NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of percutaneous mitral valve annuloplasty

Mitral regurgitation occurs when one of the four valves in the heart – the mitral valve – does not close properly, allowing blood to leak backwards. It may lead to shortness of breath and eventually heart failure (where the heart cannot pump enough blood to meet the body's needs). In this procedure, a catheter is inserted into a large vein in the groin or neck and passed through to the heart. A device is placed into a large vein that sits next to the mitral valve to constrict the valve, with the aim of making it close properly.

Introduction

The National Institute for Health and Clinical Excellence (NICE) has prepared this 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 January 2009.

Procedure name

- Percutaneous mitral valve annuloplasty

Specialty societies

- British Cardiovascular Intervention Society
- Society for Cardiothoracic Surgeons of Great Britain and Ireland.

Description

Indications and current treatment

Mitral regurgitation is characterised by backward flow of blood from the left ventricle to the left atrium during systole. It causes the left ventricle to become enlarged because of the additional workload required to maintain normal blood flow. Left untreated, moderate to severe mitral regurgitation can cause progressive congestive heart failure and eventually lead to death.

Mitral regurgitation results from failure of apposition of the mitral valve leaflets, which may be due to abnormalities of the mitral leaflets, their subvalvar apparatus (chordae and papillary muscles), or from dilation of the mitral annulus (usually due to left ventricular enlargement and often termed ‘functional’ mitral regurgitation).

Surgical treatment of severe mitral regurgitation may include partial leaflet resection, annuloplasty, chordal repair or a combination of these. Annuloplasty involves surgical placement of a supporting ring around the base of the mitral valve to reduce annular dilation, bringing the mitral valve leaflets closer together so that valve competence can be restored.

The degree of mitral regurgitation is commonly graded on a scale from 1 to 4, where grade 1 is mild, grade 2 is moderate, grade 3 is moderate to severe and grade 4 is severe.

What the procedure involves

The mitral annulus is anatomically closely related to the coronary sinus (the large vein that forms at the level of the posterior mitral annulus and drains into the right atrium at its other end). The aim of the procedure is to percutaneously place an intravascular device into the coronary sinus, which reduces the diameter of the coronary sinus when contracted and in doing so, reduces the adjacent mitral annulus.

The procedure is carried out with the patient under general or local anaesthesia, and a catheter is advanced under fluoroscopic control, usually through the jugular or femoral vein towards the coronary sinus. The device is advanced through the catheter and deployed in the coronary sinus under fluoroscopic and transoesophageal echocardiographic guidance. It is then usually anchored within the coronary sinus to minimise the likelihood of subsequent displacement. Subsequent technique details may vary according to the type of device used, but all techniques involve the percutaneous manipulation of the coronary sinus to change the shape and size of the mitral valve annulus. Transoesophageal echocardiography is used to assess the device position and whether mitral regurgitation has been reduced, and the device may be repositioned as necessary.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to percutaneous mitral valve annuloplasty. Searches were conducted of the following databases, covering the period from their commencement to 9 April 2010: 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 appendix C for details of 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	Patients with mitral regurgitation.
Intervention/test	Percutaneous mitral valve annuloplasty.
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 overview

This overview is based on approximately 93 patients from 5 case series and 2 case reports (all but one case series were reports of the first experience in humans).

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

Table 2 Summary of key efficacy and safety findings on percutaneous mitral valve annuloplasty

Abbreviations used: ACE, angiotensin-converting enzyme; AF, atrial fibrillation; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CS, coronary sinus; GCV, great cardiac vein; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MR, mitral regurgitation; MV, mitral valve; NYHA, New York Heart Association; PCA, percutaneous coronary intervention; PTMA, percutaenous transvenous mitral annuloplasty TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Schofer J (2009)[1]
Case series
Germany, Poland, Netherlands
Recruitment period: not reported
Study population: patients with functional MR demonstrated by echocardiogram and moderate heart failure
n = 48
Mean age: 64 years (implanted) and 65 years (not implanted)
Sex: 83% male
NYHA class III (37), II (9), IV (2)
Patient selection criteria: > 18 years, dilated ischaemic or non-ischaemic cardiomyopathy, moderate to severe functional MR, NYHA class II to IV, 6-minute walk distance 150–450m, LVEF< 40%, left ventricular end-diastolic diameter > 55mm.
Exclusion criteria:</td>
<td>Number of patients analysed: 30 (18 patients did not receive a device because of issues with access, insufficient functional mitral regurgitation or coronary artery compromise)
MR reduction
This was assessed according to the American Society of Echocardiography standards.
<table>
<tr><th></th><th>Baseline (n = 30)</th><th>1 month (n = 29)</th><th>6 months (n = 26)</th></tr>
<tr><td>Mitral regurgitant jet and left atrial area (%)</td><td>47.6</td><td>30.1</td><td>32.3</td></tr>
<tr><td>Regurgitant volume (ml)</td><td>35.1</td><td>22.6</td><td>24.3</td></tr>
<tr><td>Effective regurgitant orifice area (cm^2)</td><td>0.25</td><td>0.17</td><td>0.17</td></tr>
<tr><td>Vena contracta (narrowest central flow region of a jet) (cm)</td><td>0.71</td><td>0.58</td><td>0.53</td></tr>
</table>
All differences were significant from baseline to 6-month follow-up ($p < 0.001$).
Of the 24 patients with data available for follow-up at 6-months there was a 23% average MR reduction across the 5 quantitative echocardiographic measures.
Heart Function
<table>
<tr><th></th><th colspan="3">% (no)</th></tr>
<tr><th>NYHA class</th><th>Baseline (n = 30)</th><th>1 month (n = 29)</th><th>6 months (n = 26)</th></tr>
</table>
</td>
<td>Complications
13% (6/46) of patients had 7 major adverse events within the first 30 days after the procedure
<table>
<tr><th>Event</th><th>Rate (No.)</th></tr>
<tr><td>Death from multisystem organ failure*</td><td>2.2 (1/46)</td></tr>
<tr><td>MI (defined as creatine kinase ≥ 3 times the upper limit of normal measured in 8 hour intervals for 24 hours after the procedure)**</td><td>6.5 (3/46)</td></tr>
<tr><td>Coronary sinus dissection/perforation**</td><td>6.5 (3/46)</td></tr>
</table>
(This was based on intention-to-treat analysis which included patients who were not implanted with the device, but it appears to have excluded the 2 patients who withdrew from the study.)
*In a 56-year old man with a history of 3-vessel coronary artery disease, chronic renal insufficiency, and COPD 22 days after the procedure. The patient had had a repeat coronary angiogram with a normal result the day after the implant because of rise in creatine kinase-MB level. The patient then developed acute renal failure before multi-system organ failure.
**These did not require hospitalisation.</td>
<td>Follow-up issues:
2 patients withdrew before 30-day follow-up.
At 6-month follow-up 2 patients had died, 1 patient received a transplant (they were on a waiting list before the procedure) and 3 declined to return for the follow-up visit.
Study design issues:
These are results from the Mitral Annuloplasty Device European Union Study (AMADEUS)
All events were adjudicated by an independent committee.
1 patient was treated with an earlier CARILLON device.
The report includes some information about temporary or permanent devices but it was not clear which patients received each device. It is possible that it includes the patients treated with a temporary implant in Duffy (2006)[2].
The KCCQ is a 23-item</td>
</tr>
</table>

