Percutaneous Mitral Valve Repair

Number: 0880

Policy
*Please see amendment for Pennsylvania Medicaid at the end of this CPB.*

Aetna considers percutaneous mitral valve repair (PMVR) by means of the MitraClip Clip Delivery System medically necessary for persons with grade 3+ to 4+ symptomatic degenerative mitral regurgitation and at high-risk for traditional open-heart mitral valve surgery.

Aetna considers transcatheter mitral valve valve-in-valve replacement by means of the Edwards-Sapien valve experimental and investigational because it has not been proven safe and effective for this indication.

Aetna considers PMVR experimental and investigational for persons with mitral regurgitation who can be treated with open-heart surgery, persons with active inflammation of the heart (endocarditis), rheumatic mitral valve disease, blood clots present at the intended site of implant or blood clots in vessels through which access to the defect is gained, persons who cannot tolerate anti-coagulation and anti-platelet medications, persons with severe congestive heart failure (N-terminal pro-B-type natriuretic peptide (NTproBNP) greater than 10,000pg/ml), and for all other indications because its
effectiveness for these indications has not been established.

See also CPB 0558 - Percutaneous Transluminal Septal Myocardial Ablation (PTSMA) (../500_599/0558.html), CPB 0821 - Transcatheter Pulmonary Valve Implantation (0821.html), and CPB 0826 - Transcatheter Aortic Valve Implantation (0826.html).

Background
Mitral valve regurgitation, for which surgical mitral valve repair is the treatment of choice, is the second most common clinically relevant valvular heart disease in adults and has an incidence of approximately 2 % to 3 % per year (Seeburger et al, 2011).

A 2009 guideline on percutaneous mitral valve leaflet repair for mitral regurgitation (MR) was issued by the National Institute for Health and Clinical Excellence (NICE). The NICE guideline stated that evidence on the safety and efficacy of percutaneous mitral valve leaflet repair for MR stated that 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 MR, or in the context of research for patients who are not well enough for surgical mitral valve leaflet repair to treat their MR (NICE, 2009).

More recently, the Food and Drug Administration (FDA) granted Premarket Approval (PMA) to Abbott Vascular’s MitraClip device (FDA, 2013). The MitraClip Clip Delivery System consists of the MitraClip device and implant catheters. The MitraClip is a permanent implant designed to attach to the mitral valve leaflets, resulting in a double opening of the mitral valve, thus allowing greater closure and reduction of MR. The MitraClip device is inserted via catheter through the femoral vein and advanced into the heart. It is then positioned to grasp both mitral valve leaflets. Following positioning of the MitraClip device the catheter is removed. The goal of the MitraClip device is the reduction of MR to less than or equal to 2+ MR
Glower et al (2012) defined the EVEREST II study as a prospective, multi-center, randomized controlled trial (RCT) comparing percutaneous repair with the MitraClip device to mitral valve surgery in the treatment of mitral regurgitation. They reported on the patient characteristics and treatment effects on mitral repair versus replacement. Of 279 patients enrolled, 80 surgical patients underwent 82 mitral valve operations and 178 underwent an initial MitraClip procedure, of whom 37 underwent a subsequent mitral valve operation within 1 year of their index MitraClip procedure. A logistic regression model was used to predict mitral valve replacement according to valve pathology, etiology of mitral regurgitation, age, previous cardiac surgery, and treatment group which found the rate of percutaneous or surgical mitral valve repair at 1 year to be 89% (158/178) in patients initially receiving the MitraClip device versus 84% (67/80) in the surgical patients (p = 0.36). Surgical repair was performed after the MitraClip procedure in 20 (54%) of 37 patients (p < 0.001 versus surgery). In both the MitraClip device and surgery groups, mitral valve replacement was significantly associated with anterior leaflet pathology (p = 0.035). Logistic regression analysis showed that anterior leaflet pathology predicted mitral valve replacement. In 5 (13.5%) of 37 patients undergoing surgery after MitraClip therapy, replacement was performed in part because of mitral valve injury associated with the MitraClip procedure. The authors concluded that these data suggested that anterior leaflet pathology is strongly associated with mitral valve replacement in patients undergoing either de novo mitral valve surgery or surgery after MitraClip therapy. They noted that MitraClip therapy has a repair rate similar to surgery through 1 year but also imparts a risk of replacement of a potentially repairable valve.

