



Prediction of response to endobronchial coiling based on morphologic emphysema characterization of the lung lobe to be treated and the ipsilateral non-treated lobe as well as on functional computed tomography-data: correlation with clinical and pulmonary function

Christopher Kloth¹, Wolfgang Maximilian Thaiss², Jan Fritz³, Konstantin Nikolaou², Meinrad Beer¹, Jürgen Hetzel⁴, Sorin Dumitru Ioanoviciu^{5#}, Marius Horger^{2#}

¹Department of Diagnostic and Interventional Radiology, University Hospital Ulm, Ulm, Germany; ²Department of Diagnostic and Interventional Radiology, Eberhard-Karls-University, Tübingen, Germany; ³Johns Hopkins University School of Medicine, Russell H. Morgan Department of Radiology and Radiological Science, Baltimore, MD, USA; ⁴Department of Internal Medicine II, Eberhard-Karls-University, Tübingen, Germany; ⁵University Victor Babes (UMFT), Timisoara, Romania

Contributions: (I) Conception and design: M Horger, J Hetzel; (II) Administrative support: WM Thaiss, L Nikolaou; (III) Provision of study materials or patients: M Horger, J Hetzel; (IV) Collection and assembly of data: M Horger, J Hetzel, C Kloth; (V) Data analysis and interpretation: M Horger, C Kloth; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Christopher Kloth, MD. Department of Diagnostic and Interventional Radiology, University Hospital Ulm, Albert-Einstein-Allee 23, 89081 Ulm, Germany. Email: christopher.kloth@uniklinik-ulm.de.

Background: To test if the emphysema type of the targeted lobe, ipsilateral non-targeted lobe, and lobes of the contralateral lung impact outcome of endobronchial lung volume reduction (ELVR) treatment, and to document lobar volume changes in treated and non-treated lung lobes.

Methods: Thirty patients (16 men, 14 women; median age, 66±6 years; range, 48–78 years) underwent chest-computed tomography (CT) before and after endobronchial coiling for lung volume reduction (LVR) at our institution between December 2011 and March 2016. Forty-five pulmonary lobes were coiled. We classified the treated lobes into homogenous or heterogeneous emphysema phenotype based on the distribution of voxels showing tissue attenuation of less than -950 HU. Clinical response was defined as an increase or consistency in the walking distance (6MWT) 6 months after LVR-therapy. Lung volume changes were compared for treated, ipsilateral, and contralateral lobes. Additionally, pulmonary function tests (PFT), chronic obstructive pulmonary disease (COPD) assessment test (CAT), and blood gas analysis were performed.

Results: Responder (19/30, 63.3%) showed a significant improvement of 6 MWT from 281.05 to 335.26 (P=0.001). Non-responder (11/30, 36.7%) showed a decrease in 6MWT from 308.18 to 255.45 (P=0.001). Responders showed a significant reduction in CAT test from 23.23 to 20.73 points (P=0.038) and pCO₂ from 42.94 to 40.31 (P=0.001), whereas non-responders showed an increase in pCO₂ (P=0.003; from 44.27 to 47.45). There were no significant changes in PFT-parameters. In responders, there was a significant volume reduction in treated lobes from 1,627.68 to 1,519.21 mL (P=0.009). In responders, treated lobes/non-treated ipsilateral lobes were homogenous (n=11/5) and heterogeneous (n=10/28). In non-responders, treated lobes/non-treated ipsilateral were homogenous (n=5/4) and heterogeneous (n=7/16). In responders and non-responders, the emphysema phenotype in treated, ipsilateral non-treated and even contralateral lobes (P=0.250) did not differ and or change significantly before and after therapy. Only the volume of treated lobes in responders changed significantly after coiling.

Conclusions: The emphysema-phenotype in the targeted and non-targeted ipsilateral lobe has no impact

on the outcome of endobronchial coiling for LVR and also does not change significantly after treatment, whereas the volume of the treated lobe significantly decreases in responders.

Keywords: High resolution computed tomography (HRCT); lung volume reduction (LVR); endobronchial coiling; computed tomography densitometry; chronic obstructive pulmonary disease (COPD)

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Introduction

Endoscopic lung volume reduction (ELVR) techniques for the treatment of patients with advanced chronic obstructive pulmonary disease (COPD) have increasingly gained acceptance and replaced surgical treatments due to less associated morbidity and mortality (1,2). Of the different endoscopic treatment options, endobronchial valve or coil implantation has gained particular attention with growing data in support of their effectiveness (3-5). However, the target populations and the underlying pathomechanisms of the two techniques differ significantly.