Abbreviations used: ACE, angiotensin-converting enzyme; AF, atrial fibrillation; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CS, coronary sinus; GCV, great cardiac vein; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MR, mitral regurgitation; MV, mitral valve; NYHA, New York Heart Association; PCA, percutaneous coronary intervention; PTMA, percutaenous transvenous mitral annuloplasty TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography

Study details	Key efficacy findings	Key safety findings	Comments

Study details

hospitalisation in last 3 months for MI, history of CABG, unstable angina, percutaneous coronary intervention in last 30 days, moderate MR or NYHA class II, requirement for cardiac surgery within 1 year, pacing lead in CS, moderate or severe MV degeneration, rheumatic disease, severe mitral annular calcification, compromised renal function, severe tricuspid regurgitation, chronic AF

Technique: percutaneous mitral valve annuloplasty with CARILLON device (Cardiac Dimensions Inc) under general anaesthetic

Follow-up: **6 months**

Conflict of interest/source of funding: funded by Cardiac Dimensions Inc, 5 authors have stocks in the company; 2 are consultants and 3 are employees.

Key efficacy findings

I	0 (0/30)	17 (5/29)	36 (9/25)
II	20 (6/30)	62 (18/29)	52 (13/25)
III	73 (22/30)	17 (5/29)	12 (3/25)
IV	7 (2/30)	3 (1/29)	0 (0/25)

The NYHA classification was significantly reduced from an average of 2.9 at baseline to 1.8 at 6 months ($p < 0.001$).

6-minute walk test

This improved from 307 m at baseline to 387m at 1 month and 403 m at 6 months ($p < 0.001$ from baseline to 6 months). 82% (19/23) had improved by ≥ 25 m at 6 months.

Quality of life measures

Results of the KCCQ significantly improved from 47 to 69 from baseline to 6-month follow-up (0–100 scale; higher scores reflect better health status; $p < 0.001$).

The patient component of the global assessment had the following results:

Patient portion of the global assessment score	% (No.)	
	Baseline (n = 30)	6 months (n = 26)
Markedly improved	26.9 (7/26)	36.0 (9/25)
Moderately improved	30.8 (8/26)	24.0 (6/25)
Slightly improved	19.2 (5/26)	24.0 (6/25)
No change	11.5 (3/26)	8.0 (2/25)
Slightly worse	7.7 (2/26)	8.0 (2/25)
Moderately worse	0.0 (0/26)	0.0 (0/25)
Markedly worse	3.8 (1/26)	0.0 (0/25)

Key safety findings

**The CS dissection (1 patient) resolved without specific therapy. The 2 perforations occurred early in the study: one was from a stiff guidewire and did not require therapy and one from diagnostic catheter required pericardial drainage

There were no cases of device embolisation or device fracture on follow-up radiographs.

Comments

self-administered instrument which assesses physical function, symptoms, social function, self-efficacy and knowledge and quality of life (it has been suggested that a 10 point reduction in KCCQ scores has important prognostic significance).

Study population issues:

- History of coronary artery disease in 35, COPD in 11 and CABG in 17 (though history of CABG was exclusion criteria). Significantly more patients treated with a device had coronary artery disease than those without the implant (this was the only significant difference).
- 88% were on diuretics, 94% were on ACE inhibitors and 96% were on beta blockers.
- Those with a successful implantation had a more distal placement of the device.

Abbreviations used: ACE, angiotensin-converting enzyme; AF, atrial fibrillation; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CS, coronary sinus; GCV, great cardiac vein; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MR, mitral regurgitation; MV, mitral valve; NYHA, New York Heart Association; PCA, percutaneous coronary intervention; PTMA, percutaenous transvenous mitral annuloplasty TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography

Study details	Key efficacy findings	Key safety findings	Comments
Sack S (2009)[7] **Case series** Germany, Belgium, Canada Recruitment period: 2006 – 2007 Study population: symptomatic patients with functional MR (NYHA class 2 or 3) **n = 27 (29 procedures)** Mean age: 70.4 years Sex: 56% male Inclusion criteria: moderate to severe functional MR, grade 2+ to 4+ (measured by TOE) and LVEF 20-50% Exclusion criteria: organic mitral valve disease, leaflet prolapse, significant renal dysfunction (CR > 2.3 mg/dL), proximal coronary circumflex stent and left dominant coronary circulation. Technique: diagnostic PTMA implant (Viacor) with TOE to measure treatment effect; if	Number of patients analysed: **27** ***Technical success*** <u>*Diagnostic / temporary implant*</u> Of 27 patients, 8 were unable to have a diagnostic procedure because of unsuccessful venous access (6), anatomical exclusion (1), guidewire perforation (1; as in safety section). Of the19 who had a diagnostic procedure, 6 were unsuccessful in reducing MR ≥ 1 grade. Procedural success rate of diagnostic PTMA: 48% (13/27) of all patients and 68% (13/19) of those with successful placement. <u>*Permanent implant*</u> Of the remaining 13 patients with a successful diagnostic procedure, 9 went on to have the permanent implant (of the 4 in whom the permanent implant was not attempted, 2 had an unstable device and 2 had technical delivery difficulties). One of 9 with permanent implant had device fracture at 7 days as noted in safety section), therefore overall 30-day success rate of implanted devices: 62% (8/13) Three additional devices were removed percutaneously and patients were treated with surgical annuloplasty at 84, 197 and 216 days (1 for lack of efficacy and 2 because of device migration as mentioned in the safety section). Apart from 1 patient who died (see safety section), 4 patients still had the implant in place at 17, 11, 11, and 2.5 months after the procedure.	***Complications*** **Event** / **Rate (No.)** Death from progressive heart failure (not attributed to procedure) — 3% (1/29) Subclavicular haematoma — 3% (1/29) Pneumonia — 3% (1/29) Transient renal dysfunction — 3% (1/29) Circumflex stent implantation* — 3% (1/29) Pericardial effusion (centrum semiovale related)** — 3% (1/29) PTMA implant device fracture (removal percutaneously after 7 days) — 3% (1/29) PTMA migration requiring percutaneous removal and subsequent annuloplasty — 10% (3/29) Guidewire perforation*** — 3% (1/29) * this was in the first patient with a possible circumflex abnormality directly adjacent to the device, during and after intravascular ultrasound there was abrupt vessel closure with ST elevation so it was treated with stent implantation without further clinical events or myonecrosis. ** pericardiocentesis was performed, the procedure terminated and the PTMA device not inserted no PTMA used *** this occurred before the diagnostic procedure; the patient was unable to have a	**Follow-up issues**: • Echocardiography, clinical examination and laboratory assessments at 24 hours, 14, 30, 180 and 360 days. QOL at 30 and 180 days. **Study design issues**: • Patients recruited from 4 European and 1 Canadian sites. • Echocardiography assessed by both enrolling centres and the core laboratory in the USA. • Trial was done in 4 chronological periods with each group of patients having incremental technical enhancements of the device. **Study population issues**: • 17 patients had ischaemic aetiology • 10 had previous CABG procedure

Abbreviations used: ACE, angiotensin-converting enzyme; AF, atrial fibrillation; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CS, coronary sinus; GCV, great cardiac vein; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MR, mitral regurgitation; MV, mitral valve; NYHA, New York Heart Association; PCA, percutaneous coronary intervention; PTMA, percutaenous transvenous mitral annuloplasty TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography

Study details	Key efficacy findings	Key safety findings	Comments
positive effect, implantation with PTMA implant (with non-absorbable external polyester surgical suture to ensure stability) in the coronary sinus with general anaesthesia Follow-up: **up to 17 months (1 patient)** Conflict of interest/source of funding: funded by manufacturer and 1 author is employee of Viacor		diagnostic procedure. None of events had permanent sequelae.	

Abbreviations used: ACE, angiotensin-converting enzyme; AF, atrial fibrillation; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CS, coronary sinus; GCV, great cardiac vein; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MR, mitral regurgitation; MV, mitral valve; NYHA, New York Heart Association; PCA, percutaneous coronary intervention; PTMA, percutaenous transvenous mitral annuloplasty TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Webb JG (2006)[2]

Case series
Canada, Sweden
Recruitment period: not reported
Study population: patients with chronic ischaemic MR (≥ grade 2+) with previous MI
n = 5
Mean age: 67 ± 10 years
Sex: 3 male, 2 female
Exclusion criteria: LVEF < 30%, structural MV disease, mitral annular calcification, prior endocarditis or mitral surgery, creatinine > 2.0 mg/dL, CS pacing leads, anticipated revascularization, inability to take aspirin or clopidogrel or life expectancy < 1 year.
Technique: percutaneous transvenous implantation of an annuloplasty device (Viking, Edwards</td>
<td>Number of patients analysed: 5
Technical success
Successful device implantation: 80% (4/5)
In all 4 patients, the distal anchors were correctly placed at the desired locations.
In 1 patient, the device could not be advanced fully into the coronary sinus because of difficulty in obtaining coaxial guide position. A second attempt 1 month later was uneventful but unsuccessful.
Mitral regurgitation and symptoms
<table>
<tr><th></th><th>Baseline</th><th>3 months</th></tr>
<tr><td>Mitral annulus diameter (mm)</td><td>36 ± 3</td><td>35 ± 1</td></tr>
<tr><td>LVEF (%)</td><td>42 ± 11</td><td>50 ± 6</td></tr>
<tr><td>NYHA class</td><td>2.4 ± 0.5</td><td>2 ± 0.7</td></tr>
<tr><td>Mitral regurgitation grade*</td><td>3.0 ± 0.5</td><td>1.6 ± 1.1</td></tr>
</table>
*3 out of 4 patients had reduced MR grade at hospital discharge
Follow-up (3 months)
• In the 3 patients who had successful procedures and were alive at last follow-up, coronary angiogram showed no evidence of compromise of the circumflex coronary artery as a result of the device implanted in the adjacent GCV.</td>
<td>Mortality
• 1 patient died on postoperative day 148 due to progressive heart failure. The patient was considered a nonsurgical candidate because of morbid obesity and other comorbidities. Postmortem showed a well-positioned device, patent CS and patent circumflex artery.

Complications
• In the patient who had an unsuccessful procedure, attempts to implant the device led to wire perforation of the anterior interventricular vein and pericardial effusion.
• Another patient developed transient AF during cannulation of the coronary sinus.

