

CORRESPONDENCE

Should bronchoscopy be advocated to study airway remodelling and inflammation in adults with cystic fibrosis?

We read with interest the article by Regamey *et al* who reviewed the relationship of airway remodelling to inflammation in cystic fibrosis (CF).¹ The authors suggested that endobronchial biopsy studies are useful for studying airway remodelling in CF. Four studies were conducted in 91 children who underwent bronchoscopy for clinical reasons or annual routine surveillance. These studies confirmed that airway remodelling in CF appeared early in life and this is indeed of more than academic interest. However, while the authors have previously shown and claimed that biopsy procedures are safe in infants and small children, the ethics of the procedure in children have been discussed by others.²

We would like to raise concerns about the procedure in adults as well. From 1987 to 2011, Regamey *et al* found five independent studies in which bronchial biopsies were performed in only 25 adults with CF.¹ Although no major complications were reported in this small number of patients, several issues limit the use of endobronchial biopsies in adults with CF. Bronchoscopy is not the usual practice for microbiological assessment in adults with CF, in whom sputum examination is recommended.³ In a study comparing bronchoalveolar lavage (BAL) with induced sputum in 11 adults with CF having well-preserved lung function, the authors found no benefit of BAL for studying inflammatory cells and mediators.⁴ Because three subjects experienced prolonged fever and/or hypoxaemia, the authors concluded that BAL cannot be recommended in the research setting.⁴ As bronchoscopy is not part of routine practice in adults with CF, if performed, it should be done mostly as a research procedure in which risks and benefits are to be weighed carefully: CF is a progressive disease in which structural abnormalities increase with age.⁵ Enlarged bronchial vessels immediately adjacent to the airway epithelium are found in adults with CF (see figure 1). Rupture of these abnormal bronchial blood vessels into the airway lumens could be responsible for major haemoptysis, which occurs mostly in adults with CF. Although no major haemoptysis following bronchial biopsy has been reported, we suggest that the risk of biopsy-related bleeding is increased in adults with CF.

In conclusion, bronchoscopy with BAL or bronchial biopsies is an invasive procedure that is not recommended in clinical practice and may result in serious complications in adults with CF, especially in subjects with advanced lung disease. We suggest that a cautious approach is necessary when

considering studies using BAL or bronchial biopsies in adults with CF.

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Authors' response

We thank Burgel and colleagues for their valuable comments.¹ We agree that a cautious approach should be adopted when considering the use of bronchoscopy and biopsy in cystic fibrosis (CF) research. As stated in our review article,² we have confirmed the safety of endobronchial biopsy in children and infants with CF. Reassuringly, we have encountered no complications even in children with advanced lung disease. We advocate the use of endobronchial biopsy to investigate mechanisms of airway remodelling events and their relationship to infection and inflammation in children, but claim no experience of bronchoscopy in adult CF. It would be inappropriate for us to comment on the role of bronchoscopy in adults.

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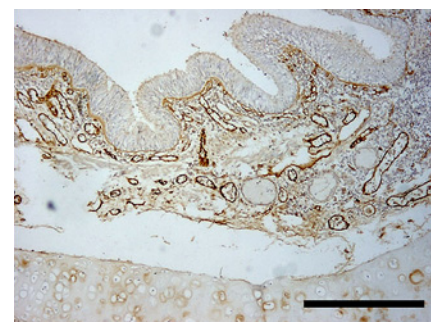


Figure 1 Representative photomicrograph demonstrating bronchial vascular remodelling in a cartilaginous airway obtained at transplantation from an adult with cystic fibrosis. A formalin-fixed paraffin embedded section was immunostained with an antibody to the endothelial marker von Willebrand factor. Numerous enlarged and tortuous airway blood vessels (brown colour) are found immediately adjacent to the airway epithelium. Bar=200 µm.

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The cloud of pulmonary embolism during COPD exacerbation

We read with great interest the paper of Chang *et al*,¹ published recently in *Thorax*. We totally agree with the fact that 'cardiac involvement may be an important determinant of prognosis in COPD exacerbations'. In their study, Chang *et al* found that patients presenting with COPD exacerbation (defined as dyspnoea, cough or sputum purulence, respiratory failure— $\text{Po}_2 < 60$ mm Hg or $\text{Pco}_2 > 45$ mm Hg—or change in mental status due to COPD) experience a worse prognosis if they also have high levels of troponin T and/or NT-proBNP.