Bronchial valve implantation is expected to reduce hyperinflation of destroyed emphysematous lung parenchyma by up to 80% in case of a complete interlobar fissure and heterogeneous emphysema phenotype (6,7). The integrity of the interlobar fissure is considered equal to invasive measurements of collateral ventilation, which annihilates the beneficial effect of one-way valves if present (7-10).

Endobronchial coiling represents an alternative ELVR technique, which acts by torquing and retracting the bronchi and nearby lung tissue, which stabilizes the bronchial tree and the adjacent lung parenchyma, thereby restoring to some extent the elastic recoil and improving respiratory function (11). Therefore, endobronchial coiling is independent of collateral ventilation and may be indicated for patients who do not qualify for valve implantation (11). Bronchial coiling has been used predominantly to treat patients with heterogeneous emphysema phenotypes (12,13), whereas later endobronchial coiling has also shown a beneficial effect in patients with homogeneous emphysema distribution (14,15).

Chest computed tomography (CT) has emerged as a major diagnostic tool for selecting patients for ELVR techniques due to its ability to characterize emphysema and pulmonary fissures (6,16). Visual assessment and now more widely available emphysema quantification are helpful for the detection and classification of homogeneous and heterogeneous phenotypes, including defining the

completeness of the interlobar fissure and target selection of the lobe with the highest degree of destruction.

The purpose of our study was to test if the emphysema type of the targeted lobe, ipsilateral non-targeted lobe, and lobes of the contralateral lung impact outcome of ELVR treatment, and to document lobar volume changes in treated and non-treated lung lobes.

Methods

Patient characteristics

The ethics board of the Medical Faculty and the University Hospital of the Eberhard-Karls University approved this retrospective data evaluation study and waived the informed consent requirement (No. 198/2016BO1).

A search of our patient information system derived 30 patients who underwent endobronchial coiling therapy for LVR at our institution between December 2011 and March 2016.

Inclusion and exclusion criteria were similar to previously reported studies in the literature (17). Main inclusion criteria were the presence of severe chronic obstructive lung disease (COLD), non-smoker (>6 months), RV >200% of predicted and absence of acute pulmonary infection. We included only patients who underwent CT examination at end-inspiratory phase before and after therapy with at least one follow-up examination. Main exclusion criteria included a change in FEV1 >15% post-bronchodilator, single-breath Hb (hemoglobin) corrected diffusion capacity (DLCO-CB) <20% predicted, CT examination with evidence of diffuse emphysema, previous lung surgery, and relevant lung diseases (e.g., bullae, bronchiectasis, lung cancer) which might have adversely affected the outcome of the study.

Twenty-eight of the 30 (93.3%) patients had stage IV COLD, and 2 (6.7%) patients had stage III COLD. Twenty-one of the patients had smoker anamnesis (70%; mean, 36.5 pack years \pm 13.5).

Table 1 Overview of implanted coils in the patients of our series

Location of coils in patients	Upper lobe	Lower lobe	Total
Right	5	4	9
Left	1	5	6
Right and left	9	6	15
Total	15	15	30

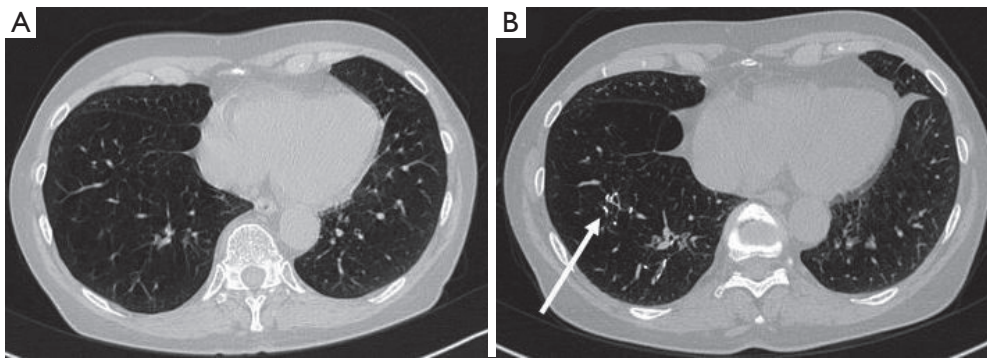


Figure 1 Axial CT images of a 60-year-old female patient before (A) and 6 months after (B) therapy with endobronchial coiling. Ten coils were implanted in the right lower lobe with therapy response after implantation (white arrow). Six-minute walking test improved from 220 to 320 m. A retraction of the lung parenchyma in the right lower lobe reduced lung volumes from 5,782 mL before to 5,522 mL after therapy. CT, computed tomography.

