BRONCHOSCOPIC INTREVENTIONS IN COPD

Ankan Bandyopadhyay

Chronic obstructive pulmonary disease (COPD) remains one of the most prevalent lung diseases in the world

Medical treatment options are limited and provide symptomatic improvements without mortality benefit

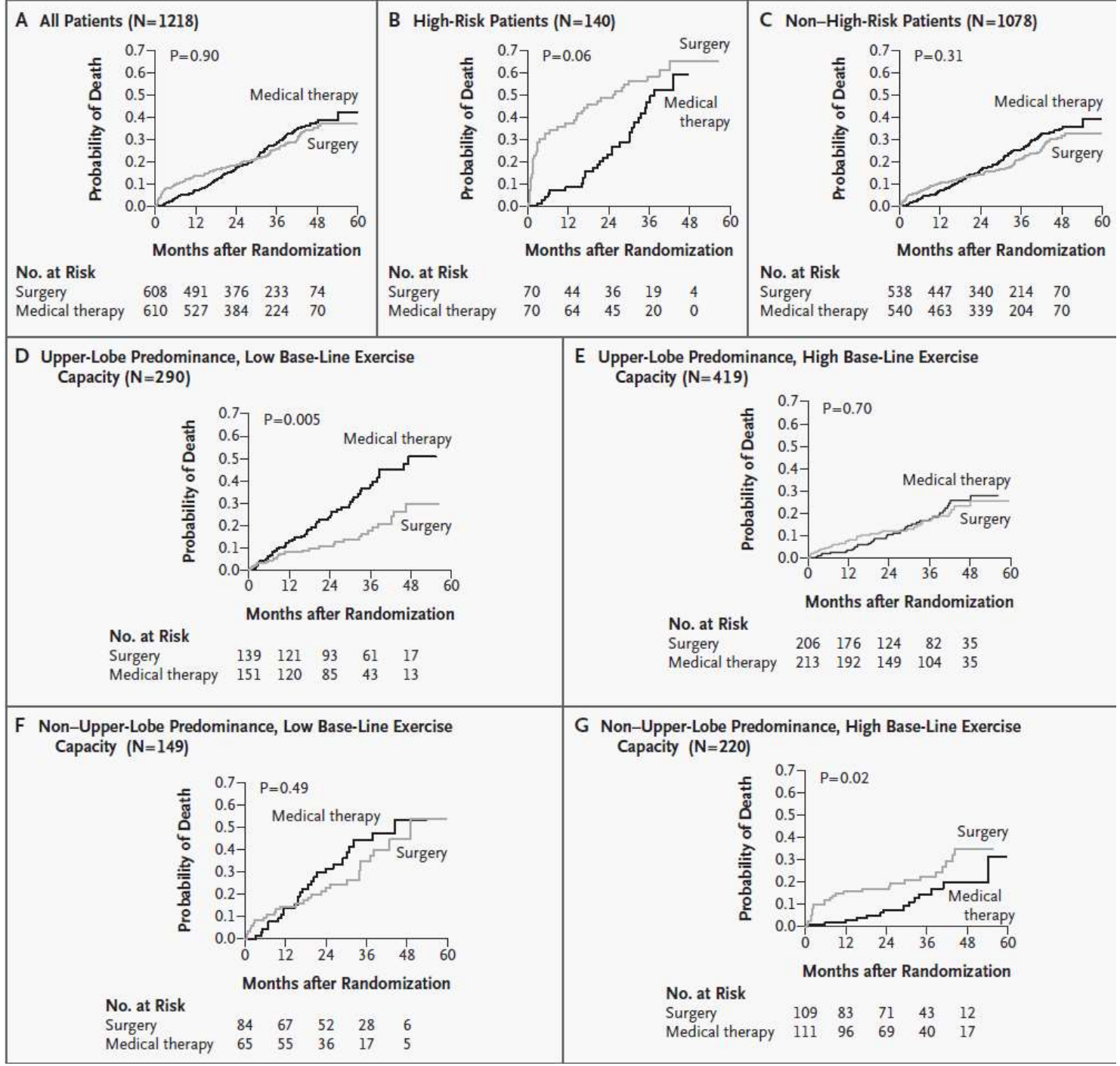
To date, supplemental oxygen for hypoxic patient and lung volume reduction surgery(LVRS) are the only medical treatments shown to improve mortality in severe COPD

LVRS has survival advantage for patients with both predominantly upper-lobe emphysema and low base-line exercise capacity.

Patients at high risk for surgery , with non–upper-lobe emphysema and high base-line exercise capacity are poor candidates for lung-volume–reduction surgery, because of increased mortality and negligible functional gain.

N Engl J Med 2003;348:2059-73

Gail G. Weinmann et al; NETT Trial www.atsjournals.org


A All Patients (N=1218)
P=0.90
Medical therapy
Surgery
Probability of Death
Months after Randomization
No. at Risk
Surgery 608 491 376 233 74
Medical therapy 610 527 384 224 70
B High-Risk Patients (N=140)
P=0.06
Surgery
Medical therapy
Probability of Death
Months after Randomization
No. at Risk
Surgery 70 44 36 19 4
Medical therapy 70 64 45 20 0
C Non–High-Risk Patients (N=1078)
P=0.31
Medical therapy
Surgery
Probability of Death
Months after Randomization
No. at Risk
Surgery 538 447 340 214 70
Medical therapy 540 463 339 204 70
D Upper-Lobe Predominance, Low Base-Line Exercise Capacity (N=290)
P=0.005
Medical therapy
Surgery
Probability of Death
Months after Randomization
No. at Risk
Surgery 139 121 93 61 17
Medical therapy 151 120 85 43 13
E Upper-Lobe Predominance, High Base-Line Exercise Capacity (N=419)
P=0.70
Medical therapy
Surgery
Probability of Death
Months after Randomization
No. at Risk
Surgery 206 176 124 82 35
Medical therapy 213 192 149 104 35
F Non–Upper-Lobe Predominance, Low Base-Line Exercise Capacity (N=149)
P=0.49
Medical therapy
Surgery
Probability of Death
Months after Randomization
No. at Risk
Surgery 84 67 52 28 6
Medical therapy 65 55 36 17 5
G Non–Upper-Lobe Predominance, High Base-Line Exercise Capacity (N=220)
P=0.02
Surgery
Medical therapy
Probability of Death
Months after Randomization
No. at Risk
Surgery 109 83 71 43 12
Medical therapy 111 96 69 40 17

Minimally invasive therapies using bronchoscopy tried with goal of reproducing the advantages of surgical LVR with less risk and procedure related morbidity

Bronchoscopic techniques include-

Unidirectional bronchial valves

Biologic and polymer based techniques to occlude lung segments

Small stents placed through airway walls to allow trapped air to exist

Thermal/Steam vapor ablation

Endobronchial coils

Targeted lung denervation

Each of these techniques attempts to reproduce some of the benefits seen in LVRS with a less invasive and less morbid procedure

Bronchoscopic interventions can be broadly divided into:

Reversible airway interventions-

Include endobronchial valves, LVRCs and transbronchial stents-

may be retrieved if complications occur

Irreversible interventions inciting an inflammatory/ fibrotic response or irreversibly plugging distal airways-

Include bronchoscopic thermal vapour ablation (BTVA) and biological LVR (BioLVR)

J Thorac Dis 2014;6(11):1640-1653

Of these interventions the largest body of evidence is currently available for endobronchial valves

J Thorac Dis 2014;6(11):1640-1653

Bronchoscopically placed endobronchial one way valves occlude airways -prevent air to enter emphysematous portions of lung but allow air and mucus to exit

Valves

Induce atelectasis of emphysematous portions of the lung

decrease air trapping

Shunting of airflow to more normal areas of lung

decrease dynamic hyperinflation of the lungs during exertion

Proc Am Thorac Soc 2008; 54:416–420

Type of Valves-Spiration Inc. and Pulmonx

Both valves are deployed bronchoscopically and are one-way valves

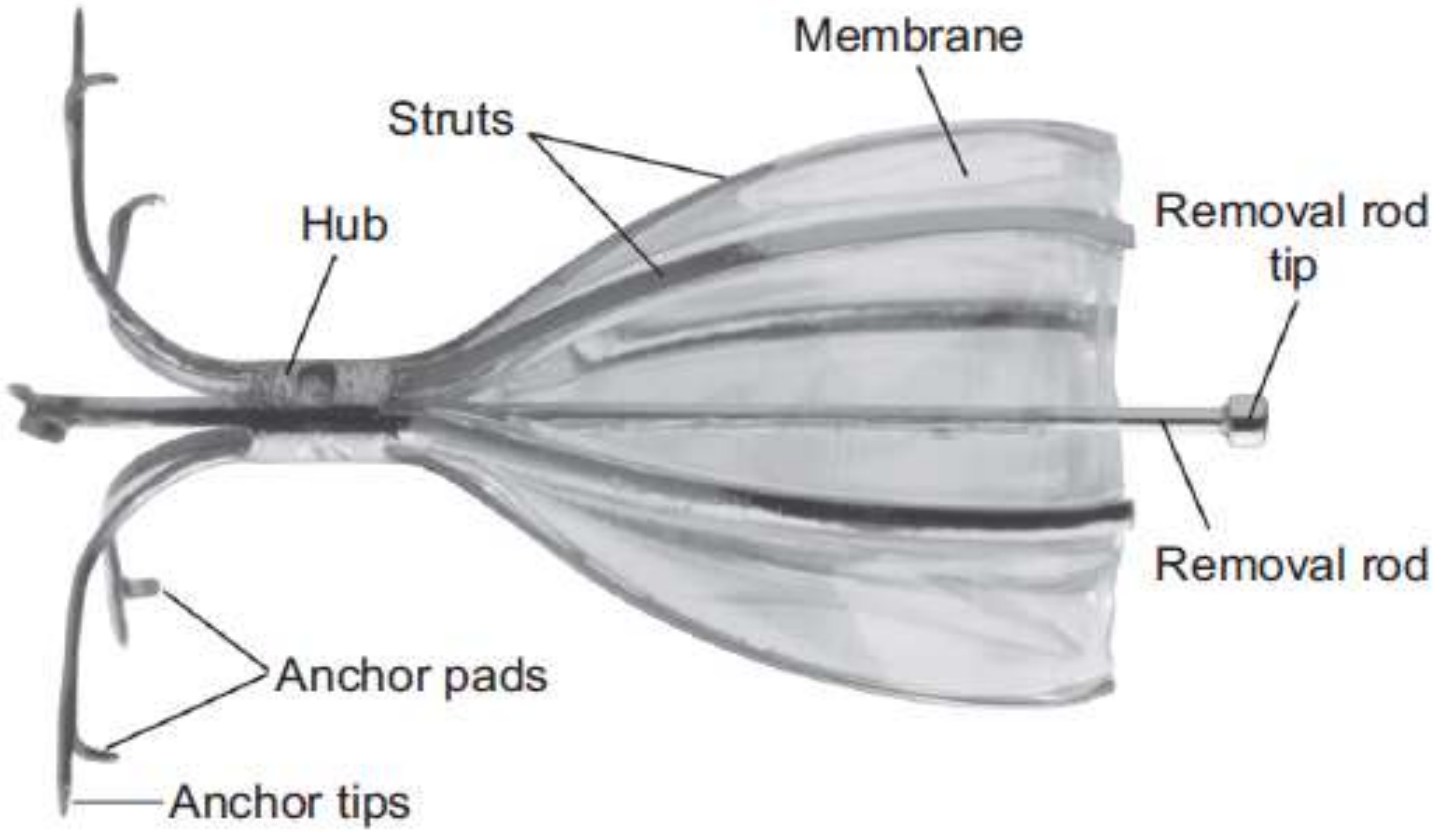
Spiration called as “intrabronchial” valve (IBV)

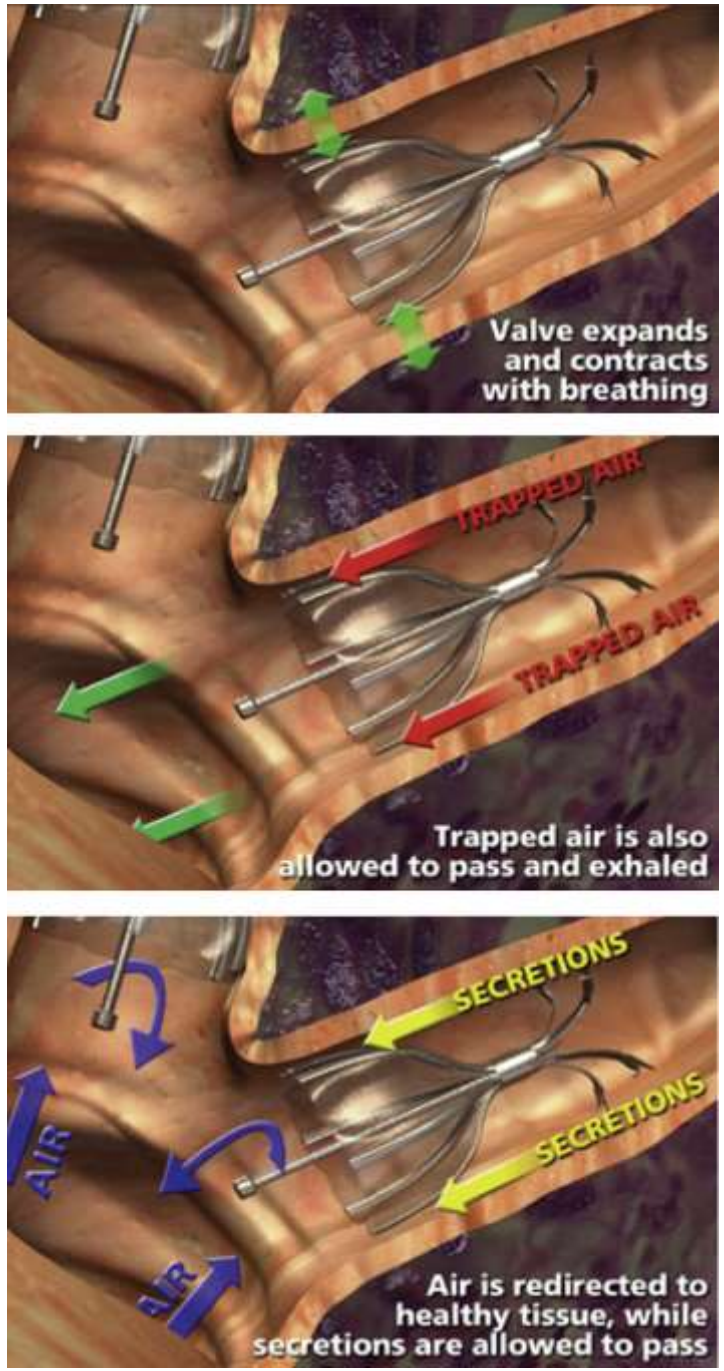
Pulmonx called as “endobronchial” valve (EBV) ; also called the Zephyr EBV

IBV being similar to an umbrella design and the EBV appearing like a fish mouth facing the proximal airways that springs opens when air or mucus is exhaled from the distal airways but stays closed during all other times.

J Thorac Dis 2014;6(S4):S407-S415

INTRABRONCHIAL VALVE UMBRELLA DESIGN




Valve expands and contracts with breathing
TRAPPED AIR
TRAPPED AIR
Trapped air is also allowed to pass and exhaled
SECRETIONS
SECRETIONS
AIR
AIR
Air is redirected to healthy tissue, while secretions are allowed to pass

The Spiration intra bronchial valve (IBV) (Olympus made) is a self-expanding nitinol frame having a central core with 5 distal anchors and 6 proximal curved radial struts

This structure supports a polyurethane membrane, which acts as a one-way umbrella valve when implanted against the bronchial wall

The central core acts as support & serves as a removal rod or helps in manipulation after initial deployment

After selection of the target airways, appropriately sized valves are chosen

J Thorac Dis 2014;6(11):1640-1653

IBV(5,6 or 7 mm size) is inserted via the working channel of a flexible bronchoscope on a catheter loader

Once in position valve is deployed so it will sit flush with the carina of the segmental bronchus

The Spiration IBV studies used a bilateral upper lobe deployment strategy without the intent to produce complete lobar atelectasis

They created redistribution of ventilation to less emphysematous airways

J Thorac Dis 2014;6(11):1640-1653

ENDOBRONCHIAL VALVES(ZEPHYR)

Zephyr endobronchial valve (EBV) (Pulmonx) consists of one-way duckbill valve attached to a nitinol (nickel-titanium alloy) self-expanding retaining frame wrapped in a silicone seal

After selection of a single target lobe, the Zephyr valves are implanted unilaterally in a 3-step process

The valve sits flush with the carina of the segmental bifurcation

The valves are removable in the event of improper positioning or complications

The Zephyr EBV studies concentrated primarily on the unilateral valve deployment with the goal of producing total lobar atelectasis

J Thorac Dis 2014;6(S4):S407-S415

EBV can be placed and removed via flexible or rigid bronchoscopy.