Hermann et al (2012) conducted a study to characterize patients with MR and atrial fibrillation (AF) treated percutaneously using the MitraClip device and compare the results with traditional surgery in this population. The study
population included 264 patients with moderately severe or severe MR assessed by an independent echocardiographic core laboratory and comparison of safety and effectiveness study endpoints at 30 days and 1 year were made using both intention-to-treat and per-protocol (cohort of patients with MR less than or equal to 2+ at discharge) analyses. Pre-existing AF was present in 27% of patients, who were older, had more advanced disease, and were more likely to have a functional etiology. Similar reduction of MR to less than or equal to 2+ before discharge was achieved in patients with AF (83%) and in patients without AF (75%, p = 0.3). Freedom from death, mitral valve surgery for valve dysfunction, and MR greater than 2+ was similar at 12 months for AF patients (64%) and for no-AF patients (61%, p = 0.3). The authors reported that at 12 months, MR reduction to less than 2+ was greater with surgery than with MitraClip, but there was no interaction between rhythm and MR reduction, and no difference in all-cause mortality between patients with and patients without AF. The authors noted that atrial fibrillation is associated with more advanced valvular disease and noncardiac comorbidities. However, they concluded that acute procedural success, safety, and 1-year efficacy with MitraClip therapy is similar for patients with AF and without AF.

Smith et al (2012) stated that catheter-based repair of MR with the MitraClip device is performed through a 22-French transseptal guiding catheter. The authors reported on the echocardiographic prevalence of iatrogenic atrial septal defects (iASDs) after the MitraClip procedure. A total of 30 subjects undergoing MitraClip repair during the roll-in phase of the EVEREST II randomized trial who had baseline, 30 day, 6 and 12 month trans-thoracic echocardiograms (TTEs) available for review were included; and patients who underwent surgery for MR within the first 12 months were excluded. Residual iASD size, right ventricular (RV) size, left atrial (LA) volume, and tricuspid/MR grade were quantified and iASDs were found at 12 months in 8 patients (27%) with a mean diameter of 6.6 ± 3.1 mm. Patients with iASD at 12 months had more residual MR, increased TR and a trend toward larger LA volumes than
non-iASD patients; 83 % of non-ASD patients were free from MR greater than 2+ at 12 months versus 38 % of those with iASD (p = 0.016). There were no other significant associations between clinical and echocardiographic variables and the persistence of iASD. The authors concluded that following MitraClip repair, persistent iASDs occur at a rate comparable to reports after other transseptal interventional procedures and did not appear hemodynamically significant. They further noted that patients with persistent iASDs had less MR reduction at 12-months and a trend toward larger LA volumes, suggesting that increased LA pressure may be a mechanism for persistent iASD.

Whitlow et al (2012) reported on the acute and 12 month results with catheter-based mitral valve leaflet repair in the EVEREST II (Endovascular Valve Edge-to-Edge Repair) High Risk Study (HRS). The EVEREST II Study assessed the safety and effectiveness of the MitraClip device in patients with significant MR at high risk of surgical mortality. This study included patients with severe MR (3 to 4+) at high risk of surgery who may benefit from percutaneous mitral leaflet repair. Study subjects included patients with severe symptomatic MR and an estimated surgical mortality rate of greater than or equal to 12 % were enrolled. A group of patients screened concurrently but not enrolled were identified retrospectively and consented to serve as a comparison group for survival in patients treated by standard care. A total of 78 patients underwent the MitraClip procedure with a mean age of 77 years. Greater than 50 % had previous cardiac surgery, 46 had functional MR and 32 had degenerative MR. MitraClip devices were successfully placed in 96 % of patients. Surgical mortality rate in the HRS and concurrent comparator group was 18.2 % and 17.4 %, respectively. The Society of Thoracic Surgeons calculator estimated mortality rate was 14.2 % and 14.9 %, respectively and the 30-day procedure-related mortality rate was 7.7 % in the HRS and 8.3 % in the comparator group (p = NS). The 12-month survival rate was 76 % in the HRS and 55 % in the concurrent comparator group (p = 0.047). In the evaluation of surviving patients with matched baseline and 12-month data,
78% had an MR grade of less than or equal to 2+. Left ventricular end-diastolic volume improved from 172 ml to 140 ml and end-systolic volume improved from 82 ml to 73 ml (both p = 0.001). New York Heart Association functional (NYHA) class improved from III/IV at baseline in 89% to class I/II in 74% (p < 0.0001). Quality of life was also evaluated and reported as improved (Short Form-36 physical component score increased from 32.1 to 36.1 [p = 0.014] with the mental component score from 45.5 to 48.7 [p = 0.065]) at 12 months. The annual rate of hospitalization for congestive heart failure in surviving patients with matched data decreased from 0.59 to 0.32 (p = 0.034).