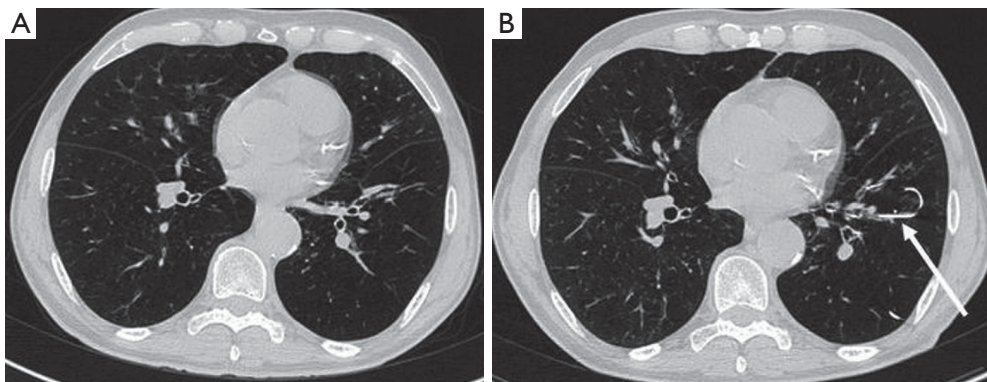


Figure 2 Axial CT images of a 78-year-old female patient before (A) and 3 months after (B) therapy with endobronchial coiling. Ten coils were implanted in the left lower lobe with therapy response after implantation (white arrow). Six-minute walking test score decreased from 200 to 120 meters. The CT images show no visible changes of emphysema and lung parenchyma. Lung volumes were essentially unchanged from 6,184 mL before to 6,180 mL after therapy. CT, computed tomography.

Eleven patients (36.7%) needed permanent oxygen therapy with a mean consumption of 2.3 liter/min. Twelve patients (40.0%) had nocturnal ventilation (NIV). An average of 15.1 coils was implanted per patient [standard deviation (SD) 5.3; range, 4–22 coils]. The distribution of

the coils is shown in *Table 1*. *Figures 1,2* show examples for each side.

Baseline chest CT examinations were performed at a mean of 54.63 days (SD \pm 49.69 days; range, 0–105 days) before endobronchial coiling. The indication for high-resolution

chest CT was made by a board-certified pulmonologist in all cases for the planning of the intervention and evaluation of results after implantation of the coils. Follow-up CT examinations were performed 121.67±147.19 days after intervention and served for evaluation of results in combination with clinical and pulmonary functional tests. A total of 97 chest CT examinations were performed including 30 baseline and 67 follow-up examinations. The mean number of CT examinations was 3±1.4 (range, 1–7 examinations per patient). All chest CT examinations were retrospectively evaluated and excluded if signs of infection or non-infectious complications like edema or hemorrhages were present. One patient had prior LVR surgery of one lung and was excluded from the final analysis. Four patients had prior contralateral endobronchial therapy for LVR with valves; however, at the time of measurement, no further valves were implanted.

High-resolution CT-technique

CT examinations were performed using a 128 row multidetector CT scanner (Somatom Definition AS Plus, Siemens Medical Systems, Erlangen, Germany), a 512×512 reconstruction matrix, a photon energy of 120 kV, a tube current of 100–150 effective mAs, and a tube rotation time of 0.5 ms. The field-of-view was adjusted for each patient to include the entirety of the chest wall and both lungs.

No IV contrast material was applied. In all patients, a spiral acquisition was obtained from the apex to the base of the lungs at end-inspiratory phase. Examinations were performed with patients in the supine position. For visual assessment, two separate CT image sets with 3 mm thick slices were created, using soft (B31f filter) and sharp (B70f filter) reconstruction algorithms. For CT densitometry and lung volume calculation, an additional CT image set with 0.6 mm thick slices was created using soft tissue kernel (B31f filter) reconstruction algorithms.