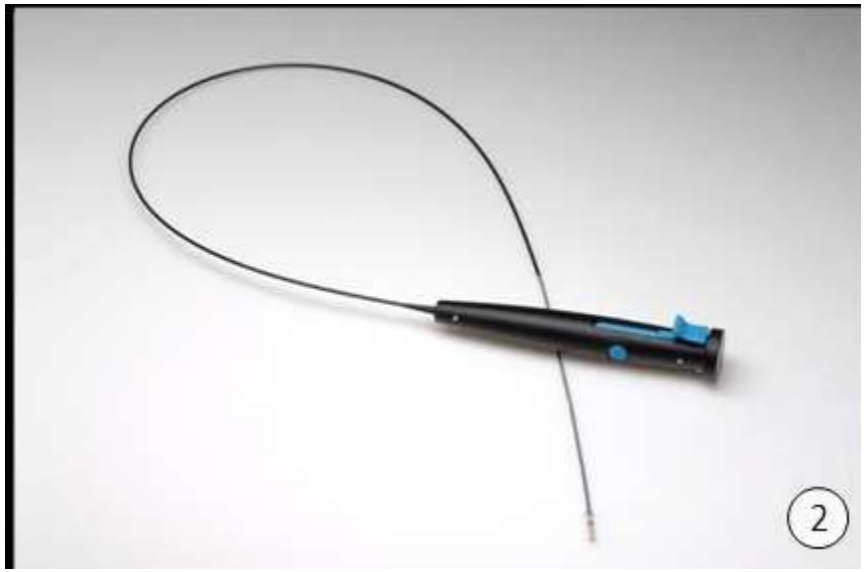
Side effects include COPD exacerbation, hemoptysis and pneumonia

Assessment of collateral ventilation is key as there is no benefit in the presence of collateral ventilation

Benefit is maximum if complete lobe occlusion and atelectasis are achieved

Benefit is modest when complete lobe occlusion is not performed or achieved

J Thorac Dis 2014;6(S4):S407-S415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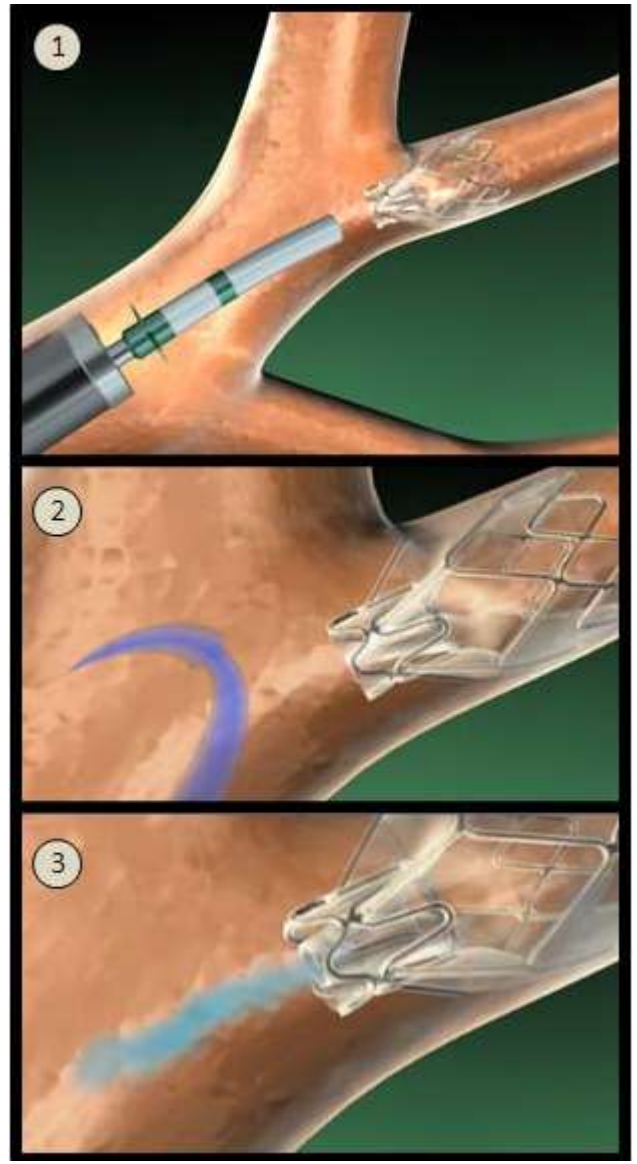
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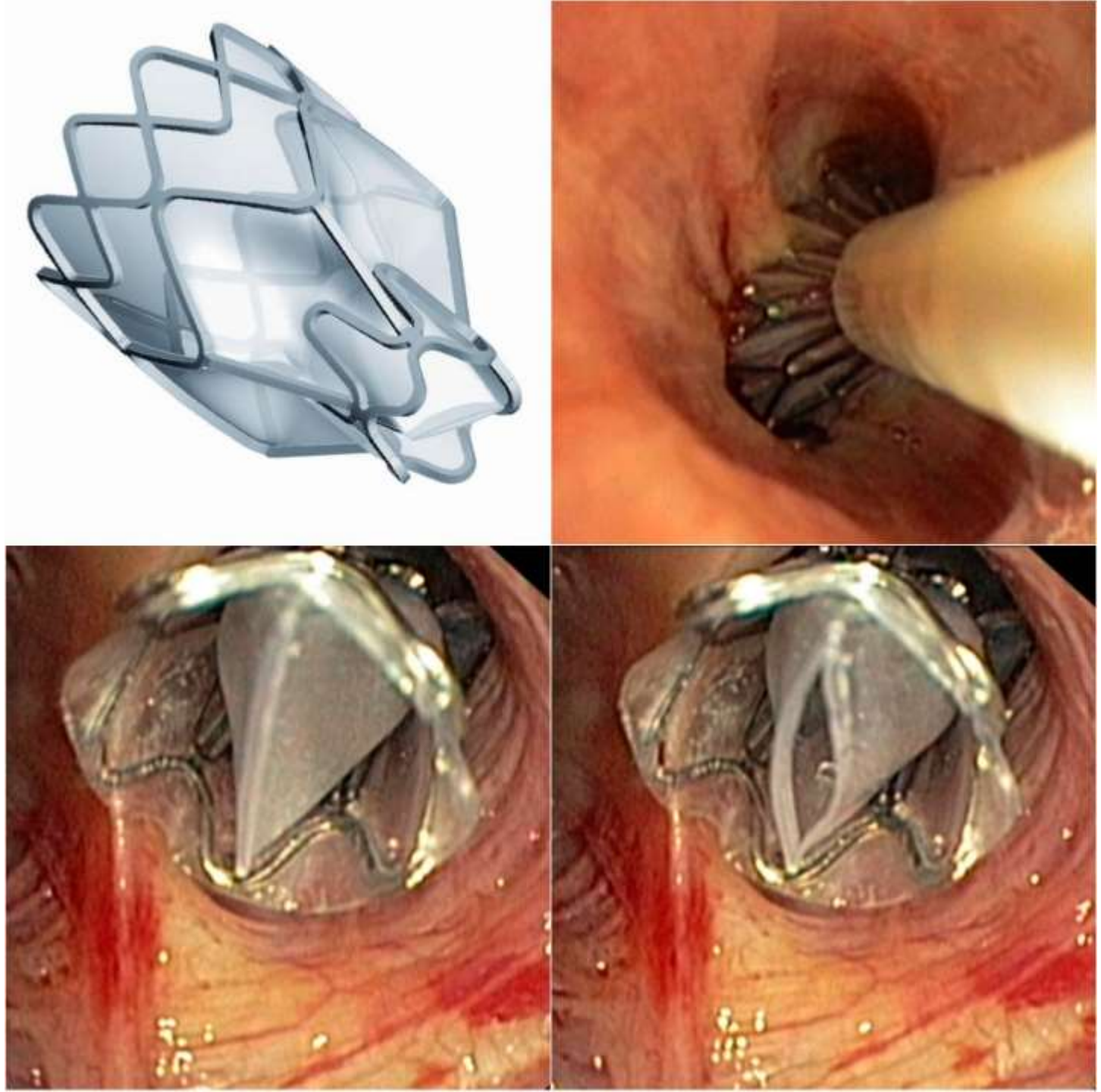

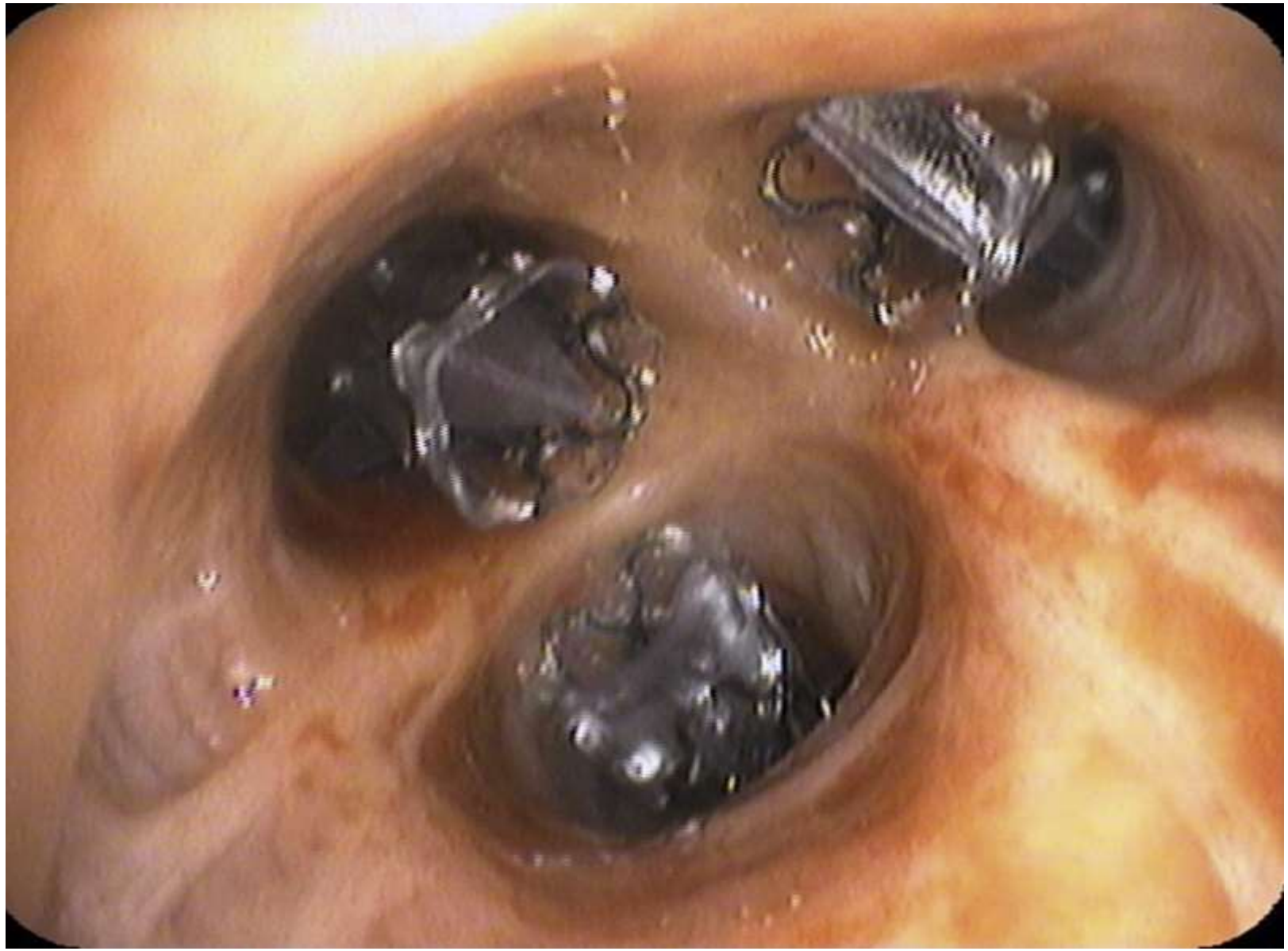

Degree of lung volume reduction and the associated clinical improvements-

more in the patients showing complete interlobar fissures on CT and EBV causing complete lobar occlusion

Complete interlobar fissures suggest absence of collateral ventilation

Incomplete fissures suggest parenchymal fusion between the lobes and collateral ventilation via channels that bypass the usual airways across the lobes

Thoracic HRCT scan used to quantify the heterogeneity of emphysema and integrity of interlobar fissure to select the patients potentially eligible for valve treatment

J Thorac Dis 2014;6(S4):S407-S415

Visual evaluation of fissure completeness is time consuming and requires assessment of fissure integrity on multiple planes of chest CT scan reconstructions.

Endoscopic catheter-based technique developed by Aljuri and Freitag which enables real- time assessment of collateral ventilation

Respirology (2014) **19**, 1126–1137

The Chartis Pulmonary Assessment System consists of a single-patient-use catheter with a compliant balloon component at the distal tip, which blocks the airway on inflation

Air flow out from the target compartment into the environment through the Chartis catheter's central lumen.

By connecting to a console, airway flow and pressure can be displayed.

Airway resistance can be calculated and collateral ventilation in isolated lung compartments can be measured during spontaneous breathing or mechanical ventilation (including jet ventilation) under general anesthesia

