NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of bronchoscopic thermal vapour ablation for upper-lobe emphysema

Emphysema is a chronic lung disease. It causes the walls of the smaller airways in the lungs to break down and creates abnormally large spaces, which do not function properly and compress the healthy parts of the lung. In this procedure, a bronchoscope (a thin tube with a camera on the end) is passed through the mouth or nose and into the lungs. It is used to deliver thermal vapour (steam) to destroy the diseased parts of the lung and allow the healthy parts to expand and work better.

Contents

Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in October 2018 and updated in March 2019.

Procedure name

- Bronchoscopic thermal vapour ablation for upper-lobe emphysema

Specialist societies

- British Thoracic Society
- Royal College of Physicians and Surgeons of Glasgow
- Royal College of Physicians
- Royal College of Physicians of Edinburgh.

Description of the procedure

Indications and current treatment

Emphysema is a chronic lung disease that typically happens with chronic obstructive pulmonary disease. In emphysema, the walls of the air sacs (alveoli) in the lungs weaken and disintegrate. This leaves behind abnormally large air spaces that stay filled with air even when the patient breathes out. The most common symptoms of emphysema are shortness of breath, coughing, fatigue and weight loss. Recurrent illnesses (such as chest infections) often lead to exacerbations, for which patients may need hospitalisation. Emphysema is usually related to smoking but other risk factors include air pollution and an inherited alpha-1-antitrypsin deficiency.

Treatment options include pulmonary rehabilitation (exercise training, breathing retraining, and patient and carer education), stopping smoking, and using inhaled or oral bronchodilators and corticosteroids. Oxygen therapy may also be needed in more severe cases. Lung volume reduction surgery is an option for patients

who experience breathlessness, and whose pulmonary function test results show severe obstruction and enlarged lungs. Surgery can be done thoracoscopically or using an open approach. Endoscopic lung volume reduction techniques include implanting valves or coils. The aim is to reduce the morbidity and mortality associated with conventional surgery.

What the procedure involves

Bronchoscopic thermal vapour (steam) ablation for upper-lobe emphysema is usually done using general anaesthesia. A bronchoscope is passed down the airway to the diseased areas of the lung. The most severely affected and hyper-inflated lung segments are targeted for treatment. A special catheter is used to deliver a patient-specific predetermined dose of thermal vapour through the bronchoscope. A balloon at the tip of the catheter is inflated to seal off the targeted area. The dose of thermal vapour depends on the mass, volume and diseased state of the affected area. The thermal vapour ablates the diseased tissue, which the body removes through the natural healing process. Multiple treatments can be done over time, targeting different segments as the patient's disease progresses. This procedure is not done when there is proven active infection in the lung. The removal of disease tissue results in a reduction of lung volume and subsequent remodelling of the lung. Lung volume reduction typically happens gradually over a 4 to 6 week period. Respiratory symptoms may worsen in the first 2 to 4 weeks after treatment.

Outcome measures

Pulmonary function tests and measures of lung volumes

FEV_1 (forced expiratory volume) – the volume of air that the patient is able to exhale in the first second of forced expiration.

FVC (forced vital capacity) – the total volume of air that one can forcibly exhale after a full inspiration.

TLC (total lung capacity) – maximum volume of air present in the lungs.

RV (residual volume) – volume of air remaining in the lungs after a full exhalation.

6MWD (6-minute walking distance test) – assesses distance walked over 6 minutes as a sub-maximal test of aerobic capacity or endurance.

Modified Medical Research Council dyspnoea scale

Measures perceived respiratory disability ranging from none (grade 0) to almost incomplete incapacity (grade 4)

Grade	Description of breathlessness
Grade 0	I only get breathless with strenuous exercise
Grade 1	I get short of breath when hurrying on level ground or walking up a slight hill
Grade 2	On level ground, I walk slower than people of the same age because of breathlessness, or I have to stop for breath when walking at my own pace on the level
Grade 3	I stop for breath after walking about 100 yards or after a few minutes on level ground
Grade 4	I am too breathless to leave the house or I am breathless when dressing

St. George's Respiratory Questionnaire (SGRQ)

The SGRQ is designed to measure health impairment in patients with respiratory disease. Three component scores are calculated for the SGRQ:

1. Symptoms – concerned with the effect of respiratory symptoms, their frequency and severity.

2. Activity – concerned with activities that cause or are limited by breathlessness.

3. Impacts – covers a range of aspects concerned with social functioning and psychological disturbances resulting from airways disease.

A total score is also calculated, which summarises the impact of the disease on overall health status. Scores are expressed as a percentage of overall impairment in which 100 represents the worst and 0 indicates the best possible health status.

BODE Index for COPD survival prediction

BODE stands for **B**ody mass index, airflow **O**bstruction, **D**yspnoea and **E**xercise capacity. It is a score that combines:

Variable	Points on BODE Index			
	0	1	2	3
FEV_1 (% predicted)	≥65	50–64	36–49	≤35
6-Minute Walk Test (metres)	≥350	250–349	150–249	≤149
mMRC dyspnoea Scale	0–1	2	3	4
Body mass index	>21	≤21		

Interpretation of BODE

	Approximate 4-year survival rates
0 to 2 points	80%
3 to 4 points	67%
5 to 6 points	57%
7 to 10 points	18%

Efficacy summary

FEV_1

In a randomised controlled trial (RCT) of 69 patients the mean improvement in FEV_1 was 11.0% in patients who had bronchoscopic thermal vapour ablation (BTVA) compared with -3.7% in patients who had medical management at 6 month follow-up ($p<0.0001$).[1] In a subgroup analysis of 54 patients with incomplete fissures, the improvement in FEV_1 was 7.6% at 6 months and 9.2% at 12 months in patients who had BTVA compared with -3.4% and -5.4% respectively in the control group ($p=0.0024$ and 0.0137).[2] In a case series of 44 patients, 55% (22/40) of patients had an increase in FEV_1 of 12% or more at 6 month follow-up and 46% (17/37) had a 12% increase or more at 12 month follow-up. The mean improvements were 141 ml and 86 ml at 6 and 12 months respectively ($p<0.05$ compared with baseline and for 12 month follow-up compared with 6 month follow-up).[3,4] In a case series of 11 patients there was a 2.6% improvement in FEV_1 at 6 month follow-up ($p=0.40$).[5]