Qualitative CT imaging analysis

All CT images were viewed at standard mediastinal (level, 35 HU; width, 450 HU) and lung (level, -700 HU; width, 1,500 HU) window settings.

Quantitative CT image analysis

We used “Syngo CT Pulmo 3D” software (SyngoVia, Siemens Healthcare, Germany) to evaluate the airway

system using image data sets with 0.6 mm thick slices. The imaging analysis process and the underlying software steps have been described elsewhere (5,6). The lung volumes of each patient were measured separately for each lung lobe. The lung and the different lobes were first automatically detected by the software and additionally manually corrected if the interlobar fissures were inaccurately delineated. We additionally confirmed the results of computer-based segmentation in the coronal and transversal planes.

Two radiologists (BLINDED and BLINDED) with 24 and 4 years of experience in interpreting chest CT examinations performed the analysis independently from each other. Both investigators were blinded to the original interpretation and the clinical situation of each patient. The emphysema phenotype was classified in each lobe using Syngo CT Pulmo 3D software (Siemens Healthcare), utilizing whole lung color-coded maps displaying the number and distribution of emphysema equivalent (density <-950 HU) lung parenchymal areas (clusters). Based on this “cluster” analysis, we classified the emphysema in each lung lobe into homogenous (almost no parenchymal area exhibiting attenuation values >-950 HU left) and heterogeneous [a mixture of parenchymal areas (patchy pattern) showing attenuation values >-950 and <-950 HU] types.

Clinical tests

Pulmonary function tests (PFT) were performed in all patients before and after endobronchial coiling according to the European Respiratory Society guidelines. PFT was performed using a Masterscreen Body plethysmograph (CareFusion GmbH, Hoechberg, Germany) in the pre-interventional setting and periodically (every 3–6 months) thereafter. Following PFT, total lung capacity (TLC), residual volume (RV), forced expiratory volume in 1 s (FEV₁), and single-breath diffusion capacity for carbon monoxide (DLCO_{c, sb}) were quantified. Additionally, every patient underwent a blood gas analysis, a 6-minute walking test (6MWT), and COPD assessment test (CAT) questionnaire. Based on changes in the 6MWT that was performed 6 months after the LVR therapy, patients were classified into two groups of responders and non-responders.

Statistics

Statistical analysis was performed using dedicated software (IBM SPSS22.0, SPSS, Armonk, USA). All results are

Table 2 Listed clinical parameters including CAT, 6 MWT and blood gas analysis

Clinical parameters	Responder (n=19)			Non-responder (n=11)		
	Before intervention	After intervention	P	Before intervention	After intervention	P
6 MWT (m)	281.05±88.31	335.26±93.47	0.001*	308.18±92.82	255.45±99.13	0.001*
CAT	23.23±7.31	20.73±6.10	0.038	21.44±7.29	24.36±4.29	0.092
Po ₂	66.31±11.33	62.78±8.97	0.371	70.00±11.11	67.72±9.63	0.262
pO ₂ saturation	85.85±11.99	88.18±4.65	0.683	91.66±3.53	90.77±2.99	0.723
PCO ₂	42.94±10.87	40.31±4.91	0.001*	44.27±10.70	47.45±9.63	0.003*
HCO ₃	27.29±2.97	27.43±3.17	0.530	27.76±4.58	28.76±6.15	0.779

*, means significant different; 6MWT, 6-minute walking test; CAT, COPD assessment test; HCO₃, bicarbonate.

expressed as mean average with standard deviation. The Kolmogorov-Smirnov test was used for the normality test including Lilliefors significance correction. Paired *t*-test was used for significance testing concerning 6MWT and CAT. Wilcoxon signed rank test was used for significance testing blood gas values and PFT parameters before and after the intervention. For comparison of lung volumes and emphysema type before and after treatment Wilcoxon signed rank test was used. Paired *t*-test was used for significance testing concerning mean lung density (MLD), high-attenuation values (HAV), and low-attenuation values (LAV). For comparing responders and non-responders, repeated measurements with Bonferroni correction were used. For each comparison, the P value for testing between the groups and time points is given. All tests were corrected for multiple measurements. Chi-square test and McNemar's test were used for analyzing emphysema distribution. Kruskal-Wallis test was used for testing difference in responders after treatment in upper and lower lobes. A value of $P < 0.025$ was considered significant.