Respirology (2014) **19**, 1126–1137


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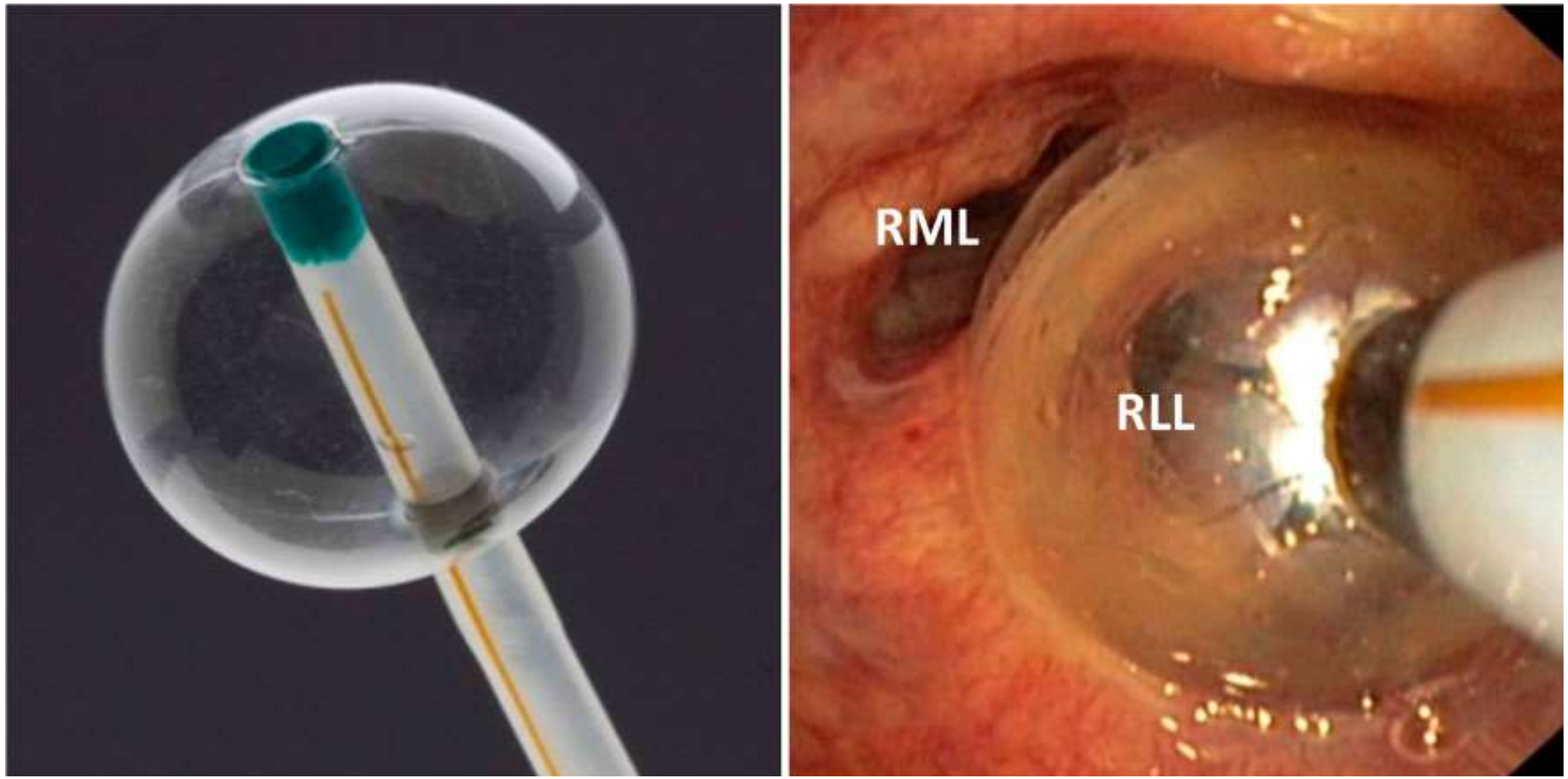
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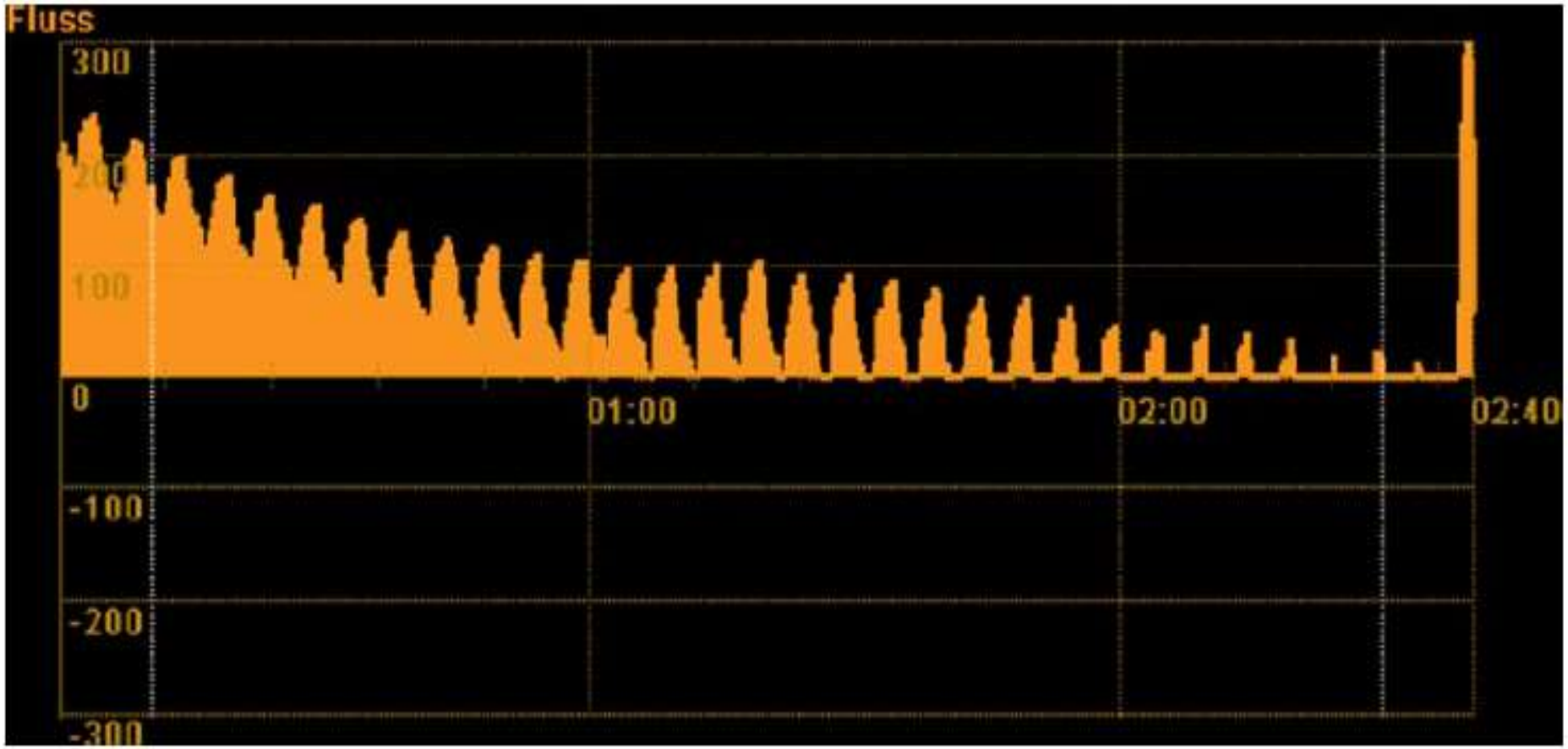

Figure 3. Chartis assessment under jet ventilation using a rigid bronchoscope. There is a reduction in target lobe ventilation within 2:30 min, indicating no collateral ventilation. Patient showed substantial improvements to valve treatment.

Herth et al in a prospective multicenter trial of EBV in COPD included 96 patients who underwent the Chartis measurement showed that patients with no evidence of collateral ventilation having median target lobar volume reduction of 55% and a mean 16% FEV1 improvement

Patients with collateral ventilation had no significant radiological or functional benefits

Chartis assessment predicted response to valve therapy with 75% accuracy

Respiration 2010; **79**: 5–13.

	Study population	Exclusion criteria	Primary outcome	Targeted lung segment	Complications	Study result	
VENT TRIAL (Not sham control) used EBV	heterogenous emphysema FEV1 15-45% TLC>100% Paco2 <50 &Pao2 >45nn of Hg	FEV1 <15%,DLCO< 20%,large bullae, PAH , unstable cardiac condition	Percent change in FEV1 &6MWT at 6 months	Unilateral complete upper lobar occlusion	Death in 2 Pt Hemoptysis (massive) Pneumonia Air leak 6.1% in EBV group &1.2% in control	FEV1 mean 6.8% 6MWt median 5.8% improvement at 6 M	More pronounced in high heterogeneity group and complete fissure group
European cohort of VENT sham controlled used EBV	SAME	SAME	FEV1, 6MWT, SGRQ	Unilateral valve placement in unilateral lobar/segmental/subsegmental bronchi with complete occlusion	COPD exacerbation, pneumonia, pneumothorax-similar in treatment and control group	Significant improvements of FEV1,SGRQ,ergometry at 6&12 months	Improvement correlate with complete fissure, successful lobar occlusion but not with heterogeneity

	Study population	Exclusion criteria	Primary outcomes	Targeted lung segments	complications	Results at 3 months	
Vincent Ninane et al in multicentric sham control European study on IBV	Advanced upper lobe predominant emphysema FEV1<45%predicted TLC>100%	FEV1 & DLCO <20% Paco2>50 Pao2<45	≥4 point improvement in SGRQ and lobar volume shift measured by HRCT	Bilateral upper lobe treatment without goal of complete lobar collapse	No difference in adverse effect in treatment &control group	24% positive response in treatment group compared to control	Mean SGRQ total score improved in both groups (treatment: -4.3±16.2; control: -3.6±10.7 SAFE but Not EFFECTIVE
D.H. Sterman et al in multicenter, prospective, open enrollment,	Severe upper lobar predominant emphysema determined by visual	similar	Safety & effectiveness of IBV	Bilateral upper lobe	valve placed in position with 99.7% success;no migration /erosion no	Significant improvement in HRQL but no improvement in FEV1	

	Study population	Exclusion criteria	Primary outcome	Targeted lung segment	Result	complications	
Ralf Eberhardt et al in complete unilateral vs partial bilateral ELVR in severe bilateral emphysema with IBV	Both upper or lower lobe predominant emphysema FEV1>40%,TLC >100%, RV>150%	6MWT distance <150 meter, Paco2>55 mm of Hg	Improvement in FEV1 &6MWT at 30 & 90 days 2ndary end point-change in SGRQ	Patients in the first group received unilateral IBV placement with complete occlusion of the worst lobe. Patients in the other group had bilateral treatment of either the lower or upper lobes, leaving out one segment on each side	At 30 days and 90 days, significant differences seen in PFT and 6MWD & in mMRC and SGRQ scores, in favor of unilateral treatment. At 90 days, FEV 1 improved by 21.4% ±10.7% in unilateral group, but not in the bilateral group	One pneumo in unilateral gr & 2 resp failure in bilateral gr	

In 2010, the Endobronchial Valve for Emphysema Palliation Trial (VENT) was published

In 2:1 randomization scheme, 321 subjects with heterogeneous emphysema and severe COPD were enrolled and 220 received the EBV treatment

Primary endpoints –improvement in FEV1 and 6-minute walk test (6MWT)

NEJM 363;13 Sep 23, 2010

Moderate sedation was used in 71.5% and general anesthesia in 28.5%

Flexible bronchoscopy was used alone (in 98.6% of the patients) or in combination with rigid bronchoscopy

Mean number of valves placed was 3.8 per patient (range, 1 to 9)

Mean (±SD) duration of the procedure was 33.8±20.5 minutes

The right upper lobe was targeted in a majority of patients (52.3%), followed by the left upper lobe (in 24.3%), the left lower lobe (in 14.0%), and the right lower lobe (in 9.3%)

NEJM 363;13 Sep 23, 2010

At 6 months, increase of 4.3% in the FEV1 in the EBV group as compared to decrease of 2.5% in the control group with mean between-group difference of 6.8% in the FEV1 (P = 0.005)

At 6 months, the distance traveled in the 6-minute walk test increased by 2.5% in the EBV group and decreased by 3.2% in the control group & a mean between-group difference was 5.8%

NEJM 363;13 Sep 23, 2010

At 12 months, the rate of the complications composite was 10.3% in the EBV group versus 4.6% in the control group (P = 0.17).

At 90 days, in the EBV group, as compared with the control group, there were increased rates of COPD exacerbation requiring hospitalization (7.9% vs. 1.1%, P = 0.03) and hemoptysis (6.1% vs. 0%, P = 0.01).

The rate of pneumonia in the target lobe in the EBV group was 4.2% at 12 months.

NEJM 363;13 Sep 23, 2010

Patients with heterogenous emphysema showed 10.7% improvement, and those with complete fissures had 16.2% improvement in FEV1 at 6 months after EBV placement.

In contrast, there were insignificant changes in FEV1 at 6 months of 2.0% in patients with low heterogeneity and 2.5% in patients with incomplete fissures.

NEJM 363;13 Sep 23, 2010

Table 2. Primary and Secondary Efficacy Outcomes in the Intention-to-Treat Population (Change from Baseline at 6 Months).*

Outcome	Endobronchial-Valve Therapy (N = 220)	Control (N = 101)	Between-Group Difference in Change from Baseline	P Value
	number (95% confidence interval)			
Primary outcome				
FEV_1				
Mean absolute percent change from baseline	4.3 (1.4 to 7.2)	−2.5 (−5.4 to 0.4)	6.8 (2.1 to 11.5)	0.005
Mean change in value from baseline — ml	34.5 (10.8 to 58.3)	−25.4 (−48.3 to −2.6)	60.0 (21.5 to 98.4)	0.002
Mean absolute percent change in predicted value from baseline	1.0 (0.2 to 1.8)	−0.9 (−1.7 to −0.1)	1.9 (0.5 to 11.2)	0.007
Distance on 6-min walk test†				
Median absolute percent change from baseline	2.5 (−1.1 to 6.1)	−3.2 (−8.9 to 2.4)	5.8 (0.5 to 11.2)	0.04
Median change from baseline — m	9.3 (−0.5 to 19.1)	−10.7 (−29.6 to 8.1)	19.1 (1.3 to 36.8)	0.02
Secondary outcome				
Mean change in score on SGRQ from baseline‡	−2.8 (−4.7 to −1.0)	0.6 (−1.8 to 3.0)	−3.4 (−6.7 to 0.2)	0.04
Mean change in score on Modified Medical Research Council dyspnea scale from baseline§	−0.1 (−0.21 to 0.09)	0.2 (0.01 to 0.37)	−0.3 (−0.50 to −0.01)	0.04
Mean change in cycle ergometry peak workload from baseline — W	0.6 (−1.5 to 2.7)	−3.2 (−4.5 to −1.9)	3.8 (0.1 to 7.5)	0.05
Median change in supplemental oxygen use from baseline — liters/day†	0.0 (−117.3 to 117.3)	0.0 (−148.2 to 148.2)	−12.0 (−76.7 to 52.7)	0.005

Table 4. Percent Changes in the FEV_1 and Distance on the 6-Minute Walk Test at 6 and 12 Months, According to Subgroup of Disease Severity.*

Subgroup and Outcome	Percent Change from Baseline at 6 Mo		Percent Change from Baseline at 12 Mo	
	Difference between EBV Group and Control Group	P Value†	Difference between EBV Group and Control Group	P Value†
	% (95% CI)		*% (95% CI)*	
High heterogeneity				
FEV_1	10.7 (3.5 to 17.9)	0.004	13.3 (5.7 to 20.9)	<0.001
Distance on 6-min walk test	12.4 (4.8 to 20.1)	0.002	7.1 (–0.8 to 14.9)	0.08
Low heterogeneity				
FEV_1	2.5 (–3.1 to 8.2)	0.38	1.5 (–4.7 to 7.6)	0.64
Distance on 6-min walk test	–1.0 (–6.4 to 8.4)	0.80	–0.6 (–6.4 to 7.7)	0.84
Complete fissure				
FEV_1	16.2 (8.8 to 23.8)	<0.001	17.9 (9.8 to 25.9)	<0.001
Distance on 6-min walk test	7.7 (–1.8 to 17.2)	0.14	3.9 (–4.0 to 11.8)	0.31
Incomplete fissure				
FEV_1	2.0 (–3.9 to 7.9)	0.51	2.8 (–3.8 to 9.4)	0.41
Distance on 6-min walk test	5.3 (–1.5 to 12.2)	0.13	4.5 (–2.7 to 11.8)	0.20

A

Degree of Heterogeneity	Percent Change in FEV_1 (Treatment–Control)	Point Estimate (95% CI)	P Value
≥25%		15.3 (5.3 to 25.3)	0.003
≥15% to <25%		5.8 (–4.5 to 16.1)	0.27
≥6% to <15%		5.9 (–1.4 to 13.1)	0.12
<6%		–0.4 (–8.8 to 8.1)	0.93

B

Degree of Heterogeneity	Percent Change in 6MWT (Treatment–Control)	Point Estimate (95% CI)	P Value
≥25%		16.2 (3.8 to 28.5)	0.009
≥15% to <25%		8.1 (–1.6 to 17.8)	0.10
≥6% to <15%		–2.7 (–16 to 10.6)	0.67
<6%		0.7 (–7.8 to 9.2)	0.89

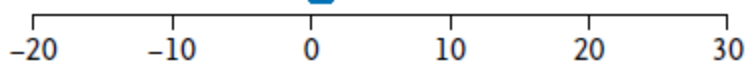

Table 3. Major Adverse Events at 90 Days.*

Event	Endobronchial-Valve Therapy (N=214)	Control (N=87)	P Value†
	no. (% [95% CI])	*no. (% [95% CI])*	
Patients with any event in the composite of major complications	9 (4.2 [1.9–7.8])	0 (0 [0.0–4.2])	0.06
Death‡	2 (0.9 [0.1–3.3])	0 (0 [0.0–4.2])	1.00
Cardiovascular event			
Arrhythmia	2 (0.9 [0.1–3.3])	0 (0 [0.0–4.2])	1.00
Congestive heart failure	0 (0 [0.0–1.1])	1 (1.1 [0.0–6.2])	0.29
Coronary artery disease	2 (0.9 [0.1–3.3])	1 (1.1 [0.0–6.2])	1.00
Pulmonary or thoracic event			
COPD exacerbation			
With hospitalization	17 (7.9 [4.7–12.4])	1 (1.1 [0.0–6.2])	0.03
Without hospitalization	3 (1.4 [0.3–4.0])	0 (0 [0.0–4.2])	0.56
Pulmonary infection	4 (1.9 [0.5–4.7])	0 (0 [0.0–4.2])	0.33
Respiratory failure‡	3 (1.4 [0.3–4.0])	0 (0 [0.0–4.2])	0.56
Pneumonia			
Not distal to valve	5 (2.3 [0.8–5.4])	2 (2.3 [0.3–8.1])	1.00
Distal to valve‡	2 (0.9 [0.1–3.3])	NA	NA
New or worsening hypercapnia§	2 (0.9 [0.1–3.3])	0 (0 [0.0–4.2])	1.00
Hypoxemia	3 (1.4 [0.3–4.0])	0 (0 [0.0–4.2])	0.56
Hemoptysis			
Massive‡	1 (0.5 [0.0–2.6])	0 (0 [0.0–4.2])	1.00
Any	12 (5.6 [2.9–9.6])	0 (0 [0.0–4.2])	0.02
Pneumothorax or air leak			
Duration of >7 days‡	3 (1.4 [0.3–4.0])	0 (0 [0.0–4.2])	0.56
Expanding	3 (1.4 [0.3–4.0])	0 (0 [0.0–4.2])	0.56
Stable	3 (1.4 [0.3–4.0])	0 (0 [0.0–4.2])	0.56
Empyema‡	0 (0 [0.0–1.7])	0 (0 [0.0–4.2])	NA
Noncardiac chest pain	1 (0.5 [0.0–2.6])	0 (0 [0.0–4.2])	1.00

In the USA VENT study the mean response to EBV treatment was significantly increased in patients having higher emphysema heterogeneity over patients with lower emphysema heterogeneity

Emphysema heterogeneity was not critical for determining positive outcomes in European VENT study

Arschang Valipour et al in their study of analysed 416 COPD patients with advanced emphysema and hyperinflation across Europe and USA, who were randomized to EBV (n5284) or conservative therapy (n5132)

Quantitative image analysis used to compare the volume of the targeted lobe at baseline and at 6 months to determine target lobe volume reduction .