St George's Respiratory Questionnaire (SGRQ)

In the randomised controlled trial (RCT) of 69 patients the mean improvement in SGRQ score was 9.7 points in patients who had BTVA compared with no improvement in patients who had medical management at 6 month follow-up ($p=0.0021$).[1] In the subgroup analysis of 54 patients with incomplete fissures, the improvement in SGRQ score was 6.8 at 6 months and 9.4 at 12 months in patients who had BTVA compared with 0.6 and 1.0 respectively in the control group ($p=0.1089$ and 0.0712).[2] In the case series of 44 patients the mean improvements in SGRQ score were 14.0 and 11.0 points at 6 and 12 months respectively ($p=0.05$ compared with baseline).[3,4] In the case series of 11 patients the SGRQ total score was 49.1 at 6 month follow-up compared with 64.4 at baseline (p value not reported).[5]

Residual volume

In the RCT of 69 patients the difference in residual volume between the treatment and control groups was -302.5 ml (95% confidence interval [CI] -542.6 to -62.4) at 6 month follow-up (p=0.0145).[1] In the subgroup analysis of 54 patients with incomplete fissures, the residual volume decreased by 261.3 and 108.8 ml at 6 and 12 months in patients who had BTVA compared with increases of 44.4 and 111.1 ml respectively in the control group (p=0.0477 and 0.1991).[2] In the case series of 44 patients the mean improvements in residual volume were 406 and 303 ml at 6 and 12 months respectively (p<0.05 compared with baseline).[3,4]

6-minute walk distance (6MWD)

In the RCT of 69 patients the difference in 6MWD between the treatment and control groups was 30.5 metres (95% CI -1.5 to 62.4, p=0.0614) at 6 month follow-up.[1] In the subgroup analysis of 54 patients with incomplete fissures, the distance increased by 13.7 and 6.2 metres at 6 and 12 months in patients who had BTVA compared with decreases of 10.6 and 4.8 metres respectively in the control group (p=0.1718 and 0.5389).[2] In the case series of 44 patients the mean improvements in 6MWD were 46.5 and 18.5 metres at 6 and 12 months respectively (p<0.001 for 6 months compared with baseline).[3,4]

BODE index

In the case series of 44 patients the mean improvements in BODE index were 1.48 and 1.25 units at 6 and 12 months respectively (p<0.001 compared with baseline).[3,4]

Modified Medical Research Council (mMRC) score

In the case series of 44 patients the mean improvements in mMRC were 0.90 and 0.83 units at 6 and 12 months respectively (p<0.001 compared with baseline).[3,4]

Lung tissue volume change

In the RCT of 69 patients the treated upper lobe was reduced by 16% at 6 month follow-up (assessed by CT).[1]

Safety summary

Chronic obstructive pulmonary disease (COPD) exacerbation

COPD exacerbation within 6 months of treatment or randomisation was reported in 24% (11/45) of patients who had BTVA and 4% (1/24) of patients in the control group in the RCT of 69 patients. These exacerbations resolved with standard medical care, with no mechanical ventilation or respiratory failure. One patient

died 84 days after treatment from complications related to COPD exacerbation. The data and safety monitoring board judged this to be possibly related to treatment.[1] COPD exacerbation was reported in 20.4% (9/44) of patients within 6 months of treatment; 11.4% (5/44) of patients had an exacerbation beyond 6 months of treatment.[2] COPD exacerbation was reported in 36.4% (4/11) of patients in the case series of 11 patients; 2 exacerbations were considered to be serious and the patients needed hospitalisation.[5]

Pneumonia or pneumonitis

Pneumonia or pneumonitis within 6 months of treatment or randomisation was reported in 18% (8/45) of patients who had BTVA and 8% (2/24) of patients in the control group in the RCT of 69 patients.[1] Pneumonia was reported in 13.6% (6/44) of patients within 6 months of treatment in the case series of 44 patients.[3,4] Pneumonitis was reported in 18.2% (2/11) of patients in the case series of 11 patients; 1 was considered to be serious and the patient needed hospitalisation.[5]

Pneumothorax

Pneumothorax within 6 months of treatment or randomisation was reported in 1 patient who had BTVA and no patients in the control group in the RCT of 69 patients. The pneumothorax was asymptomatic and resolved without the need for a chest tube or surgery.[1]

Haemoptysis

Haemoptysis within 6 months of treatment or randomisation was reported in 1 patient who had BTVA and no patients in the control group in the RCT of 69 patients.[1] Haemoptysis was reported in 6.8% (3/44) of patients within 6 months of treatment in the case series of 44 patients.[3,4]

Respiratory tract infection

Respiratory tract infection was reported in 11.4% (5/44) of patients within 6 months of treatment and in 1 patient more than 6 months after treatment in the case series of 44 patients.[3,4]

Cardiac adverse events

Ventricular fibrillation was reported in 1 patient within 6 months of BTVA in the case series of 44 patients. Cardiac insufficiency and right heart failure were each reported in 1 patient more than 6 months after BTVA in the same study.[3,4] Atrial tachycardia, which was considered to be serious, was reported in 1 patient in the case series of 11 patients; the patient needed hospitalisation.[5]

Other

End-stage COPD, gastroesophageal reflux, post-treatment inflammation reaction, right upper quadrant abdominal pain, and urinary retention were each reported in 1 patient within 6 months of BTVA in the case series of 44 patients. Acute dyspnoea and investigation of diabetes were each reported in 1 patient more than 6 months after BTVA in the same study.[3,4] Serious anxiety was reported in 1 patient in the case series of 11 patients; the patient needed hospitalisation.[5]

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never happened). For this procedure, specialist advisers described the following anecdotal adverse event: treatment of the wrong area because of the patient coughing during administration, causing dislodgement of the balloon catheter. They did not describe any additional theoretical adverse events.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to bronchoscopic thermal vapour ablation for upper-lobe emphysema. The following databases were searched, covering the period from their start to 22 January 2019: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	People with upper-lobe emphysema.
Intervention/test	Bronchoscopic thermal vapour ablation.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on 124 patients from 1 randomised controlled trial (reported in 2 studies) and 2 case series (1 of which was reported in 2 studies).[1–5]

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) are listed in the appendix.

