

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional procedure consultation document

Balloon pulmonary angioplasty for chronic thromboembolic pulmonary hypertension

When a blood clot forms in one of the deep veins in the legs, it is called a deep vein thrombosis. The clot can become loose and be carried in the blood to the lungs. Here, it can block an artery (a blood vessel), which can affect blood flow to the lungs. Blood clots in the lungs may dissolve over time but they do not always dissolve completely, leaving the artery narrowed. This restricts blood flow through the lungs leading to shortness of breath, dizziness, tiredness, chest pain and, eventually, heart failure. In this procedure, a balloon is inserted into an artery in the lungs, through a vein in the neck or groin. The balloon is then positioned at the site of narrowing and inflated to widen the artery. The aim is to improve blood flow through the lungs.

The National Institute for Health and Care Excellence (NICE) is examining balloon pulmonary angioplasty for chronic thromboembolic pulmonary hypertension 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 provisional recommendations about balloon pulmonary angioplasty for chronic thromboembolic pulmonary hypertension.

This document summarises the procedure and sets out the provisional recommendations made by the Advisory Committee. It has been prepared for public consultation. The Advisory Committee particularly welcomes:

- comments on the provisional 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 provisional 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- The Advisory Committee will then prepare draft guidance which will be the basis for NICE's guidance on the use of the procedure in the NHS.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: 26 January 2016

Target date for publication of guidance: April 2016

1 Provisional recommendations

- 1.1 Evidence on the safety of balloon pulmonary angioplasty for chronic thromboembolic pulmonary hypertension shows the potential for serious but well-recognised complications. In relation to efficacy:

- For patients for whom pulmonary endarterectomy is considered to be unsuitable (because of comorbidities or the distribution of their arterial disease), evidence on efficacy is adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance, consent and audit.
- For patients for whom pulmonary endarterectomy is considered to be suitable, evidence on efficacy is inadequate, especially in the long term. Therefore, for these patients, this procedure should only be used with special arrangements for clinical governance, consent and audit or research.

1.2 Clinicians wishing to offer balloon pulmonary angioplasty for chronic thromboembolic pulmonary hypertension to patients for whom pulmonary endarterectomy would be suitable should:

- Inform the clinical governance leads in their NHS trusts.
- Ensure that patients understand the uncertainty about the procedure's efficacy, especially in the long term, and provide them with clear written information. In addition, the use of NICE's information for the public [\[\[URL to be added at publication\]\]](#) is recommended.
- Audit [\[URL to audit tool to be added at publication\]](#) and review clinical outcomes of all patients having balloon pulmonary angioplasty for chronic thromboembolic pulmonary hypertension (see section 7.1).

1.3 Patient selection and treatment should only be done in units specialising in the management of chronic thromboembolic

pulmonary hypertension and with a regular practice in pulmonary endarterectomy.

- 1.4 NICE encourages further research into balloon pulmonary angioplasty for chronic thromboembolic pulmonary hypertension. Details of patient selection, all complications, and subsequent treatments and interventions for pulmonary hypertension should be collected. Reports should include quality-of-life outcomes, long-term efficacy outcomes and survival. NICE may update the guidance on publication of further evidence.

2 Indications and current treatments

- 2.1 Chronic thromboembolic pulmonary hypertension is a progressive disease. It is caused by obstruction of the pulmonary arteries (from main to subsegmental levels) by pulmonary emboli that have not resolved but which have become organised. This causes narrowing of the pulmonary arteries, an increase in the resistance to blood flow and a rise in pressure within the pulmonary arteries. Progression of pulmonary hypertension may occur because of gradual remodelling of unobstructed pulmonary vasculature in response to the haemodynamic changes.
- 2.2 Early symptoms include chest pain, shortness of breath, fatigue, dizziness, peripheral cyanosis and oedema. If left untreated, chronic thromboembolic pulmonary hypertension often leads to right heart failure and ultimately death.
- 2.3 Medical treatment includes anticoagulants to prevent recurrent venous thromboembolism and in-situ pulmonary artery thrombosis. Vasodilators may be used to reduce pulmonary hypertension. Pulmonary endarterectomy is a surgical procedure that aims to

remove the obstructing thromboembolic material. However, the procedure may not be suitable for all patients because of comorbidities or because smaller peripheral pulmonary arteries are affected.

3 The procedure

3.1 Balloon pulmonary angioplasty (BPA) aims to reduce pulmonary hypertension by dilating stenoses in the main or subsegmental pulmonary arteries. The procedure is usually done using a local anaesthetic, with the patient fully anticoagulated. A standard right heart catheterisation is done through the internal jugular vein or femoral vein. The stenosed and occluded arteries that need treatment are identified using selective pulmonary angiography. A balloon catheter is advanced through the stenosis or occlusion, over a guide wire. The balloon is then inflated to dilate each target artery. Between 1 and 6 segmental or subsegmental arteries may be treated during each BPA procedure. The procedure may be repeated until desired haemodynamic measurements are attained.

