493. Endoscopic lung volume reduction: the growing evidence

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The influence of emphysema heterogeneity on the magnitude of benefit following endoscopic thermal vapor ablation (InterVapor™) in patients with heterogeneous emphysema

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Introduction: Endoscopic thermal vapor ablation (InterVapor™) has been demonstrated to induce lung volume reduction through the local delivery of heated water vapor to targeted lung segments. We examined patient subgroups based on emphysema heterogeneity for differential responses.
Methods: Subgroup analysis from a single-arm trial of InterVapor (single upper lobe treatment at 10 cal/g of tissue) in patients with upper lobe predominant emphysema. Inclusion criteria: FEV_1 15%-45% predicted, RV>150%, TLC>100%, 6 minute walk distance (6MWD)>140 m, DLCO>20%. Primary efficacy endpoints: FEV_1 ≥12% or SGRQ ≥-4 units at 6 months. Secondary efficacy: lung volumes (body plethysmography, HRCT), mMRC dyspnea, and 6MWD. Endpoints were analyzed for associations (Pearson correlation) and categorized based on tertiles of heterogeneity index (HI) (lower to upper lobe tissue to air ratio from HRCT).
Results: 44 patients received InterVapor. Demographics: 50% men, age 63 years, FEV_1 0.86 L (31% predicted), SGRQ 59 units, 6MWD 300 m. Results at 6 and 12 months (mean change from baseline):

	HI<1.45 (n=15)		HI 1.45–≤1.90 (n=15)		HI>1.90 (n=14)	
	6 mo	12 mo	6 mo	12 mo	6 mo	12 mo
Lobar reduction (%)	34	31	44	44	66	59
RV (mL)	–203	–88	–311	–304	–753	–559
FEV1 (mL)	119	67	139	94	168	96
FEV1 (%Δ)	16	9	14	10	21	12
mMRC	–0.64	–0.67	–0.93	–0.54	–1.17	–1.36
6MWD (m)	34	2	65	19	40	36
SGRQ (units)	–15	–6	–13	–12	–14	–14

Conclusion: Efficacy from InterVapor for the treatment of heterogeneous emphysema appears to increase with increasing HI (i.e. upper lobe predominance). HI should be considered when projecting the magnitude of benefit after InterVapor.

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Associations among one-year efficacy outcomes following endoscopic thermal vapor ablation (InterVapor™) for heterogeneous emphysema

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Background: The understanding of interactions or associations over the long-term may assist in understanding and predicting changes over time in chronic diseases such as emphysema. The associations among various COPD efficacy endpoints are variable; however, the degree of correlation is often important in examining the consistency of the results across measures not considered redundant.
Objectives: Determine the correlations of improvements in patient-reported outcomes, exercise capacity and BODE score with lung function and lobar volume

reduction (LoVR) measured by CT after 1-year post-InterVapor for heterogeneous emphysema.
Methods: Single-arm trial of InterVapor in patients with upper lobe emphysema. Patient criteria: FEV_1 15% - 45% predicted, age 40-75 years, RV>150%, TLC>100%, 6 minute walk distance (6MWD)>140 m, DLCO>20%, previous pulmonary rehabilitation. Endpoints included: spirometry, body plethysmography, SGRQ, mMRC dyspnea, 6MWD and LoVR (CT). Pearson correlation coefficients were calculated for associations of changes from baseline to 12 months.
Results: 44 patients received InterVapor. Mean age: 63 years, men 50%, FEV_1 0.86 (31% predicted), RV 237% predicted, DLCO 35% predicted, SGRQ 59 units, 6MWD 300 m, mMRC 2.9.

	SGRQ	BODE	mMRC	6MWD
FEV1	–0.37*	–0.67*	–0.47*	0.42*
FVC	–0.26	–0.40*	–0.33*	0.31
RV	0.21	0.54*	0.45*	–0.35*
TLC	–0.02	0.32	0.27	–0.05
FRC	0.15	0.49*	0.41*	–0.34
IC	–0.21	–0.27	–0.23	0.37
LoVR	0.31	0.53*	0.52*	–0.47*

*p<0.05.