Separation of the nitinol bridge segment of the device was documented in 3 of 4 patients who had successful procedures on routine follow-up chest radiographs at 22, 28 and 81 days. Migration of the anchors was not observed. Although there were no adverse events associated with device separation, feasibility study enrolment was discontinued.</td>
<td></td>
</tr>
</table>

Abbreviations used: ACE, angiotensin-converting enzyme; AF, atrial fibrillation; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CS, coronary sinus; GCV, great cardiac vein; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MR, mitral regurgitation; MV, mitral valve; NYHA, New York Heart Association; PCA, percutaneous coronary intervention; PTMA, percutaenous transvenous mitral annuloplasty TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Lifesciences Inc) in the coronary sinus with local anaesthesia Follow-up: **at least 3 months** Conflict of interest/source of funding: 5 authors are consultants to the manufacturer			

Abbreviations used: ACE, angiotensin-converting enzyme; AF, atrial fibrillation; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CS, coronary sinus; GCV, great cardiac vein; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MR, mitral regurgitation; MV, mitral valve; NYHA, New York Heart Association; PCA, percutaneous coronary intervention; PTMA, percutaenous transvenous mitral annuloplasty TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Duffy SJ (2006)[3]

Case series
Australia
Recruitment period: not reported
Study population: patients undergoing scheduled coronary angiography with heart failure and functional MR (grade 2+ to 4+)
n = 5
Mean age: 52.2 years
Sex: 4 male, 1 female
Patient selection: ≥ 18 years, NYHA class II or III, LVEF 30–45%.
Exclusion criteria: decompensate heart failure < MV prosthesis or annuloplasty ring, pacing electrode, MR pathology, severe mitral calcification, coronary stent adjacent to CS or GCV, heart failure (non-dilated), cerebrovascular event within 3 months, potential pregnancy, supine systolic BP < 85 mm Hg, serum</td>
<td>Number of patients analysed: 5

Technical success
The CS was successfully cannulated in all but 1 (in whom the GCV was too small).

Presence of MR
<table>
<tr><th></th><th>Baseline</th><th>Postoperatively</th><th>p value</th></tr>
<tr><td>Mitral annular dimension (mm)</td><td>35.5 ± 4.7</td><td>32.2 ± 4.6</td><td>0.02</td></tr>
<tr><td>MR area mm^2 (as measured by colour Doppler)</td><td>98.3 ± 43.6</td><td>83.3 ± 35.1</td><td>0.09</td></tr>
<tr><td>MR jet (% of left atrial area)</td><td>36 ± 18</td><td>30 ± 14</td><td>0.11</td></tr>
</table>
Procedural outcomes
<table>
<tr><th></th><th>value</th></tr>
<tr><td>Procedure time (min)</td><td>44 ± 10</td></tr>
<tr><td>Fluoroscopy time (min)</td><td>16.7 ± 3.9</td></tr>
<tr><td>Contrast volume (ml)</td><td>58 ± 54</td></tr>
</table>
</td>
<td>There were no reported complications.</td>
<td>Follow-up issues:
• Not described.

Study design issues:
• This was a feasibility study to test safety, deployability, tensioning and recapturing of a specially designed temporary implant (the Schofer (2009)[1] publication used the permanent version of the implant from this manufacturer).
• Patients in this study may be included in Schofer publication.
• It was not reported when each implant was removed and if the patients were then implanted with the permanent implant.

Study population issues:
• 1 patient had previous CABG
• 3 ischaemic cardiomyopathy, 1 non-ischaemic, 1 unknown
• 2 patients were in AF
• 4 were being treated</td>
</tr>
</table>

Abbreviations used: ACE, angiotensin-converting enzyme; AF, atrial fibrillation; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CS, coronary sinus; GCV, great cardiac vein; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MR, mitral regurgitation; MV, mitral valve; NYHA, New York Heart Association; PCA, percutaneous coronary intervention; PTMA, percutaenous transvenous mitral annuloplasty TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography

Study details	Key efficacy findings	Key safety findings	Comments
creatinine > 0.18 mmol/L, epicardial vessels crossing within 75% of proximal end of CS or GCV, anatomical CS abnormality, CS diameter < 3.5mm, hospitalization in last 3 months for MR, unstable angina, CABG, or PCI Technique: placement of temporary Percutaneous Mitral Annuloplasty Device (PMAD) with 2 components: a distal anchor and central element (Cardiac Dimensions, Inc); using light sedation Follow-up: **not reported (appears to be postoperatively)** Conflict of interest/source of funding: funded by The National Health and Medical Research Council of Australia; primary author disclosed a 'financial or other interest' in the subject; 1 author was employed by Cardiac Dimensions Inc; 1 author is supported by			with beta blockers, 4 with diuretics, 2 with digoxin and all were receiving ACE inhibitors or angiotensin receptor antagonists. The authors noted that all patients were receiving the maximum tolerated medical therapy at the time of the procedure.

Abbreviations used: ACE, angiotensin-converting enzyme; AF, atrial fibrillation; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CS, coronary sinus; GCV, great cardiac vein; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MR, mitral regurgitation; MV, mitral valve; NYHA, New York Heart Association; PCA, percutaneous coronary intervention; PTMA, percutaenous transvenous mitral annuloplasty TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
the Atherosclerosis Trust (UK)			

Abbreviations used: ACE, angiotensin-converting enzyme; AF, atrial fibrillation; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CS, coronary sinus; GCV, great cardiac vein; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MR, mitral regurgitation; MV, mitral valve; NYHA, New York Heart Association; PCA, percutaneous coronary intervention; PTMA, percutaenous transvenous mitral annuloplasty TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Dubreuil O (2007)[4]

Case series
Canada
Recruitment period: 2005 to 2006
Study population: patients with ischaemic MR (grade 2+ to 4+) and NYHA functional class II or III
n = 4
Mean age: 63 years
Sex: 75% male

Patient selection criteria: TTE and angiography confirming grades ≥ 2+ mitral regurgitation, type II and/or IIIB Carpentier’s pathophysiological classification with annulus diameter > 35 mm.
Exclusion criteria: abnormal leaflets or morphological mitral apparatus abnormality, creatinine > 2.5 mg/dl.