Table 2 Summary of key efficacy and safety findings on bronchoscopic thermal vapour ablation for upper-lobe emphysema

Study 1 Herth F (2016)

Details

Study type	**Randomised controlled trial (STEP-UP)**
Country	Australia, Austria, Germany, Ireland, UK (13 centres)
Recruitment period	2013 to 2014
Study population and number	**n=69** (45 bronchoscopic thermal vapour ablation, 24 standard medical management [control group]) **Patients with severe upper-lobe predominant emphysema**
Age and sex	• Bronchoscopic thermal vapour ablation group: mean age 64 years; 51% (23/45) male • Control group: mean age 63 years; 54% (13/24) men
Patient selection criteria	Age 45 to 75 years, upper lobe-predominant heterogeneous emphysema (>15% difference in lung density between targeted upper lobe segment and its respective lower lobe, and hyperinflation), FEV_1 between 20% and 45% predicted, total lung capacity at least 100% predicted, substantial hyperinflation, post-rehabilitation 6-minute walk test greater than 140 metres, and non-smoking for at least 6 months before study enrolment. Patients with incomplete fissures or collateral ventilation were not excluded from the trial. Exclusion criteria included any condition that would interfere with the completion of study follow-up assessments or bronchoscopy or would adversely affect study outcomes, and those patients with pulmonary hypertension, clinically significant bronchiectasis, or recent chronic obstructive pulmonary disease (COPD) exacerbations.
Technique	• Bronchoscopic vapour ablation was done as a 2 stage procedure; 1 segment was targeted during the first treatment session and up to 2 segments were targeted during the second session 13 weeks later. The protocol restricted treatment to 1 upper lobe per session. CT quantitative analysis software was used to do a sub-lobar analysis and measure the tissue mass and air volume of each segment, to establish which segments to treat and determine the appropriate treatment time. The target dose was 8.5 calories per gramme of lung tissue. A CT scan was done 6 months after treatment to assess lung volume reduction. • Standard medical treatment comprised removal of risk factors such as smoking, medical therapy with 1 or more bronchodilators, pulmonary rehabilitation, and inhaled corticosteroids.
Follow-up	**6 months**
Conflict of interest/source of funding	Study was funded by Uptake Medical.

Analysis

Follow-up issues: Of the 45 patients who had thermal vapour ablation, 2 (4.4%) missed their 3 month 6-minute walk test follow-up, 1 missed their 3 month spirometry follow-up and 1 patient died from exacerbation. Three (6.7%) patients in the thermal vapour ablation group missed their 6 month spirometry follow-up, 2 of whom missed their entire 6 month follow-up visit. Four (16.7%) patients in the control group missed their 3 month 6-minute walk test, 1 of whom missed their entire 3 month follow-up visit and 1 patient withdrew from the study.

Study design issues: Multicentre randomised controlled open-label trial. Randomisation was based on a computer-generated blocked randomisation scheme, which was not disclosed to the sites or the sponsor. Study personnel and patients were not masked to group allocation. The primary efficacy endpoints were the change in FEV_1 and St George's Respiratory Questionnaire (SGRQ-C) scores between the treatment and control groups at 6 months, analysed by intention to treat. The sample size was calculated using 80% power, a type I error rate of 0.05 and a 2:1 randomisation allocation.

Study population issues: Baseline characteristics were similar in the 2 groups. Incomplete fissures were recorded in at least 1 lung in 78% of all enrolled patients in both groups. The mean SGRQ-C scores at baseline were 57.7 in the treatment group and 57.3 in the control group.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **69 (45 compared with 24)**

5 patients in the thermal ablation group had only 1 treatment session: 1 was not eligible for a second session because of extensive improvement at 3 months, 2 patients were excluded because of health-related complications, 1 patient was found to be currently on anticoagulants and 1 patient died before the second treatment session.

Primary efficacy endpoints

	BTVA group		Control group		Difference between groups (95% CI)	p value
	n	Mean (SD)	n	Mean (SD)		
Change in FEV_1, %						
3 months*	43	8.2% (17.5%)	22	-1.8% (10.1%)	10.1% (3.2 to 16.9)	0.0047
6 months	41	11.0% (16.2%)	23	-3.7% (11.1%)	14.7% (7.8 to 21.5)	<0.0001
Change in SGRQ-C, points						
3 months*	44	-7.2 (12.2)	22	-0.6 (11.0)	-6.6 (-12.4 to -0.9)	0.0243
6 months	42	-9.7 (14.4)	23	-0.0 (9.8)	-9.7 (-15.7 to-3.7)	0.0021

*3-month data were collected before the second treatment session

Segmental and lobar tissue volume changes at 6 months in the treatment group, % volume change

	First treatment (n=40), mean (SD)	Second treatment (n=36), mean (SD)
Reduced segment(s)	-42% (26%)	-33% (20%)
Preserved segment(s)	+11% (32%)	+11% (21%)
Treated upper lobe	-12% (15%)	-16% (13%)
Preserved middle lobe or lingula	+14% (54%)	+8% (10%)
Preserved lower lobe	+8% (17%)	+8% (14%)

Secondary efficacy endpoints – absolute difference between groups

	3 months		6 months	
	Difference (95% CI)	p value	Difference (95% CI)	p value
6MWD, metres	29.4 (-3.1 to 61.8)	0.0748	30.5 (-1.5 to 62.4)	0.0614
FEV_1, ml	80.5 (18.6 to 142.4)	0.0117	130.8 (63.6 to 198.0)	0.0002
Forced vital capacity, ml	163.7 (-15.1 to 342.5)	0.0717	243.1 (57.0 to 429.3)	0.0115
Total lung capacity, ml	-2.4 (-233.0 to 228.1)	0.9832	-77.6 (-313.6 to 158.4)	0.5111
Residual volume, ml	-44.1 (-305.9 to 217.7)	0.7374	-302.5 (-542.6 to -62.4)	0.0145
Functional residual capacity (thoracic gas volume), ml	-35.4 (-288.9 to 218.0)	0.7809	-130.9 (-368.9 to 107.2)	0.2758

