Lung Clearance Index (LCI) predicts time to pulmonary exacerbation in children with CF

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Lung Clearance Index (LCI) is a promising endpoint for use in CF clinical trials. Since correlation with validated clinical endpoints has not yet been established, we investigated the association between baseline LCI and risk of respiratory tract exacerbations (RTE) in children with CF.

Methods: During a prospective observational study, baseline LCI (N2 washout), FEV1 and CFQR respiratory domain (CFQRres) were measured. RTE, defined as an increase in respiratory symptoms treated with IV antibiotics, were recorded during one year. Whether baseline LCI predicted RTE was assessed with a Poisson regression model and Kaplan–Meier plots. LCI z-scores were calculated from values in 57 healthy children.

Results: In 63 children with CF (median age 12.4 years, range 5–19), mean LCI z-score was 5.3 (SD 4.6) and mean FEV1 z-score –0.9 (SD 1.3). CFQRres correlated with LCI (R = –0.43, p < 0.001), but not with FEV1 (R = 0.24, p = 0.051). In the 53 patients with a normal FEV1, CFQRres and LCI were still correlated (R = –0.44, p < 0.002).

During the 12 months follow up, 25 patients (40%) experienced 47 RTE. LCI and FEV1 were predictors of RTE. Time to first RTE decreased with worsening LCI quartiles (Log Rank test, p < 0.001). Similarly, compared to the quartile with the lowest LCI, yearly RTE rate ratio in increasing LCI quartiles was 2.8 (95%CI 1.6–13.9, p = 0.205), 4.7 (95%CI 1.0–21.4, p = 0.046) and 13.6 (95%CI 3.2–57.0, p < 0.001). In the group with normal FEV1, LCI but not FEV1 z-score was still a predictor of RTE.

Conclusion: Baseline LCI predicts the risk of RTE in children with CF, even in the subgroup with normal FEV1. These data further support the use of LCI as a surrogate outcome in CF clinical trials.

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