

Endobronchial valve insertion to reduce lung volume in emphysema

Interventional procedures guidance

Published: 20 December 2017

www.nice.org.uk/guidance/ipg600

Your responsibility

This guidance represents the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take this guidance fully into account, and specifically any special arrangements relating to the introduction of new interventional procedures. The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the [Yellow Card Scheme](#).

Commissioners and/or providers have a responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful

discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties. Providers should ensure that governance structures are in place to review, authorise and monitor the introduction of new devices and procedures.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

This guidance replaces IPG465.

1 Recommendations

- 1.1 Current evidence on the safety and efficacy of endobronchial valve insertion to reduce lung volume in emphysema is adequate in quantity and quality to support the use of this procedure provided that standard arrangements are in place for clinical governance, consent and audit. Find out what standard arrangements mean on the NICE interventional procedures guidance page.
- 1.2 Patient selection should be done by a multidisciplinary team experienced in managing emphysema, which should typically include a chest physician, a radiologist, a thoracic surgeon and a respiratory nurse.
- 1.3 Patients selected for treatment should have had pulmonary rehabilitation.
- 1.4 The procedure should only be done to occlude volumes of the lung where there is no collateral ventilation, by clinicians with specific training in doing the procedure.

2 Indications and current treatments

- 2.1 Emphysema is a chronic lung disease in which 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 smoking related but may also be inherited.

- 2.2 Treatment options include pulmonary rehabilitation (exercise training, breathing retraining, and patient and carer education), smoking cessation, and the use of inhaled or oral bronchodilators and corticosteroids. Oxygen therapy may also be indicated 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. Such surgery can be done thoracoscopically (using video-assisted thoracoscopy or thoracotomy) or using an open approach (using a sternotomy or thoracotomy). Lung transplantation surgery may also be an option. Certain therapies under clinical investigation such as coiling, use of sealants and thermal ablation may be used in regional lung disease.

3 The procedure

- 3.1 The aim of insertion of endobronchial valves (also known as intrabronchial valves) to reduce lung volume in emphysema is to achieve atelectasis of selected lung segments. It uses an endoscopic approach, which is less invasive than open or thoracoscopic lung volume reduction surgery. Before the procedure, it is usual practice to assess the presence of collateral ventilation (when air enters a lobe of the lung through a passage that bypasses the normal airway). A surrogate for this is CT scanning to assess the completeness of fissures. A functional approach, specially developed for use before airway valve insertion, involves a specially designed balloon catheter with a flow sensor.
- 3.2 Endobronchial valve insertion is done with the patient under sedation or general anaesthesia. Using a delivery catheter passed through a bronchoscope, a synthetic valve is placed in the target location and fixed to the bronchial wall. The valve is designed to prevent air inflow during inspiration but to allow air and mucus to exit during expiration. Several valves may be needed (1 or more for each segment of the lung to be treated). Patients may sometimes be given antibiotics or corticosteroids. Two devices with different designs are available for

interventional lung volume reduction – 1 is duckbill shaped and the other umbrella shaped.

4 Efficacy

This section describes efficacy outcomes from the published literature that the committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#).