Conclusion: Among lung function tests, FEV_1 appeared to correlate the strongest with health outcomes, followed by RV and FRC at one year. The strong correlation of outcomes with LoVR are consistent with the proposed mechanism of action.

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The influence of baseline exercise tolerance on long-term efficacy outcomes following endoscopic thermal vapor ablation (InterVapor™) in patients with heterogeneous emphysema

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Introduction: The NETT noted that baseline exercise tolerance may influence long-term outcomes following lung volume reduction. The association of baseline six minute walk distance (6MWD) to outcomes was examined in a study of endoscopic thermal vapor ablation in patients with heterogeneous emphysema.
Methods: Post hoc subgroup analysis from the Vapor trial, a multicenter single-arm trial of InterVapor (single upper lobe treatment at 10 cal/g) in patients with upper lobe emphysema. Inclusion: FEV_1 15%-45% predicted, RV>150%, TLC>100%, 6MWD>140 m, DLCO>20%, prior pulmonary rehabilitation. Outcomes included spirometry, body plethysmography, lobar volume reduction (LoVR) by HRCT, SGRQ, mMRC dyspnea, and 6MWD. Endpoints were dichotomized based on two thresholds for baseline 6MWD.
Results: 44 patients received InterVapor. Demographics: 50% men, age 63 years, FEV_1 0.86 L (31% predicted), SGRQ 59 units, 6MWD 300 m. Results at 6 and 12 months (mean change from baseline):

	FEV1 (%) 6 / 12 mo	LoVR (%) 6 / 12 mo	6MWD (m) 6 / 12 mo	SGRQ (units) 6 / 12 mo	RV (L) 6 / 12 mo
<300 (n=22)	14.3 / 8.8	–54.0 / –51.6	31.7 / 26.7	–13.7 / –11.6	–0.413 / –0.330
≥300 (n=22)	18.8 / 11.4	–42.2 / –39.2	58.6 / 9.7	–15.7 / –9.6	–0.400 / –0.281
<350 (n=31)	16.5 / 12.6	–45.1 / –46.7	40.6 / 28.6	–14.0 / –11.0	–0.383 / –0.351
≥350 (n=13)	17.5 / 5.5	–51.9 / –41.6	58.7 / –12.7	–16.3 / –9.6	–0.453 / –0.193

Conclusion: Baseline 6MWD was associated with differences that were most prominent with the subsequent 6MWD and SGRQ at 12 months. Other outcomes showed no consistent pattern of association. A bias such as regression to the mean cannot be ruled out in this analysis.

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Chartis evaluation of collateral ventilation versus HRCT assessment, in predicting clinical outcomes following endobronchial valve therapy (EBV) in COPD patients

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Studies suggest EBV insertion in heterogeneous severe COPD is most effective in patients with no collateral ventilation (CV-ve) involving the targeted lobe.
Aim: To determine whether Chartis evaluation could predict clinical outcomes in COPD pts having EBV insertion and who were assessed as having a complete fissure by HRCT.
Methods: A prospective parallel group study with all pts screened with HRCT. Destruction scores were determined for each lobe, fissure integrity was assessed in both lungs. Only pts with >10% differential in destruction scores and complete fissures (for the targeted lobe) were enrolled. All had lung function tests, 6 min walk, differential V/Q, and SGRQ scoring at baseline/30/90 days after EBV placement. Pts had Chartis testing of CV prior to EBV placement, but EBV was placed irrespective of the Chartis result.
Results: 49 pts were screened. 9 had intact fissures on HRCT assessment and went onto Chartis Assessment and EBV placement. All had EBV placed in the left upper lobe and lingula. 7 pts were CV-ve on Chartis: 2 were CV+ve. In the CV-ve group. FEV1 [mean(SD)] increased from baseline 0.69(0.15) to 0.93(0.19)L; p<0.025; at 90 days. TLC decreased from 6.55 (1.28)L to 6.00 (1.11)L. p<0.01. SGRQ scores at 90 days were also significantly lower -43.2(10.5) vs 61.2 (8.7) p<0.01. The two subjects in the CV+ve group had no change in lung function.
Conclusion: When used as a supplement to HRCT, Chartis assessment of CV predicts improvement in lung function and clinical outcomes in pts with severe COPD undergoing EBV therapy. Chartis should be incorporated into decision pathways relating to EBV insertion.

