WS7.1 LCI measured with nitrogen multiple breath washout is higher than mass spectrometer SF6 washout in children with cystic fibrosis

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Objectives: The lung clearance index (LCI) obtained from SF6 multiple breath washout (MBW) is a more sensitive index of airway dysfunction than spirometry in cystic fibrosis (CF) [1]. LCISF6 values are lower and show stronger agreement between laboratories than historical LCI_{N2} using conventional N2 analyzers. We compared FRC and LCI results obtained using both a mass spectrometer SF6 MBW and a new indirect N2 MBW system (Exhalyzer D, Eco Medics AG) in CF children. The results are expressed as mean(SD) if not stated otherwise.
Methods: 19 children (13M) median age 10.0 y, (range 6.4–16.5y), with median FEV1.0 of 92% (range 67–121%) performed a MBW SF6, N2 and body plethysmography (FRCp) during the same day when in stable condition. LCI_{N2} and LCI_{SF6} correlated significantly (R^2 0.642, $p = 0.00006$) but LCI_{N2} and FRC_{N2} was significantly higher than LCI_{SF6} and FRC_{SF6}, being 8.87 (2.34) vs 7.31(1.48), $p = 0.0004$ and 1.629 (0.569) litres vs 1.416 (0.495), $p = 0.006$ respectively. FRCp was different to FRC_{SF6} 1.496 (0.364) litres, $p = 0.041$ but not to FRC_{N2}. Compared to healthy controls (ULN_{N2} 7.33) only seven children had a LCI_{N2} below ULN_{N2}).
Conclusions: Compared to the SF_6 method, the newN2 MBW method gives FRC_{N2} values closer to the FRCp values. The N2 MBW method also results in a higher LCI. The cause for this unknown but two possible mechanisms may be a more complete washin phase and the production of body nitrogen during the washout. Since the ULN is similar in healthy for both methods, N2 MBW might be even more sensitive than SF6 MBW to detect early CF lung disease.

Reference(s)

[1] Gustafsson et al. Eur Respir J. 2003; 22: 972–9.

WS7.2 Lung clearance index: comparison of helium and nitrogen washout

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Objectives: Lung clearance index (LCI) is a sensitive measure of small airway function, the site of early CF lung disease. LCI can be determined using different inert gasses. Therefore, we wanted to compare the discriminate validity of LCI using helium washout (LCI_{He}) versus LCI using nitrogen washout (LCI_{N2}).
Methods: LCI was measured in healthy children (HC; $n = 59$ for N_2 and $n = 65$ for He) and children with CF (CF; $n = 62$ for N_2 and $n = 65$ for He) with the Ecomedics set-up using either He or N_2 washout. At least 2 acceptable tests with FRC within 10% of smallest value were required. The CF clinical score (CFCS) (Kanga) was determined by a physician blinded to LCI result.
Results: Test success rate nor coefficient of variation (CV) differed between LCI_{He} and LCI_{N2}, nor between HC and CF (overall success rate for LCI 84%, mean CV 5.6%). Both LCI_{He} and LCI_{N2} discriminated between HC and CF but the range of values obtained in CF was larger for LCI_{N2}. AUC in ROC analysis was 0.866 for LCI_{N2} and 0.804 for LCI_{He}. LCI_{N2} correlated with FEV_1% pred ($r = -0.729$, $p < 0.001$) as did LCI_{He} ($r = -0.334$, $p = 0.014$). LCI_{N2} correlated with CFCS ($r = 0.608$, $p < 0.001$), but LCI_{He} did not ($p = 0.061$). There was a close correlation ($r = 0.723$, $p < 0.001$) between LCI_{He} and LCI_{N2}, but LCI_{N2} was systematically higher than LCI_{He} and this difference increased as LCI increased.
Conclusions: Both LCI_{He} and LCI_{N2} discriminate between CF and HC, but LCI_{N2} has a greater discriminate validity than LCI_{He} since the range of values obtained in CF, but not in HC, is higher. There is a close correlation between LCI_{He} and LCI_{N2} but values differ and only LCI_{N2} correlates with clinical score. Therefore, both systems are not interchangeable.