Results

Response classification to endobronchial coiling based on 6MWT

Based on changes in the 6MWT that was performed 6 months after LVR therapy, patients were classified into responders and non-responders. Accordingly, 19 were classified into responders (63.3%) with a change from 281.05±88.31 meters to 335.26±93.47 ($P=0.001$) meters, whereas 11 were classified as non-responders (36.7%) yielding a mean walking distance of 308.18±92.82 meters and 255.45±99.13 meters after intervention ($P=0.001$).

In 16/30 patients, the interlobar fissure was moderately or severely incomplete on both sides, whereas 8/16 patients with incomplete fissure were responders and 8/16 patients were non-responders.

Other clinical parameters (CAT, blood gas analysis, PFT)

Clinical parameters are shown in *Table 2*. In responders, the CAT test decreased from 23.23±7.31 to 20.73±6.10 points ($P=0.038$), whereas in non-responders there was a decrease from 24.44±7.29 to 24.36±4.29 points ($P=0.092$). In responders, there was a significant decrease in pCO₂ from 42.94±10.87 to 40.31±4.91 ($P=0.001$), whereas in non-responders there was a significant increase in pCO₂ from 44.27±10.70 to 47.45±9.63 ($P=0.003$). *Table 3* shows the results of PFT in responders and non-responders.

Lung volumes and CT quantification

In responders, there was a statistically significant volume reduction of the treated lobe from 1,627.68±531.75 mL before to 1,519.21±458.47 mL after therapy ($P=0.009$), whereas in non-responders, there was an increase of volume from 1,424.18±335.38 mL before, to 1,428.36±317.15 mL after therapy ($P=0.722$). Ipsilateral non-targeted lobes of both responders and non-responders showed a strong, but non-significant tendency of increasing volumes after therapy from 1,073.18±607.88 to 1,106.56±652.09 mL ($P=0.137$) and 1,015.76±516.70 to 1,034.52±528.10 mL ($P=0.455$), respectively. The LAV decreased in the treated lobe in responders and increased in non-responders, whereas HAV slightly decreased from 30.98±8.93 to 27.41±7.35 HU and increased in non-responders from 24.05±5.63 to 25.46±5.06 HU (*Table 4*). *Figures 3,4* show representative cases.

Table 3 PFT-parameters and their temporal course after endobronchial coiling in responders and non-responders

Pulmonary function parameters	Responder (n=19)					Non-responder (n=11)				
	Before intervention		After intervention		P	Before intervention		After intervention		P
	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
TLC	8.15	1.62	8.04	1.88	0.496	8.69	2.21	7.73	1.56	0.359
Pre TLC %	138.88	14.72	137.50	17.74	0.570	149.80	43.10	133.76	11.40	0.445
RV, L	7.81	8.39	5.49	1.54	0.331	6.56	1.87	5.43	0.98	0.508
Pre RV %	255.71	42.56	245.47	54.46	0.281	298.74	106.40	244.01	26.67	0.508
RV%TLC	70.03	7.26	68.17	9.08	0.691	74.18	10.39	70.83	8.34	0.374
Pre RV%TLC	175.48	22.74	169.96	26.26	0.496	184.29	25.16	174.45	19.66	0.314
VC, L	2.38	0.87	2.48	0.99	0.394	2.08	1.25	2.25	1.05	0.359
Pre VC %	69.60	16.84	73.55	20.67	0.334	58.54	25.03	66.57	20.63	0.285
FEV ₁ , L	2.44	6.38	0.88	0.32	0.777	0.78	0.35	0.81	0.32	0.284
Pre FEV ₁ %	30.02	13.12	33.75	8.45	0.478	28.88	9.25	31.74	10.29	0.169
DLCOC _{SB}	2.90	1.29	2.82	1.09	0.480	2.42	0.77	2.51	1.24	0.273
Pre DLCOC _{SB} %	34.27	10.72	33.72	9.37	0.410	28.90	4.25	30.09	12.45	0.273

PFT, pulmonary function testing; 6MWT, 6-minute walking test; TLC, total lung capacity; RV, residual volume; FEV₁, forced expiratory volume in 1 s; DLCOC_{SB}, single-breath diffusion capacity for carbon monoxide; Pre, percentage of the measured values to the predicted values.