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 In a case series of 18 patients treated by balloon pulmonary angioplasty (BPA) for chronic thromboembolic pulmonary hypertension, the survival rate was 89% (16/18) after a mean follow-up of 34 months.

- 4.2 In a non-randomised retrospective comparative study of 53 patients treated by BPA (n=29) or pulmonary endarterectomy (PEA; n=24), the mean pulmonary arterial pressure decreased from 39.4 mmHg to 21.3 mmHg ($p<0.001$) in the BPA group at 1 week follow-up and from 44.4 mmHg to 21.6 mmHg ($p<0.001$) in the PEA group at 2 week follow-up. In the same study, the mean right atrial pressure decreased from 5.5 mmHg to 2.6 mmHg ($p=0.013$) in the BPA group at 1 week follow-up and from 10.2 mmHg to 6.0 mmHg (not significant) in the PEA group at 2 week follow-up. Also, the mean cardiac index increased from 2.2 litre/min/m² to 2.7 litre/min/m² ($p<0.001$) in the BPA group at 1 week follow-up and from 2.1 litre/min/m² to 2.8 litre/min/m² ($p=0.005$) in the PEA group at 2 week follow-up.
- 4.3 In a case series of 68 patients with a mean follow-up of 2.2 years after the last BPA session, the mean pulmonary arterial pressure decreased from 45.4 mmHg to 24.0 mmHg ($p<0.01$). In the same study, the mean right atrial pressure decreased from 8.1 mmHg to 1.9 mmHg ($p<0.01$), and the mean cardiac index increased from 2.2 litre/min/m² to 3.2 litre/min/m² ($p<0.01$). In the case series of 18 patients with a mean follow-up of 3 years, the mean pulmonary arterial pressure decreased from 42 mmHg to 33 mmHg ($p=0.002$) and the mean cardiac index changed from 2.0 litre/min/m² to 2.1 litre/min/m² (not significant).
- 4.4 In the case series of 18 patients, the mean New York Heart Association class (range from I to IV: I indicating no limitation of physical activity because of heart failure and IV indicating severe limitation of physical activity because of heart failure) improved from 3.3 to 1.8 ($p<0.001$) at a mean follow-up of 3 years after the last BPA session. In the case series of 68 patients, all patients

were categorised as having World Health Organization (WHO) Class III or IV pulmonary hypertension (marked or severe limitation of physical activity because of pulmonary hypertension) before treatment. At a mean follow-up of 2.2 years after the last BPA session, 96% (64/67) of patients were categorised as having WHO functional class I or II pulmonary hypertension (no or slight limitation of physical activity because of pulmonary hypertension) and 5% (3/67) of patients were categorised as having WHO functional class III pulmonary hypertension.

- 4.5 In the non-randomised retrospective comparative study of 53 patients treated by BPA (n=29) or PEA (n=24), the mean 6-minute walking test distance increased from 295 m to 397 m in the BPA group ($p < 0.001$; follow-up period not reported). No results were reported for the PEA group. In the case series of 18 patients, the mean 6-minute walking test distance increased from 191 m to 454 m ($p < 0.0001$) at a mean follow-up of 3 years after the last BPA session.
- 4.6 In a case series of 20 patients, the mean time that patients were able to carry out cardiopulmonary exercise tests increased from 6.5 minutes to 9.2 minutes ($p = 0.017$) 3 months after the last BPA session. The mean total workload (peak watts) reached during cardiopulmonary exercise testing increased from 86 watts to 111 watts ($p = 0.001$) and the mean peak oxygen consumption during cardiopulmonary exercise testing increased from 13.6 ml/kg/ml to 17.0 ml/kg/ml ($p < 0.01$).
- 4.7 In the non-randomised retrospective comparative study of 53 patients treated by BPA (n=29) or PEA (n=24), mean B-type natriuretic peptide levels decreased from 210 pg/ml to 41 pg/ml

($p=0.01$) in the BPA group and from 263 pg/ml to 74 pg/ml ($p=0.022$; follow-up period not reported) in the PEA group. In the case series of 68 patients, mean B-type natriuretic peptide levels decreased from 330 pg/ml to 35 pg/ml ($p<0.01$) at a mean follow-up of 2.2 years after the last BPA session. In the case series of 20 patients, the proportion of patients who were Troponin T positive decreased from 60% (12/20) to 15% (3/20) 3 months after the last BPA session ($p=0.001$).

