Response to NHS Chief Executive’s Open Call for Evidence and Ideas

Respondent ID: 168

Organisation name: THE SOCIETY FOR CARDIOTHORACIC SURGERY IN GREAT BRITAIN

Type of response: Document and case study
Natural History of Mitral Regurgitation
Proper opening and closure of the mitral valve requires the coordinated function of multiple anatomic structures. Specifically, the leaflets, valve annulus, chordae tendineae and papillary muscles as well as both left chambers of the heart must function properly to enable effective valve function. Malfunction of one or more of these structures can cause the valve leaflets to close inadequately causing the valve to leak. Patients with mitral regurgitation (MR) may remain asymptomatic for years. Over time, left ventricular dilatation and dysfunction occurs in an attempt to accommodate the increased volume load and maintain cardiac output. In the meantime, the left atrium (LA) dilates under the excess volume load and this may eventually result in atrial fibrillation and in some cases atrial thrombus and embolisation.

The average annual risk of developing an indication for surgery in patients with severe MR due to prolapse, who were asymptomatic or minimally symptomatic and had normal LV and RV function at rest, has been reported as 10.3%. More than half of the patients studied were receiving medical therapy. Ultimately, chronic volume overloading of the LV results in contractile dysfunction, symptoms of heart failure, and an increased risk of sudden death. Patients with severe symptomatic MR have a poor prognosis with an annual mortality rate of 5% per year without surgical intervention. Progressive heart failure is the usual cause of death, but sudden death, stroke, and endocarditis are other causes of death.
The MitraClip (Abbott Laboratories)

The MitraClip System (developed by Evalve but now acquired by Abbott Laboratories) is a catheter-based device designed to perform an edge-to-edge repair of the mitral valve while the heart is beating as an alternative to the conventional surgical approach. The MitraClip System includes a MitraClip device, a Steerable Guide Catheter and a Clip Delivery System that enables placement of the Clip on the mitral valve leaflets resulting in permanent leaflet approximation and a double mitral valve orifice. The procedure is performed in the cardiac catheterisation laboratory with echocardiographic and fluoroscopic guidance while the patient is under general anaesthesia.

To access the left heart, standard transseptal catheterisation is performed. The guide catheter is then percutaneously inserted into the femoral vein. The delivery catheter is the inserted into the guide and the MitraClip device is positioned above the mitral valve. Manipulation of the steering mechanism on the handles of the guide and delivery catheter positions the MitraClip device on the mitral valve. The MitraClip device is actuated (i.e., opened and closed, locked, deployed) through manipulation of levers on the handle of the delivery catheter.

To date the clinical efficacy and safety of the MitraClip system has been assessed in two clinical trials (EVEREST I and II Trials) in 47 US and Canadian Hospitals. EVEREST I was the initial feasibility trial which studied 55 patients. EVEREST II is a randomized controlled trial including over 300 patients with eligible patients randomised to MitraClip or surgery. Patients not suitable for randomisation due to high risk of surgery were included in a ‘High risk registry’. The EVEREST II trial reported at EuroPCR in 2010. Data from 107 patients included in EVEREST I and the high risk registry arm of EVEREST II have been reported in abstract form.

In the published data (from 107 patients in the EVEREST trials) 91% of patients were free from major adverse event associated with the procedure.
Although an initial learning curve is expected the procedural success rate in the EVEREST data was 90%, with 61% of patients receiving 1 MitraClip, 29% of patients requiring 2 devices, and 10% of patients having no device delivered. This represents the earliest experience of this device and going forward procedural success is likely to be higher than this.

NICE Interventional Procedure Guidance 309 (published August 2009) stated that:

*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.*

Since publication of this guidance, new evidence has emerged for MitraClip. In the EVEREST II trial, 279 patients with grade 3 or 4 MR were randomised in a 2:1 design to the MitraClip system (n=184) or surgical repair or replacement (n=94). Patients were either symptomatic (with EF >25% and LVESD ≤55mm) or asymptomatic (with one or more of: EF 25-60%, LVESD ≥40mm, new onset AF or pulmonary hypertension). The mitral valve anatomy was carefully specified (mitral valve area ≥4cm², leaflet flail width <15mm and gap <10mm, and patients with leaflet tethering - coaptation depth >11mm and length <2mm – were excluded). In the device group, 178 actually underwent treatment, and procedural success was achieved in 137. In the control group 80 underwent treatment (86% repair).