Table 4 Results of CT-densitometry performed for emphysema phenotype classification

CT-densitometry parameters	Responder (n=19)					Non-responder (n=11)				
	Before intervention		After intervention		P	Before intervention		After intervention		P
	Mean	SD ±	Mean	SD ±		Mean	SD ±	Mean	SD ±	
Lung volume (mL)										
Total	6,820.22	1,578.78	6,775.77	1,635.55	0.606	6,456.81	1,324.51	6,570.36	1,191.94	0.271
Treated lobe	1,627.68	531.75	1,519.21	458.47	0.009*	1,424.18	335.38	1,428.36	317.15	0.722
Ipsilateral lobes	1,073.18	607.88	1,106.56	652.09	0.137	1,015.76	516.70	1,034.52	528.10	0.455
Contralateral lobes	1,403.21	547.37	1,407.15	548.39	0.649	1,467.56	437.77	1,501.52	431.39	0.075
CT densitometry										
MLD	-887.94	14.21	-884.61	13.46	0.086	-886.18	9.41	-887.63	5.48	0.496
HAV	1.07	0.32	1.00	0.23	0.024*	0.85	0.15	0.88	0.15	0.234
LAV	30.98	8.93	27.41	7.35	0.423	24.05	5.63	25.46	5.06	0.493

CT, computed tomography; SD, standard deviation; MLD, mean lung density; HAV, high attenuation values; LAV, low attenuation values.

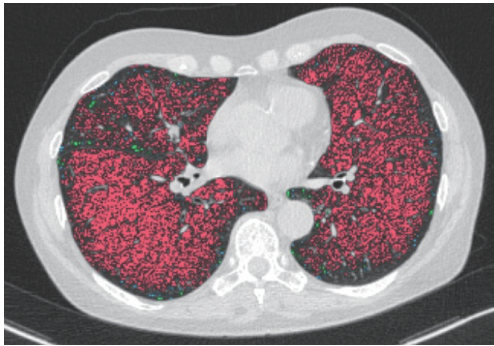


Figure 3 Axial CT image of a 78-year-old female patient with chronic obstructive lung disease grade IV before therapy with endobronchial coiling. The patient was a heavy smoker with a history of 35 pack years. The cluster analysis demonstrates homogenous emphysema areas (color coded display of emphysema-equivalent attenuation values). The patient had a 6-minute walking test of 360 meters. The inspiratory lung volume was 5,782 mL and the expiratory lung volume was 4,792 mL. CT, computed tomography.

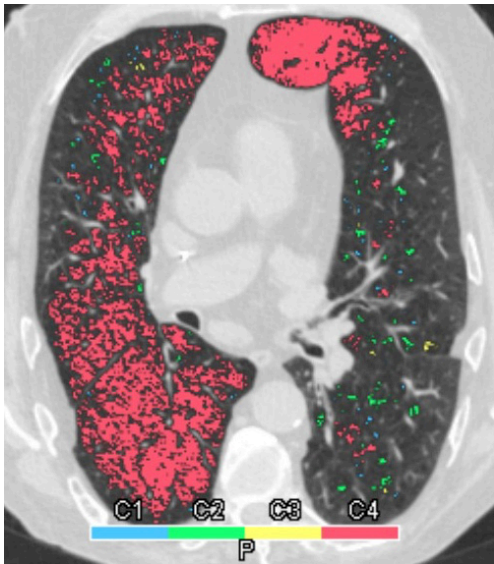


Figure 4 Axial CT image of a 64-year-old male patient with chronic obstructive lung disease grade IV before therapy with endobronchial coiling. The patient had a history of smoking with 30 pack years. The cluster analysis demonstrates heterogeneous emphysema with multiple areas of different emphysema peculiarity. The patient had a 6-minute walking test of 260 meters. The inspiratory lung volume was 6,099 mL and the expiratory lung volume was 4,939 mL. CT, computed tomography.