Technique: temporary</td>
<td>Number of patients analysed: 3

Operative success
Coronary sinus was cannulated in all but 1 case.
(this patient had extreme angulation of the CS ostium so a sheath could not be advanced)

Presence of MR
In the 3 patients successfully cannulated, MR was reduced from grade 2+ to 3+ at baseline to 1 to 1+ postoperatively (determined by echocardiography).
Outcomes in the 3 patients who were successfully cannulated:
<table>
<tr><th></th><th>Baseline</th><th>Postoperatively</th></tr>
<tr><td>Mean effective regurgitation orifice (cm^3)</td><td>0.25 ± 0.06</td><td>0.07 ± 0.03</td></tr>
<tr><td>Mean regurgitant volume (ml)</td><td>45.4 ± 24.4</td><td>13.3 ± 7.3</td></tr>
<tr><td>Mean mitral annulus diameter on diastole (mm)</td><td>40.1</td><td>35.6</td></tr>
<tr><td>Mean mitral annulus diameter on systole (mm)</td><td>40.3</td><td>35.2</td></tr>
</table>
Procedural outcomes
<table>
<tr><th></th><th>value</th></tr>
<tr><td>Procedure time (min)</td><td>93 ± 33</td></tr>
<tr><td>Fluoroscopy time (min)</td><td>32 ± 6</td></tr>
<tr><td>Contrast volume (ml)</td><td>99 ± 33</td></tr>
</table>
The patients were treated with an average of 2 rods.</td>
<td>Mortality
1 of the patients who was successfully cannulated and later treated with the Edwards Mitral annuloplasty ring and tricuspid annuloplasty, died 16 days after surgery from complications. (no other details provided)</td>
<td>Follow-up issues:
• Not described.

Study design issues:
• This was a pilot study to test safety and efficacy; it is the first published report of this device used in humans.
• TTE and TOE at baseline, TOE after each rod adjustment.
• Final determination of change in MR was made by independent unblended echocardiologist.
• After temporarily placement of rods, measurements were taken and patients who were successful underwent further MV surgery (1 had Edwards Mitral annuloplasty ring, another had a mammary and venous graft and MV replacement, another had Edwards Mitral annuloplasty ring and tricuspid annuloplasty).
• Carpentier’s pathophysiological</td>
</tr>
</table>

Abbreviations used: ACE, angiotensin-converting enzyme; AF, atrial fibrillation; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CS, coronary sinus; GCV, great cardiac vein; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MR, mitral regurgitation; MV, mitral valve; NYHA, New York Heart Association; PCA, percutaneous coronary intervention; PTMA, percutaenous transvenous mitral annuloplasty TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography

Study details	Key efficacy findings	Key safety findings	Comments
percutaneous transvenous mitral annuloplasty (PTMA rods, Viacor) placed in the coronary sinus under general anaesthesia Follow-up: **not reported (appears to be immediately postoperatively)** Conflict of interest/source of funding: funded with a grant from the French Federation Cardiology, PTMA catheters were provided free of charge from Viacor.			classification includes stat of leaflets (ie. type I is normal leaflet motion, type II is leaflet prolase and type III is restricted leaflet motion) and the restriction in diastole and systole (A – both diastolic and systolic restrictions; B – systolic restrictions) **Study population issues**: • The first 3 patients went on to have MV surgery immediately afterwards. • Medical management was not described.

Abbreviations used: ACE, angiotensin-converting enzyme; AF, atrial fibrillation; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CS, coronary sinus; GCV, great cardiac vein; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MR, mitral regurgitation; MV, mitral valve; NYHA, New York Heart Association; PCA, percutaneous coronary intervention; PTMA, percutaenous transvenous mitral annuloplasty TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography

Study details	Key efficacy findings	Key safety findings	Comments
Palacios IF (2007)[5] **Multiple case report** USA Recruitment period: not reported Study population: patients with functional ischaemic mitral regurgitation (NYHA II to IV) about to have clinically indicated mitral valve repair n = **2** Age: 48 and 56 years Sex: 1 male, 1 female Patient selection criteria: > 18 years old, grades 2+ to 4+ mitral regurgitation with preserved leaflet anatomy, LVEF > 30% Exclusion criteria: history of CABG, MI or PCI in last 3 months, calcified mitral annulus or subvalvular apparatus, prior MV surgery, CS pacing leads, left atrial thrombus or left atrial	Number of patients analysed: **2** ***Patient 1*** This patient had a decrease in MR grade from 2+ to 1+ after the procedure. Septal sinus systolic reduction by 29%. ***Patient 2*** This patient had a decrease in MR grade from 3+ to 1+ after the procedure. Septal-lateral systolic reduction by 31%.	There were not procedural complications.	**Follow-up issues**: • Not reported. **Study design issues**: • This was the first-in-human study for this device which intended to evaluate the safety and efficacy of the system in patients immediately prior to surgical mitral valve repair. **Study population issues**: • Patient 2 had a prior MI.