Binary responder analysis at 3 and 6 months

	FEV_1 ≥12%	SGRQ-C		FEV_1 ≥12% or SGRQ-C ≤-8 points	6MWT ≥26 metres
		≤-4 points	≤-8 points		
Treatment group: % responders					
3 months	32%	67%	49%	64%	35%
6 months	50%	70%	53%	70%	42%
Control group: % responders					
3 months	18%	27%	18%	36%	20%
6 months	13%	39%	17%	30%	23%

Safety

Serious adverse events and hospital admissions, n (%)

	BTVA group (n=45)			Control group (n=24)
	After treatment session 1	After treatment session 2	0 to 180 days of treatment overall*	0 to 180 days of randomisation overall
COPD exacerbation	6 (13%)	6 (15%)	11 (24%)	1 (4%)
Pneumonia or pneumonitis	6 (13%)	3 (8%)	8 (18%)	2 (8%)
Pneumothorax	0	1 (3%)	1 (2%)	0
Haemoptysis	0	1 (3%)	1 (2%)	0
Death	1 (2%)	0	1 (2%)	0
Any serious respiratory adverse event	10 (22%)	9 (23%)	16 (36%)	3 (13%)

* 180 days after treatment session 1 or 90 days after treatment session 2

The pneumothorax was asymptomatic and resolved without the need for a chest tube or surgery.

Exacerbations and pneumonia resolved with standard medical care, with no mechanical ventilation or respiratory failure.

One patient died 84 days after treatment from complications related to COPD exacerbation. The data and safety monitoring board judged this to be possibly related to treatment.

Abbreviations used: BTVA, bronchoscopic thermal vapour ablation; CI, confidence interval; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second; 6MWD, 6-minute walk distance; SD, standard deviation; SGRQ, St George's Respiratory Questionnaire

Study 2 Gompelmann D (2016)

Details

Study type	**Randomised controlled trial (subgroup analysis of STEP-UP data)**
Country	Australia, Austria, Germany, Ireland, UK (13 centres)
Recruitment period	2013 to 2014
Study population and number	**n=54** (35 bronchoscopic thermal vapour ablation, 19 standard medical management [control group]) **Patients with severe upper-lobe predominant emphysema and incomplete fissures**
Age and sex	Not reported for patient subgroup
Patient selection criteria	See study 1 for inclusion and exclusion criteria. This analysis only included patients with collateral ventilation (if either of the treated lobes was adjacent to a fissure that was <90% complete, the patient was assumed to have collateral ventilation).
Technique	• Bronchoscopic vapour ablation was done as a 2 stage procedure; 1 segment was targeted during the first treatment session and up to 2 segments were targeted during the second session 13 weeks later. The protocol restricted treatment to 1 upper lobe per session. CT quantitative analysis software was used to do a sub-lobar analysis and measure the tissue mass and air volume of each segment, to establish which segments to treat and determine the appropriate treatment time. A CT scan was done 6 months after treatment to assess lung volume reduction. • Standard medical treatment comprised removal of risk factors such as smoking, medical therapy with 1 or more bronchodilators, pulmonary rehabilitation, and inhaled corticosteroids.
Follow-up	**12 months**
Conflict of interest/source of funding	The STEP-UP study was funded by Uptake Medical.

Analysis

Follow-up issues: No losses to follow-up were described. At the 12 month follow-up, 1 patient in the bronchoscopic thermal vapour ablation group had died and 1 patient in the control group had withdrawn from the study.

Study design issues: Post-hoc subgroup analysis of trial described in study 1. The subgroup is a large majority of the full cohort.

Study population issues: Patients are a subgroup of those included in Herth FJ, 2016 (study 1). All patients were considered to have collateral ventilation, based on the presence of incomplete fissures in either lung (fissure integrity <90% for left oblique fissure or combination of right oblique fissure and horizontal fissure for the right).

Key efficacy and safety findings

Efficacy

Number of patients analysed: **54 (35 compared with 19)**

Results for primary efficacy endpoints

	BTVA group (n=35)	Control group (n=19)	Difference between groups (95% CI)	p value
Change in FEV_1, %				
3 months	7.9	-1.2	9.1 (0.1 to 18.1)	0.0056
6 months	7.6	-3.4	10.9 (3.6 to 18.4)	0.0024
12 months	9.2	-5.4	14.6 (3.1 to 26.7)	0.0137
Change in SGRQ-C (points)				
3 months	-7.7	-2.2	-5.5 (0.5 to -11.5)	0.0697
6 months	-6.8	-0.6	-6.1 (1.3 to -13.7)	0.1089
12 months	-9.4	-1.0	-8.4 (0.7 to -17.5)	0.0712

Results for secondary efficacy endpoints

	BTVA group (n=35)	Control group (n=19)	Difference between groups (95% CI)	p value
Change in FEV_1, ml				
3 months	64.4	-22.8	87.2 (7.5 to 166.9)	0.0326
6 months	58.1	-31.1	89.2 (20.4 to 158.0)	0.0122
12 months	65.0	-46.7	111.7 (18.5 to 204.9)	0.0198
Change in forced vital capacity, ml				
3 months	87.6	-96.1	183.8 (-16.1 to 383.5)	0.0706
6 months	97.1	-88.3	185.4 (-24.0 to 394.8)	0.0813
12 months	98.2	-96.1	194.3 (-50.4 to 439.0)	0.1170
Change in residual volume, ml				
3 months	-52.9	-27.8	-25.2 (-383.3 to 333.1)	0.8884
6 months	-261.3	44.4	-305.7 (-608.1 to -3.3)	0.0477
12 months	-108.8	111.1	-214.1 (-559.3 to 119.5)	0.1991
Change in functional residual capacity (thoracic gas volume), ml				
3 months	-64.7	-11.1	-53.6 (-443.9 to 336.7)	0.7838
6 months	-119.4	16.7	-136.0 (-459.8 to 187.6)	0.4021
12 months	-126.5	122.2	-248.7 (-581.7 to 84.3)	0.1399
Change in 6-minute walk distance (metres)				
3 months	12.1	-19.9	32.0 (6.6 to 70.6)	0.1021
6 months	13.7	-10.6	24.3 (-10.9 to 59.5)	0.1718
12 months	6.2	-4.8	10.8 (-24.9 to 46.9)	0.5389

