

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional procedure consultation document

Endobronchial valve insertion to reduce lung volume in emphysema

Emphysema is a chronic lung disease that causes the walls of the smaller airways in the lungs to break down. This creates abnormally large spaces that fill with air, reducing the amount of air that reaches the healthy parts of the lung. In this procedure, a thin flexible tube with a camera on the end (bronchoscope) is moved through the nose or mouth into the lungs and small, one-way valves are then placed in the airways leading to the damaged parts of the lungs. The aim is to reduce the airflow to the damaged parts, allowing more air to reach the healthy areas.

The National Institute for Health and Care Excellence (NICE) is examining endobronchial valve insertion to reduce lung volume in emphysema and will publish guidance on its safety and efficacy to the NHS. NICE's interventional procedures advisory committee has considered the available evidence and the views of specialist advisers, who are consultants with knowledge of the procedure. The advisory committee has made draft recommendations about endobronchial valve insertion to reduce lung volume in emphysema.

This document summarises the procedure and sets out the draft recommendations made by the advisory committee. It has been prepared for public consultation. The advisory committee particularly welcomes:

- comments on the draft recommendations
- the identification of factual inaccuracies
- additional relevant evidence, with bibliographic references where possible.

Note that this document is not NICE's formal guidance on this procedure. The recommendations are provisional and may change after consultation.

The process that NICE will follow after the consultation period ends is as follows.

- The advisory committee will meet again to consider the original evidence and its draft recommendations in the light of the comments received during consultation.
- The advisory committee will then prepare draft guidance which will be the basis for NICE's guidance on the use of the procedure in the NHS.

For further details, see the [Interventional Procedures Programme process guide](#), which is available from the NICE website.

Through its guidance NICE is committed to promoting race and disability equality, equality between men and women, and to eliminating all forms of discrimination. One of the ways we do this is by trying to involve as wide a range of people and interest groups as possible in the development of our interventional procedures guidance. In particular, we aim to encourage people and organisations from groups who might not normally comment on our guidance to do so.

In order to help us promote equality through our guidance, we should be grateful if you would consider the following question:

Are there any issues that require special attention in light of NICE's duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations between people with a characteristic protected by the equalities legislation and others?

Please note that NICE reserves the right to summarise and edit comments received during consultations or not to publish them at all where in the reasonable opinion of NICE, the comments are voluminous, publication would be unlawful or publication would otherwise be inappropriate.

Closing date for comments: 25 September 2017

Target date for publication of guidance: December 2017

1 Draft 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.

- 1.2 Patient selection should be done by a multidisciplinary team experienced in managing emphysema.
- 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 such as coiling, use of sealants and thermal ablation may be particularly useful 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. Different devices of slightly varying designs are available for this procedure – 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 a duckbill-shaped endobronchial valve (EBV) insertion and 3 RCTs of patients (n=372) treated by an 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 (mean difference [MD] 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 (MD 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 (MD 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).

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 patients having SMC group. One RCT (n=321) found no statistically significant difference in the

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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 , $p=0.029$, $I^2=0\%$).

- 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, there was statistically significantly better quality of life in patients treated by duckbill EBV compared with those having SMC (MD -7.29 units, 95% CI -11.12 to -3.45 , $p=0.0002$, $I^2=67\%$) 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 and 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 valves (EBV) 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.
- 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 the umbrella valve in 1 RCT included in the SR. It was also reported 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 day 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.

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.

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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.

7 Further information

- 7.1 For related NICE guidance, see the [NICE website](#).
- 7.2 This guidance is a review of NICE's interventional procedure guidance on [insertion of endobronchial valves for lung volume reduction in emphysema](#).

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