Value of bronchial wall measurements in computed tomography in patients after lung transplantation

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Purpose

To prospectively evaluate the diagnostic value of quantitative airway wall measurements of 3D thin section computed tomography (CT) for the diagnosis of bronchiolitis obliterans syndrome (BOS) following lung transplantation.
Methods and Materials

The prospective study had been approved by the local ethics committee.

Study participants

The study group comprised 90 lung transplant patients who underwent 141 paired thin-section CT and lung function tests. Fifty-three patients were male and 37 female with a mean age of 45 years (range 18-65 years) at time of examination. For 85 patients it was the first transplantation, 5 patients underwent a re-transplantation. 84 patients had a double-lung transplantation and 6 patients received a heart-lung transplantation, none of the patients underwent single-lung transplantation.

Mean time delay between transplantation and CT examination was 11 month (range 5 - 65 month). Twenty-four CT and PFT were performed in patients with clinical diagnosis of BOS. Of these 15 were BOS stage 3, 2 were BOS stage 2 and 7 were BOS stage 1. 126 patients underwent CT examinations and PFT on the same day, in 13 patients the interval was 1 - 2 weeks and in 3 patients it was 3 - 4 weeks.

CT data acquisition

CT examinations were carried out at full inspiration (insp) and full expiration (exp) with a 64 row MDCT (Lightspeed VCT, GE healthcare, Milwaukee, United States) under spirometric control, no intravenous contrast medium was used. The CT data were acquired using 120 kV, 100 mAs, a rotation time of 0.8 s and a pitch of 0.984, the slice collimation during acquisition was 1.25. Data reconstruction yielded 1.25mm slices with an interval of 1mm using a "standard" reconstruction kernel (soft tissue). The field of view (FOV) was adapted to the size of the patient's lung. No separate reconstructions of the right or left lung were performed.

Lung function tests

Pulmonary function tests (PFT) were performed using body plethysmography (BodyScope N, Ganshorn Medizin Electronic. GMBH, Münnerstadt/Niderlauer, Germany) and the measured values were related to the predicted values calculated according to Quanjer et al.. Spirometry was performed according to the guidelines provided by the American Thoracic Society and European Respiratory Society.

Quantification of airway wall parameters
For the automatic quantification of airway wall thickness (WT) and wall area percentage (WA%), dedicated software (MEVIS airway examiner, Fraunhofer MEVIS Bremen, Germany) was applied (figure 1). After fully automatic segmentation of the bronchial tree, a central pathway through the bronchial structures was calculated. WT, and WA% were automatically measured for each cross sectional image perpendicular to the central pathway after segmentation of the wall contours. Areas not appropriate for measurement, i.e. branching points or areas of adherence of bronchial wall and vascular structures, were automatically excluded from measurement. For the quantitative analysis two bronchial branches were chosen: the posterior basal segmental bronchus (B10) of the right lung and the apicoposterior segmental bronchus (B01) of the left lung. The path of a bronchus was divided in anatomical sections following the anatomic branching from lobar, segmental to subsegmental and sub-sub-segmental: each ramification defines the beginning of a new section. Bronchi up to the 7th generation were consistently identified in all scans. More peripheral bronchi up to the 10th generation could not be identified in all scans and were only considered if automatic segmentation was succesful in inspiration and expiration. Only bronchial sections with at least 10 valid measurements were included in the analysis.

Statistical analysis

Statistical tests were performed with PASW statistics (ver. 18.0, SPSS Inc., Chicago, USA, 2006). The Kolmogorov-Smirnov-test was used to test normal data distribution. Correlation of PFT with CT measurements obtained for WT and WA% in in- and expiratory CT scans was tested using Spearman's rank correlation coefficient.

Airway wall parameters of stable lung transplant recipients were compared to those of patients with manifest BOS with independent samples t-test. WA% and WT measured in inspiration were compared to expiratory values using a paired samples t-test. To further evaluate the influence of lung volume on bronchial wall measurements an univariate analysis of variance for WT and WA% in inspiration and expiration corrected for lung volume comparing patients with and without BOS was performed.
Fig. 1: Bronchial wall measurements with MeVis Airway Examiner. A three-dimensional image of the tracheobronchial tree was provided (B) which allowed the selection of the bronchus to be evaluated (yellow border). For visualization, curved multiplanar reformation (D) and cross sectional images perpendicular to the central path were applied (C) with the viewing direction along the bronchial path. The original dataset is shown in (A), the selected bronchus is tagged with a cross line. The location for measurements of the bronchial wall was visualized with a yellow line for the inner and a red line for the outer borderline of bronchial wall (C).