Safety

Serious adverse events and hospital admissions, n (%)

	BTVA group (n=35)		Control group (n=19)	
	Days after treatment		Days after randomisation	
	0 to 180	181 to 365	0 to 180	181 to 365
COPD exacerbation	3 (9)	0	1 (5)	2 (11)
Pneumonia or pneumonitis	8 (23)	0	1 (5)	1 (5)
Pneumothorax	1 (3)*	0	0	0
Haemoptysis	0	0	0	0
Death	1 (3)	0	0	0
Any respiratory serious adverse events	9 (26)	0	2 (11)	3 (16)

* Incidental finding at follow-up, resolved without intervention

One patient died 84 days after treatment from complications related to COPD exacerbation. The data and safety monitoring board judged this to be possibly related to treatment.

Abbreviations used: BTVA, bronchoscopic thermal vapour ablation; CI, confidence interval; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second; SGRQ, St George's Respiratory Questionnaire

Study 3, 4 Herth F (2012), Snell G (2012)

Details

Study type	**Case series**
Country	Australia, Austria, Germany, Ireland, US
Recruitment period	2009 to 2011
Study population and number	**n=44** **Patients with upper lobe predominant emphysema**
Age and sex	Mean 63 years; 50% (22/44) men
Patient selection criteria	*Key inclusion criteria*: Upper lobe predominant emphysema determined by high-resolution CT, age 40 to 75 years, FEV_1 between 15% and 45% predicted, residual volume >150% predicted, total lung capacity >100%, diffusing capacity for carbon monoxide >20% predicted, 6-minute walk distance >140 metres, partial pressure of CO_2 <55 mmHg and partial pressure of O_2 >45 mmHg, non-smoking ≥4 months, and recent participation in pulmonary rehabilitation. *Key exclusion criteria*: known alpha-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 (peak systolic pulmonary artery pressure ≥45 mmHg or mean pulmonary artery pressure ≥35 mmHg).
Technique	The InterVapor system (Uptake Medical Corp., US) was used. Selection of the lung targeted for treatment was based on the degree of heterogeneity and other anatomical factors. The vapour dose was 10 calories per gramme of tissue.
Follow-up	**12 months**
Conflict of interest/source of funding	Study was sponsored by the manufacturer of InterVapor, Uptake Medical Corp., US.

Analysis

Follow-up issues: Data were not available for 4 (9.1%) patients at 6 months (2 missed visits, 1 withdrawn, 1 serious adverse event) and for 7 (15.9%) at 12 months (1 missed visit, 4 withdrawn, 2 serious adverse events).

Study design issues: Pooled data from 2 open-label, single-arm studies. The primary efficacy endpoint was the proportion of patients with an improvement from baseline of more than 12% in FEV_1 or 4 or more units in St George's Respiratory Questionnaire (SGRQ) total score. The BODE (body mass index, obstruction, dyspnoea, exercise) index was also calculated. All adverse events were reported throughout the trial with the primary diagnosis adjudicated by an independent physician. No correction for multiple comparisons was made. Post-hoc subgroup analyses were done based on GOLD (Global Initiative for Chronic Obstructive Lung Disease) stage and heterogeneity index (HI; calculated as the ratio of lower to upper lobe tissue mass to air volume). Patients were categorised as low or high HI based on the median value.

Study population issues: The mean SGRQ total score at baseline was 58.9. The SGRQ and 6-minute walk distance test were consistent with significant impairment. Lung function testing indicated GOLD stage III/IV disease and substantial gas trapping with hyperinflation.

Other issues: Efficacy outcomes and safety outcomes beyond 6 months have been extracted from Herth F et al. (2012). Safety events that happened within 6 months of the procedure were reported in Snell et al. (2012).

Key efficacy and safety findings

<table>
<tr>
<th>Efficacy</th>
<th>Safety</th>
</tr>
<tr>
<td>
Number of patients analysed: 44

The primary endpoint was reached by 84% of evaluable patients at 6 months and 78% at 12 months.

Mean improvement in FEV_1
• 6 month follow-up=141 ml
• 12 month follow-up=86 ml
p<0.05 compared with baseline and for 12 month follow-up compared with 6 month follow-up.
At 6 months, 58% (23/40) of patients had ≥100 ml improvement in FEV_1 and 55% (22/40) had an increase ≥12%; 50% (20/40) of patients had an increase ≥15%.
At 12 months, 49% (18/37) of patients had ≥100 ml improvement in FEV_1 and 46% (17/37) had an increase ≥12%; 41% (15/40) had an increase ≥15%.

Mean improvement in residual volume
• 6 month follow-up=-406 ml
• 12 month follow-up=-303 ml
p<0.05 compared with baseline

Pulmonary function (absolute change and change in percent of predicted normal from baseline), mean (SD)
<table>
<tr><th></th><th colspan="2">6 months (n=40)</th><th colspan="2">12 months (n=37)</th></tr>
<tr><th></th><th>Absolute</th><th>% predicted</th><th>Absolute</th><th>% predicted</th></tr>
<tr><td>FVC (ml)</td><td>271 (455)*</td><td>7.9 (12.2)*</td><td>249 (429)*</td><td>8.5 (13.4)*</td></tr>
<tr><td>FEV_1/FVC</td><td>0.02 (0.04)*</td><td>-</td><td>0.00 (0.05)^</td><td>-</td></tr>
<tr><td>TLC (ml)</td><td>-220 (445)*</td><td>-3 (8)*</td><td>-65 (532)^</td><td>-0.1 (11)^</td></tr>
<tr><td>FRC (ml)</td><td>-369 (615)*</td><td>-12 (20)*</td><td>-167 (624)^</td><td>-5 (21)^</td></tr>
<tr><td>IC (ml)</td><td>149 (403)*</td><td>-</td><td>101 (495)</td><td>-</td></tr>
<tr><td>RV/TLC</td><td>-0.03 (0.06)*</td><td>-</td><td>-0.04 (0.07)</td><td>-</td></tr>
<tr><td>DLCO (ml/min/mmHg)</td><td>0.32 (1.34)</td><td>1.5 (8.2)</td><td>0.46 (1.77)</td><td>1.2 (8.3)</td></tr>
</table>
* p<0.05 compared with baseline; ^p<0.05 12 months compared with 6 months