The 12 month per protocol success rate was 72% in the device group and 88% in the surgery group. Success was defined as freedom from death, need for MV surgery or re-operation for MV dysfunction and MR>grade 2 at 12m. Urgent or emergency surgery (or re-operation) was required in 2.2% of the device group and 4.3% of the control group. Major end-points were significantly lower in the device group (8.3% vs 42.6%) but this difference was almost entirely down to the definition of major bleeding and requirement for transfusion in the surgical group. Although the inclusion of bleeding/transfusion in the end-points has been criticised, the trialists have pointed out the literature related to adverse outcomes of surgical patients requiring transfusion. Deaths and major strokes occurred in 1.1% and 2.1% of the device and surgical arms. At 12 months, deaths in the actually treated patients were 4.5% and 6.8%, MV surgery (or re-operation) was required in 6.7% and 2.7% and MR grade >2 was seen in 16.4% and 2.7% respectively. Significant reverse LV remodelling was seen in both groups. NYHHA status I and II was seen in 97.6% in the device group and 87.9% in the surgical group and quality of life scores were similar. Results were similar for the sub-groups treated for functional or degenerative MR.

These results confirmed preliminary reports from the EVEREST cohorts suggesting the device can result in significant reduction in severity of MR, reverse LV remodeling and sustained improvement in symptoms as judged by NYHA class (77%
improved, 17% no change, 6% deteriorated in the original cohorts). At 36 months freedom from death was 94% and freedom from death or surgery 75%. These data demonstrate the MitraClip is a device that can be implanted as part of a low risk procedure in patients with degenerative or functional MR and may be associated with significant benefit to patients. However it should be noted that the trial is relatively small with < 100 patients in the surgically treated arm.

The Abbott MitraClip has been awarded a CE mark, and is now being introduced into a small number of centres in Europe.

Conclusions
Transcatheter valve techniques represent the most exciting developments in cardiovascular intervention since percutaneous coronary intervention. Over the next decade these valve techniques are likely to become increasingly important. The MitraClip represents the latest innovation in the treatment of structural heart disease. In the short term the majority of patients who may benefit from this technique have heart failure and functional or “secondary” MR. The results of surgery in these patients are disappointing with high procedural mortality and morbidity. The use of the MitraClip would aim to improve their symptoms of heart failure and reduce the length of hospitalisation and therefore may result in significant financial benefit.

COMMISSIONING PRINCIPLES / GUIDELINES

1. The epidemiology of mitral regurgitation is not fully established and identifying the numbers of cases that would be amenable to either percutaneous or surgical mitral valve repair is not yet possible.

2. Widespread commissioning is not currently justified. An economic analysis of the EVEREST II results is required.

3. Nonetheless, there is clear evidence that many patients are disabled secondary to degenerative and functional mitral regurgitation, and that many of these patients are amenable to such repair techniques.

4. There is a clinical case for offering MitraClip to a selected group of patients within the NHS.

5. In patients suitable for surgical intervention surgery should still be the treatment of choice.

6. In patients unsuitable for surgical intervention, but suitable for MitraClip, NHS funding in exceptional circumstances would be appropriate.
7. We strongly recommend commissioning a limited volume of activity to establish an initial UK experience in part to assist in the interpretation of the results of the above trial.

8. There should be a degree of sensible geographic distribution of those centres who are commissioned (so that there are no regional or post code differences in access to this technology). BCIS and SCTS will suggest criteria that will help commissioners identify providers who should be supported (see appendix 1).

9. We would envisage up to 8 centres commissioned to 20-25 patients per centre (This model is also financially advantageous given the vending strategy of the company).

10. Centres should have on site cardiac surgery including a surgeon with expertise in mitral valve repair techniques. They should have specialist cardiac imaging services (including transoesophageal and 3D echocardiography and preferably have access to MRI), and a formal and high volume heart failure service. Expert echocardiographic input is mandatory in patient selection and clip implantation.

11. Patients should not be selected by any individual specialty. Patient evaluation and selection must be through a structured MDT process to include two interventional cardiologists with the appropriate skills and interests, a cardiologist with expertise in cardiac imaging, at least one specialist mitral valve repair surgeon and a heart failure specialist. Input from others such as cardiac anaesthetists and elderly care physicians may be appropriate for individual cases.