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Results

Airway dimensions

WT was measured in 2,978 bronchial sections (1,784 in inspiratory scans, 1,194 in expiratory scans) and WA% in 2,975 bronchial sections (1,786 in inspiratory scans, 1,189 in expiratory scans). The difference of WT in in- and expiration could be calculated for 1,079 bronchial sections.

WT continuously decreased when moving from central (mean WT insp section 1: 1.76 mm) to peripheral bronchial segments (mean WT insp section 8: 0.81 mm) (table 1). For all segments mean WT and mean WA% were significantly larger (paired t-test) in expiration than in inspiration (p<0.001, table 1, figure 2) except for WT in section 1 (main bronchus).

Correlation of airway wall parameters and lung function parameters

Kolmogorov-Smirnov-test showed that the datasets for bronchial wall measurement and PFT were partially not normally distributed. Thus, Spearman's rank correlation coefficient was used for testing the correlation between CT morphologic and lung function parameters.

Analysis did not find correlations between overall WT, WA% and WTdiff with lung function parameters in in- and expiration (table 2 and table 3).

When analysing the data according to bronchial sections a moderate correlation was found between PEF and the ratio of PEF/PEFpredicted with WT insp in section 10 (table 2) (P<0.05). For all other airway parameters no statistically meaningful correlation with lung function parameters could be found (all r<0.5, table 2 and table 3).

Comparison of airway wall parameters in patients with and without BOS

Twenty-five examinations were performed in patients with clinically manifest BOS in which WT and WA% were measured in 469 bronchial sections. These were compared to WT and WA measurements of 2,509 and 2,506 bronchial sections, respectively, in patients without clinical evidence for BOS.

Mean WT in inspiration was slightly higher in patients with BOS than in patients without BOS (table 4), but the difference did not yield statistical significance. WA% in inspiration in patients with BOS was significantly different from measurements in stable lung transplant recipients in bronchus sections 1, 2, 4, 5 and 7 (table 4). WT and WA% in expiration as well as WTdiff were not significantly different in the two patient groups. WT and WA
% were significantly larger in expiration than in inspiration in patients with and without BOS (table 1).

Lung volumes in inspiration in patients with BOS (mean: 4,903 ml) were lower than in patients without BOS (mean: 5,302 ml), the difference was not significant (p=0.173). Lung volumes in expiration in patients with BOS (mean: 3,178 ml) were significantly larger than in patients without BOS (mean: 2,495 ml, p=0.001). Lung volume difference between inspiration and expiration was significantly smaller in patients with BOS (mean: 1,840 ml) than in patients without BOS (mean: 2,815 ml, p<0.001) (table 5).

Univariate analysis of variance for WA% in expiration revealed a significant influence of lung volume on WA% in most bronchial sections. There was a significant difference of WA% in inspiration in patients with and without BOS if WA% was corrected for lung volume (table 6). However, variability of bronchial wall measurements was high and values for WA% in inspiration for patients with and without BOS overlapped considerably (figure 3). WT in in- and expiration and WA% in expiration did not show significant differences in both groups even if corrected for lung volume.
Fig. 2: Cross sectional images perpendicular to the central path of a segmental bronchus (B10) in a patient without (a+b) and with BOS (c+d) in inspiration (a+c) and expiration (b+d).

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Table 1: Mean airway wall parameters in inspiration and expiration according to bronchial sections.

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Table 2: Spearman’s rank correlation coefficient for WT and WA% in inspiration for universe (all) bronchial sections and divided into bronchial sections (1-10).

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Table 3: Spearman's rank correlation coefficient for WT and WA% in expiration for universe bronchial sections (all) and divided into bronchial sections (1-8).

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Table 4: Mean airway wall parameters in patients without and with BOS and the significance of these groups calculated with the independent samples t-test.

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Table 5: Mean lung volumes in inspiration (lung vol insp) and expiration (lung vol exp) and the difference between inspiration and expiration (lung vol diff) in patients with and without BOS.

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**Table 6:** Univariate analysis of variance for WT and WA% in inspiration and expiration comparing patients with and without BOS corrected for lung volume.

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<th>WA% insp Sig. BOS</th>
<th>WT insp Sig. Vol</th>
<th>WT insp Sig. BOS</th>
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**Fig. 3:** Boxplot showing descriptive statistics for WA% in patients with and without BOS according to bronchial sections. Despite significant differences in WA% between patients with and without BOS there is a high range of values with overlap of both patients groups.

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Conclusion

For the whole patient group, WA% in inspiration without and with correction of underlying lung volume was a significantly larger in patients with BOS as compared to patients without BOS. However, measurements showed a high variability and a considerable overlap which questions the value of WA% as the single morphologic parameter to discriminate between patients with and without BOS.
References


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