Eur Respir J 2014; 43: 387–396

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Changes in BODE were predicted by baseline BODE and correlated significantly with lobar exclusion and lung volumes at 6 months.

The likelihood of benefit was less than half in both groups. Patients in whom TLVR was obtained had greater improvements in clinical outcome

Eur Respir J 2014; 43: 387–396

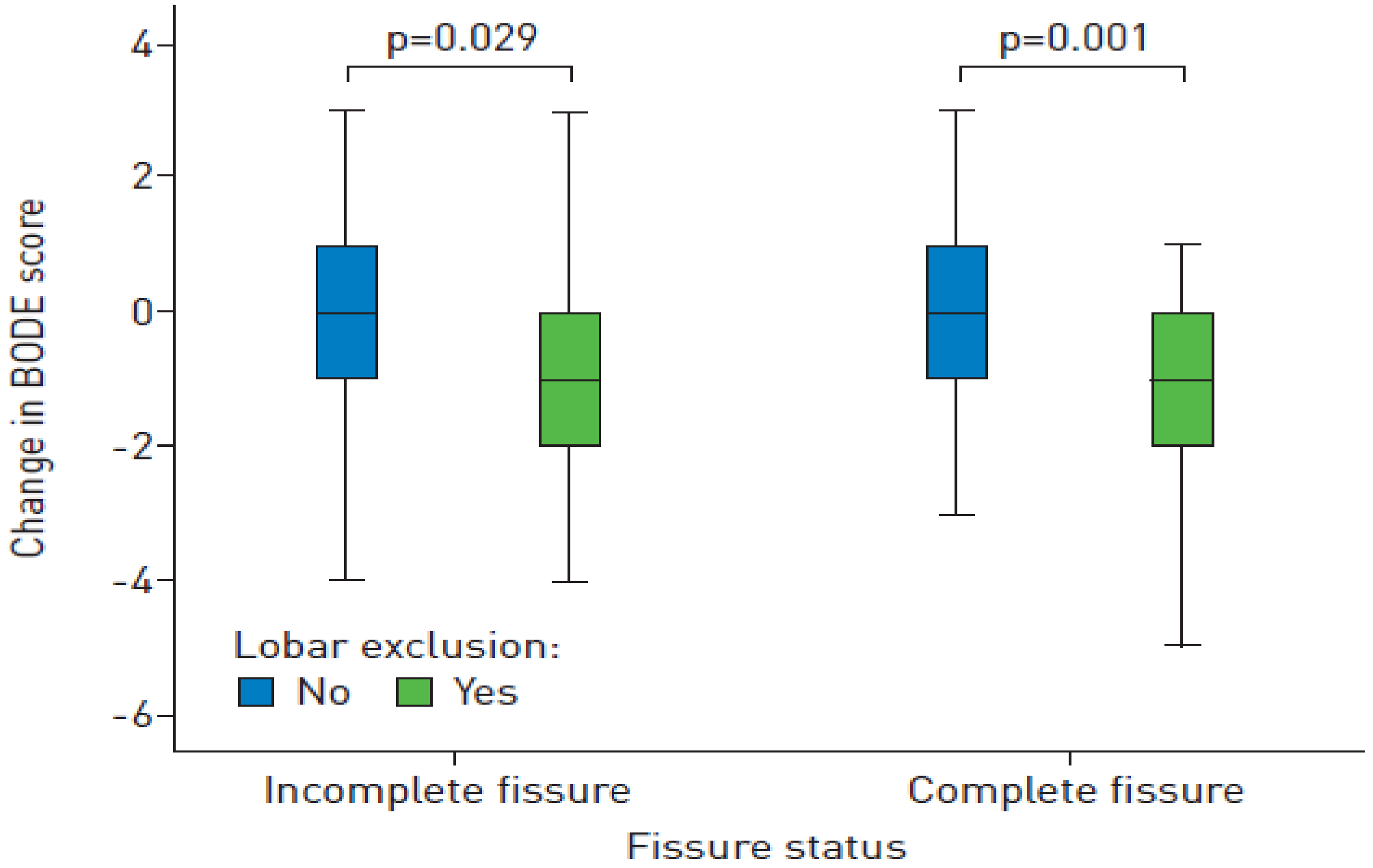

p=0.029
p=0.001
4
2
0
-2
-4
-6
Change in BODE score
Lobar exclusion:
No
Yes
Incomplete fissure
Complete fissure
Fissure status

TABLE 2 Clinical, functional and radiological outcomes presented as percentage of population in patients treated with endobronchial valve therapy and controls at 6 months according to fissure status

	Treatment group			Control group
	Complete fissure	Incomplete fissure	p-value	
Subjects n	110	174		132
Radiological outcomes				
TLVR >50%	32.5	4.1	<0.001	0.0
TLVR 20–50%	22.0	15.3		2.0
TLVR ⩽20%	30.1	67.3		82.2
Missing	15.4	13.3		15.8
Clinical and functional outcomes (cut-off)				
FEV_1 (12% pred)	46.7	15.8	<0.001	16.5
6-min walk distance (26 m)	45.3	42.1	0.352	35.5
SGRQ (4 points)	41.7	44.4	0.394	30.2
mMRC (1 point)	35.7	32.8	0.385	14.7
BODE index (1 point)	41.0	46.9	0.242	24.7

Data are presented as %, unless otherwise stated. p-values were obtained by comparison of frequencies by crosstabs and Chi-squared tests. TLVR: target lobar volume reduction; FEV_1: forced expiratory volume in 1 s; % pred: % predicted; SGRQ: St George's Respiratory Questionnaire; mMRC: modified Medical Research Council dyspnoea scale; BODE: body mass index, airflow obstruction, dyspnoea and exercise capacity scale.

Bronchoscopic lung volume reduction with endobronchial valves for patients with heterogeneous emphysema and intact interlobar fissures (the BeLieVeR-HIFi study): a randomised controlled trial

Claire Davey, Zaid Zoumot*, Simon Jordan, William H McNulty, Dennis H Carr, Matthew D Hind, David M Hansell, Michael B Rubens, Winston Banya, Michael I Polkey, Pallav L Shah, Nicholas S Hopkinson*

Single-centre, double-blind sham-controlled trial in patients with both heterogeneous emphysema and a target lobe with intact interlobar fissures on CT of the thorax.

Target lobe selection based on CT appearance alone

Measurements of collateral ventilation using the Chartis balloon catheter system were made in all participants so that the accuracy of the two approaches could be compared.

Endobronchial valves were placed to occlude segmental bronchi leading to the target lobe collapse (irrespective of the Chartis results).

50 patients were enrolled to receive valves (n=25) or sham valve placement (control, n=25)

In the bronchoscopic lung volume reduction group, FEV1 increased by a median 8.77% versus 2.88% in the control group.

The success rate of valve placement was higher than in previous studies because only patients with intact interlobar fissures on CT were included

Cases of positive collateral ventilation assessed using the Chartis system were associated with no benefit from treatment

There may be possibility of an additive role of Chartis system in improving patient selection

	BLVR		Control (n=24)	p value*
	All (n=23)	CV-positive excluded (n=19)		
FEV_1	9 (39%)	..	1 (4%)	0·0044
>15% improvement	..	9 (47%)	1 (4%)	0·0022
RV	11 (48%)	..	7 (29%)	0·24
0·35 L reduction[20]	..	11 (58%)	7 (29%)	0·07
6MWD	12 (52%)	..	4 (17%)	0·012
26 m improvement[24]	..	12 (63%)	4 (17%)	0·004
Endurance cycle time	10 (43%)	..	2 (8%)	0·008
105 s improvement[23]	..	9 (47%)	2 (8%)	0·005
SGRQc	11 (48%)	..	11 (46%)	1·0
4 points reduction[21]	..	11 (58%)	11 (46%)	0·5
CAT	13 (57%)	..	7 (29%)	0·080
2 points reduction[22]	..	13 (68%)	7 (29%)	0·015

Data are n (%). CV-positive=collateral ventilation using Chartis system. BLVR=bronchoscopic lung volume reduction. FEV_1=forced expiratory volume in 1 s. RV=residual volume. 6MWD=6 min walking distance. SGRQc=St George's respiratory questionnaire for chronic obstructive pulmonary disease (COPD). CAT=COPD assessment test score. *Fisher's exact test (this analysis does not include imputed values).

Table 5: **Responder rates according to lung function, health status, and exercise criteria**

COMPLICATIONS OF BRONCHOSCOPIC VALVE PLACEMENT

Hemoptysis

Pneumothorax

Acute exacerbation of COPD

The overall rate of post-procedural pneumothorax reported to be 6% [Gompelmann *et al.* 2014b]

Risk increase up to 30% with higher target lobar volume reduction [Valipour *et al.* 2014].

Cause of pneumothorax-

Untreated ipsilateral lobe expands to occupy the newly created space in the thoracic cavity after valve placement

Shifting of volumes on one side of the lung, which may rapid in some cases, is associated with tensioning and tearing of the already compromised lung tissue.

The magnitude of the lobar volume shift proportional to size of the target lobe reduction

This shifting of volume to the nontreated ipsilateral lobe result in rupture of blebs or bullae causing a pneumothorax

Respirology (2014) 19, 1126–1137

Other mechanism is parenchymal rupture as the lobes shift volumes due to preexisting pleural adhesion

In above conditions pneumothorax result in a bronchopleural fistula that could cause pneumothorax expansion over time if not treated by chest tube insertion.

Respirology (2014) 19, 1126–1137

Other less common manifestation is pneumothorax ex vacuo

Acute lobar collapse results in a sudden increase in the negative intrapleural pressure surrounding the collapsed lobe.

Gas originating from the ambient tissues and blood are drawn into the pleural space surrounding the collapsed lobe while the seal between the visceral and parietal pleura of the adjacent lobe or lobes remains intact

Here a bronchopleural fistula is not present and the pleural air would resolve spontaneously over time without the need for tube thoracostomy

Respirology (2014) 19, 1126–1137

CONCLUSION-

Complete lobar occlusion to produce the desired volume reduction necessary for significant clinical effectiveness.

The presence of inter-lobar collateral ventilation (CV) interferes with lobar collapse despite adequate positioning and function of one-way valves.

As more than half of severe emphysema patients have significant inter-lobar CV Indirect evaluation of CV via the assessment of fissure completeness required for accurate patient selection

The selection of the target lobe for bronchial occlusion is crucial

Most affected emphysematous lobe usually selected

Confirmation by low-baseline regional perfusion of the target lobe enhance clinical results

Existence of expandable ipsilateral lobes with less emphysematous destruction required for desirable clinical effectiveness after valve treatment

Chest 2013; **144**: 1578–86

LUNG VOLUME REDUCTION COILS

LVRC is a technique for bronchoscopic treatment of severe COPD using a nitinol coil that is delivered to the mid lung airways under fluoroscopy in a sheath which keeps it straightened .

The LVR coil is designed to improve the elastic recoil of lung tissue and reduce the airway resistance and hyperinflation in emphysema patients.

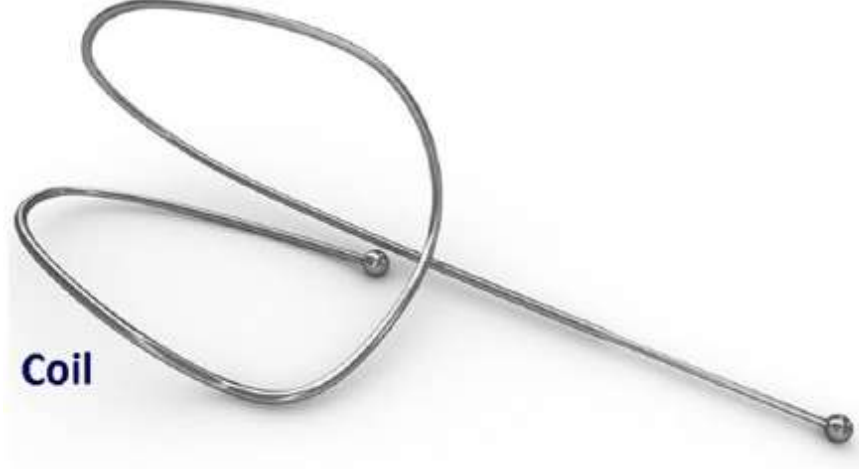
Reduction of the residual volume (RV) of the hyperinflated lung improves diaphragmatic function and inspiratory muscle function.

It is effective on heterogeneous and homogeneous emphysema and is independent of collateral ventilation.

Patients with large bullae are unlikely to benefit from the technique

J Thorac Dis 2014;6(S4):S407-S415

Coil



Catheter

Forceps

Cartridge

Guidewire

STEPS OF LVRS

Bronchoscope navigated to the target airway and positioned at the ostium of a subsegmental airway

Both the catheter and guidewire inserted into the working channel of the bronchoscope

Guidewire advanced and navigated into the distal targeted airway under fluoroscopy guidance; minimum 3 cm away from the pleura

Guidewire is hold fixed in position relative to the bronchoscope and catheter is advanced distally up to but not past the point where the tip of the catheter is aligned with the tip of the guidewire.