WS7.3 Relationships between lung clearance index (LCI), patient reported symptoms and health related quality of life (HRQoL) in CF

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Objective: To assess the relationship between LCI, patient reported symptoms and HRQoL.
Methods: Stable patients recruited from adult & paediatric Belfast CF centres completed age appropriate versions of CFQ-R. Domain scores range 0–100, with higher scores indicating better function. Participants completed three MBW tests, using 0.2%SF_6 and a modified Innocor^{TM}device. Spirometry was performed to ATS/ERS standards. Patients were grouped according to lung function results. The Kruskal-Wallis and Jonckheere-Terpstra tests were used assess for differences between groups and trends.
Results: Data was collected for 39 patients (22M:17F), age mean(SD) 18.8(11.3) range 6–49 yrs. $FEV_1$86.4(17.9)%pred (normal >80%pred). Mean (SD) LCI 8.2 (2.1) (normal <7.4). LCI correlated negatively with FEV_1%pred ($r = -0.57$) $p < 0.0001$. A comparison of LCI, FEV_1 values and CFQ-R domains scores are displayed in table 1.

Comparison of LCI, FEV1 values and CFQ-R domains

Group	Proportion of patients	Median CFQ-R score (IQR)		
		Respiratory symptoms domain	Treatment burden domain	Body image domain
Co-normal LCI & FEV1	38%	75.0 (16.7)	88.9 (22.2)	100.0 (11.1)
Abnormal LCI with normal FEV1	21%	75.0 (17.4)	83.3 (19.5)	100.0 (11.1)
Normal LCI with abnormal FEV1	10%	80.6 (26.4)	66.7 (25.0)	100.0 (8.3)
Co-abnormal LCI & FEV1	31%	66.7 (27.8)	66.7 (33.3)	66.7 (33.3)

No significant differences were found across groups for respiratory symptoms ($p = 0.132$) or treatment burden ($p = 0.06$) but differences for body image were significant ($p = 0.014$). Significant trends across the order of the groups (co-normal to co-abnormal) was observed in the treatment burden ($p = 0.013$) and body image ($p = 0.008$) domains. No other differences or trends where observed with any other domains of CFQ-R.
Conclusions: Results show that there is a pattern in some HRQoL domains dependent on severity of lung function as measured by LCI and FEV_1.

WS7.4 Does lung clearance index predict time to pulmonary exacerbation?

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Objectives: Lung Clearance Index (LCI) is a sensitive measure of small airway function, the site of early CF lung disease. In cross sectional studies, abnormal LCI values correlate to bronchiectasis detected on chest CT scan. In short term studies LCI is responsive to intervention. However, more longitudinal studies are required to prove the prognostic value of LCI. The objective of this study was to evaluate the relation between baseline LCI value and time to pulmonary exacerbation.
Methods: LCI was measured in 54 children with CF using the Ecomedics nitrogen washout set-up. Treating physicians were blinded to LCI result. Patients were followed during the subsequent year and time to pulmonary exacerbation (TtoPE) as defined by Fuchs (increase in symptoms and need for IV antibiotics) was registered.
Results: At baseline mean age was 11.6 yrs (SD 4.2), mean FEV_1% pred 91.5% (SD 17.0) and mean LCI 11.8 (SD 3.7). TtoPE was significantly shorter in subjects with LCI above upper limit of normal (ULN) ($n = 34$) compared to patients with normal LCI ($n = 20$) (log rank test $p = 0.020$). When patients were divided in quartiles according to baseline LCI, TtoPE was significantly shorter in subjects in increasing LCI quartiles (log rank test for trend $p < 0.001$). When only patients with FEV_1 >80% were considered, TtoPE was still shorter in the group with LCI above ULN ($n = 25$) compared to patients with normal LCI ($n = 18$) (log rank test $p = 0.049$).
Conclusions: LCI predicts TtoPE, also when only the subgroup of children with FEV_1 above 80% is considered.