SGRQ total score and domains, change in scores from baseline
<table>
<tr><th></th><th>6 months</th><th>Change</th><th>12 months</th><th>Change</th></tr>
<tr><td>Symptoms</td><td>43.2 (24.0)</td><td>-11.9 (21.8)*</td><td>48.5 (25.4)</td><td>-6.4 (25.4)</td></tr>
<tr><td>Activity</td><td>64.4 (20.4)</td><td>-14.7 (17.7)*</td><td>68.3 (19.6)</td><td>-10.3 (16.9)*^</td></tr>
<tr><td>Impact</td><td>32.1 (21.3)</td><td>-14.0 (16.1)*</td><td>33.0 (21.1)</td><td>-12.7 (13.2)*</td></tr>
<tr><td>Total</td><td>43.8 (19.5)</td><td>-14.0 (15.1)*</td><td>46.2 (19.2)</td><td>-11.0 (14.0)*</td></tr>
</table>
* p=0.05 compared with baseline; ^p<0.05 12 months compared with 6 months

The SGRQ total score improved by the minimal clinically important difference of 4 units in 29 evaluable patients (72.5%) at 6 months and 25 patients (67.6%) at 12 months (p<0.001).

Mean improvement in 6MWD (metres)
• 6 month follow-up=46.5, p<0.001
• 12 month follow-up=18.5
</td>
<td>
There were 39 serious adverse events in 23 (52.3%) patients; 22 events were respiratory.

29 events happened in the first 6 months after the procedure (1 was in the first week, 10 had onset between 9 and 30 days, 9 were between 31 and 90 days and 8 were beyond 90 days after the procedure):
• End-stage COPD, n=1
• COPD exacerbation, n=9
• Gastroesophageal reflux, n=1
• Haemoptysis, n=3
• Pneumonia, n=6
• Post-treatment inflammation reaction, n=1
• Respiratory tract infection, n=5
• Right upper quadrant abdominal pain, n=1
• Urinary retention, n=1
• Ventricular fibrillation, n=1

10 serious adverse events occurred beyond 180 days in 8 patients:
• COPD exacerbation, n=5
• Respiratory tract infection, n=1
• Investigation of diabetes, n=1
• Acute dyspnoea, n=1
• Cardiac insufficiency, n=1
• Right heart failure, n=1

1 patient died 67 days after treatment secondary to end-stage lung disease. Another patient died 350 days after treatment because of complications after lobectomy for aspergillus infection of the untreated lung.

Number of patients with serious adverse events during the first 30 days by subgroup:
• GOLD III=5
• GOLD IV=6
• Heterogeneity index<1.6=4
• Heterogeneity index>1.6=7
</td>
</tr>
</table>

Mean improvement in mMRC score (units)

- 6 month follow-up=0.90, p<0.001
- 12 month follow-up=0.83, p<0.001

Mean improvement in BODE index (units)

- 6 month follow-up=1.48, p<0.001
- 12 month follow-up=1.25, p<0.001

Changes in efficacy outcomes according to GOLD stage disease severity, mean (SD)

	Baseline	Change at 6 months	Change at 12 months
GOLD stage IV (n=22)			
Lobar volume (ml)	1474 (484)	-690 (692)*	-772 (734)*
FEV_1 (ml)	715.9 (202.5)	142.0 (182.9)*	108.9 (182.25)*
RV (ml)	4970.5 (1033.7)	-302.0 (780.4)	-335.6 (908.3)
SGRQ total score	63.7 (11.9)	-17.4 (16.9)*	-12.7 (15.0)*
6MWD (metres)	270.6 (65.8)	48.7 (78.5)*	25.6 (72.1)^
mMRC score	3.0 (0.7)	-0.8 (1.1)*	-0.9 (0.8)*
GOLD stage III (n=22)			
Lobar volume (ml)	1503 (488)	-743 (565)*	-735 (601)*
FEV_1 (ml)	1005.5 (215.2)	139.5 (152.4)*	64.7 (167.5)^
RV (ml)	4989.6 (1114.0)	-510.0 (643.4)*	-270.0 (641.3)
SGRQ total score	54.1 (14.5)	-10.6 (12.7)*	-9.4 (13.1)*
6MWD (metres)	329.3 (77.5)	44.4 (55.4)*	10.9 (54.5)
mMRC score	2.8 (0.8)	-1.0 (1.1)*	-0.7 (1.1)*

* p=0.05 compared with baseline; ^p<0.05 12 months compared with 6 months

Changes in efficacy outcomes according to heterogeneity index

	Baseline	Change at 6 months	Change at 12 months
GOLD stage IV (n=22)			
Lobar volume (ml)	1630 (580)	-963 (704)^	-1078 (753)^
FEV_1 (ml)	870 (249)	183 (197)^	139 (200)*
RV (ml)	5053 (923)	-654 (738)*	-571 (837)*
SGRQ total score	55.9 (12.7)	-12.5 (17.0)*	-13.2 (13.6)^
6MWD (metres)	297.0 (93.6)	48.4 (55.7)*	25.0 (59.8)
mMRC score	2.9 (0.8)	-1.2 (1.1)^	-1.0 (1.2)
GOLD stage III (n=22)			
Lobar volume (ml)	1347 (309)	-484 (431)	-426 (304)
FEV_1 (ml)	852 (262)	102 (125)*	36 (131)^
RV (ml)	4907 (1202)	-182 (627)	-63 (645)
SGRQ total score	61.8 (14.9)	-15.3 (13.5)	-9.0 (14.4)*
6MWD (metres)	302.9 (58.0)	44.8 (77.3)*	12.3 (68.3)^
mMRC score	2.9 (0.7)	-0.7 (1.0)*	-0.7 (0.7)

