CORRESPONDENCE

Reasons for heterogeneous change in LCI in children with cystic fibrosis after antibiotic treatment

With great interest we read the paper of Horsley *et al*.[1] In their prospective observational study they showed significant improvement in indices of ventilation capacity (spirometry) and ventilation heterogeneity (multiple-breath washout (MBW)) after a course of intravenous antibiotics in subjects with cystic fibrosis (CF). There was considerable heterogeneity of lung clearance index (LCI) response as observed previously.[2] Here we aim to disentangle underlying physiological mechanisms of this heterogeneous response.

We assessed changes of lung function parameters before and after 23 courses of intravenous antibiotics in 19 children with CF aged 5–18 years. Children performed arterial blood oxygen measurement, nitrogen MBW,[3 4] body plethysmography and spirometry.

We observed a very heterogeneous change in LCI, with a mean decrease from 13.2 to 12.9, (p=0.41), and clear improvement in 7 of 23 subjects (>1 lung turnovers, see online supplementary figure S1). Spirometric indices improved significantly (see online supplementary table S1).

We found that change in LCI and moment ratio is best explained by change in functional residual capacity from MBW (FRC_{MBW}) minus residual volume (RV) (figure 1, see online supplementary figure S2). To our knowledge there is currently no established expression for this parameter.

In multivariable regression analysis, change of FRC_{MBW}—RV and ventilation homogeneity of conductive airways (Scond) explained 58% variability of delta LCI (R^2, see online supplementary table S2). These results suggest that improvement of LCI after antibiotic treatment in this patient group can be explained by: less secretion and obstruction (better ventilation of conductive airways=lower Scond), better ventilated lung units (net increase of expired tracer gas=FRC_{MBW}) and less hyperinflation (lower RV). Depending on the dominating effect and the resulting time constant of overall ventilated lung units,[2] LCI will change accordingly in the individual, explaining heterogeneous results.

The picture for moment ratio change is comparable, but understandably more influenced by peripheral ventilation (Sacin) (see online supplementary table S3 and figure S2).

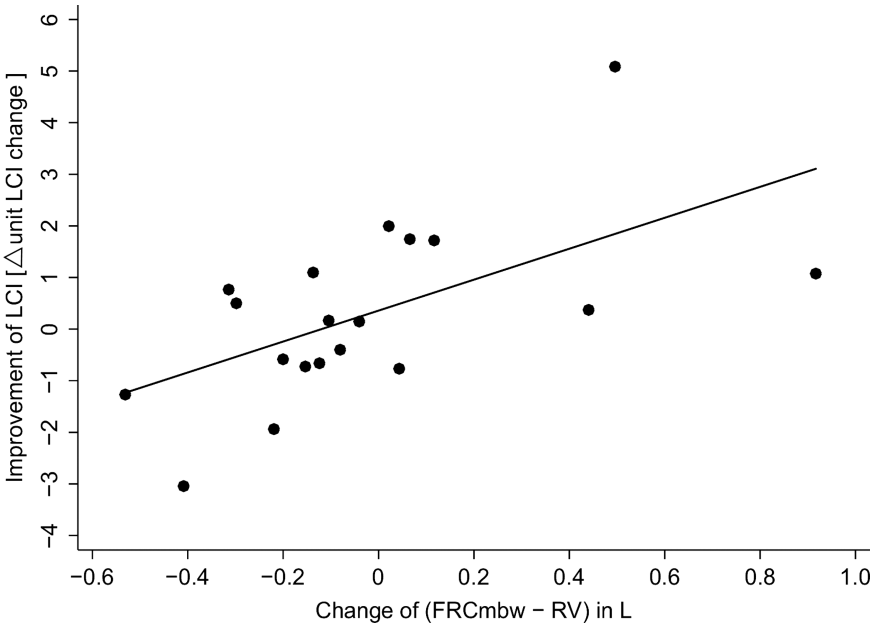

Figure 1 Association of lung clearance index (LCI) improvement and change in FRC_{MBW}—RV. Improvement of LCI (Δ LCI before minus after treatment) and change of functional residual capacity from nitrogen multiple-breath washout (FRC_{MBW}) minus residual volume (RV) from body plethysmography after 19 antibiotic courses in children with cystic fibrosis.

Change in abnormal LCI remains complex and is determined by several components contributing to overall ventilation heterogeneity, generated at different levels of the lung. We speculate that in severe CF lung disease airway collapse might hamper decrease of RV and consequently improvement of LCI. Thus, depending on the magnitude of reversibility of the single components, LCI seems to be a marker suited to monitor changes better [5] or less good in the course of CF lung disease.

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