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Pneumothorax as a predictor of beneficial outcome following endoscopic lung volume reduction

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Introduction: Patients developing significant target lobe volume reduction (TLVR) following endobronchial valve (EBV) treatment experience great improvement in clinical outcome measures. A prospective multicenter study confirmed an improvement in FEV1, SGRQ and 6MWD in patients with a TLVR > 350 ml. However, the risk of pneumothorax increases in case of rapid TLVR by parenchymal rupture. Therefore it is thought, that a pneumothorax is a predictor of beneficial outcome following EBV therapy.
Objective: To evaluate the impact of the pneumothorax on outcome following EBV treatment.
Methods: Retrospective analysis of a multicenter trial evaluating the impact of the pneumothorax on outcome following EBV treatment. All patients underwent chest x-ray the same day of EBV implantation for exploration of pneumothorax. 30 days following valve implantation, TLVR assessed by high resolution computed tomography (HRCT) and clinical outcome measures (FEV1, SGRQ, 6MWT) were evaluated.
Results: 96 emphysema patients received EBV therapy, of which 41 patients experienced a TLVR > 350 ml. In totally, 8 patients (8.3%) experienced a pneumothorax following EBV placement. TLVR values were available for 6 out of the 8 patients. All 6 achieved TLVR > 350ml cut off for the study. The mean TLVR as well as the improvement in FEV1 was greater in the group of patients who experienced a pneumothorax (n=6; mean TLVR -2273.2 ml, mean % FEV1 23.8±10.6) compared to those who did not (n=35; mean TLVR -1222.1 ml, mean % FEV1 22.3±24.01). All patients required chest drainage and recovered within 3-14 days.
Conclusion: The event of pneumothorax seems to be a predictor of a great outcome following EBV therapy.

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Outcome of endobronchial valve (EBV) placement in lower lobes and in low heterogeneous patients

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Introduction: VENT and Chartis studies showed clinical benefit when EBV's

(PulmonX, CA, USA) are placed to achieve lobar occlusion in patients with complete fissures/absent collateral ventilation. There was no restriction on site of valve placement and patients with a range of heterogeneity scores were treated.
Objective: To evaluate clinical outcomes in patients treated with EBV in lower lobes and in patients with low heterogeneity.
Methods: Analysis of the VENT subgroup with complete fissures with lobar occlusion and analysis of patients in the Chartis study with absent collateral ventilation and who achieved target lobe volume reduction of > 350ml.
Results: In the Chartis subgroup, 12 patients were treated in left lower lobe (LLL) with a % improvement in FEV_1 at 30 days of 17.5% ±20.8 and SGRQ of -14.6 points ±14.4. Five patients were treated in right lower lobe (RLL) with a Δ FEV_1 of 40.7% ±27.4 and a Δ SGRQ of -18.6 points ±15.2. In the VENT subgroup, 11 patients were treated in LLL, resulting in a ΔFEV_1 at 6 and 12 months of 18.1% ±20.0 and 13.1% ±20.2 respectively. In the 4 RLL patients, ΔFEV_1 was 22.9% ±22.8 and 23.6% ±15.8. Δ SGRQ was -7.5 points ±19.1 and -7.5±15.0 at 6 months in LLL and RLL respectively.
In the VENT subgroup, 26 patients had heterogeneity score of ≤15% with a mean change in FEV_1 at 12 months of 15.4% ±25.1 compared to 31.1±28.8 in the 35 patients with a score > 15%. In the Chartis subgroup, 14 had a score of ≤15% and showed a mean change in FEV_1 of 15.9% ±16.1 at 30 days compared to 26.4% ± 27.9 in the 20 patients with a score > 15%.
Conclusion: A clinical relevant response can be obtained after EBV in lower lobes and in patients who are not highly heterogeneous.

