Specific ventilation inequality and dead space components of lung clearance index in patients with asthma and cystic fibrosis

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**Background**

Lung clearance index (LCI) is a widely reported marker of gas mixing inefficiency within the airways that is derived using the multiple breath inert gas washout (MBW) technique. We developed two novel parameters, LCI$_{vent}$ and LCI$_{ds}$, to reflect the components of increased LCI due to (i) unequal convective ventilation between relatively large lung units, and (ii) increased respiratory dead space, respectively. We hypothesised that these parameters would be repeatable, would effectively discriminate between healthy controls and patients with asthma and cystic fibrosis (CF), and would distinguish between different sub-phenotypes of these diseases.

**Methods**

Washout data from sixty-six healthy control subjects, seventy-four patients with asthma, and forty-one patients with CF were fitted to a two-compartment model of gas mixing, and the parameters LCI$_{vent}$ and LCI$_{ds}$ were calculated.

**Results**

LCI$_{vent}$ and LCI$_{ds}$ were markedly elevated in patients with CF, and mildly elevated in patients with asthma, compared to controls, as illustrated in Figure 1. LCI$_{ds}$ was significantly raised in CF patients with chronic *P. aeruginosa* colonisation compared to those without chronic colonisation (1.49 vs 1.34, p = 0.004). LCI, LCI$_{vent}$ and LCI$_{ds}$ were significantly raised in CF patients with a severe genotype compared to those with a mild genotype. No significant differences were observed between any of the asthma sub-phenotypes (severe vs non-severe, poorly-controlled vs not poorly controlled, exacerbator vs non-exacerbator, and eosinophilic vs non-eosinophilic) with respect to any MBW parameter. The intraclass correlation
coefficients of $LCI_{vent}$ and $LCI_{ds}$ exceeded 0.85 in the asthma and CF groups, and 0.60 in controls.

**Conclusion**

The novel parameters $LCI_{vent}$ and $LCI_{ds}$ are repeatable and effectively discriminate between sub-phenotypes of CF, although their utility in asthma is currently unproven. Further studies are required to determine their utility in other airway diseases such as chronic obstructive pulmonary disease, to investigate their role as outcome measures in clinical trials, and to delineate their structural correlates.