Number of patients with serious adverse events over 12 months by subgroup:

- GOLD III=9
- GOLD IV=14
- Heterogeneity index<1.6=10
- Heterogeneity index>1.6=13

Abbreviations used: FEV_1, forced expiratory volume in 1 second; mMRC, modified Medical Research Council dyspnoea scale; RV, residual volume; SD, standard deviation; 6MWD, 6-minute walking distance; SGRQ, St George's Respiratory Questionnaire

Study 5 Snell G (2009)

Details

Study type	**Case series**
Country	Australia
Recruitment period	Not reported
Study population and number	**n=11** **Patients with severe heterogenous emphysema**
Age and sex	Mean 62 years; 18% (2/11) male
Patient selection criteria	Inclusion criteria: age >40 and <80 years, heterogenous upper lobe emphysema on high-resolution CT, FEV1>15% and <45% predicted, diffusion capacity of the lung for carbon monoxide >20% predicted, total lung capacity >100% predicted, residual volume >150% predicted, post-rehabilitation 6-minute walk test >140 metres, PCO_2≤50 mmHg, PO_2≥45 mmHg (on room air), non-smoking for 4 months before study enrolment. Patients were on optimal medical management. Exclusion criteria: deficiency of alpha-1-antitrypsin or clinically significant asthma, chronic bronchitis, or bronchiectasis, body mass index <15 or >35 kg/m^2, history of surgical or bronchoscopic lung volume reduction, bullectomy, lobectomy or thoracoscopic operation, more than 3 hospitalisations in previous 12 months for respiratory infections, pulmonary arterial systolic pressure ≥45 mmHg.
Technique	Device: Uptake Medical BTVA treatment system. A conservative unilateral low-dose (5 calories thermal vapour energy/gramme of tissue) for upper lobe treatment was used. All patients were offered postoperative prophylactic antibiotics, inhaled bronchodilators, and supplemental oxygen as determined by arterial oxygen saturations.
Follow-up	**6 months**
Conflict of interest/source of funding	Financial, technical and equipment support was provided from the sponsor Uptake Medical Corp., US.

Analysis

Follow-up issues: No losses to follow-up were described.

Study design issues: Small feasibility and safety study. The primary endpoint was to assess all adverse events secondary to the bronchoscopic thermal vapour ablation (BTVA) treatment during 6 months of follow-up. Serious adverse events were defined as fatal or life-threatening events, an event needing unexpected hospitalisation or an event resulting in permanent disability. The study was generally not powered to detect statistical differences in efficacy endpoints.

Study population issues: The mean SGRQ total score at baseline was 64.4.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **11**

Mean length of hospital stay = 1.7 days (range 1 to 5)

Overall, there were no significant changes in CT-calculated total lung volume.

Mean decrease in target lobar volume at 6 months = 16% (range -75% to 1%).

The extent of the volume loss in the BTVA target area correlated with the improvement in SGRQ (r=0.83).

Respiratory function test outcomes, mean (range)

Variable	Baseline	1 month	3 months	6 months	% change	p value
FEV_1, L	0.77	0.82 (0.48 to 1.08)	0.81 (0.56 to 1.21)	0.79 (0.49 to 1.18)	+2.6	0.40
FEV_1, % predicted	32 (22 to 39)	34 (22 to 44)	34 (20 to 43)	33 (17 to 45)		
FVC, L	2.28 (1.35 to 2.93)	2.38 (1.56 to 3.13)	2.37 (1.70 to 2.95)	2.27 (1.66 to 2.93)	-0.4	0.45
FVC, % predicted	72 (46 to 92)	75 (56 to 92)	74 (58 to 91)	72 (52 to 97)		
RV, L	4.16 (4.00 to 5.85)	3.99 (2.96 to 5.39)	3.98 (2.90 to 5.58)	4.13 (2.99 to 5.77)	-1.0	0.46
RV, % predicted	219 (166 to 320)	209 (159 to 267)	208 (164 to 284)	216 (155 to 312)		
DLCO	7.7 (4.5 to 10.5)	8.1 (5.9 to 10.9)	8.6 (4.2 to 13.3)	9.0 (5.1 to 12.1)	+15.9	0.01
DLCO % predicted	33 (20 to 44)	35 (27 to 45)	37 (21 to 56)	38 (24 to 49)		
6MWD, metres	359 (233 to 495)	-	360 (208 to 540)	362 (210 to 527)	+1.0	0.69

MRC dyspnoea score

- Baseline=2.6
- 6 months=2.1

SGRQ total score

- Baseline=64.4 (range 37 to 84)
- 6 months=49.1 (range 32 to 64)

Change in SGRQ impact score at 6 months=-16.3 (range -53 to 3)

Change in SGRQ activity score at 6 months=-21.0 (range -72 to 22)

Change in SGRQ symptom score at 6 months=-10.1 (range -43 to 30)

Safety

There were no intraoperative adverse events.

'Nonserious' events after the procedure, consistent with the effects of anaesthesia and bronchoscopy, were reported in 10 of 11 patients. The commonest included nausea, cough, mild to moderate haemoptysis, and transient fatigue.

There were 7 COPD exacerbations in 4 patients (3 were judged to be infectious and 4 were non-infectious).

There were 2 bouts of pneumonitis, 1 probable infection-based on day 6 and 1 non-infectious inflammatory pneumonitis on day 4.

Serious adverse events (all needed hospitalisation for a mean of 4.6 days [range 2 to 8])

- COPD exacerbations, n=2
- Pneumonitis, n=1
- Anxiety, n=1
- Atrial tachycardia, n=1

Abbreviations used: BTVA, bronchoscopic thermal vapour ablation; DLCO, diffusion capacity of the lung for carbon monoxide; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; MRC, Medical Research Council; RV, residual volume; SGRQ, St George's Respiratory Questionnaire; 6MWD, 6-minute walk distance

Validity and generalisability of the studies

- The evidence included 1 randomised controlled trial, which was open-label.
- The randomised controlled trial compared efficacy and safety with standard medical treatment.
- One of the studies was a subgroup analysis of the randomised controlled trial, which only included patients with incomplete fissures.
- There were no data beyond 12 months of follow-up.
- One of the studies was a feasibility study and used a lower dose than the other studies.[5] This is likely to have an effect on the efficacy and safety outcomes.
- All the studies were sponsored by the company that manufactures the device used for the procedure.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure.