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Lung volume reduction coil treatment for patients with emphysema: 6-month multicenter feasibility results
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Rationale: The Lung Volume Reduction Coil (LVRC, PneumRx USA) is a bronchoscopic device for the treatment of emphysema. A previous pilot study showed safety and effectiveness in severe upper-lobe heterogeneous emphysema. In this multicenter study (NCT0122098, NCT01328899) we investigated whether LVRC is safe and effective for the treatment of upper- and lower-lobe heterogeneous and homogeneous emphysema.
Methods: 71 subjects underwent two separate bronchoscopic treatments using LVR Coils under anesthesia using fluoroscopy (142 procedures). Over 1350 LVR Coils were placed with median 10 Coils (range 5-15) placed per procedure in 48±24 minutes. Safety was evaluated by recording all SAEs and AEs; effectiveness was measured by SGRQ, pulmonary function and exercise testing through 255 days ± 47 days.
Results: 71 subjects (42F/29M, 62±8 yrs), FEV1: 29±6%, RV: 247±50%, RV/TLC: 66±9 and SGRQ: 63±12 were analyzed. SAEs reported during the Treatment Recovery Period (≤30 days post treatment) for the 142 procedures included exacerbation (8), pneumonia (10), pneumothorax (1), chest pain (3) and hemoptysis (1). SAEs reported post Treatment Recovery Period, up to 295 days included exacerbation (14), pneumonia (8), pneumothorax (1) and chest pain (1); and no hemoptysis. At 255±47 days post treatment, study subjects exhibited an absolute ΔFEV_1 +14±25%, ΔRV -0.51±0.81L, Δ6MWT +43±72 m and ΔSGRQ -11±13 points (all statistically significant, p≤0.001).
Conclusion: LVRC treatment is safe and demonstrated clinically significant improvements in effectiveness in severe upper and lower lobe heterogeneous and homogeneous emphysema.

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Heterogeneous and homogenous emphysema both respond to lung volume reduction coil treatment
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Rationale: The Lung Volume Reduction Coil (LVRC, PneumRx USA) is a bronchoscopic device for the treatment of patients with heterogeneous emphysema. In this study we investigated if the LVRC has potential in the treatment of homogenous emphysema.
Methods: Using a post-hoc blinded CT analysis we tested the impact of degree of heterogeneity on 6-month outcome in patients after bilateral LVRC treatment in two recent trials (NCT01220908, NCT01328899). First, digital lobar CT emphysema scores were assessed using the % destruction below -950HU for both lungs. <25% difference between the ipsilateral lobes of both lungs was regarded homogeneous. Secondly, a visual pattern approach was used grading from 0 (no damage) to 4 (bullous disease). A difference of ≤1 point in one of the lungs was regarded as homogeneous disease.
Results: 53 patients, 61.8y (±7.4), FEV1 33.8%pred (±9.8), RV 246%pred (±53) RV/TLC 60.6 (±9.1) were analyzed. Digital CT analyses identified 15 homogenous cases with a ΔFEV1 +7.8% (±11.9), ΔRV -0.77L (±0.55), Δ6MWD +41m (±85), ΔSGRQ -13.4pts (±11.3) and 38 heterogeneous cases with a ΔFEV1 +15.9% (±31.8), ΔRV -0.48L (±0.83), Δ6MWD +42m (±80), ΔSGRQ -10.9pts (±15.3). The visual approach resulted in 34 homogeneous cases with a ΔFEV1 +10% (±16), ΔRV -0.49L (±0.66), Δ6MWD +44m (±85), ΔSGRQ -9.6pts (±12.9), and 29 heterogeneous cases with a ΔFEV1 +18.3% (±37), ΔRV -0.61L (±0.85), Δ6MWD +42m (±59), ΔSGRQ -13.4pts (±15.3). Only FEV1 was different (p<0.01) between the two phenotypes.
Conclusion: LVRC treatment also results in significant and clinically relevant improvements in patients with homogenous emphysema. These results warrant a prospective evaluation on LVRC in homogenous disease.