NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional procedure consultation document

Transapical transcatheter mitral valve-in-valve implantation for a failed surgically-implanted mitral valve bioprosthesis

When the mitral valve in the heart is not working properly, it may be replaced with a bioprosthetic valve (a valve made of animal tissue or a combination of animal tissue and other materials) during open heart surgery. If this new valve then fails, another major open heart operation is usually needed to replace it. In this procedure, a second bioprosthetic valve can be placed within the first valve without the need for repeat open heart surgery. This is done using a tube (catheter) inserted through the skin of the chest and through the wall of the heart across the existing mitral prosthetic valve. The new valve is then implanted through the catheter.

The National Institute for Health and Care Excellence (NICE) is examining transapical transcatheter mitral valve-in-valve implantation for a failed surgically-implanted mitral valve bioprosthesis 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 transapical transcatheter mitral valve-in-valve implantation for a failed surgically-implanted mitral valve bioprosthesis.

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- The Advisory Committee will then prepare draft guidance which will be the basis for NICE's guidance on the use of the procedure in the NHS.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: 25 September 2015

Target date for publication of guidance: December 2015

1 Provisional recommendations

These recommendations apply only to patients for whom open surgical valve implantation is unsuitable.

1.1 The current evidence on the safety of transapical transcatheter mitral valve-in-valve implantation for a failed surgically-implanted

mitral valve bioprosthesis shows the potential for serious complications. However, this is in patients for whom open surgical valve implantation is unsuitable, who have severe symptoms and a high risk of death. The evidence on efficacy shows generally good symptom relief in the short term, but is based on very small numbers of patients. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research.

1.2 Clinicians wishing to do transapical transcatheter mitral valve-in-valve implantation for a failed surgically-implanted mitral valve bioprosthesis should:

- Inform the clinical governance leads in their NHS trusts.
- Ensure that patients understand the uncertainty about the procedure's safety and efficacy 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.
- Enter details about all patients having transapical transcatheter mitral valve-in-valve implantation for a failed surgically-implanted mitral valve bioprosthesis onto the National Institute for Cardiovascular Outcomes Research database (NICOR) and review local clinical outcomes.

1.3 Patient selection should be done by a multidisciplinary team including interventional cardiologists, cardiac surgeons, a cardiac anaesthetist and an expert in cardiac imaging. The multidisciplinary team should determine the risk level for each patient and review their suitability for alternative medical or surgical treatments.

1.4 Transapical transcatheter mitral valve-in-valve implantation for a failed surgically-implanted mitral valve bioprosthesis should only be done by clinicians and teams with special training and experience in complex endovascular cardiac interventions, including regular experience in transcatheter valve implantation procedures. Units doing these procedures should have both cardiac and vascular surgical support for emergency treatment of complications.

1.5 NICE encourages further research into transapical transcatheter mitral valve-in-valve implantation for a failed surgically-implanted mitral valve bioprosthesis. This may include prospective observational studies. Studies should include details on patient selection, functional outcomes, quality of life, survival and complications. Studies should report long-term follow-up of clinical outcomes and valve durability. NICE may update this guidance on publication of further evidence.

2 Indications and current treatments

2.1 Mitral valve replacement is done for severe mitral valve stenosis, mitral regurgitation or a combination of both. Symptoms of severe mitral valve disease typically include shortness of breath, fatigue and palpitations (arising from atrial fibrillation).

2.2 If symptoms of mitral valve disease are sufficiently severe, valve replacement with an artificial prosthesis (bioprosthetic or mechanical) may be done by open heart surgery in patients who are well enough for this kind of operation. Bioprosthetic valves have some advantages over mechanical valves, but they are more likely to degenerate and fail over time. This can result in severe stenosis or regurgitation, needing replacement of the bioprosthetic valve.

2.3 The standard treatment for a failed bioprosthetic valve is repeat open heart surgery to replace the valve. Repeat open heart surgery is associated with a higher risk of morbidity and mortality than primary surgery. Transapical transcatheter mitral valve-in-valve implantation is a less invasive alternative when repeat open heart surgery is considered to have a high risk. It avoids the need for cardiopulmonary bypass and can be used to treat failed bioprosthetic mitral valves originally placed during open heart surgery.

3 The procedure

3.1 The procedure is done with the patient under general anaesthesia and using imaging guidance including fluoroscopy, angiography and transoesophageal echocardiography. Prophylactic antibiotics and anticoagulants are given before and during the procedure. Temporary peripheral extracorporeal circulatory support (usually through the femoral vessels) is sometimes used.

3.2 The mitral valve is accessed surgically via apical puncture of the left ventricle using an anterior or left lateral minithoracotomy (transapical approach). A guidewire is placed across the existing mitral prosthetic valve and into a pulmonary vein. A balloon catheter delivery system is then advanced over the guidewire. When there is severe prosthetic mitral valve stenosis, a balloon valvuloplasty may be done first. The inner diameter of the degenerated valve is measured using transoesophageal echocardiography to establish the size of new bioprosthetic valve needed. Using the delivery system, the new bioprosthetic valve is then introduced, manipulated into position and slowly deployed within the degenerated mitral valve under fluoroscopic and

echocardiographic guidance. Often, rapid ventricular pacing is used to reduce movement of the heart. After valve deployment, the catheter delivery system, guidewires and pacing wires are removed and the chest wound is closed. Valve performance is then assessed using echocardiography and fluoroscopy.

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 23 patients treated by transcatheter mitral valve-in-valve implantation for degenerated mitral bioprosthetic valves, the procedure was successful in 100% of patients. Procedural success was defined according to the Valve Academic Research Consortum-2 definition (device success and no occurrence of in-hospital or 30-day death). In 1 procedure, implantation through the left atrium via a right thoracotomy was unsuccessful (because the delivery system failed to align properly) but was successfully done via a left thoracotomy and transapical approach.