The investigators concluded that the MitraClip device reduced MR in a majority of patients deemed at high risk of surgery, resulting in improvement in clinical symptoms and significant left ventricular reverse remodeling over 12 months.

Andalib et al (2014) conducted a systematic review to evaluate the outcomes of mitral valve surgery in octogenarians with severe symptomatic mitral regurgitation (MR) and meta-analysis of data on octogenarians who underwent mitral valve replacement (MVR) or mitral valve repair (MVRpr). Their search yielded 16 retrospective studies. Using Bayesian hierarchical models, they estimated the pooled proportion of 30-day mortality, postoperative stroke, and long-term survival. The pooled proportion of 30-day postoperative mortality was 13% following MVR (10 studies, 3,105 patients, 95% credible interval (CI): 9 to 18%), and 7% following MVRpr (6 studies, 2,642 patients, 95% CI: 3 to 12%). Furthermore, pooled proportions of post-operative stroke were 4% (6 studies, 2,945 patients, 95% CI: 3 to 7%) and 3% (3 studies, 348 patients, 95% CI: 1 to 8%) for patients undergoing MVR and MVRpr, respectively. Pooled survival rates at 1 and 5 years following MVR (4 studies, 250 patients) were 67% (95% CI: 50 to 80%) and 29% (95% CI: 16 to 47%), and following MVRpr (3 studies, 333 patients) were 69% (95% CI: 50 to 83%) and 23% (95% CI: 12 to 39%), respectively. The authors concluded that surgical treatment of MR in octogenarians is associated with high peri-operative mortality and poor long-term survival with an uncertain benefit on quality of life and that these data
highlight the importance of patient selection for operative intervention and suggest that future transcatheter mitral valve therapies such as transcatheter mitral valve repair (TMVr) and/or transcatheter mitral valve implantation (TMVI), may provide an alternative therapeutic approach in selected high-risk elderly patients.

Armstrong et al (2013) reported on the predictors of the number of MitraClip devices implanted during percutaneous repair of mitral regurgitation (MR), and the long-term reduction in MR. In the EVEREST trials, 1 or 2 MitraClip devices were implanted to reduce MR, as needed. Pre-procedural TTE and transesophageal echocardiograms (TEE) of 233 subjects who received 1 or 2 MitraClip devices in the EVEREST II Study were analyzed. TEEs were reviewed for etiology of MR and pathoanatomic features of the valve, valve apparatus, and the regurgitant jet and follow-up MR was assessed by TTE post-procedure and at 12 months. A total of 97 subjects (42 %) had 2 MitraClip devices implanted. Those subjects with quantitatively more severe MR were more likely to receive 2 devices [mean regurgitant volume (RV) 45.9 ± 21.9 versus 36.3 ± 18.5 ml, p < 0.001]. Multi-variate analysis showed increased anterior leaflet thickness (OR 1.7 per mm, p = 0.007) and greater baseline RV (OR 1.21 per 10 ml, p = 0.01) were associated with increased odds of implanting 2 devices. The frequency of 2+ MR or less at discharge was similar regardless of the number of devices implanted. The authors concluded that after propensity matching, patients had quantitatively similar MR at 12-month follow-up, regardless of whether 1 or 2 MitraClip devices were implanted (p = 0.6). The authors concluded that subjects with thicker anterior mitral leaflets and more severe MR were more likely to receive 2 MitraClip devices. Immediate and long-term reduction in MR was similar regardless of the number of devices implanted at the time of the procedure.