- 4.1 A systematic review (SR) and meta-analysis included 5 randomised controlled trials (RCTs) of patients (n=703) treated by duckbill-shaped endobronchial valve (EBV) insertion and 3 RCTs of patients (n=372) treated by umbrella-shaped EBV insertion, both compared with standard medical care (SMC). These 2 groups were analysed separately. In a meta-analysis of the 5 RCTs of duckbill EBV insertion compared with SMC, there was a statistically significant difference in 1% change from baseline in forced expiratory volume in 1 second (FEV₁) in favour of duckbill EBV insertion (standardised mean difference [SMD] 0.48, 95% confidence interval [CI] 0.32 to 0.64, p<0.00001, I²=42). In 2 RCTs (n=143) from the same meta-analysis, a 2% increase in FEV₁ was statistically significantly more frequent in patients treated by duckbill EBV than in those treated by SMC at 90-day follow-up (SMD 0.77, 95% CI 0.43 to 1.11, p<0.00001, I² = 0%). In the other 3 RCTs (n=560) from the same meta-analysis, a 2% increase in FEV₁ was statistically significantly more frequent in patients treated by duckbill EBV than in those treated by SMC at 6-month follow-up (SMD 0.40, 95% CI 0.22 to 0.58, p<0.00001, I²=41%). One RCT (n=73), which studied patients treated by the umbrella EBV, reported no statistically significant difference in FEV₁ measurements at 3-month follow-up (MD 0.90 litres, standard deviation [SD] 0.34) compared with patients having SMC (0.87 litres, SD 0.34, p=0.065). A second RCT (n=22) of the umbrella EBV reported statistically significantly improved FEV₁ measurements in patients treated unilaterally (21.4%, SD 10.7%) but not in patients treated bilaterally (-3.1%, SD 15.0; MD 24.50%, 95% CI 13.61 to 35.39). The SR reported a statistically significantly larger change in FEV₁ from baseline in patients with heterogeneous emphysema treated by duckbill EBV than in patients with homogeneous emphysema having the same treatment (MD 16.36%, 95% CI 9.02 to 23.71, p=0.00001, I²=0%, n=137, 2 RCTs).

- 4.2 In 3 RCTs (n=542) included in the SR there was a statistically significant increase in FEV₁ from baseline in patients without collateral ventilation treated by duckbill EBV (MD 18.15%, 95% CI 11.81 to 24.49; p=0.000001, I²=0%). Three RCTs (n=542) reported no statistically significant increase in FEV₁ after duckbill EBV treatment in patients with collateral ventilation (MD 2.48%, 95% CI -2.63 to 7.59, p=0.34, I²=0%). The SR reported that 2 RCTs showed statistically significant increases in FEV₁ in patients with intact interlobar fissures as a surrogate for the absence of collateral ventilation (MD 17.80%, 95% CI 7.78 to 27.82, n=68; and MD 17.23%, 95% CI 8.10 to 26.36, n=93). In an RCT of 97 patients without collateral ventilation, an increase in FEV₁ of greater than 12% from baseline was statistically significantly more frequent in patients treated by duckbill EBV (56% [36/64]) than in patients treated by SMC (3% [1/31], p<0.001) at 6-month follow-up.
- 4.3 The SR reported a meta-analysis of 4 of the RCTs (n=379) of patients treated with duckbill EBV in whom the 6-minute walking distance test was used to assess exercise capacity. The analysis showed a statistically significant increase in exercise capacity from baseline compared with SMC (MD 38.12 m, 95% CI 8.68 to 67.56, p=0.011, I²=78%). There was high variability between the studies. Three RCTs included in the SR reported a statistically significantly higher number of patients able to walk 26 m or more in the EBV-treated group compared with the SMC group. One RCT (n=321) found no statistically significant difference in the number of patients able to walk more than 26 m between the duckbill EBV and SMC groups (p=0.28). The SR reported a meta-analysis of 2 RCTs (n=316) that showed a statistically significant difference in exercise capacity from baseline favouring patients having SMC compared with patients treated by umbrella EBV (MD -19.54 m, 95% CI -37.11 to -1.98, p=0.029, I²=0%). In the RCT of 97 patients without collateral ventilation, an increase in 6-minute walking distance of more than 26 m from baseline values was statistically significantly more frequent in patients treated by duckbill EBV (52% [33/63]) than in patients treated by SMC (13% [4/31], p<0.001) at 6-month follow-up.
- 4.4 Five RCTs (n=695) included in the SR reported on quality of life measured by the St. George's respiratory questionnaire (SGRQ, 100 being the worst and 0 the best possible health status). In this analysis, patients treated by duckbill EBV had statistically significantly better quality of life than those having SMC (MD -7.29 units, 95% CI -11.12 to -3.45, p=0.0002, I²=67%) at a maximum follow-up of 12 months. The SR reported a meta-analysis of 2 RCTs (n=350) that showed no

statistically significant difference in SGRQ score between patients treated by umbrella EBV and those having SMC (MD 2.64 units, 95% CI -0.28 to 5.56, $p=0.076$, $I^2=28\%$, high-quality evidence).

- 4.5 The specialist advisers listed the key efficacy outcomes to be lung function measurements, health status, exercise capacity, improvement in breathlessness, reduction in lung volume, and quality of life.

