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Title: Multiple breath washout in bronchiolitis obliterans syndrome following paediatric lung transplantation

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Body: Aim: Bronchiolitis obliterans syndrome (BOS) is a significant cause of morbidity and mortality following lung transplantation. Lung Clearance Index (LCI) measured by multiple breath washout (MBW) detects early structural lung damage in other paediatric obstructive lung disease. The aim was to determine the pattern of LCI values in children with BOS. Methods: Retrospective analysis of MBW and spirometry data from subjects transplanted between 2002-2010 (date of annual MBW testing introduction). BOS staging was defined using published "all age" reference equations. LCI in BOS 0, 0p and 1 were compared. Results: 50/56 (89%) subjects had MBW performed (n=162): mean (SD:range) 3.1 (1.85:1-9) times over a mean (SD: range) follow up 1069 (613: 196-2613) days. Abnormal LCI values (>7.5) were common post transplant (63/114 tests, 55%). LCI was increased in subjects with BOS. All those with persistent LCI>10 (n=8) died from severe BOS. Two distinct BOS patterns were seen: gradual vs. very rapid FEV1 decline. Despite infrequent testing, earlier LCI signal was seen in some (3/8) but not all 8 subjects (e.g. not those with rapid FEV1 decline).

	BOS stage post transplant			
	No BOS	Any BOS	BOS 0p	BOS ≥1
Number of MBW tests	70	46	38	8
LCI	7.34 (5.83-11.13)	7.90 (6.32-14.70)*	7.73 (6.32-13.14)*	12.3 (6.51-14.70)*Φ
LCI > 7.5	33/70 (47.1%)	32/46 (69.5%)	25/38 (65.8%)	7/8 (87.5%)

Data displayed as median (range). p<0.05 vs. *No BOS or ΦBOS 0p

Conclusion: LCI is frequently abnormal post lung transplantation. LCI is significantly elevated in BOS, and appears to increase with BOS severity. An early signal of subsequent outcome may exist but optimal frequency of testing is yet to be determined.