Abbreviations used: ACE, angiotensin-converting enzyme; AF, atrial fibrillation; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CS, coronary sinus; GCV, great cardiac vein; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MR, mitral regurgitation; MV, mitral valve; NYHA, New York Heart Association; PCA, percutaneous coronary intervention; PTMA, percutaenous transvenous mitral annuloplasty TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography

Study details	Key efficacy findings	Key safety findings	Comments
diameter < 40 mm and body weight < 50 kg. Technique: percutaneous septal sinus shortening using the PS3 System (Ample Medical) inserted under direct visualisation with general anaesthesia or conscious sedation Follow-up: **not reported** Conflict of interest/source of funding: not reported			

Abbreviations used: ACE, angiotensin-converting enzyme; AF, atrial fibrillation; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CS, coronary sinus; GCV, great cardiac vein; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MR, mitral regurgitation; MV, mitral valve; NYHA, New York Heart Association; PCA, percutaneous coronary intervention; PTMA, percutaenous transvenous mitral annuloplasty TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography

Study details	Key efficacy findings	Key safety findings	Comments
Mueller D (2008)[6] **Case report** Germany Recruitment period: 2007 Study population: 58-year-old male with history of coronary artery disease complicated by inapparent inferior myocardial infarction n = **1** Technique: percutaneous mitral valve annuloplasty with MONARC™ device (Edward Lifesciences) Follow-up: Follow-up: **event occurred at unspecified follow-up** Conflict of interest/source of funding: not reported	Number of patients analysed: **1** A 58-year-old patient who was treated with a dual-chamber implantable cardioverter-defibrillator in 2003 to address impaired LVEF was treated with a Monarc™ device 4 years later to address increasing mitral regurgitation which accompanied further impairment of LVEF. Initially, the patient's mitral reflow was reduced (on both echocardiography and clinical assessments) and NYHA class improved to II (initial classification not reported). During the follow-up period, the patient developed third-degree atrioventricular block, becoming pacemaker dependent. Echocardiography revealed left-bundle-branch block under right ventricular stimulation and severe left ventricular asynchrony. The patient was then treated with a cardiac resynchronisation device with an increase in NYHA functional class (from III to II) and an improved 6-minute walking test (175m to 240m).		**Follow-up issues**: • Time from procedure to event not reported.

Efficacy

Reduction in mitral regurgitation assessed by echocardiography

A case series of 48 patients of whom 30 patients were successfully treated with a mitral annuloplasty device reported significantly less mitral jet regurgitant, volume, effective regurgitant orifice area and vena contracta (narrowest central flow region of a jet) from baseline to 6 months ($p < 0.001$ for all)[1].

In addition to this case series, a number of small case series reported on the first experience of device implantation in humans. A case series of 5 patients reported that of the 4 who had an annuloplasty device successfully implanted, mitral regurgitation grade decreased from an average of 3.0 at baseline to 1.6 at 3-month follow-up (significance not stated)[2].

Another case series of 5 patients treated with a temporary implant reported a significantly improved mitral annular dimension and mitral regurgitant area (as measured by colour Doppler) postoperatively ($p = 0.02$ and $p = 0.09$). There was also a decrease in mitral regurgitant jet but this was not statistically significant[3].

A case series of 4 patients reported that mitral regurgitation grade decreased in the 3 patients successfully treated with a temporary implant (from 2+ to 3+ at baseline to 1 to 1+ postoperatively). The same study reported a postoperative reduction in mean regurgitant volume, mean effective regurgitation orifice and mitral annulus diameter on diastole and systole in the 3 patients successfully treated with a temporary implant (significance not given)[4].

In a multiple case report of 2 patients treated with septal sinus shortening, both patients had a reduction in mitral regurgitation from grades 2+ and 3+, respectively, to 1+[5].

Clinical outcomes

The case series of 48 patients reported that New York Heart Association (NYHA) classification was significantly reduced from an average of 2.9 at baseline to 1.8 at 6-month follow-up ($p < 0.001$). The same study reported that 6-minute walk test results improved significantly from an average of 307 m at baseline to 403 m at 6 months ($p < 0.001$)[1].

The case series of 5 patients reported NYHA class improved from an average of 2.4 at baseline to 2 at 3-month follow-up[2].

Patient-reported quality of life

The case series of 48 patients reported significantly increased scores from the Kansas City Cardiomyopathy Questionnaire (assesses physical function, symptoms, social function, self-efficacy and knowledge and quality of life) from 47 at baseline to 69 at 6-month follow-up (scale 0–100 with higher scores better, $p < 0.001$)[1].

Device removal

A case series of 27 patients, in which the permanent device was successfully implanted in 9 patients, reported that 1 patient required percutaneous removal of the device and subsequent surgical annuloplasty because of a lack of efficacy (time of event not clear) [7].

Safety

Death

The case series of 48 patients reported 1 death 22 days after the procedure in a patient with a history of coronary artery disease, chronic obstructive pulmonary disease and chronic renal insufficiency. The patient initially presented with an increased creatine kinase level and then developed acute renal failure followed by multisystem organ failure[1].

The case series of 27 patients, in which the permanent device was successfully implanted in 9 patients, reported that 1 patient died from progressive heart failure 180 days after the procedure, but this was not attributed to the device[7].

The case series of 5 patients reported progressive heart failure resulting in death 148 days after the procedure in 1 patient who was not eligible for surgical treatment because of morbid obesity and other comorbidities. The device was shown to be well-positioned with a patent coronary sinus and circumflex artery on a postmortem examination[2].

The case series of 4 patients reported death in 1 patient who was initially treated with a temporary implant followed by ring annuloplasty and tricuspid annuloplasty 16 days after the procedure[4].

Other

The case series of 48 patients reported coronary sinus dissection in 1 patient which resolved without treatment and coronary sinus perforation in 2 patients – 1 from a stiff guidewire, which did not require treatment, and the other from the diagnostic catheter, which required pericardial drainage[1].

The same study reported myocardial infarction (defined as an increase in creatine kinase by greater than or equal to 3 times the upper normal limit) in 6.5% (3/46) of patients within 24 hours after the procedure; these patients did not require admission to hospital.

The case series of 27 patients reported that 3 patients had the device removed percutaneously and were treated with subsequent surgical annuloplasty. This was because of device fracture in 1 patient after 7 days and device migration in 2 patients. Another patient was unable to have the diagnostic procedure because of guidewire perforation (no other details provided)[7].

The same study reported pericardial effusions requiring pericardiocentesis, transient renal dysfunction, pneumonia, and subclavicular haematoma in 1 patient each. The patient who received the first device implantation appeared to have a circumflex abnormality directly adjacent to the device. On intravascular ultrasound, there was an abrupt vessel closure and ST elevation, which was successfully treated with stent implantation.

