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Title: The lung clearance index correlates with markers of pulmonary deterioration in patients with cystic fibrosis

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Body: Background and aim: Lung clearance index (LCI) is obtained by multiple breath washout (MBW) and is a sensitive marker of early lung disease in patients with cystic fibrosis (CF). LCI is increasingly used as an endpoint in clinical trials, although the knowledge of its prognostic value is limited. We aimed to show whether LCI is correlated with clinical markers of lung disease. Methods: In this prospective study 60 patients with CF in clinical stable condition underwent lung function tests, MBW and blood sampling. Infective exacerbations and decline in FEV1 during the study period (mean 3.1years) were recorded, Pearson's correlation coefficients were calculated. Results: 59 Patients completed the study with a mean (range) age of 14.5 (8.9;21.9) years and FEV1%pred 87 (44;136)%.

	FEV1%pred	FEF75%pred	VO2max%pred	pO2	PCO2
LCI	-0.802 (<0.001)	-0.717 (<0.001)	-0.385 (=0.015	-0.671 (<0.001)	0.384 (=0.004)
FEV1%pred		0.851 (<0.001)	0.517 (<0.001)	0.748 (<0.001)	-0.389 (=0.004)
	C-reactive Protein	Fibrinogen	Immunoglobulin G	decline in FEV1%pred	Infective exacerbations requiring iv antibiotics
LCI	0.543 (=0.056)	0.421 (<0.001)	0.585 (<0.001)	0.517 (<0.001)	0.626 (<0.001)
FEV1%pred	-0.449 (<0.001)	-0.351 (=0.009)	-0.569 (<0.001)	-0.534 (<0.001)	-0.540 (<0.001)

the table gives pearson´s correlation coefficients (p in brackets)

Conclusions: LCI and FEV1 both correlate well with clinical status and with known surrogate parameters of CF lung disease. This supports that LCI is a clinical relevant parameter and encourages its use as an endpoint in clinical trials in CF. Abbrevations: FEV1%pred: forced expiratory volume in 1 second percent predicted FEF75%pred: forced expiratory flow at 75 percent forced vital capacity VO2max%pred: maximal oxygen uptake percent predicted.