Interventional procedures

- Endobronchial valve insertion to reduce lung volume in emphysema. NICE interventional procedures guidance 600 (2017). Available from http://www.nice.org.uk/guidance/IPG600
- Insertion of endobronchial nitinol coils to improve lung function in emphysema. NICE interventional procedures guidance 517 (2015). Available from http://www.nice.org.uk/guidance/IPG517
- Lung volume reduction surgery for advanced emphysema. NICE interventional procedures guidance 114 (2005). Available from http://www.nice.org.uk/guidance/IPG114

NICE guidelines

- Chronic obstructive pulmonary disease in over 16s: diagnosis and management. NICE clinical guideline 101 (2010). Available from http://www.nice.org.uk/guidance/CG101

Additional information considered by IPAC

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate.
Two Specialist Advisor Questionnaires for bronchoscopic thermal vapour ablation for upper-lobe emphysema were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme was unable to gather patient commentary for this procedure.

Company engagement

A structured information request was sent to 1 company who manufactures a potentially relevant device for use in this procedure. NICE received 1 completed submission. This was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

None other than those described above.

References

1. Herth F, Valipour A, Shah P, et al. (2016) Segmental volume reduction using thermal vapour ablation in patients with severe emphysema: 6-month results of the multicentre, parallel-group, open-label, randomised controlled STEP-UP trial. The lancet respiratory medicine 4: 185–93
2. Gompelmann D, Eberhardt R, Schuhmann M, et al. (2016) Lung Volume Reduction with Vapor Ablation in the Presence of Incomplete Fissures: 12-Month Results from the STEP-UP Randomized Controlled Study. Respiration; international review of thoracic diseases 92: 397–403
3. Herth FJF, Ernst A, Baker KM, et al. (2012) Characterization of outcomes 1 year after endoscopic thermal vapor ablation for patients with heterogeneous emphysema. International journal of chronic obstructive pulmonary disease 7: 397–405
4. Snell G, Herth FJF, Hopkins P, et al. (2012) Bronchoscopic thermal vapour ablation therapy in the management of heterogeneous emphysema. The European respiratory journal 39: 1326–33
5. Snell GI, Hopkins P, Westall G, et al. (2009) A feasibility and safety study of bronchoscopic thermal vapor ablation: a novel emphysema therapy. The annals of thoracic surgery 88: 1993–8

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	22/01/2019	Issue 1 of 12, January 2019
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	22/01/2019	Issue 1 of 12, January 2019
HTA database (CRD website)	22/01/2019	-
MEDLINE (Ovid)	22/01/2019	1946 to January 21, 2019
MEDLINE In-Process (Ovid) & Medline ePub ahead (Ovid)	22/01/2019	January 21, 2019
EMBASE (Ovid)	22/01/2019	1974 to 2019 Week 03

Trial sources searched 25/05/2018

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched 25/05/2018

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- EuroScan
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	Emphysema/
2	Pulmonary Emphysema/
3	emphysema*.tw.
4	or/1-3
5	Bronchoscopy/
6	bronchoscop*.tw.

7	Ablation Techniques/
8	((steam* or vapour* or water*) adj4 ablat*).tw.
9	*Steam/
10	or/5-9
11	4 and 10
12	(Intervapor or BTVA).tw.
13	11 or 12
14	(2008* or 2009* or 201*).ed.
15	13 and 14 (506)
16	Animals/ not Humans/
17	15 not 16

Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Gompelmann D, Shah PL, Valipour A, et al. (2018) Bronchoscopic Thermal Vapor Ablation: Best Practice Recommendations from an Expert Panel on Endoscopic Lung Volume Reduction Respiration 95 (6)	Review	After the procedure, patients should be strictly monitored to proactively detect symptoms of localized inflammatory reaction that may temporarily worsen the clinical status of the patient and to detect complications. As the data are still very limited, BTVA should be performed within clinical trials or comprehensive registries where the product is commercially available.	All the relevant studies described in the review have been included in table 2 or the appendix.
Gompelmann D, Heussel CP, Eberhardt R, et al. (2012) Efficacy of bronchoscopic thermal vapor ablation and lobar fissure completeness in patients with heterogeneous emphysema Respiration; international review of thoracic diseases 83: 400-6	Case series n=44	Lobar fissure integrity has no or minimal influence on BTVA-induced lung volume reduction and improvements in clinical outcomes.	Results from the same study are already included (study 3 and 4 in table 2).
Gompelmann D, Eberhardt R, Ernst A, et al. (2013) The localized inflammatory response to bronchoscopic thermal vapor ablation Respiration 86: 324-331	Case series n=44	Patients with more prominent respiratory symptoms in the first 30 days following BTVA experience greater efficacy. The clinical manifestations of the localised inflammatory response are predictive of long-term clinical benefits.	Results from the same study are already included (study 3 and 4 in table 2).
Iftikhar IH, McGuire FR and Musani AI (2014) Efficacy of bronchoscopic lung volume reduction: a meta-analysis International journal of chronic obstructive pulmonary disease 9: 481-91	Review and meta-analysis	The preliminary findings of our meta-analysis signify the importance of most methods of bronchoscopic lung volume reduction. The magnitude of the effect on selected primary outcomes shows noninferiority, if not equivalence, when compared to what is known for surgical lung volume reduction.	Includes other techniques for bronchoscopic lung volume reduction and only 1 trial on bronchoscopic thermal vapour ablation.
Rustagi N, Singh S, Dutt N, et al. (2019) Efficacy and safety of stent, valves, vapour ablation, coils and sealant therapies in advanced emphysema: A meta-analysis Turkish Thoracic Journal 20: 43-60	Review and meta-analysis	Bronchoscopic thermal vapour ablation appears promising, but it has not yet been adequately studied to derive any robust conclusion.	Includes other techniques for bronchoscopic lung volume reduction and only 2 trials on bronchoscopic thermal vapour ablation, which

			are already included in table 2.