The case series of 5 patients reported that attempts to implant the device in the 1 patient who was not successfully implanted led to wire perforation of the anterior interventricular vein and pericardial effusion. Another patient in this study developed transient atrial fibrillation during cannulation of the coronary sinus[2].

A case report described a patient who was treated with an annuloplasty device 4 years after treatment with a cardioverter-defibrillator to address impaired left ventricular ejection fraction. Despite initially responded favourably (NYHA class improved to class II), the patient developed atrioventricular block during the follow-up period resulting in the patient becoming dependent on a pacemaker. The patient was treated with a cardiac resynchronisation device which resulted in an improved 6-minute walk test (175 to 240 m) and the NYHA functional class returning from III to II (the time of occurrence after implantation was not reported)[6].

Validity and generalisability of the studies

- There are no comparative studies between best medical management and the procedure.
- The existing case series include very few patients and the maximum period of follow-up is 6 months.
- There are a number of different types of devices that can be used to manipulate the coronary sinus percutaneously to change the shape and size of the mitral valve annulus. These include rings, rods and nitinol ribbons that attach at anchors on each end.
- A number of studies included were pilot studies which tested the use of a temporary implant.
- The use of anaesthetic varied from the use of local sedation to local and general anaesthesia.

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. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Percutaneous mitral valve leaflet repair for mitral regurgitation. NICE interventional procedures guidance 309 (2009). Available from http://www.nice.org.uk/IPG309
- Thoracoscopically assisted mitral valve surgery. NICE interventional procedures guidance 245 (2007). Available from www.nice.org.uk/IPG245

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 does not represent the view of the society.

Dr Michael O'Sullivan, British Cardiovascular Intervention Society, Mr Clifford Barlow, Mr Peter Braidley, Mr Ramesh Patel, Society for Cardiothoracic Surgery in Great Britain and Ireland.

- One Specialist Adviser highlighted that this procedure will be performed on its own in rare cases when mitral continence is type I (failure of apposition); otherwise, it will require additional procedures, either on the leaflet or at submitral valvular level. Other Specialist Advisers also highlight that this procedure only addresses annular dilation, only 1 aspect of the pathology of mitral regurgitation.
- One Specialist Adviser mentioned specifically the importance of addressing the downward displacement of the papillary muscle, which is not addressed with this procedure.
- One Specialist Adviser, who performs this procedure surgically, stated that this procedure does not encircle all of the valve annulus as proposed but brings a portion of the posterior annulus anteriorly. The same Specialist Adviser commented that the bridge spring-wire may shorten at body temperature and that this may have implications for ensuring correct placement at body temperature.

- Comparator procedures include surgery with cardiopulmonary bypass and surgical mitral valve annuloplasty (for selected patients). One Adviser commented that this procedure will be used in patients who are not suitable for surgery, so the comparator is pharmacological therapy.
- Key efficacy outcomes include mitral valve competence in the short (1 year), medium (5 years), and long term (10 years) for patients with degenerative disease, reduction in mitral regurgitation and mitral annular area, improved left ventricular function, improved NHYA classification, increase in 6-minute walk distance, increase in quality of life scores and survival and reduced hospital admissions for patients with advanced heart failure.
- Theoretical adverse events include compression of the coronary artery while accessing through the coronary sinus causing ischaemia or death, coronary sinus rupture, cardiac perforation, compromise of coronary venous return, bleeding from coronary sinus, coronary sinus and cardinal vein thrombosis, coronary sinus erosion, progressive stenosis and deformation of the mitral valve orifice, progressive elongation and rupture of the chordal apparatus supporting the mitral valve leaflet where the mechanism of the regurgitation has not been evaluated in detail, fixed posterior mitral annulus (a dynamic structure changing its shape and orifice size during the entirety of the cardiac cycle), undetected stress fracture that may endure due to long-term deformation forces in action in the annulus, inability to remove the device, and device migration, embolisation, or fracture.
- Anecdotal adverse events include cardiac tamponade.
- The Specialist Advisers highlighted the importance of a multidisciplinary team for the selection of patients for this procedure and also for performing the procedure (there should also be access to standby cardiac surgery).

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme was unable to obtain patient commentary for this procedure.

Issues for consideration by IPAC

- Please see ‘Validity and generalisability of the studies’ section.
- Long-term echocardiographic follow-up (more than 1 year) needed to assess residual mitral regurgitation.

References

1. Schofer J, Siminiak T, Haude M et al. (2009) Percutaneous mitral annuloplasty for functional mitral regurgitation: Results of the CARILLON mitral annuloplasty device european union study. Circulation 120: 326–33.

2. Webb JG, Harnek J, Munt BI et al. (2006) Percutaneous transvenous mitral annuloplasty: Initial human experience with device implantation in the coronary sinus. Circulation 113: 851–5.

3. Duffy SJ, Federman J, Farrington C et al. (2006) Feasibility and short-term efficacy of percutaneous mitral annular reduction for the therapy of functional mitral regurgitation in patients with heart failure. Catheterization and Cardiovascular Interventions 68: 205–10.

4. Dubreuil O, Basmadjian A, Ducharme A et al. (2007) Percutaneous mitral valve annuloplasty for ischemic mitral regurgitation: first in man experience with a temporary implant. Catheterization & Cardiovascular Interventions 69: 1053–61.

5. Palacios IF, Condado JA, Brandi S et al. (2007) Safety and feasibility of acute percutaneous septal sinus shortening: First-in-human experience. Catheterization and cardiovascular interventions 69: 513–8.

6. Mueller D, Tschoepe C, and Spencker S. (2008) Cardiac resynchronization therapy in a patient with a mitral annuloplasty device. Pacing & Clinical Electrophysiology 31: 1074–6.

7. Sack S, Kahlert P, Bilodeau L et al. (2009) Percutaneous transvenous mitral annuloplasty: initial human experience with a novel coronary sinus implant device. Circulation: Cardiovascular Interventions 2:27–284.

