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

A. Lindblad1, B. Houltz2, M. Rosberg3, L. Bergh2, P. Gustafsson4. 1 Sahlgrenska University Hospital, Pediatrics, Gothenburg, Sweden; 2 Sahlgrenska University Hospital, Clinical Physiology, East Hospital, Gothenburg, Sweden; 3 Queen Silvia Childrens Hospital, Paediatric Clinical Physiology, Gothenburg, Sweden; 4 Central Hospital, Pediatrics, Skicde, Sweden

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]. LCI SF6 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 (Exalyzer 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 yrs. (range 6.4−16.5y) with median FEV1 of 92% (range 67−121y) performed a MBW SF6, N2 and body plethysmography (FRCP) during the same day when in stable condition. LCI N2 and LCI SF6 correlated significantly (R2 0.642, p=0.00006) but LCI N2 and FRCP N2 was significantly higher than LCI SF6 and FRCP SF6, being 8.73 (1.44) vs 7.31 (1.46), p=0.0004 and 1.069 (0.590) litres vs 1.33 (0.951), p=0.006 respectively. FRCP was different to FRCSF6 1.496 (0.364) litre but p=0.041 but not to FRCPSF6. Compared to healthy controls (ULN N2 7.33) only seven children had a LCI N2 below ULN N2.

Conclusions: Compared to the SF6 method, the new N2 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)

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

J. Ophoff1, E. Vermuele1, M. Proesmans1, K. De Boeck1. 1 University of Leuven, Pediatric Pulmonology, Leuven, Belgium

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 (LCHₑ) versus LCI using nitrogen washout (LCIₑN₂).

Methods: LCI was measured in healthy children (HC, n=59 for N₂ and n=65 for He) and children with CF (CF; n=62 for N₂ and n=65 for He) with the Ecomedics set-up using either He or N₂ 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 LCHₑ and LCIₑN₂, nor between HC and CF (overall success rate for LCI 84%, mean CV 5.6%). Both LCHₑ and LCIₑN₂ discriminated between HC and CF but the range of values obtained in CF was larger for LCIₑN₂. AUC in ROC analysis was 0.866 for LCIₑN₂ and 0.804 for LCHₑ, LCIₑN₂ correlated with FEV₁% pred (r=−0.729, p<0.001) as did LCHₑ (r=−0.334, p=0.014). LCIₑN₂ correlated with CFCS (r=0.608, p<0.001), but LCHₑ did not (p=0.061). There was a close correlation (r=0.723, p<0.001) between LCHₑ and LCIₑN₂, but LCIₑN₂ was systematically higher than LCHₑ and this difference increased as LCIₑ increased.

Conclusions: Both LCHₑ and LCIₑN₂ discriminate between CF and HC, but LCIₑN₂ has a greater discriminate validity than LCHₑ since the range of values obtained in CF, but not in HC, is higher. There is a close correlation between LCHₑ and LCIₑN₂ but values differ and only LCIₑN₂ 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

K. O’Neill1, T. Johnston1, M. Tunney1, J.S. Elborn1, J.M. Bradley2. 1 Queen’s University Belfast. CF & Airways Microbiology Research Group. Belfast, United Kingdom; 2 University of Ulster, Health and Rehabilitation Sciences Research Institute, Belfast, United Kingdom

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%SF₆ and a modified Innocor™ 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 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. FEV₁ 86.4(17.9)%pred (normal >80%pred). Mean (SD) LCI 8.2 (2.1) (normal <7.4). LCI correlated negatively with FEV₁%pred (r=−0.573 p < 0.0001). A comparison of LCI, FEV₁ values and CFQ-R domains scores are displayed in table 1.

Comparison of LCI, FEV₁ values and CFQ-R-R domains are displayed

<table>
<thead>
<tr>
<th>Group</th>
<th>Proportion of patients</th>
<th>Median CFQ-R score (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co-normal LCI &amp; FEV₁</td>
<td>38%</td>
<td>75.0 (16.7)</td>
</tr>
<tr>
<td>Abnormal LCI with normal FEV₁</td>
<td>21%</td>
<td>75.0 (17.4)</td>
</tr>
<tr>
<td>Normal LCI with abnormal FEV₁</td>
<td>10%</td>
<td>80.6 (26.4)</td>
</tr>
<tr>
<td>Co-abnormal LCI &amp; FEV₁</td>
<td>31%</td>
<td>66.7 (27.8)</td>
</tr>
</tbody>
</table>

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 FEV₁.

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

E. Vermuele1, J. Ophoff1, M. Proesmans1, K. De Boeck1. 1 University of Leuven, Pediatric Pulmonology, Leuven, Belgium

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 relationship between baseline LCI values 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 (ToPE) as defined by Ehrlich (increase in symptoms and need for IV antibiotics) was registered.

Results: At baseline mean age was 11.6yrs (SD 4.2), mean FEV₁%pred 91.5% (SD 17.0) and mean LCI 11.8 (SD 3.7). ToPE 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, ToPE was significantly shorter in subjects in increasing LCI quartiles (log rank test for trend p<0.001). When only patients with FEV₁ >80% were considered, ToPE 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 ToPE, also when only the subgroup of children with FEV₁ above 80% is considered.