Lancet Respir Med 2013;1: 233–40

Radiopaque markers on the guidewire used to measure the airway length

Guidewire removed from the catheter while maintaining the catheter position

The desired size coil loaded into the cartridge

The coil delivered into the catheter by advancing the forceps and coil

Distal end of the coil is aligned with the distal end of the catheter. Positioning of the coil is made using fluoroscopy

Lancet Respir Med 2013;1: 233–40

An assistant hold the bronchoscope fixed relative to the patient

Coil is deployed using fluoroscopy by withdrawing the catheter with one hand, while holding the coil position fixed with the forceps using the other hand

Position of the coil is verified under fluoroscopy and the coil is released by unlocking the forceps

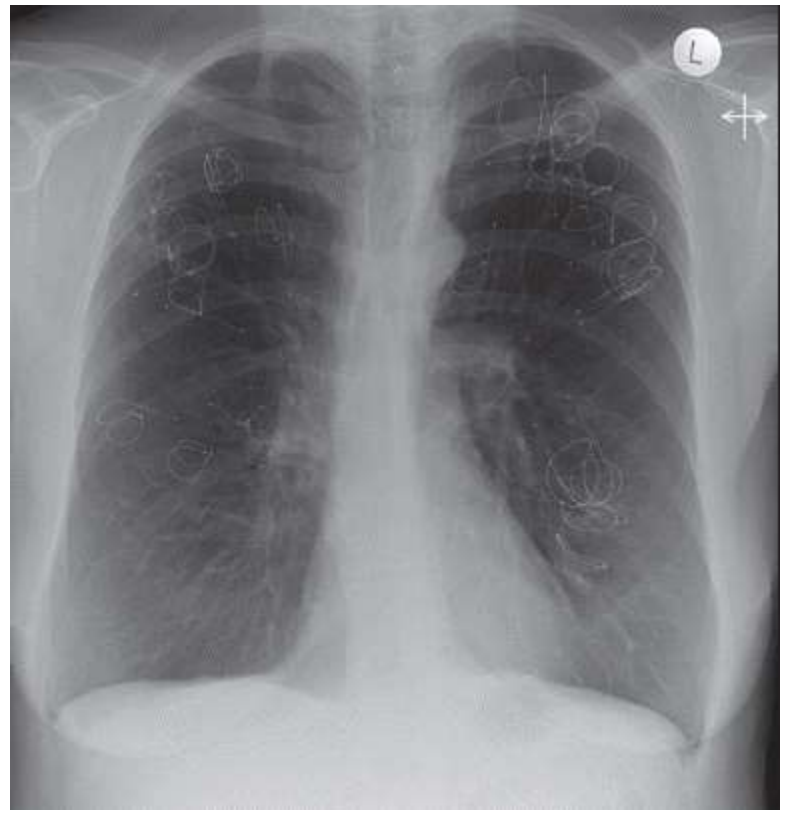
Forceps are removed from the catheter

Lancet Respir Med 2013;1: 233–40

On average, 10–12 coils are placed per upper lobe and 10–14 per lower lobe treatment

Generally, both sides of the lung are treated, and this is performed in two separate bronchoscopic procedures with 1–2 months in between

Klooster et al. Exp Rev Med Devices 11: 481–489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Endobronchial coils for the treatment of severe emphysema with hyperinflation (RESET): a randomised controlled trial

Pallav L Shah, Zaid Zoumot, Suveer Singh, Stephen R Bicknell, Ewen T Ross, John Quiring, Nicholas S Hopkinson, Samuel V Kemp, for the RESET trial Study Group

Patients with severe emphysema (aged ≥35 years) randomly allocated one-to-one ratio to either LVRC treatment (treatment group) or best medical care (usual care group)

Primary endpoint - the difference in response in the St George's Respiratory Questionnaire (SGRQ) between treatment and usual care groups at 90 days

Inclusion criteria

Aged ≥35 years

High resolution CT scan indicates unilateral or bilateral emphysema

High resolution CT scan indicates homogeneous or heterogeneous emphysema

A post-bronchodilator FEV1 ≤45% predicted

Total lung capacity >100% predicted

Patient has marked dyspnoea score ≥2 on modified Medical Research Council scale of 0–4

Patient has stopped smoking for a minimum of 8 weeks before enrolment

Exclusion criteria

change in FEV1 greater than 20% post-bronchodilator

A single-breath diffusing capacity for carbon monoxide <20% predicted

A history of recurrent clinically significant respiratory infection

An uncontrolled pulmonary hypertension defined by right ventricular pressure >50 mm Hg or evidenced by echocardiogram

An inability to walk >140 m in 6 min

Evidence of other diseases that can compromise survival—eg, lung cancer or renal failure

Pregnant or lactating

	Treatment (n= 23)	Usual care (n= 23)	p value*
Primary outcome			
SGRQ ≥4-point improvement	15 (65%)	5 (22%)	0·01
SGRQ ≥8-point improvement	13 (57%)	3 (13%)	0·01
Secondary outcome			
Respiratory volume: 0·35-L reduction	13 (57%)	4 (17%)	0·01
6-min walk test: 26-m improvement	17 (74%)	4 (17%)	<0·0003
FEV_1: 10% improvement	13 (57%)	6 (26%)	0·07

Data are n (%). *Fisher's Exact Test. SGRQ=St George's Respiratory Questionnaire. FEV_1= forced expiratory volume in 1 s.

Table 3: **Responder analysis of primary and secondary efficacy outcomes in the intent-to-treat population (change from baseline at 90 days after final treatment)**

	Treatment (23 patients, 44 procedures)			Usual care (23 patients)			p value‡
	Events (n)*	Patients (n)	Incidence (%)†	Events (n)	Patients (n)	Incidence (%)†	
Treatment recovery periods§							
Device removal	0	0	0%	0	0	0%	NA
Exacerbation	2	2	5%	1	1	4%	>0·99
Haemoptysis	0	0	0%	0	0	0%	NA
Lower respiratory tract infection¶	2	2	5%	0	0	0%	0·49
Pneumothorax	2	2	5%	0	0	0%	0·49
Respiratory failure	0	0	0%	0	0	0%	NA
Total	6	6	15%	1	1	4%	0·02
Post-treatment periods‖							
Device removal	0	0	0%	0	0	0%	NA
Exacerbation	3	2	7%	2	2	9%	>0·99
Haemoptysis	0	0	0%	0	0	0%	NA
Lower respiratory tract infection¶	0	0	0%	1	1	4%	>0·99
Pneumothorax	0	0	0%	0	0	0%	NA
Respiratory failure	0	0	0%	0	0	0%	NA
Total	3	2	7%	3	3	13%	>0·99

Patients with both upper and lower lobar distribution of emphysema and homogeneous distribution of emphysema were benifited.

Long term benefits of LVRS is not established in this study.

Effectiveness of Endobronchial Coil Treatment for Lung Volume Reduction in Patients with Severe Heterogeneous Emphysema and Bilateral Incomplete Fissures: A Six-Month Follow-Up

Konstantina Kontogianni[a] Vasiliki Gerovasili[a] Daniela Gompelmann[a]
Maren Schuhmann[a] Claus Peter Heussel[b] Felix J.F. Herth[a] Ralf Eberhardt[a]

Departments of [a]Pulmonology and Respiratory Care Medicine and [b]Diagnostic and Interventional Radiology, Thoraxklinik at the University of Heidelberg, Heidelberg, Germany

Twenty-six patients with chronic obstructive pulmonary disease (COPD), 13 males and 13 females, aged 66 ± 8 years with heterogeneous emphysema and incomplete fissures included in this retrospective analysis

The coils implanted unilaterally in the upper or lower lobe

Patients were followed up at 30, 90 and 180 days after treatment and

changes in pulmonary function test

6-minute-walk-test (6MWT) values

mMRC) dyspnea scale and

SGRQ recorded.

	Baseline (n = 26)	30-day follow-up (n = 26)	90-day follow-up (n = 25)	180-day follow-up (n = 22)	p value
Pulmonary lung function					
FEV_1, l	0.67±0.17	0.74±0.21*	0.78±0.25*	0.73±0.21 (n = 21)	<0.001
FEV_1, % predicted	26±8	29±8	30±9*	29±8 (n = 21)	<0.001
VC, l	1.97±0.64	2.15±0.70	2.34±0.78*	2.29±8.7 (n = 21)	0.001
VC, % predicted	58±18	64±17	68±19*	70±19* (n = 21)	0.001
RV, l	6.17±1.6	5.52±1.16*	5.57±1.65*	5.75±1.28 (n = 21)	0.005
RV, % predicted	279±53	251±38	247±60*	265±47 (n = 21)	0.005
TLC, l	8.16±1.72	7.72±1.36	7.93±1.65	8.05±1.56 (n = 21)	NS
TLC, % predicted	141±20	133±13	135±17	145±19 (n = 21)	NS
RV/TLC	75±8	71±7	69±10*	72±9 (n = 21)	0.001
Exercise capacity (6MWT), m	216±107	247±105* (n = 25)	262±97* (n = 23)	262±112 (n = 19)	0.001
Questionnaire scores					
SGRQ					
Total	65±12 (n = 25)	56±13* (n = 25)	58±13* (n = 24)	59±13 (n = 20)	0.009
Impact	54±18*	47±17	47±18	49±18	0.032
Activity	86±12	80±18	84±10	82±13	NS
Symptoms	64±18	53±24	47±16*	52±25	0.012
mMRC (dyspnea)	3.0±1.1	2.6±1.3	2.6±1.2	2.4±1.3 (n = 22)	NS

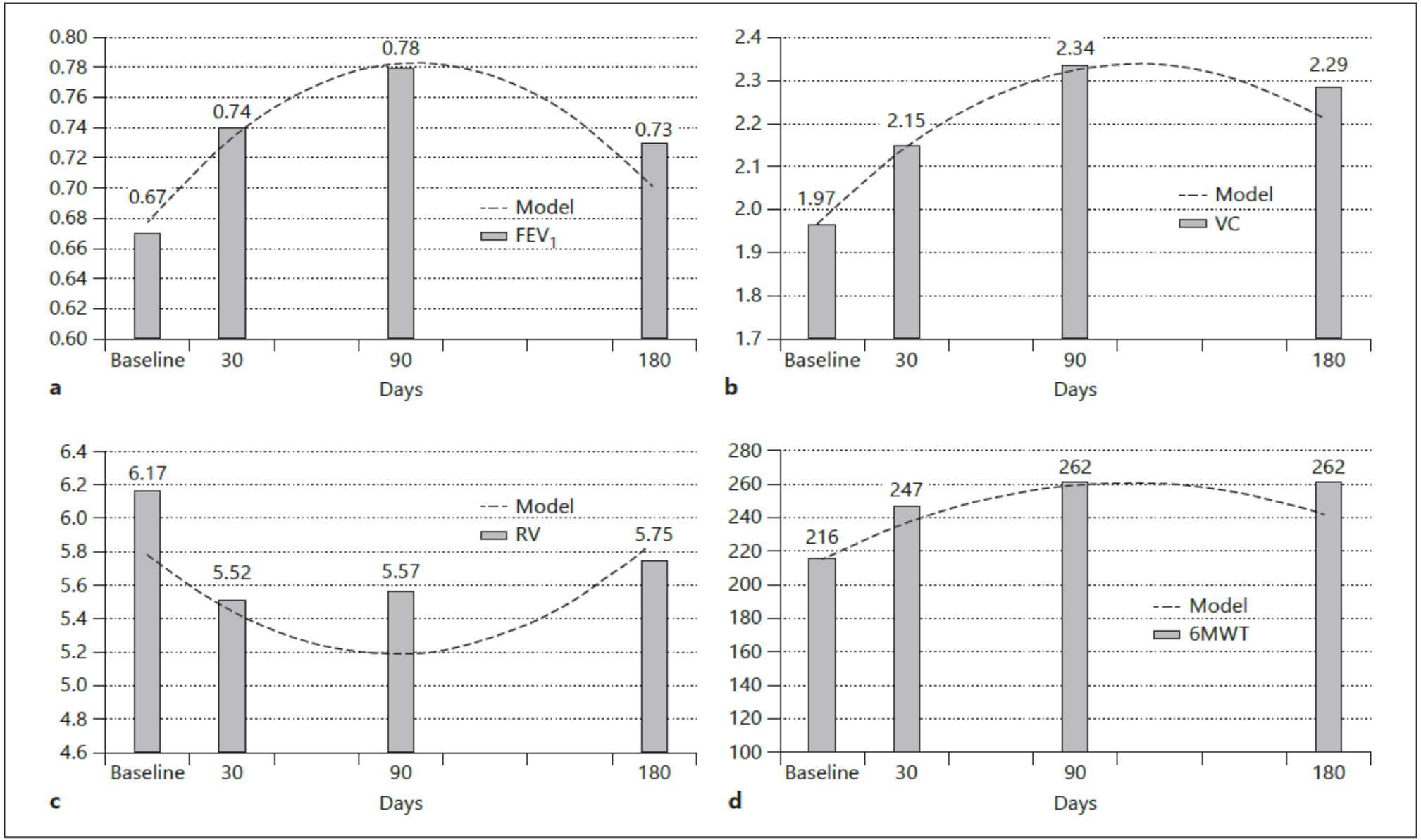


Fig. 5. FEV_1 (**a**), VC (**b**), RV (**c**) and 6MWT (**d**) in 26 patients who underwent LVRC treatment at baseline and at 30, 90 and 180 days after the intervention (bars represent mean values and lines represent predicted values according to the fitted quadratic model).

AIRWAY BIPASS

Small endobronchial vents placed bronchoscopically through holes made directly in the airway wall to allow direct flow of trapped air in the emphysematous lung is called airway bypass

By creating holes in the airways and stenting them open with drug eluting stents, they will remain open and allow emphysematous areas of lung with trapped air to escape to the larger airways more easily

Doppler probe used to interrogate the target site for the hole to ensure there is no vessel at that location.

J Thorac Dis 2014;6(11):1640-1653

The Exhale drug-eluting stent is composed of stainless steel and silicone and contains paclitaxel, which is intended to inhibit fibrotic responses .

For airway bypass up to six stents placed(maximum of two stents per lobe, excluding the right middle lobe) per individual

J Thorac Dis 2014;6(11):1640-1653

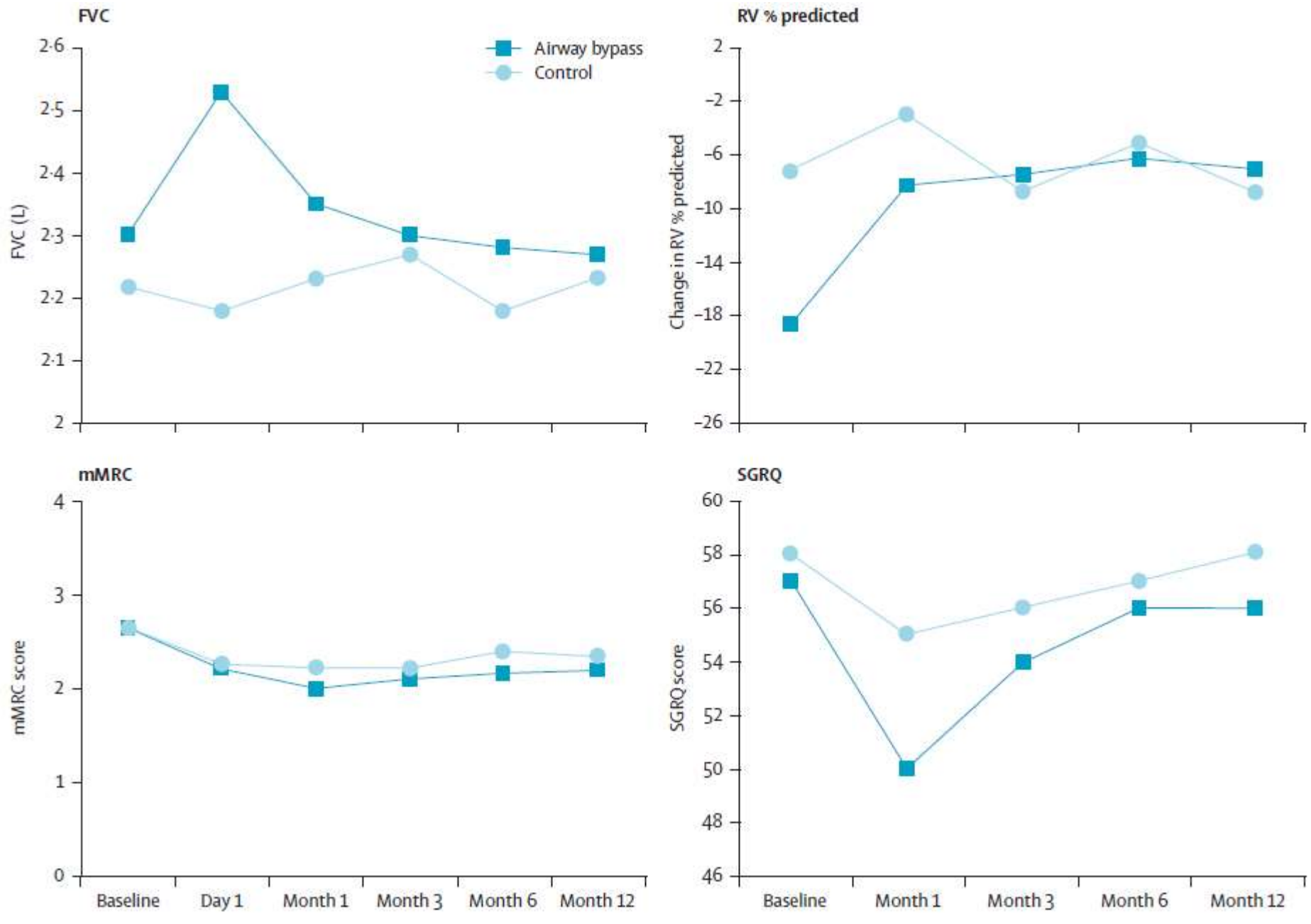
The exhale airway stents for emphysema (EASE) trial was a prospective randomized, double-blind, sham-controlled study published in 2011 studied 315 subjects with homogenous emphysema and with severe hyperinflation -ratio of RV to total lung capacity of ≥0.65

Primary efficacy endpoint was at least a 12% increase in FVC and at least 1-point decrease in the mMRC dyspnea score from baseline

Addition of drug eluting stents for the EASE trial was an attempt to prevent granulation obstruction of the vents.

- No difference between treatment and sham groups seen in the efficacy or safety endpoints at 6 or 12 months

- Initially the vents produced an improvement in lung function but the vents tended to become obstructed over time with granulation tissue or mucus and the improvements were not sustainable over time.