Appendix A: Additional papers on percutaneous mitral valve annuloplasty

The following table outlines the studies that are considered potentially relevant to the 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
Jerzykowska O, Kalmucki P, Woloszyn M et al. (2010) Echocardiographic evaluation of percutaneous valve repair in patients with mitral regurgitation using the CARILLON system. Kardiologia Polska 68:57–63.	Case series n = 9 (with Carillon system) Follow-up = 1 month	Statistically significant improvement in vena contracta and ratio of the jet area to the left atrial area ($p < 0.05$ and 0.005).	Larger studies in table 2.
Siminiak T, Firek L, Jerzykowska O et al. (2007) Percutaneous valve repair for mitral regurgitation using the Carillon Mitral Contour System. Description of the method and case report. Kardiologia Polska 65: 272–8.	Case report n = 1 Follow-up = at least 4 months	Significant reduction of mitral regurgitation jet was observed. The patient was discharged 4 days after the procedure. During follow-up visits, the patient continued to improve generally and in exercise capacity. The patient was NHYA class 1 at last follow-up.	Patient was part of AMADEUS trial so likely already included in Schofer (2009)[1].
Siminiak T, Hoppe UC, Schofer J et al. (2009) Effectiveness and safety of percutaneous coronary sinus-based mitral valve repair in patients with dilated cardiomyopathy (from AMADEUS trial). American Journal of Cardiology 104:565–70.	Case series n = 43 (30 treated with implants) Follow-up = not reported	Mitral regurgitation decreased from 3.0 at baseline to 2.0 after implantation. (not clear why this study reports less patients with attempted implantation than Schofer 2009[1]; also follow-up for outcomes is not reported in this study).	Patients from AMADEUS trial already reported on in Schofer (2009)[1].

Appendix B: Related NICE guidance for percutaneous mitral valve annuloplasty

Guidance	Recommendations
Interventional procedures	**Percutaneous mitral valve leaflet repair. NICE interventional procedures guidance 309 (2009).** 1.1. Evidence on the safety and efficacy of percutaneous mitral valve leaflet repair for mitral regurgitation is currently inadequate in quality and quantity. Therefore, this procedure should only be used: • with special arrangements for clinical governance, consent and research for patients who are well enough for surgical mitral valve leaflet repair to treat their mitral regurgitation, or • in the context of research for patients who are not well enough for surgical mitral valve leaflet repair to treat their mitral regurgitation. 1.2. Clinicians wishing to undertake percutaneous mitral valve leaflet repair for mitral regurgitation in patients who are well enough for surgical mitral valve leaflet repair to treat their mitral regurgitation should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that patients and their carers understand the uncertainty about the procedure's safety and efficacy and provide them with clear written information. In addition, the use of NICE's information for patients ('Understanding NICE guidance') is recommended (available from www.nice.org.uk/IPG309publicinfo). 1.3. The NHS Information Centre for Health and Social Care runs the UK Central Cardiac Audit Database. Clinicians should enter details about patients who are well enough to have surgical mitral valve leaflet repair to treat their mitral regurgitation and who are treated by percutaneous mitral valve leaflet repair onto this database (www.ccad.org.uk). 1.4. Clinicians wishing to undertake percutaneous mitral valve leaflet repair for mitral regurgitation in patients who are not well enough for surgical mitral valve leaflet repair should do so in the context of research studies. Research outcomes should include the effect on symptoms, change in functional status and effective measures of cardiac function, in addition to clear documentation of adverse events and survival. 1.5. Patient selection and treatment should be carried out in specialist units (with access to emergency cardiac surgery) by a multidisciplinary team, including an interventional cardiologist (with expertise in echocardiography or with

	support from an echocardiologist) and a cardiac surgeon. 1.6. This procedure should only be carried out by clinicians with specific training. 1.7. NICE is aware of current clinical trials involving this procedure, and may review the procedure on publication of further evidence. **Thoracoscopically assisted mitral valve surgery. NICE interventional procedures guidance 245 (2007).** 1.8. Evidence from large case series supports the safety and efficacy of thoracoscopically assisted mitral valve surgery. Therefore, clinicians wishing to use this procedure should do so with normal arrangements for clinical governance and consent. 1.9. Thoracoscopically assisted mitral valve surgery is technically demanding. Surgeons undertaking it should have special expertise and specific training in thoracoscopic cardiac surgery, and should perform their initial procedures with an experienced mentor.

Appendix C: Literature search for percutaneous mitral valve annuloplasty

Database	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	09/04/2010	April 2010
Database of Abstracts of Reviews of Effects – DARE (CRD website)	09/04/2010	-
HTA database (CRD website)	09/04/2010	-
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	09/04/2010	April 2010
MEDLINE (Ovid)	09/04/2010	1950 to March Week 5 2010
MEDLINE In-Process (Ovid)	09/04/2010	April 8, 2010
EMBASE (Ovid)	09/04/2010	1980 to 2010 Week 13
CINAHL (NLH Search 2.0)	09/04/2010	-
BLIC (Dialog DataStar)	23/11/2009	-

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

1	(mitral adj3 regurgit*).tw.
2	(mr adj3 regurgit*).tw.
3	(mitral adj3 incompet*).tw.
4	(mitral adj3 insuff*).tw.
5	Mitral Valve Insufficiency/
6	((mitral or cardiac or heart or bicuspid or left atrioventricular) adj valve*).tw.
7	(incompet* or insuff*).tw.
8	6 and 7
9	or/1-5
10	8 or 9
11	((endovascular* or percutaneous* or transcatheter* or catheter* or transvenous*) adj3 (annuloplasty or surg* or reconstruct* or repair*)).tw.
12	PTMA.tw.
13	(percutaneous* adj3 coron* adj3 sinus*).tw.
14	monarc*.tw.

15	viking*.tw.
16	cardiac dimensions carillon.tw.
17	carillon mitral contour system.tw.
18	viacor.tw.
19	st jude.tw.
20	mitraclip.tw.
21	or/11-20
22	10 and 21
23	Animals/ not Humans/
24	22 not 23