4.8 In the case series of 68 patients, the proportion of patients who used endothelin receptor agonists decreased from 52% (35/68) to 37% (25/67) and the proportion of patients who used phosphodiesterase-5 inhibitor decreased from 40% (27/68) to 28% (19/67) at a mean follow-up of 2.2 years after the last BPA session ($p<0.05$ for both drug groups).

4.9 The specialist advisers listed the following key efficacy outcomes: symptomatic improvement; improved functional status (WHO classification, 6-minute walk test); improved haemodynamics; improved tissue perfusion and increased rapidity of pulmonary venous phase during angiography; improved quality of life; improved cardiopulmonary exercise testing; and improved survival.

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 In-hospital death was reported in 1 patient in the balloon pulmonary angioplasty (BPA) group in a non-randomised retrospective

comparative study of 53 patients treated by BPA (n=29) or pulmonary endarterectomy (PEA; n=24) for chronic thromboembolic pulmonary hypertension. This death was due to infection caused by a central venous catheter used to administer epoprostenol. In the same study, perioperative death was reported in 2 patients from the PEA group within 16 days of surgery. Both patients had severe pulmonary hypertension and low cardiac output, and needed constant cardiopulmonary support.

5.2 Death due to right heart failure was reported in 1 patient, 28 days after their third BPA session, in a case series of 68 patients. There was a severe reperfusion pulmonary injury during the BPA session, which exacerbated the patient's right heart failure.

5.3 Death due to right ventricular failure was reported in 1 patient, 7 days after BPA, in a case series of 18 patients. The patient developed segmental pulmonary oedema in all dilated areas and was receiving mechanical ventilation. In the same study, death due to recurrent aspiration pneumonia was reported in 1 patient, 16 months after their first BPA session. In a case series of 20 patients, death due to acute right ventricular failure was reported in 1 patient, within 2 hours of his first BPA session. In the same study, death due to acute pulmonary embolism was reported in 1 patient 9 days after his first BPA session. Also, death due to chronic right heart failure was reported in 1 patient 15 months after the last BPA session.

5.4 Wire perforation (blood vessels not specified) was reported after 5% (4/86) of BPAs but not after any PEAs in the non-randomised retrospective comparative study of 53 patients. Pulmonary artery perforation was reported after 2% (5/255) of BPAs in the case

series of 68 patients. Two of these patients were treated by emergency transcatheter coil embolisation. Perforation of the pulmonary artery in the right lower lobe was reported in 1 patient in the case series of 18 patients; this was treated by coil occlusion.

5.5 Femoral artery pseudoaneurysm was reported in 17% (3/18) of patients in the case series of 18 patients. These patients were obese and needed femoral arterial access for monitoring during BPA. All were successfully treated by surgical repair or mechanical compression.

5.6 Reperfusion pulmonary oedema was reported in 61% (11/18) of patients in the case series of 18 patients; 4 cases were identified at the time of catheterisation and 7 were identified up to 48 hours after surgery. The patients were treated with diuretics and oxygen, and 3 needed additional mechanical ventilation. Reperfusion pulmonary oedema was reported in 35% (7/20) of patients in the case series of 20 patients; they were treated by supplementary oxygen therapy and diuretics.

5.7 Severe haemoptysis was reported after 4% (3/86) of BPAs and 13% (3/24) of PEAs in the non-randomised retrospective comparative study of 53 patients. Mild to moderate haemoptysis was reported in 50% (6/12) of patients in a case series of 12 patients.

5.8 Haemosputum or desaturation was reported after 28% (24/86) of BPAs and 13% (3/24) of PEAs in the non-randomised retrospective comparative study of 53 patients. Breathlessness and desaturation were each reported in 3 patients in a case series of 8 patients. In the same study, atrial arrhythmia and subcutaneous haematoma were each reported in 1 patient.

- 5.9 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 the following anecdotal adverse events: acute kidney injury and anaphylactic shock, both caused by contrast medium, and exposure to high radiation in patients needing repeat procedures. They considered that the cardiovascular collapse and cardiac tamponade were theoretical adverse events.

6 Committee comments

- 6.1 The Committee was advised about the [New International CTEPH Database](#), hosted by the International CTEPH Association, which will collect data on the epidemiology and long term outcomes of chronic thromboembolic pulmonary hypertension.

7 Further information

- 7.1 This guidance requires that clinicians doing the procedure make special arrangements for audit. NICE has identified relevant audit criteria and is developing an audit tool (which is for use at local discretion). This tool will be available when the guidance is published.
- 7.2 For related NICE guidance, see the [NICE website](#).

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