FVC
Airway bypass
Control
FVC (L)
2·6
2·5
2·4
2·3
2·2
2·1
2
RV % predicted
Change in RV % predicted
2
-2
-6
-10
-14
-18
-22
-26
mMRC
mMRC score
4
3
2
1
0
SGRQ
SGRQ score
60
58
56
54
52
50
48
46
Baseline
Day 1
Month 1
Month 3
Month 6
Month 12

BIOLOGIC LUNG VOLUME REDUCTION

Biologic lung volume reduction reduces lung volume by administration of a fibrinogen biopharmaceutical suspension and thrombin solution that polymerize in situ to form a hydrogel

Hydrogel contains biodegradable complexes of poly-L-lysine and chondroitin sulfate that initiate a localized inflammatory reaction that collapses, remodels, and volume-reduces areas of emphysematous lung over 3 to 6 weeks

J Thorac Dis 2014;6(S4):S407-S415

Am J Respir Crit Care Med Vol 179. pp 791–798, 2009

Biologic Lung Volume Reduction in Advanced Upper Lobe Emphysema

Phase 2 Results

Gerard J. Criner[1], Victor Pinto-Plata[2], Charlie Strange[3], Mark Dransfield[4], Mark Gotfried[5], William Leeds[6], Geoffrey McLennan[7], Yael Refaely[8], Sanjiv Tewari[9], Mark Krasna[10], and Bartolome Celli[2]

[1]Temple University, Philadelphia, Pennsylvania; [2]Caritas-St. Elizabeth's Medical Center, Boston, Massachusetts; [3]Medical University of South Carolina, Charleston, South Carolina; [4]University of Alabama Birmingham, Birmingham, Alabama; [5]Pulmonary Associates, Phoenix, Arizona;

Gerard et al. in their study of biologic lung volume reduction selected patients of GOLD stage three or stage four upper lobe predominant emphysema on HRCT thorax who were not eligible or had refused LVRS

Objective - Assess the safety and therapeutic dose of BioLVR hydrogel in upper lobe predominant emphysema.

PROCEDURE

The most damaged lung segments selected for BioLVR by HRCT.

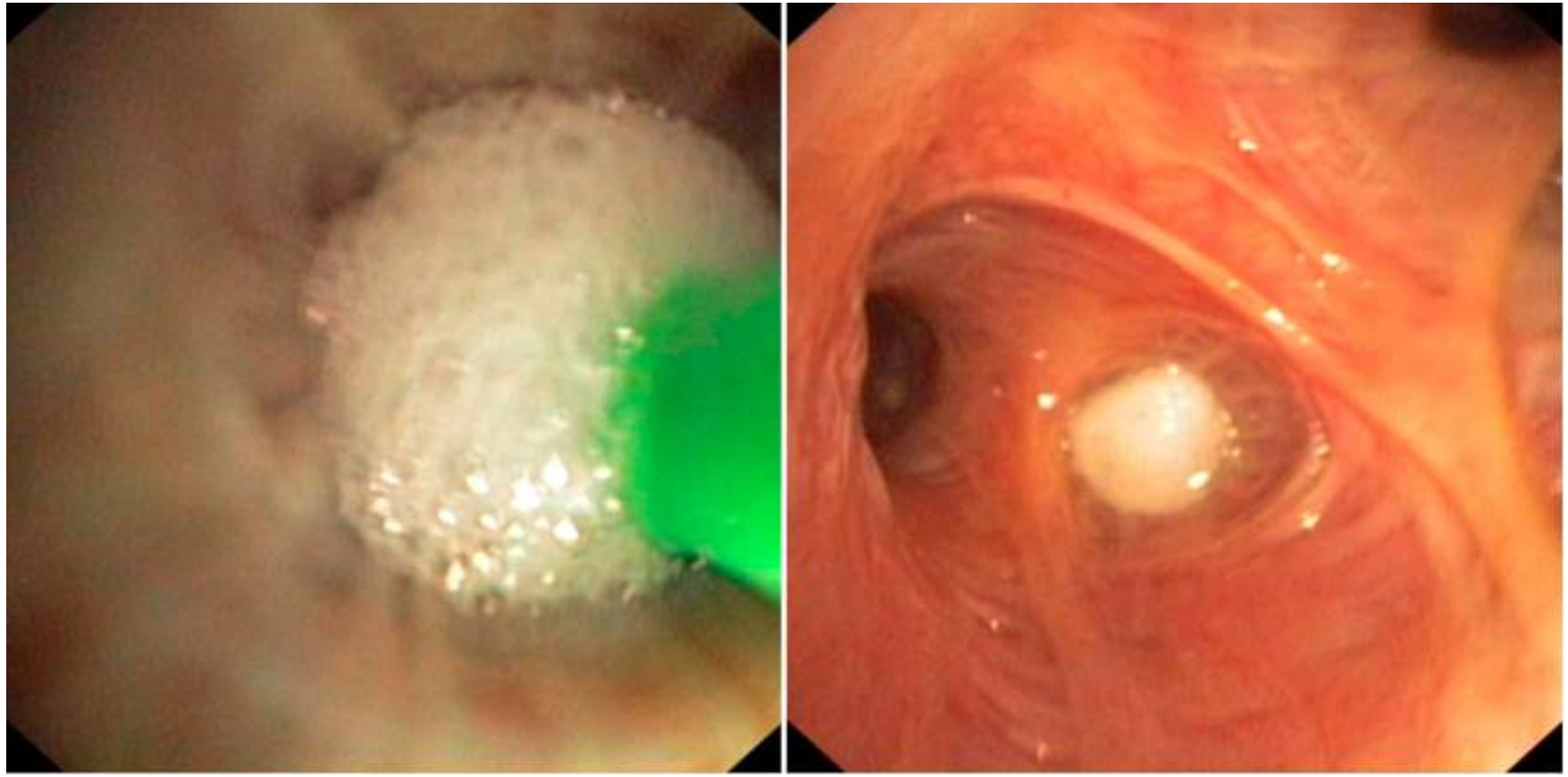
The flexible bronchoscope advanced into the subsegmental orifice of the airway selected for treatment and wedged to prevent reagent backflow during administration

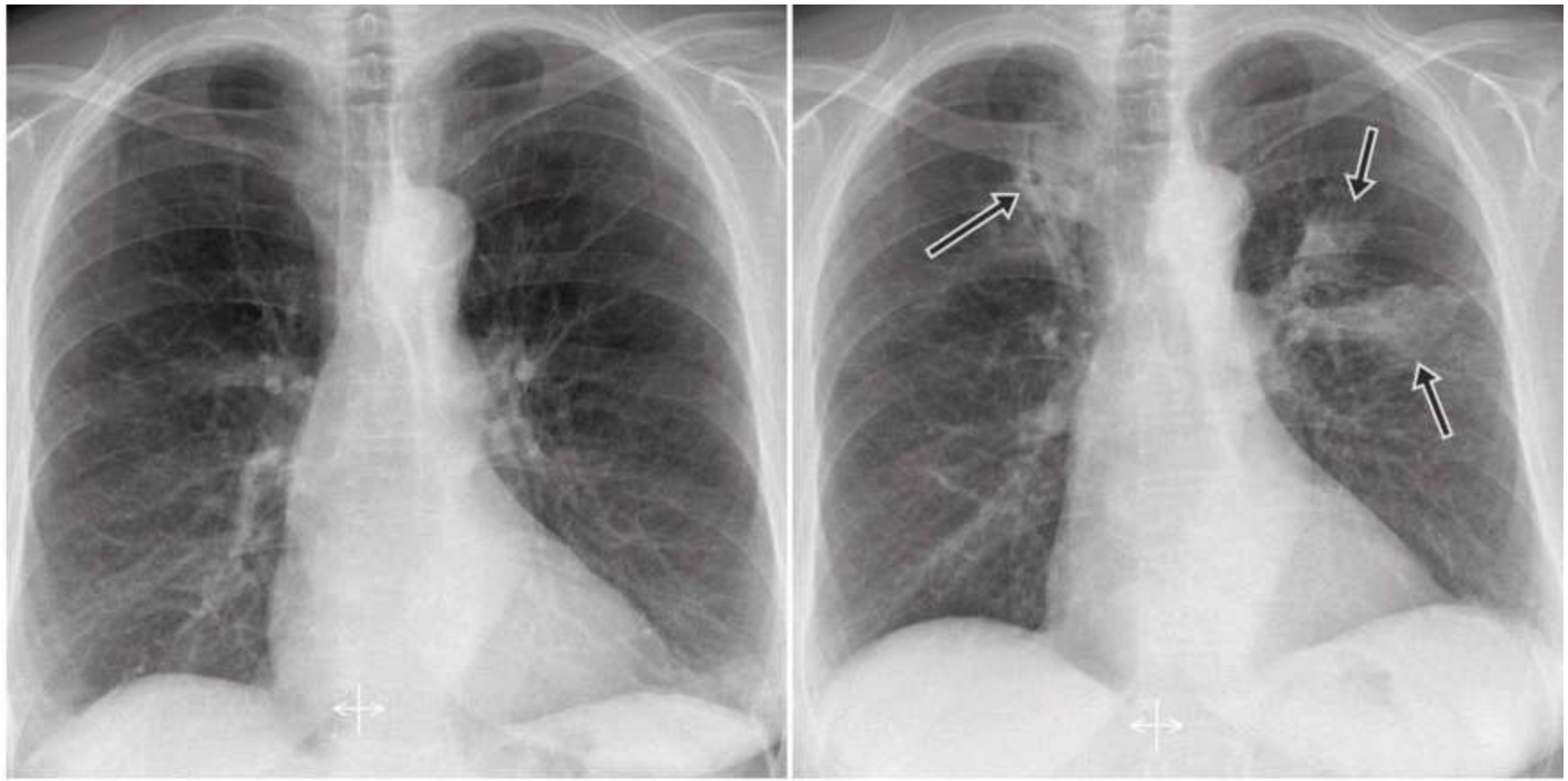
Dual lumen catheter guided distally under direct vision until the tip reached 3 to 4 cm beyond the end of the bronchoscope

Syringes containing the two reagents, fibrinogen suspension and thrombin solution connected to the appropriate luer connectors of the catheter and proportionately delivered using a handheld administration device over 10 to 15 seconds to ensure rapid polymerization of the hydrogel

Immediately after delivery of the hydrogel, 60 ml of air injected twice through the instrument channel of the scope to push the reagents peripherally

After 30 seconds bronchoscope repositioned at the next treatment site





Hydrogel administered to eight sub segmental sites (four in each upper lobe) involving:

low-dose treatment (n = 28) with 10 ml per site (LD)

high-dose treatment (n 5=22) with 20 ml per site (HD)

Reduction in residual volume to TLC ratio at 12 weeks (primary efficacy outcome) achieved with both LD(-6.4 ± 9.3%; P = 0.002) and HD (-5.5± 9.4%; P = 0.028) treatments

Improvements in pulmonary function in HD(6mo:ΔFEV1+15.6%;P=0.002; ΔFVC+9.1%;P=0.034) greater than in LD patients (6mo: ΔFEV1+6.7%; P=0.021; ΔFVC+5.1%; P = 0.139)

LD- and HD-treated groups both demonstrated improved symptom scores and health-related quality of life.

No deaths during the course of study

Complications-

Procedure-related COPD exacerbations

Post procedure inflammatory reaction causing fever ,malaise ,transient SOB

	Mortality AT 90 DAYS	Serious complications		
LVRS	5.5% National Emphysema trial	58%		
EBV	1%	8 to 10%		
Airway Bipass	3%	27%		
Bio LVR	Nil	8%		

Endoscopic thermal vapor ablation for patients with heterogeneous emphysema

Bronchoscopic thermal vapor ablation (BTVA) is a permanent, non-blocking technique based on delivering heated water vapor via a disposable bronchoscopic catheter to emphysematous lung parenchyma within a targeted region.

Vapor induces inflammatory reaction & fibrosis resulting in lung volume reduction.

This remodeled lung tissue does not inflate and reinflate as a result of interlobar collateral ventilation

J Thorac Dis 2014;6(S4):S407-S415

Vapor therapy for COPD delivers thermal energy in the form of heated water vapor to target subsegments of the lung.

Performed via a disposable catheter introduced through the working channel of a flexible bronchoscope under moderate sedation.

Subsegments targeted based upon the degree of heterogeneity

Energy dose of 5 to 10 calories per estimated gram of tissue is delivered to the selected subsegments.

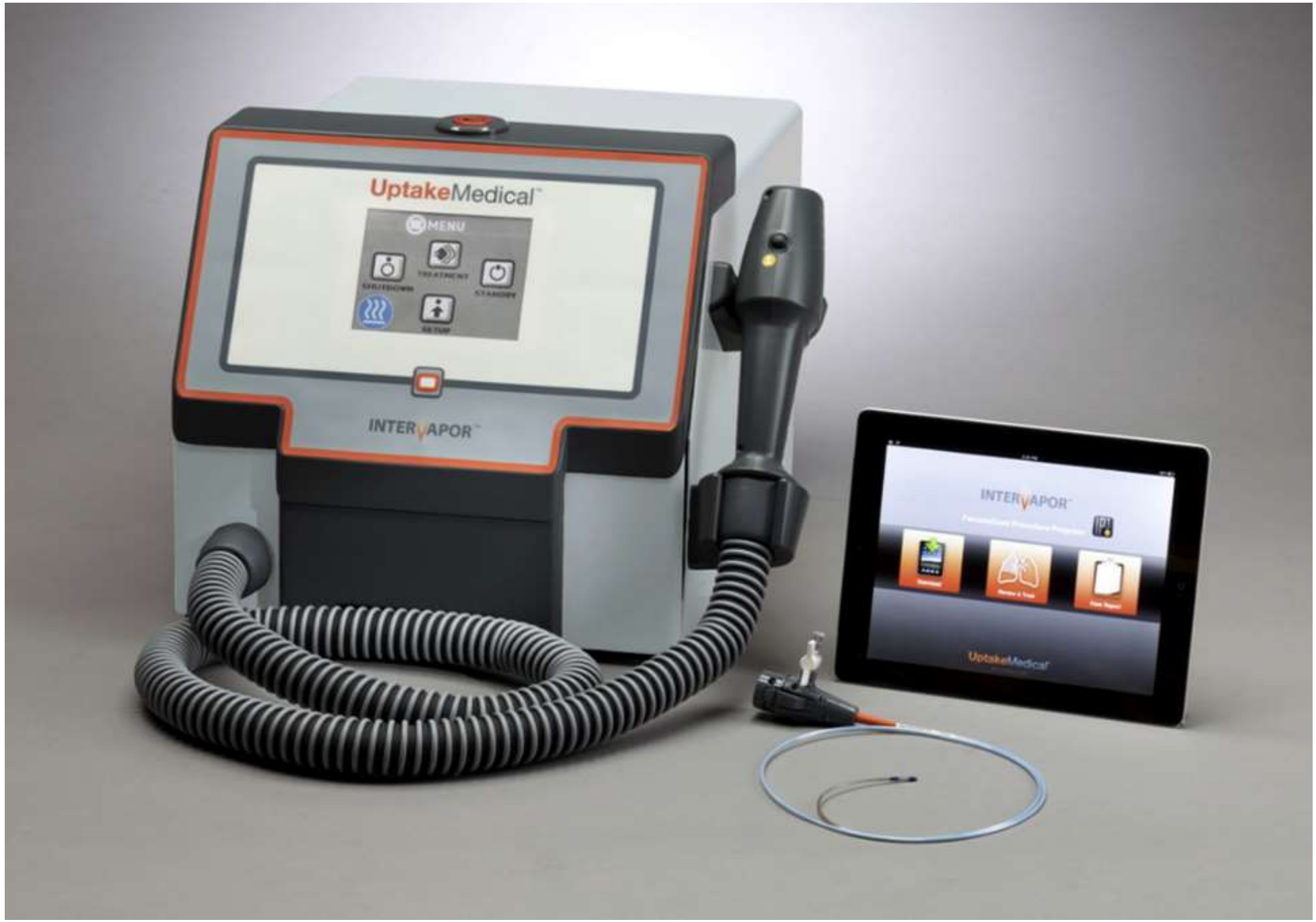
Thermal energy leads to an inflammatory response causing contraction fibrosis and atelectasis - lung volume reduction.

J Thorac Dis 2014;6(S4):S407-S415

No association between efficacy following BTVA and fissure integrity.

