Lung Clearance Index (LCI) Identifies Severe Ventilation Inhomogeneity and Gas Trapping in Obstructive Lung Disease with Low Total Lung Capacity

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Background

Obstructive lung diseases are characterized by heterogeneous patterns of airway dysfunction and ventilation, which can be quantified using Lung Clearance Index z-score (LCI_z). However, Total Lung Capacity z-score (TLC_z) should not be measured with multiple-breath washout (MBW-N2), because MBW does not reliably determine absolute lung volumes and may underestimate TLC. Therefore, combining LCI_z with TLC_z may better distinguish hyperinflated (emphysematous-like) from apparently restricted (airway closure-prone) phenotypes than spirometry or MBW_N2 alone.

Methods

A cohort of 11,309 subjects from A.O.U. Policlinico Umberto I – Sapienza Università di Roma performed spirometry and nitrogen multiple-breath washout (MBW-N2). Then, they were classified by airflow obstruction defined as FEV_1/FVC z-score < −1.645. They also were stratified according to TLC_z into three groups: Restricted (below the lower limit of normal, LLN), Normal, and Hyperinflated (above the upper limit of normal, ULN). Ventilation inhomogeneity (LCI_z) was compared across these groups.

Results

TLC_z and LCI_z showed a bimodal pattern across the FEV_1/FVC z-score spectrum. Among obstructed subjects, those with low measured TLC had the greatest ventilation inhomogeneity, with an LCI_z of 7.13, compared with 3.67 in hyperinflated subjects. This apparent low-volume phenotype may not reflect anatomical restriction, but rather severe gas trapping and airway closure, resulting in large volumes of trapped gas that are poorly accessible to washout and therefore not captured by MBW-derived lung volume measurements. In contrast, hyperinflated subjects showed lower LCI_z, consistent with less severe ventilation inhomogeneity despite increased lung volumes. Thus, a reduced TLC_z in the presence of obstruction may represent a functional "micro-lung", reflecting severe disventilation and substantial unmeasured trapped volume.

Conclusion

In obstructive lung disease, LCI_z combined with TLC_z may provide a more informative physiological characterization. Markedly increased LCI_z in subjects with apparently reduced TLC may identify severe gas trapping rather than true restriction, whereas hyperinflated phenotypes show comparatively lower ventilation inhomogeneity. Thus, a "smaller" measured lung volume in an obstructed patient may signals critical unmeasured volume and maximum ventilatory impairment.

References

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