Emphysema phenotype

The distribution of emphysema types between the treated, ipsilateral untreated, and contralateral lobes are shown in *Table 5*. There was no significant difference between responders and non-responders ($P=0.825$). Overall, the distribution of emphysema showed a significant difference between the lobes ($P=0.005$) before therapy in both ipsilateral and contralateral non-treated lung lobes, but not in treated lobes. In non-responders, there were no significant differences between emphysema phenotypes before ($P=0.280$) and after therapy ($P=0.378$). In responders, the emphysema phenotype of treated ($P=0.999$), ipsilateral non-treated ($P=0.687$), and contralateral lobes ($P=0.250$) did not change significantly after therapy. Similarly in non-responders, the emphysema phenotype of treated ($P=0.250$), ipsilateral non-treated ($P=0.999$), and contralateral lobes ($P=0.999$) did not change significantly either. There were no significant differences between treated upper and lower lobes ($P=0.310$) in responders.

Receiver operating characteristics (ROC)

The cuff-off value for a response after therapy based on LAV measurements at baseline was significant for a LAV of 23.47 or lower in inspiration (sensitivity/1-specificity/AUC/P value 78.59%/50.0%/0.792/0.007) (*Figure 5*). There were no significant cuff-off values for MLD, HAV, and PFT.

Discussion

The selection of the most appropriate lobe for lung volume reduction (LVR) with endobronchial coiling is important to optimize outcomes in patients with severe COPD. For this purpose, different morphologic and functional methods have been proposed, which are mostly based on the differentiation of homogeneous and heterogeneous emphysema phenotypes (16,18,19). While this differentiation can be performed visually on high-resolution CT images of the chest, quantification of lung parenchymal density may be more accurate, and calculation of the distribution of emphysema equivalent areas has become practicable based on the so-called “cluster analysis” (20). In order to understand which impact the interplay of different lobar phenotypes could potentially have in a patient, we performed lobar-based phenotype

Table 5 Emphysema phenotype in treated, ipsilateral and contralateral non-treated lobes before and after coiling

Type of emphysema	Responder (19 patients)		Non-responder (11 patients)	
	Before intervention	After intervention	Before intervention	After intervention
Overall lobes		n=95		n=55
Homogenous emphysema	25/95 (26.3%)	26/95 (27.4%)	11/55 (20.0%)	7/55 (12.7%)
Heterogeneous emphysema	70/95 (73.7%)	69/95 (72.6%)	44/55 (80.0%)	48/55 (87.3%)
Treated lobes		n=21		n=11
Treated lobes homogenous	11/21 (52.3%)	10/21 (47.6%)	4/11 (36.4%)	7/11 (63.6%)
Treated lobes heterogenous	10/21 (47.7%)	11/21 (52.4%)	7/11 (63.6%)	4/11 (36.4%)
Ipsilateral lobes		n=33		n=21
Ipsilateral homogenous	5/33 (15.2%)	8/33 (24.2%)	4/21 (19.0%)	1/21 (4.8%)
Ipsilateral heterogenous	28/33 (84.8%)	26/33 (75.8%)	17/21 (81.0%)	20/21 (95.2%)
Contralateral lobes		n=36		n=23
Contralateral homogenous	10/36 (27.8%)	8/36 (22.2%)	2/23 (8.6%)	4/23 (17.4%)
Contralateral heterogenous	26/36 (72.2%)	28/36 (77.8%)	21/23 (91.4%)	19/23 (82.6%)

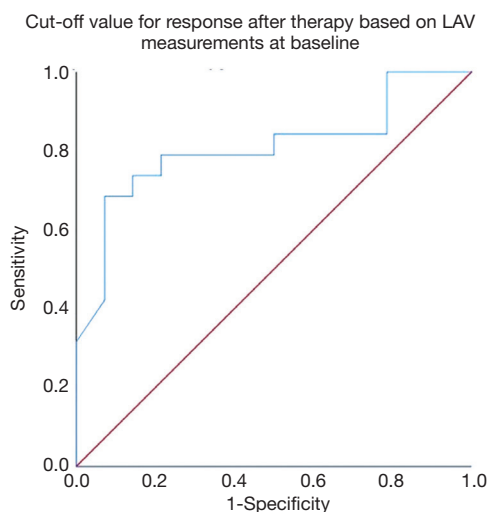


Figure 5 Receiver-operating characteristic analysis derived a significant cut-off value for response after therapy based on LAV measurements at baseline. There was a cut-off value for the low attenuation values of 23.47 or lower in inspiration, which showed a sensitivity of 78.59% and a specificity of 50% (area under the curve, 0.792; $P=0.007$). LAV, low-attenuation values.

analysis of the targeted lobe, and also of the nontargeted ipsilateral and contralateral lung lobes.

