evidence-based diagnostic and therapeutic protocols for CVID, much work remains to be done. We agree that at present, there is insufficient evidence to recommend a yearly HRCT scanning protocol for all (asymptomatic) pediatric patients with CVID. Given the low prevalence of CVID, multi-center studies, e.g., as currently initiated by the Chest CT in Antibody Deficiency Group (5, 14) will be needed.

Current management of pulmonary complications in CVID requires a multitude of clinical skills and expertise, and the indication for HRCT scanning is currently included in this expert judgment for an individual patient. Collaborative studies that include HRCT will lead to more structural and evidence-based diagnosis and treatment of CVID-related pulmonary complications.

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References

1. Touw CM, van de Ven A, de Jong PA, et al. Detection of pulmonary complications in common variable immunodeficiency. *Pediatr Allergy Immunol* 2010; **21**: 793–805.
2. van de Ven AAJM, van Montfrans JM, Terheggen-Lagro SW, et al. A CT scan score for the assessment of lung disease in children with common variable immunodeficiency disorders. *Chest* 2010; **138**: 371–9.
3. Aghamohammadi A, Moin M, Kouhi A, et al. Chromosomal radiosensitivity in patients with common variable immunodeficiency. *Immunobiology* 2008; **213**: 447–54.
4. Cunningham-Rundles C, Bodian C. Common variable immunodeficiency: clinical and immunological features of 248 patients. *Clin Immunol* 1999; **92**: 34–48.
5. Kainulainen L, Varpula M, Liippo K, Svedstrom E, Nikoskelainen J, Ruuskanen O. Pulmonary abnormalities in patients with primary hypogammaglobulinemia. *J Allergy Clin Immunol* 1999; **104**: 1031–6.
6. Manson D, Reid B, Dalal I, Roifman CM. Clinical utility of high-resolution pulmonary computed tomography in children with antibody deficiency disorders. *Pediatr Radiol* 1997; **27**: 794–8.
7. Newson T, Chippindale AJ, Cant AJ. Computed tomography scan assessment of lung disease in primary immunodeficiencies. *Eur J Pediatr* 1999; **158**: 29–31.
8. Thickett KM, Kumararatne DS, Banerjee AK, Dudley R, Stableforth DE. Common variable immune deficiency: respiratory manifestations, pulmonary function and high-resolution CT scan findings. *QJM* 2002; **95**: 655–62.
9. Busse PJ, Farzan S, Cunningham-Rundles C. Pulmonary complications of common variable immunodeficiency. *Ann Allergy Asthma Immunol* 2007; **98**: 1–8.
10. Park JE, Beal I, Dilworth JP, Tormey V, HADDOCK J. The HRCT appearances of granulomatous pulmonary disease in common variable immune deficiency. *Eur J Radiol* 2005; **54**: 359–64.
11. Bates CA, Ellison MC, Lynch DA, Cool CD, Brown KK, Routes JM. Granulomatous-lymphocytic lung disease shortens survival in common variable immunodeficiency. *J Allergy Clin Immunol* 2004; **114**: 415–21.
12. Kim R, Meyer KC. Therapies for interstitial lung disease: past, present and future. *Thorax* 2008; **2**: 319–38.
13. Lucas M, Lee M, Lortan J, Lopez-Granados E, Misbah S, Chapel H. Infection outcomes in patients with common variable immunodeficiency disorders: relationship to immunoglobulin therapy over 22 years. *J Allergy Clin Immunol* 2010; **125**: 1354–60.
14. <http://www.chest-ct-group.eu>. 2010: Ref Type: Generic