5 Safety

This section describes safety outcomes from the published literature that the committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#).

- 5.1 Mortality was not statistically significantly different in patients treated by duckbill endobronchial valve (EBV) insertion compared with patients having standard medical care (SMC; odds ratio [OR] 1.07, 95% confidence interval [CI] 0.47 to 2.43, $I^2=0$) in a meta-analysis of 5 randomised controlled trials (RCTs; $n=703$) included in a systematic review (SR). Mortality was not statistically significantly different in patients treated by umbrella EBV compared with those having SMC (OR 4.95, 95% CI 0.85 to 28.94, $p=0.076$, $I^2=0\%$) in a meta-analysis of 2 RCTs ($n=350$) in the SR. One patient died from tension pneumothorax 4 days after valve insertion in a case series of 91 patients. One patient died from a pneumothorax-induced cardiac arrest within 30 days of duckbill EBV insertion in 1 RCT of 97 patients.
- 5.2 The rate of adverse events was statistically significantly higher in patients treated by duckbill EBV compared with those having SMC (OR 5.85, 95% CI 2.16 to 15.84) in a meta-analysis of 3 RCTs ($n=482$) in the SR. Serious adverse events were reported on 22 occasions in patients treated by umbrella EBV and in 6 patients having SMC in 1 RCT ($n=277$) included in the SR. The rate of adverse events was statistically significantly higher in patients treated by umbrella EBV than in those having SMC (OR 3.41, 95% CI 1.48 to 7.84) in a meta-analysis of 2 RCTs ($n=350$) in the SR.
- 5.3 Chronic obstructive pulmonary disease (COPD) exacerbation episodes were not

- statistically significantly more frequent in patients treated by duckbill EBV (64% [16/25]) compared with those having SMC (80% [20/25]) in an RCT (n=50) reported in the SR (p=0.42). COPD exacerbation episodes were reported in patients treated with the umbrella valve in 2 RCTs included in the SR: 7 in the valve group and 2 in the SMC group in 1 RCT (n=277) and 2 in the valve group and 2 in the SMC group in another RCT (n=22).
- 5.4 Respiratory failure occurred on 4 occasions in patients treated by umbrella valve in 1 RCT included in the SR, and in 1 patient in a case series of 343 patients without collateral ventilation treated by duckbill EBV.
- 5.5 Pneumonia episodes were not statistically significantly more frequent in patients treated by duckbill EBV (n=2) compared with patients having SMC (n=0) in an RCT (n=50) reported in the SR (p=0.49). The pneumonia rate was not statistically significantly different in patients treated by duckbill EBV (6% [2/34]) compared with those having SMC (3% [1/34]) in 1 RCT reported in the SR (p=1.0). Pneumonia distal to the valve was reported in 4% (9/220) of patients treated by duckbill EBV in 1 RCT included in the SR. Pneumonia distal to the valve was reported in 7% (6/91) of patients and bacterial bronchitis was reported in 1 of 91 patients in the case series of 91 patients at 12-month follow-up. Pneumonia was reported in 1 of the 14 patients who were treated bilaterally by EBV in a case series of 49 patients. Pneumonia distal to the valve was reported in 5% (2/40) of patients treated by EBV in a case series of 40 patients.
- 5.6 Pneumothorax episodes were not statistically significantly more frequent in patients treated by duckbill EBV (n=2) compared with patients having SMC (n=1) in an RCT (n=50) reported in the SR (p=1.0). The pneumothorax rate was reported as 26% (11/43) and 18% (6/34) in patients treated by duckbill EBV in 2 RCTs included in the SR. Pneumothorax occurred on 3 occasions in patients treated by umbrella EBV in 1 RCT included in the SR. The pneumothorax rate was 6% (25/421) in a case series of 421 patients treated by duckbill EBV; the mean duration of pneumothorax in this study was 11 days (range 2 to 73 days). Pneumothorax occurred in 10% (35/343) of patients in the case series of 343 patients. Pneumothorax within 12 months of valve insertion was reported in 12% (11/91) of patients in the case series of 91 patients; 5 of these were judged to be serious and definitely device related. Pneumothorax was reported in 21% (3/14) of patients in the bilateral group and in 8% (3/35) of patients in the unilateral