This observation is explained by the mechanism of action, which does not rely on obstruction of large airways

Gompelmann et al. Respiration 2012;83:400–406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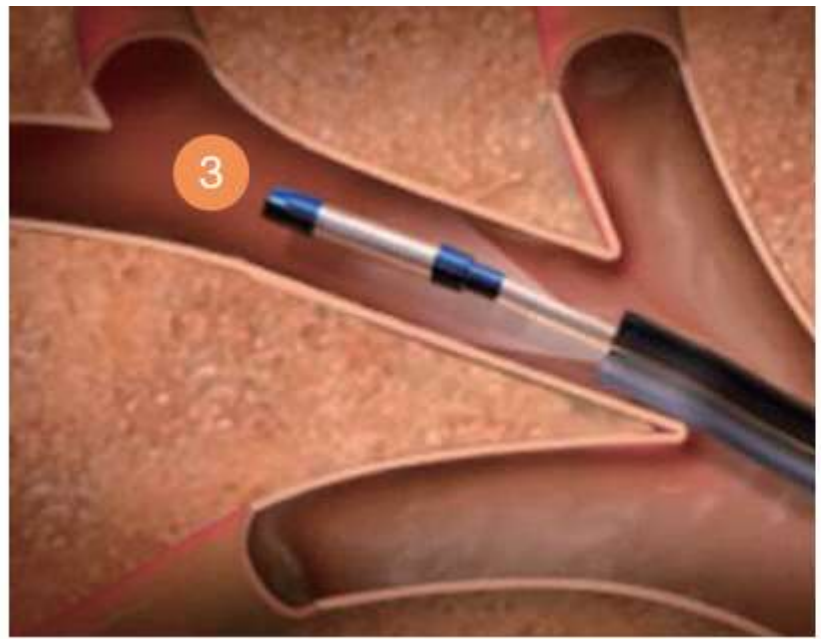
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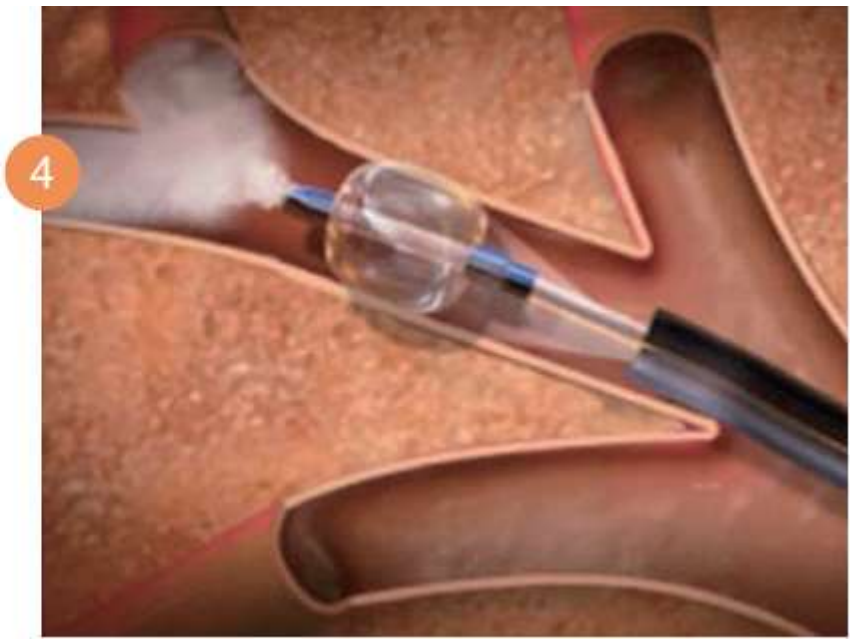
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The results of this procedure are permanent

Felix JF Herth et al in the study of thermal vapour ablation in heterogenous emphysema delivered thermal energy to the airways of an upper lobe through the direct administration of heated water vapor.

The system consists of a vapor generator, a catheter directed through a flexible bronchoscope

- International Journal of COPD 2012:7 397–405

The procedure plan based on the calculated amount of energy (10 calories per gram of tissue) for each lung segment targeted for treatment .

The amount of tissue determined from software analysis .

Treatment time 3- 10 seconds per airway treated.

- International Journal of COPD 2012:7 397–405

key inclusion criteria :

upper lobe predominant emphysema determined from HRCT,

Aged 40 to 75 years, FEV1 between 15% and 45% predicted,

residual volume (RV) .150% predicted,

total lung capacity > 100%,

diffusing capacity for carbon monoxide >20% predicted,

6MWD > 140 m,

partial pressure of CO2 >55 mmHg and

partial pressure of O2 >45 mmHg,

nonsmoking >4 months

International Journal of COPD 2012:7 397–405

Exclusion criteria were:

known α-1-antitrypsin deficiency,

clinically significant asthma,

chronic bronchitis or bronchiectasis,

recent pneumothorax, bullae . 1/3 of lobe, thoracotomy,

left ventricular ejection fraction < 40%, and

pulmonary hypertension

- International Journal of COPD 2012:7 397–405

Improvement in	At 6 months	At 12 months	P value				
FEV1 mean(SD)	141(166ml,17 %)	86(174ml,10 %)	<0.001				
SGRQ Mean(SD)	-14 units	-11 units					
Residual volume Mean(SD)	-406 ml(714 ml)	-303ml (776 ml)	<0.001				
BODE index Mean(SD)	1.48(1.75)	1.25(1.75)	<0.001				
6MWD	46.5m(67.1m)	18.5m(63.7m)					

For patients with GOLD stage III and IV disease, improvements from baseline at 6 months were similar, while improvements at 12 months were more robust in GOLD stage IV patients

Conclusion-Unilateral lobar Inter Vapor treatment of heterogeneous emphysema improved lung function and health outcomes 1 year following treatment.

The magnitude of improvement was larger at 6 months compared to 12 months.

Targeted lung denervation for moderate to severe COPD

Cholinergic parasympathetic nerves innervate both large and small airways Dominant innervation to human lungs.

Acetylcholine released from these nerves regulates airway smooth muscle tone, mucus secretion, and local inflammation through interaction with muscarinic receptors .

Pulmonary parasympathetic activity is enhanced in COPD, and is the dominant reversible component of airway obstruction in this disease

Slebos D-J, et al. Thorax 2015;70:411–419

Targeted lung denervation (TLD) –

Bronchoscopic therapy ablates parasympathetic innervation of the lungs

Similar to mechanism of action of anticholinergic drugs.

TLD therapy is delivered via a dual-cooled radiofrequency (RF) catheter

It target tissue heating at depth producing a narrow band of ablation around the main bronchi

Minimizing effects of heating to the inner surface of the airway

Slebos D-J, et al. Thorax 2015;70:411–419

When RF current passes from the electrode through the airway and surrounding tissues - tissues are heated

Coolant continuously circulated through the electrode and balloon- removes heat from the surface of the airway wall

Slebos D-J, et al. Thorax 2015;70:411–419

NET EFFECT- Targeted tissue ablation at depth with minimal heating and damage of the inner surface of the airway

Targeted tissue ablation disrupt motor axons within bronchial nerve branches

Block parasympathetic signaling to the lungs

Decrease neuronal release of acetylcholine

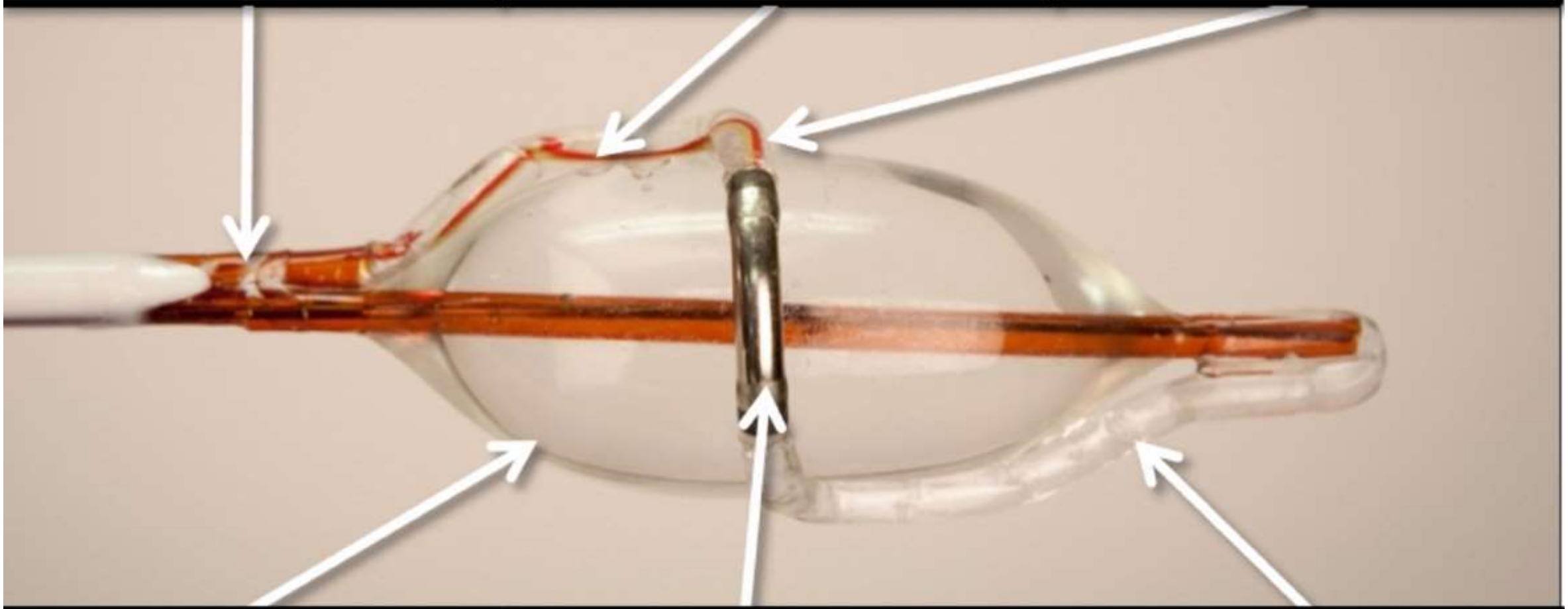
Decrease in acetylcholine reduces airway obstruction in the whole lung by decreasing smooth muscle tone and mucous production

Slebos D-J, et al. Thorax 2015;70:411–419

Catheter Shaft

Thermocouple and Power Line

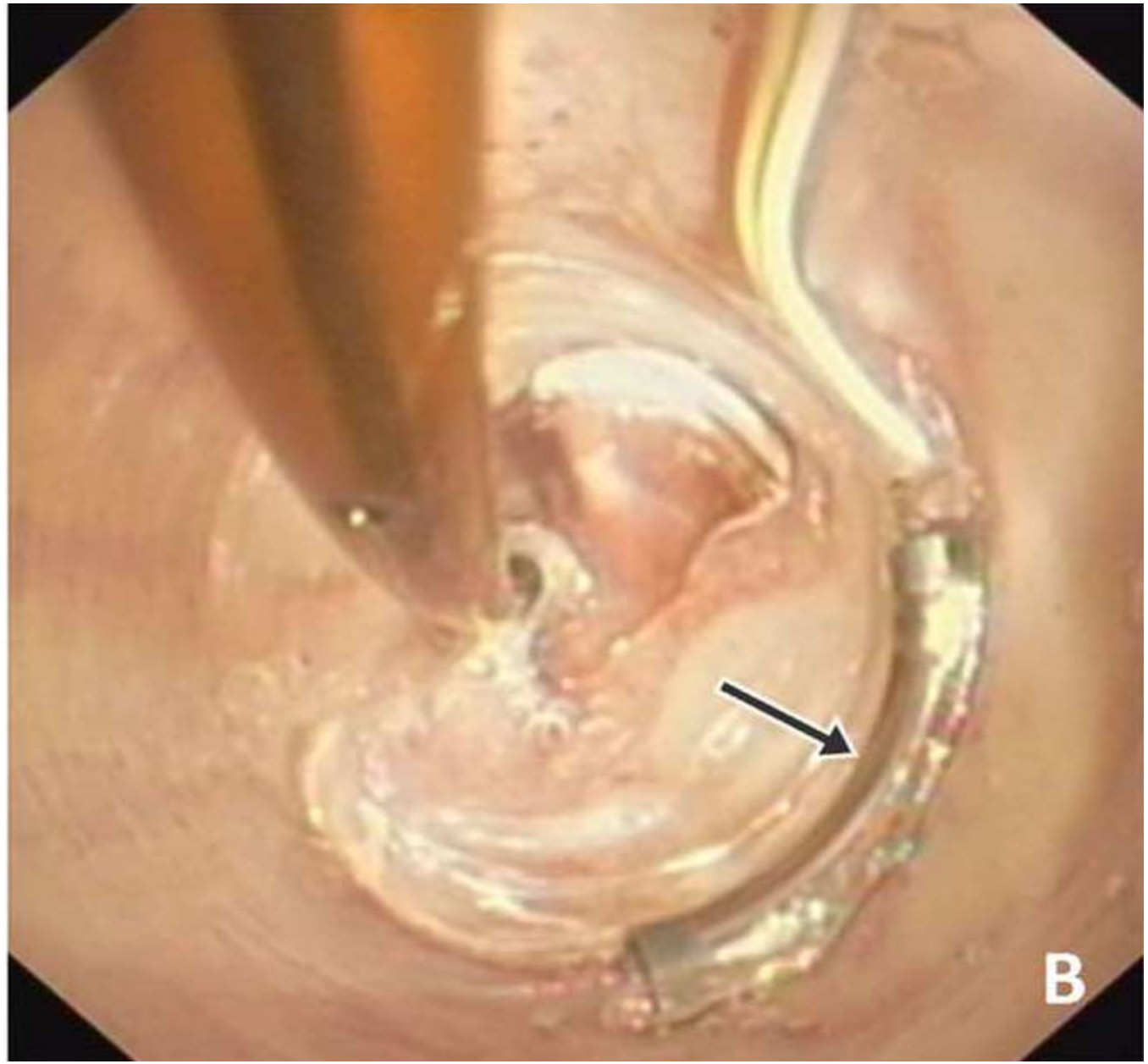
Coolant Inflow Conduit



Balloon

Electrode

Coolant Outflow Conduit


B

Dirk-Jan Slebos et al in their 1-year, prospective, multicentre study evaluated TLD in patients with COPD (FEV1/ FVC <0.70; FEV1 30%–60% predicted)

This non-randomised, prospective, sequential, two-dose study conducted at two sites in South Africa and one in The Netherlands

Patients underwent staged TLD at 20 watts (W) or 15 W following baseline assessment off bronchodilator

Slebos D-J, et al. Thorax 2015;70:411–419

Procedures performed via rigid bronchoscopy under general anaesthesia

The dual-cooled catheter placed through the rigid bronchoscope, and a flexible bronchoscope placed beside it for visualization

The electrode placed and activated to achieve complete circumferential treatment

Total balloon inflation times were approximately 3 min per activation

Slebos D-J, et al. Thorax 2015;70:411–419

The initial subjects were treated with 20 watts (W) in all positions except for the posterior-medial aspects of the left bronchus, where the power was reduced to 15W due to the proximity of the oesophagus

After a protocol amendment, additional patients underwent treatment with a more distal placement of the electrode along the medial wall to avoid the thin tissue of the carina, and a lower 15 W energy level in all position

Slebos D-J, et al. Thorax 2015;70:411–419

Bronchoscopic and fluoroscopic visualisation was used to guide the electrode positioning throughout treatment

To maximise safety 2 therapeutic procedures done per patient with the second bronchus being treated 30 days after the first

No special post procedure medications were required

Use of tiotropium stopped 7 days prior to and after the procedure

Slebos D-J, et al. Thorax 2015;70:411–419

Eligible patients were ≥40 years of age with moderate to severe COPD with a 15% or greater relative increase in FEV1 following inhalation of 80 µg ipratropium bromide

Exclusion criteria-

Pulmonary hypertension,

CHF

Polycythaemia,

COPD exacerbation or active respiratory infection within the past 4 weeks

More than 3 respiratory-related hospitalisations within 1 year of enrolment

Previous lung surgery

Slebos D-J, et al. Thorax 2015;70:411–419

Study End Point-

Decrease in the individual patient's FEV1 by any amount at all follow-up time points or an adverse event related to device