We found that the emphysema phenotype in the targeted lobe has no association with the response to endobronchial

coiling. Our data support more recent reports, which similarly found that the emphysema phenotype may not influence the treatment outcome (21). Interestingly, the emphysema phenotype in the ipsilateral, untreated lung lobes also did not influence the patient outcome; however, there was a predominance of heterogeneous emphysema phenotypes in our cohort. We found no relevant difference in terms of response between the groups with either homogeneous emphysema of treated and non-treated ipsilateral lobes or heterogeneous emphysema of treated and non-treated ipsilateral lobes. The same was true also for the contralateral lung lobes. Hence, the choice of the most proper lung lobe to be treated by endobronchial coiling seems indeed not to be influenced by the emphysema phenotype, which is in contrast to valve-based LVR (16). Accordingly, the pre-interventional work-up of patients undergoing endobronchial coiling may be simplified compared to other LVR procedures. Nonetheless, for evaluation of response and treatment monitoring, CT densitometry and volumetry of lung parenchyma proved very useful (22). Notably, classification of response in our series was based on results of 6MWT, which were also in concordance with those of the CAT test and blood gas analysis. However, the PFT parameters which are used for routine patient evaluation did not change significantly either in the responder or non-responder group, indicating a major limitation for routine response evaluation in this clinical setting. Our non-responder group had worse

PFT at baseline, which is similar to previous studies (5,14). However, the difference in the absolute values was more extensive in our group, which suggests that the effectiveness of coiling may be limited in the setting of poor baseline PFT parameters.

To the best of our knowledge, this is the first report considering not only the impact of the emphysema phenotype of the treated lobe but also of the ipsilateral and contralateral lobes, and thus provides an opportunity to understand the potential mechanical effect on the post-interventional respiratory function. The strategy of pre-interventional lobe selection for endobronchial LVR has been addressed previously (2,16). Generally, the lobes with the greatest degree of destruction have been chosen for endobronchial treatment. However, at least for valve placement, the consideration of the emphysema phenotype is still an issue of debate. More recent data have emphasized the role of lobar deflation in expiration, showing that morphological criteria based exclusively on inspiratory CT densitometry only partially reflect the deflation of particular lung lobes, and may be of limited value as a sole predictor for target lobe selection in LVR. Contrary to endobronchial valve implantation, which aims at volume reduction of the most affected (destroyed) lung lobe by precluding inflation through a one-way bronchial valve, coiling leads to mechanical volume reduction through the distribution of increased radial tension throughout the airway network, while tethering opens small airways to prevent collapse (23). Coiling also causes a significant decrease in the cross-sectional area of treated segment bronchi in inspiration and a slight increase in expiration accompanied by a volume reduction and stabilizes the bronchial tree (5). Our data support this pathomechanistic interpretation of the role of endobronchial coiling in that there is no relevant change in volume and attenuation of the other lung lobes, but only of the treated lobe after endobronchial coiling. Only in responders did we find a slight volume increase of the ipsilateral lobe and a mild decrease in density. However, improvement in respiratory function seemed mainly secondary to the decrease of hyperinflation of treated lung lobes.

In our cohort, 8/30 patients (26.6%) showed lower lobe-dominant emphysema. In 4 cases, these patients were responders, and in 4 cases the patients were non-responders. According to the current literature (24), our group showed an upper lobe dominant emphysema pattern; however, without consequence for the outcome.

Our study has limitations. First, the number of treated lobes is relatively low for comprehensive statistical

analysis. Second, we had a predominance of heterogeneous emphysema phenotype in the ipsilateral and contralateral non-treated lobes, which may have also influenced comprehensive statistical analysis.

In conclusion, we found that the phenotype of lung emphysema in the targeted and non-targeted ipsilateral lobes had no significant impact on the outcome of endobronchial coiling for LVR and also did not change significantly after treatment, whereas statistically significant changes in lobar volume were found solely in the treated lobe in responders.

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Footnote

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Ethical Statement: The ethics board of the Medical Faculty and the University Hospital of the Eberhard-Karls University approved this retrospective data evaluation study and waived the informed consent requirement (No. 198/2016BO1).

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