However, a potential important confounding factor may explain a part of their results: undiagnosed pulmonary embolism (PE), mimicking (or induced by) COPD exacerbation. Troponin and BNP are factors associated with poor prognosis in PE.² COPD is associated with an increased risk of deep venous thrombosis and PE (particularly during exacerbation) and with an increased risk of fatal PE.³ In particular, COPD is associated with increased risk of death from undiagnosed PE.⁴

The real incidence of PE during exacerbation of COPD is not clearly known, ranging from 1.5% to 24.7%⁵ corresponding to the incidence of elevated troponin and BNP, as noted by Chang *et al* in their cohort. Therefore, it would be of great interest if Chang *et al* could provide us some precise answers:

- ▶ In how many of the 250 patients a PE has been evoked and/or eliminated?
- ▶ How many patients were under efficient anticoagulant drugs at inclusion?
- ▶ How many patients received thromboprophylaxis, as a significant number of patients included presented other PE risk factors such as malignancy or cerebrovascular diseases?

Because of reserved prognosis of COPD patients with PE, and of the availability of preventive and curative specific drugs, COPD patients admitted with exacerbation and with abnormal cardiac biomarkers may require a PE screening and effective thromboprophylaxis if PE has been ruled out.

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Authors' response

We thank Bertoletti and colleagues for raising the important issue of pulmonary embolism (PE) in the exacerbation of chronic obstructive pulmonary disease (COPD).¹ Although we did not routinely investigate for PE in our cohort, we excluded any patients with suspected or confirmed PE from the study.² Unfortunately, it is difficult to detect thromboembolic events in this population and it is possible that we included some patients with subclinical pulmonary emboli. It is also plausible that this contributed to the association between elevated cardiac biomarkers and mortality. However, we think that this is unlikely to be the only mechanism.

Thromboprophylaxis was administered to some patients during their admission depending on their immobility and other risk factors, but this would not have influenced the NT-proBNP or troponin T results obtained on presentation. We did not collect information on pre-existing anticoagulation therapy on admission to the study.

Further research into the mechanism linking elevated cardiac biomarkers and mortality in COPD exacerbation is needed. We agree with Bertoletti and colleagues that investigating the contribution of concurrent PE is important, as this is something that can be treated.

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Thorax 2011;**66**:A128–A129 doi:10.1136/thoraxjnl-2011-201054c.151. P151 Cost of pulmonary rehabilitation is offset by reduction in healthcare utilisation. The author list and author affiliations for this poster should read: ¹ S Kibe, ¹ D Ford, ² S Hart. 1 Scarborough General Hospital, Scarborough, UK; 2 Castle Hill Hospital, Hull, UK.

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Thorax 2011;**66**:A133–A134 doi:10.1136/thoraxjnl-2011-201054c.163. P163 Factors influencing histological confirmation of diagnosis in lung cancer patients. The author list for this poster should read: S Chandramouli, M Cheema, J Corless. Wirral Lung Unit, Arrowe Park Hospital, Wirral CH49 5PE, UK.

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Thorax 2011;**66**:A162–A163 doi:10.1136/thoraxjnl-2011-201054c.233. P233 Judicious use of oximetry can help deliver cost effective sleep service. The author list and affiliation for this poster should read: C L Collins, B Balakrishnan, J Madieros, M Sovani. Queen's Medical Centre, Nottingham University Hospitals, Nottingham, UK.

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Thorax 2011;**66**:A140 doi:10.1136/thoraxjnl-2011-201054c.179. P179 The changing numbers and indications of mediastinoscopy procedures performed following the introduction of endobronchial ultrasound at a UK tertiary centre. The author list and affiliations for this poster should read: ¹ M Bakir, ² R Breen, ² A Quinn, ² J King, ¹ G Santis. 1 Kings College London, London, UK; 2 Guy's and St Thomas' NHS Foundation Trust, London, UK.