Slebos D-J, et al. Thorax 2015;70:411–419

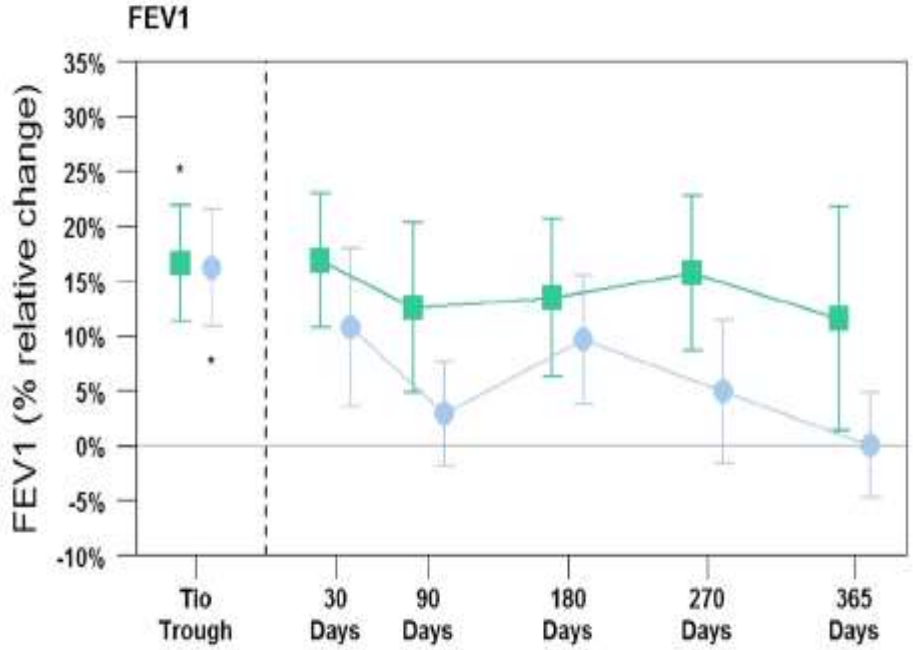
Improvements in lung function, exercise capacity, and HRQL were observed in the 20 W cohort with statistical significance achieved for

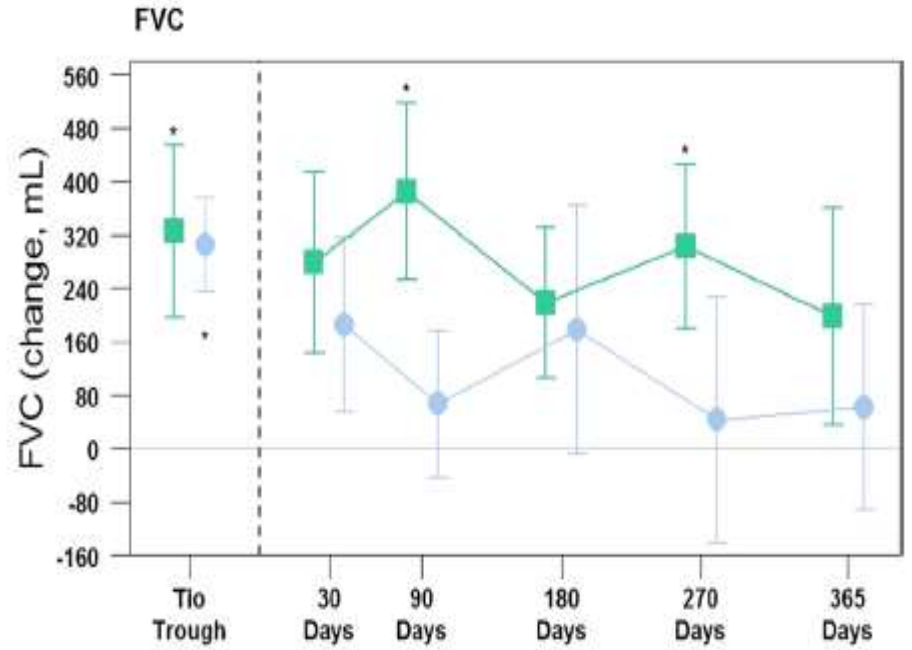
FVC at 90 days (p=0.016) and 270 days (p=0.036)

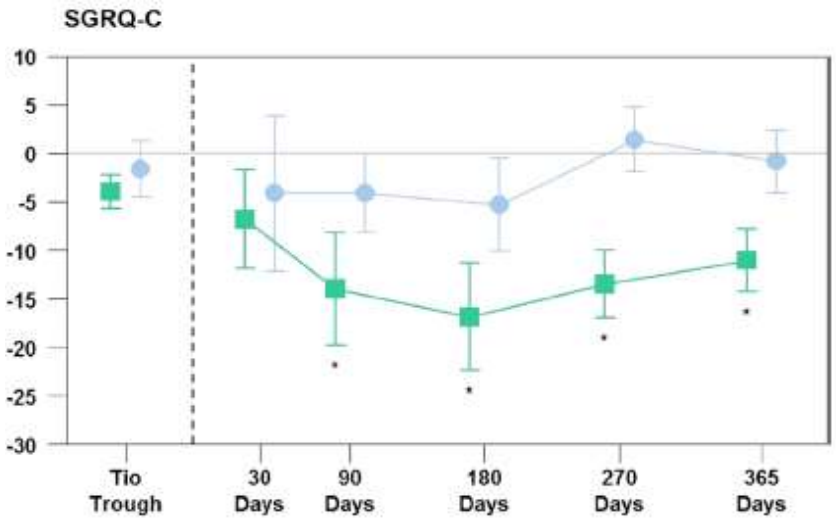
SGRQ at 90 days (p=0.042), 180 days (p=0.019), 270 days (p=0.008) and 1 year (p=0.011)

Improvements larger than those seen in the 15 W cohort

Slebos D-J, et al. Thorax 2015;70:411–419


FEV1
FEV1 (% relative change)
35%
30%
25%
20%
15%
10%
5%
0%
-5%
-10%
Tio Trough
30 Days
90 Days
180 Days
270 Days
365 Days


FVC
FVC (change, mL)
560
480
400
320
240
160
80
0
-80
-160
Tio Trough
30 Days
90 Days
180 Days
270 Days
365 Days


SGRQ-C
10
5
0
-5
-10
-15
-20
-25
-30
Tio Trough
30 Days
90 Days
180 Days
270 Days
365 Days


20W
15W

Table 2 Summary of adverse events through 1 year

	20 watt cohort n=12		15 watt cohort n=10		All n=22	
RF dosage, watt Adverse event	Adverse event frequency n=60 (%)	Subject * frequency (%)	Adverse event frequency n=39 (%)	Subject* frequency (%)	Adverse event frequency n=99 (%)	Subject* frequency (%)
Device-related non-serious						
Bronchial perforation (carina)	2 (3)	2 (17)	–	–	2 (2)	2 (9)
Bronchial stenosis	1 (2)	1 (8)	–	–	1 (1)	1 (5)
Bronchial ulceration	1 (2)	1 (8)	–	–	1 (1)	1 (5)
COPD Exacerbation	–	–	1 (3)	1 (10)	1 (1)	1 (5)
Granulomas	1 (2)	1 (8)	–	–	1 (1)	1 (5)
Worsening of FEV_1†	–	–	1 (3)	1 (10)	1 (1)	1 (5)
Device related-serious						
Gastroparesis	–	–	1 (3)	1 (10)	1 (1)	1 (5)
Procedural related-serious (related or reported within 2 days of either procedure)						
Anaphylactic reaction	1 (2)	1 (8)	–	–	1 (1)	1 (5)
COPD exacerbation	–	–	1 (3)	1 (10)	1 (1)	1 (5)

CONCLUSION-

TLD is novel bronchoscopic treatment concept for symptomatic patients suffering from COPD.

TLD is feasible, safe and well tolerated.

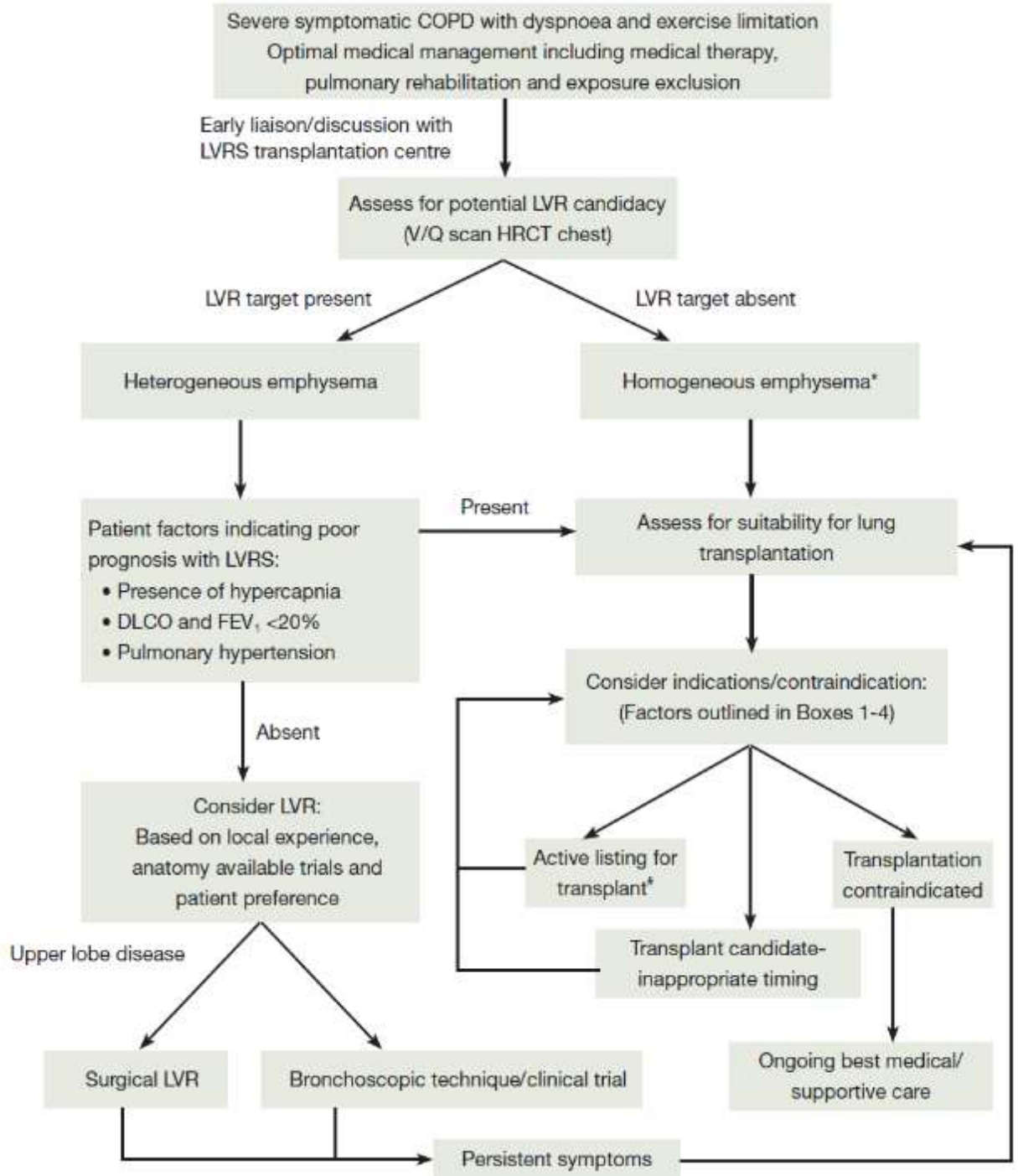
TLD has the potential to overcome many of the limitations of inhaled drugs for the treatment of COPD

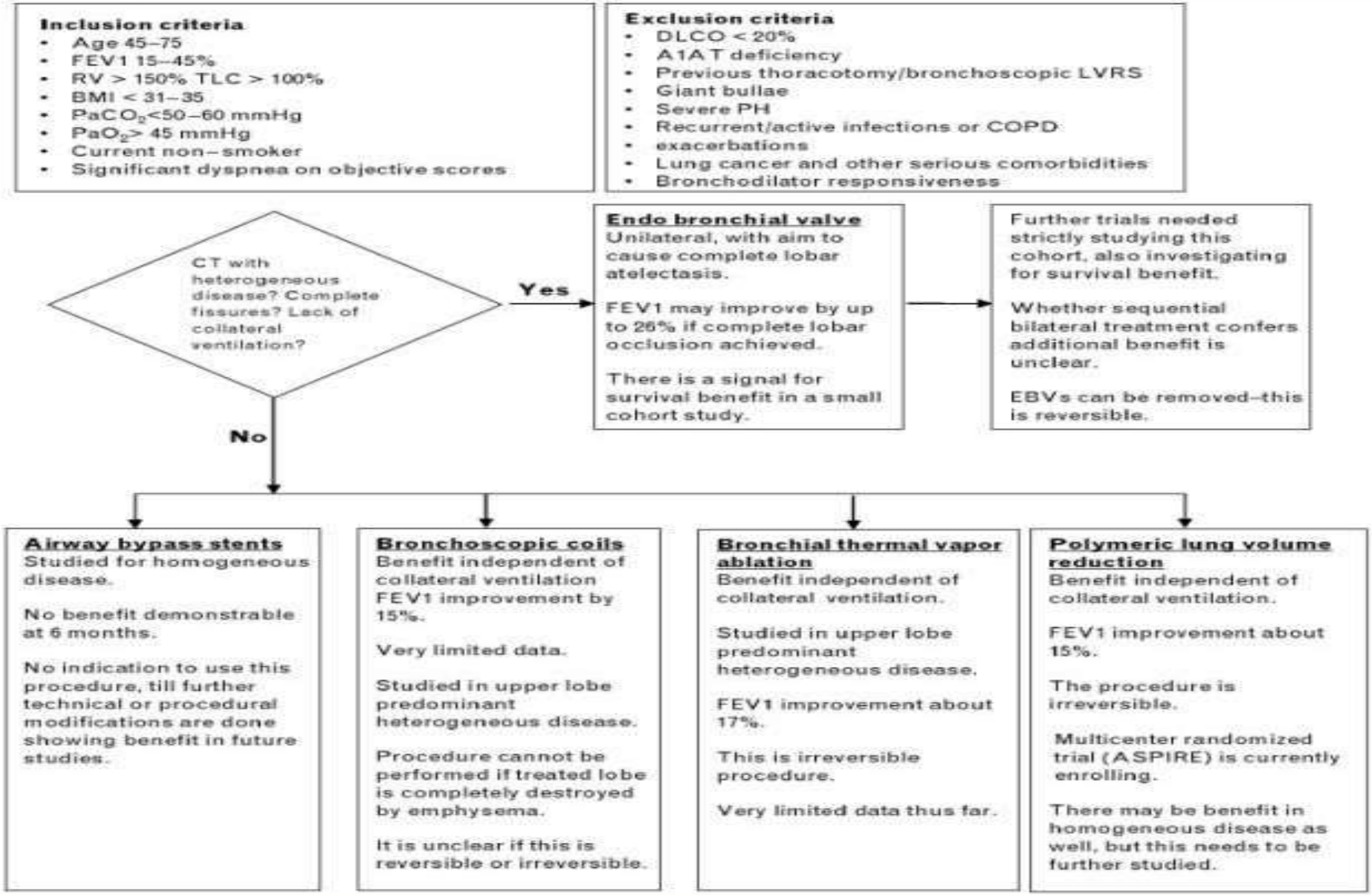
TLD may eliminate inhaler compliance issues .

TLD not be subject to the peak and trough variations seen with drugs

TLD eliminate variable regional drug delivery and deposition in patients with obstructive lung disease by ablating the nerves that travel throughout the bronchial tree independent of regional airflow obstruction.

Combination of TLD & inhaled anticholinergic drugs, may have a synergistic effect in reducing airway obstruction and mucus production


Severe symptomatic COPD with dyspnoea and exercise limitation
Optimal medical management including medical therapy, pulmonary rehabilitation and exposure exclusion
Early liaison/discussion with LVRS transplantation centre
Assess for potential LVR candidacy (V/Q scan HRCT chest)
LVR target present
LVR target absent
Heterogeneous emphysema
Homogeneous emphysema*
Patient factors indicating poor prognosis with LVRS:
• Presence of hypercapnia
• DLCO and FEV1 <20%
• Pulmonary hypertension
Present
Assess for suitability for lung transplantation
Absent
Consider indications/contraindication: (Factors outlined in Boxes 1-4)
Consider LVR: Based on local experience, anatomy available trials and patient preference
Active listing for transplant*
Transplantation contraindicated
Transplant candidate-inappropriate timing
Upper lobe disease
Surgical LVR
Bronchoscopic technique/clinical trial
Ongoing best medical/ supportive care
Persistent symptoms



TAKE HOME MESSAGE

Among BLVR surgery, EBV placement is shown to be safe & effective in long term follow up for 1 yr but no mortality benefit has been established as compared to conventional lung volume reduction surgery.

Other procedures like bioLVR and LVRC are effective but long term follow up not available to establish their safety and efficacy.

At present EBV is not available in INDIA.

More RCC is required to see long term benefits and side effects of EBV in patients of COPD with complete fissure before implementing to our clinical practice.