12. Patients selected will be those who are symptomatic in spite of conventional treatment, or who have parameters that would normally lead to consideration of mitral repair surgery (LV parameters, pulmonary hypertension, atrial fibrillation etc).

13. There should be formal training of the implanting team which should include:
   
a. Didactic theoretical training

b. Simulator training if available

c. A visit to an experienced centre to observe MitraClip procedures
d. Support for the initial cases at any site by a proctor or clinical specialist

14. All activity should be captured via centralised data collection (c.f. TAVI) although this will require the resource to allow BCIS and the SCTS to develop an appropriate dataset with CCAD. This should include appropriate follow-up data to determine echocardiographic and clinical parameters.

15. Further evaluation is necessary and an RCT of MitraClip in “functional” MR should be encouraged.

APPENDIX 1; Suggested criteria for selection of centres that wish to undertake Mitraclip procedures.

1. Centres with on-site cardiac surgery.
2. Surgical experience of MV operations
3. Significant experience in MV repair techniques (>50 per year) with >/=1 surgeon with the appropriate experience and clinical results.
4. On site transoesophageal and 3D echocardiography with routine experience in the use of intra-operative transoesophageal echocardiography.
5. MRI scanning availability is desirable.
6. Formal heart failure programme and regional or supra-regional links to heart transplantation centre.
7. Formal mitral valve programme with MDT discussion of mitral patients.
8. Business plan commitment from the hospital management team to support the programme.
9. Local commissioner agreement for a designated number of procedures.
10. Available catheter laboratory availability to support the programme.
11. Implantation team made up of at least two operators who are dedicated to the programme – either two interventional cardiologists or one interventional cardiologist working with a cardiac surgeon.
12. MDT to be made up of: cardiac surgeon(s) with experience in mitral valve repair, interventional cardiologist(s)/cardiac surgeon with training in the Mitraclip procedure, cardiologists with expertise in cardiovascular imaging, at least one cardiologist or cardiac surgeon without experience in either repair or interventional structural heart techniques, and at least one cardiothoracic anaesthetist dedicated to the programme. An elderly care physician may be included as deemed appropriate for selected patients.
13. Demonstrable compliance with national data submission to CCAD, both via the SCTS cardiac surgery database, BCIS database and UK TAVI registry (if appropriate).
14. Commitment to work with the device manufacturers to conform to the training and proctoring arrangements.
15. On-site cardiovascular research capabilities with appropriate support team.

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In recent years interventional cardiology and cardiac surgery have participated in numerous innovations which have served to radically improve patient outcomes and reduce costs.

Transcatheter valve techniques represent a new wave of cardiac innovations which show great potential. They need to be systematically introduced and evaluated to ensure early access for those in need and the best value for the NHS.

On the basis of the experience with trans-aortic valve implantation, the SCTS and BCIS have identified the opportunity for a more structured approach to the introduction of these technologies which may be of wider relevance to the innovation agenda.

The attached document, written on behalf of the SCTS and BCIS and ratified by the National Committee for New Cardiovascular Technologies, summarises the position in relation to transcatheter mitral valve intervention using the MitraClip system (Abbott Vascular). It concludes with a series of commissioning principles, some of which are condition and device-specific and others of which are more generic in character. The latter include the:

- need to commission a limited volume of activity to establish UK experience;
- desirability of sensible geographic distribution to promote equitable access;
- importance of designating a number of centres with a minimum level of activity to develop and support good standards of clinical practice;
- need for centralised data collection to help in the development of clinical parameters.

One of the benefits of this approach would be the early involvement of commissioners, assisted by the likely transfer of responsibility for new cardiovascular technologies to the proposed NHS Commissioning Board (NHSCB) under the reforms presently going through Parliament. The parallel introduction of an innovation fund would both help to speed the adoption of new technologies and to ensure the sort of structured approach we are proposing. A very small percentage of the NHSCB’s specialised commissioning budget would be sufficient to support this project.

The Professional Societies and the National Committee for New Cardiovascular Technologies have discussed the implementation of the programme outlined in the position statement and have a very clear view as to how this can be effected. This approach has the complete support of Abbott Vascular.

We believe that this represents a unique collaboration between clinicians, the Professional Societies and industry in the roll-out and initial clinical evaluation of a new cardiovascular technology. Moreover, this provides a template that could be applied to the introduction of new technologies in the future.

We would welcome an early opportunity to discuss these proposals in more detail.

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