4.2 In the case series of 23 patients, survival at 30 day follow-up was 100%. At a median follow-up of 753 days (range 376 days to 1119 days), survival rate calculated using Kaplan–Meier analysis was 90%. In a case series of 6 patients, 5 patients were alive and had not had any valve-related events at a median follow-up of 70 days (range 25 days to 358 days).

4.3 In the case series of 23 patients, there was improvement in New York Heart Association (NYHA) functional class after the

procedure. Before treatment, 96% (22/23) of the patients were in NYHA class III/IV and 1 patient was in class II. At last follow-up (range 376 days to 1119 days), 96% (22/23) of the patients had clinically improved to NYHA class I/II. One patient with hypertrophic obstructive cardiomyopathy continued to be in NYHA class III despite satisfactory valve function and septal ablation.

4.4 In the case series of 23 patients, there was a significant decrease in the mean mitral transvalvular pressure gradient after implantation (from 11.1 ± 4.6 mmHg to 6.9 ± 2.2 mmHg, p=0.014).

4.5 In the case series of 23 patients, mitral regurgitation reduced from severe or moderate regurgitation (in 61% [14/23] and 17% [4/23] of patients respectively) at baseline to mild or no regurgitation (in 52% [12/23] and 48% [10/23] of patients respectively) at discharge.

4.6 The specialist advisers listed key efficacy outcomes as: correct and stable positioning of a new valve; valve function (that is, no valvular or paravalvular regurgitation, no significant pressure gradient across the valve, and no left ventricular outflow tract obstruction); symptom improvement; survival; and long-term durability of the valve.

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 a case series of 349 patients treated by transcatheter mitral valve-in-valve implantation for degenerated mitral bioprosthetic

valves, 30-day all-cause mortality was reported as 9% (32/349) and 30-day cardiovascular death was reported as 6% (21/349). One patient died in a case series of 7 patients (mortality rate 14%); this patient had an unsuccessful transseptal approach for transcatheter mitral valve-in-valve implantation, which resulted in embolisation and the need for conversion to a prolonged open operation. The patient developed multisystem failure and died on the second postoperative day.

5.2 An all-cause mortality rate of 10% (2/23) at a median follow-up of 753 days was reported in a case series of 23 patients. Death was from respiratory failure in 1 patient (at 45 days) in whom the transatrial approach was converted to transapical implantation, and was from an unknown cause (defined as cardiovascular according to Valve Academic Research Consortum-2) in 1 patient (on day 135).

5.3 In-hospital fatal pneumonia (on day 34, due to respiratory failure) was reported in 1 patient with chronic obstructive pulmonary disease in the case series of 7 patients. The patient needed reintubation, but later died.

5.4 Major stroke was reported in 3% (11/349) of patients in the case series of 349 patients at a median follow up of 408 days. Major periprocedural stroke (complicated by nosocomial pneumonia and acute renal injury needing temporary renal replacement therapy) was reported in 1 patient in the case series of 23 patients. This patient had a prolonged intensive care stay and died on day 45 with respiratory failure, despite renal and neurological recovery.

5.5 Major bleeding was reported in 26% (6/23) of patients in the case series of 23 patients (further details were not reported).

5.6 Late bleeding at the apical site was reported in 33% (2/6) of patients in a case series of 6 patients. One patient needed a further thoracotomy on day 4 because of haemothorax and had an uneventful recovery. One patient became haemodynamically compromised on day 6 and needed cardiopulmonary resuscitation, but died of haemorrhagic shock because of acute bleeding from the apical wound.

5.7 Gastrointestinal bleeding (caused by anticoagulation and sepsis 2 months after the procedure) was reported in 1 patient in the case series of 6 patients. The patient was admitted to hospital but no signs of endocarditis were found.

5.8 Bioprosthesis thrombosis (3 months after transcatheter mitral valve-in-valve implantation) was reported in a case report of 1 patient. The patient had increasing shortness of breath and transoesophageal echocardiography revealed symptomatic and severe mitral valve stenosis with unusual leaflet thickening. After antithrombotic treatment, there was a significant decrease in transvalvular gradient and significant regression of the leaflet thickening.

5.9 Acute kidney injury (Acute Kidney Injury Network staging 2 and 3) was reported in 11% (39/349) of patients in the case series of 349 patients with a median follow-up of 408 days. Further details were not reported.

5.10 Permanent pacemaker implantation (on day 3 for pre-existing atrioventricular conduction disturbance) was needed in 1 patient in the case series of 23 patients.

5.11 An incisional hematoma was reported in 1 patient in the case series of 23 patients (further details were not reported).

5.12 Atrial clot (detected at 6-month follow-up echocardiogram) was reported in 1 patient in the case series of 23 patients. The patient was asymptomatic with no embolic events but treated with systemic anticoagulation.

5.13 Haemothorax (drained with a thoracostomy tube) was reported in 1 patient in the case series of 23 patients.

5.14 Implantation of a second transapical transcatheter mitral valve-in-valve was needed (at 2 months; because of acute heart failure) in 1 patient in the case series of 23 patients. Echocardiography showed 4-5 mm atrial migration of the valve, which caused severe valvular regurgitation. A second transapical transcatheter mitral valve-in-valve implantation was done with no complications or valvular regurgitation.

5.15 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 described left ventricular outflow tract obstruction as an anecdotal adverse event. They considered that the following were theoretical adverse events: incorrect positioning of the transcatheter valve, paravalvular regurgitation, mitral stenosis and surgical wound infection.

6 Further information

6.1 For related NICE guidance, see the NICE website.

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August 2015