group in the case series of 49 patients treated by EBV. One patient had contralateral pneumothorax 15 days after the procedure in the case series of 40 patients. Pneumothorax occurred in 1% (5/343) of patients reported in the case series of 343 patients. Pneumothorax happened in 18% (70/381) of patients treated by EBV with duckbill or umbrella valves in the case series of 381 patients. In these 70 patients, pneumothorax resolved under observation in 13% (9/70), and 87% (61/70) needed chest tube insertion. In 51% (31/61) of patients pneumothorax did not resolve and valve removal was necessary. Persistent fistula (despite chest drain and valve removal) was present in 45% (14/31) of patients and required further intervention. In the same study 73% (51/70) of cases of pneumothorax happened within 3 days of EBV treatment.

- 5.7 Four episodes of valve expectoration were reported in 1 RCT (n=50) of the duckbill EBV included in the SR. Valve replacement was reported in 7% (3/43) of patients treated by duckbill EBV in 1 RCT (n=93) included in the SR. Valve expectoration, migration or aspiration were reported on 14 occasions in 1 RCT (n=171) of duckbill EBV reported in the SR. Valve replacement was needed in less than 1% (3/343) of patients reported in the case series of 343 patients. Valve migration was reported in 14% (2/14) of patients treated bilaterally by duckbill EBV in the case series of 49 patients. Valve removal (duckbill EBV) was needed in 2 cases in 1 RCT (n=50), in 12% (5/43) of patients in another RCT and in 14% (21/220) of patients in another RCT included in the SR. Valve removal was reported in 18% (16/91) of patients in the case series of 91 patients treated by duckbill EBV, and in 1 patient treated by EBV in the case series of 40 patients.
- 5.8 Haemoptysis was reported in less than 1% (1/220) of patients treated by duckbill EBV in 1 RCT included in the SR. Mild haemoptysis occurred in 1 of 343 patients in the case series of 343 patients. Haemoptysis was reported in 14% (2/14) of patients treated bilaterally by EBV in the case series of 49 patients.
- 5.9 Bronchospasm was reported in 1 patient treated by umbrella EBV in 1 RCT included in the SR. Bronchospasm within 3 days of the procedure was reported in 9% (8/91) of patients in the case series of 91 patients. One of these was described as serious, and associated with respiratory failure and myocardial infarction that began the evening after the procedure; the patient had further episodes of bronchospasm and the valves were removed on day 21. A second patient had valve removal on day 3 because the bronchospasm did not resolve.

- 5.10 Placement of a valve in the incorrect lobe was reported in 1% (3/220) of patients in 1 RCT included in the SR.
- 5.11 Hypoxia was reported in 1% (4/343) of patients, fistula in less than 1% (2/343), pleural effusion in less than 1% (2/343) and increased sputum in less than 1% (1/343) of patients in the case series of 343 patients. Injury to bronchi was reported in 3% (3/91) of patients in the case series of 91 patients (not further described). In the same case series, 2% (2/91) of patients reported transient hypercarbia; 1 patient needed overnight ventilator support.
- 5.12 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 done so). For this procedure, specialist advisers listed no anecdotal adverse events in addition to those in the literature. They considered that the following were theoretical adverse events: worsening of hypercapnia and pulmonary hypertension.

6 Committee comments

- 6.1 Most of evidence on the efficacy of this procedure came from patients with heterogeneous emphysema. The committee was told that the valves can also be used in patients with homogenous emphysema.
- 6.2 The committee noted that there are different devices available for this procedure, and that the published evidence shows they may have different efficacy profiles.
- 6.3 There is a [UK lung volume reduction trial and national database for lung volume reduction procedures](#) into which some patients treated by endobronchial valve insertion could be entered.

7 Further information

- 7.1 Patient commentary was sought but none was received.

Information for patients

NICE has produced information on this procedure for patients and carers ([information for the public](#)). It explains the nature of the procedure and the guidance issued by NICE, and has been written with patient consent in mind.

ISBN: 978-1-4731-2755-5

Endorsing organisation

This guidance has been endorsed by [Healthcare Improvement Scotland](#).