Foster et al (2013) conducted an analysis to determine the extent of reverse remodeling at 12 months after successful percutaneous reduction of MR with the MitraClip device; 49 of
64 patients with 3+ and 4+ MR who achieved acute procedural success after treatment with the MitraClip device had moderate or less MR at 12-month follow-up. Baseline and 12-month echocardiograms were compared between the group with and without left ventricular (LV) dysfunction. In patients with persistent MR reduction and pre-existing LV dysfunction, there was a reduction in LV wall stress, reduced LV end-diastolic volume, LV end-systolic volume and increase in LV ejection fraction in contrast to those with normal baseline LV function, who showed reduction in LV end-diastolic volume, LV wall stress, no change in LV end-systolic volume, and a fall in LV ejection fraction. Patients with pre-existing LV dysfunction demonstrated reverse remodeling and improved LV ejection fraction after percutaneous mitral valve repair.

Lim et al (2014) studied the treatment of MR in patients with severe degenerative MR (DMR) at prohibitive surgical risk undergoing transcatheter mitral valve repair with the MitraClip. A prohibitive risk DMR cohort was identified by a multi-disciplinary heart team that retrospectively evaluated high risk DMR patients enrolled in the EVEREST II studies. The study enrolled 141 high risk DMR; 127 of these patients were retrospectively identified as meeting the definition of prohibitive risk and had one-year follow-up data (median of 1.47 years) available. Patients were elderly (mean age of 82 years), severely symptomatic (87 % NYHA Class III/IV), and at prohibitive surgical risk (STS score 13.2 ± 7.3 %). MitraClip was successfully implanted in 95.3 %; hospital stay was 2.9 ± 3.1 days. Major adverse events at 30 days included death in 6.3 %, myocardial infarction in 0.8 %, and stroke in 2.4 %. Through 1 year there were a total of 30 (23.6 %) deaths, with no survival difference between patients discharged with MR less than or equal to 1+ or MR = 2+. A majority of surviving patients (82.9 %) remained MR less than or equal to 2+ at 1 year and 86.9 % were in NYHA Functional Class I or II. Left ventricular end-diastolic volume decreased (125.1 ± 40.1 ml to 108.5 ± 37.9 ml, p < 0.0001, n = 69 survivors with paired data). SF-36 quality-of-life scores improved and hospitalizations for heart failure were reduced in patients whose MR was reduced. The
authors concluded that transcatheter mitral valve repair in prohibitive surgical risk patients is associated with safety and good clinical outcomes, including rehospitalization decrease, functional improvements and favorable ventricular remodeling at 1 year.

Mauri et al (2013) conducted a study to evaluate 4-year outcomes of percutaneous repair versus surgery for mitral regurgitation. Patients with grade 3+ or 4+ MR were randomly assigned to percutaneous repair with the MitraClip device or conventional mitral valve surgery in a 2:1 ratio (184:95). Patients prospectively consented to 5 years of follow-up. At 4 years, the rate of the composite endpoint of freedom from death, surgery, or 3+ or 4+ MR in the intention-to-treat population was 39.8 % versus 53.4 % in the percutaneous repair group and surgical groups, respectively (p = 0.070). Rates of death were 17.4 % versus 17.8 % (p = 0.914), and 3+ or 4+ MR was present in 21.7 % versus 24.7 % (p = 0.745) at 4 years of follow-up, respectively. Surgery for mitral valve dysfunction, however, occurred in 20.4 % versus 2.2 % (p < 0.001) at 1 year and 24.8 % versus 5.5 % (p < 0.001) at 4 years. The authors concluded that patients treated with percutaneous repair of the mitral valve more commonly required surgery to treat residual MR; however, after the first year of follow-up, there were few surgeries required after either percutaneous or surgical treatment and no difference in the prevalence of moderate-severe and severe MR or mortality at 4 years.

Puls et al (2014) conducted a study to identify predictors of midterm mortality and heart failure rehospitalisation after percutaneous mitral valve repair with MitraClip. A total of 150 consecutive patients were followed for a median of 463 days. Survival analyses were performed for baseline characteristics, risk scores and failure of acute procedural success (APS) defined as persisting MR grade 3+ or 4+. Univariate significant risk stratifiers were tested in multivariate analyses using a Cox proportional hazards model. Overall survival was 96 % at 30 days, 79.5 % at 12 months, and 62 % at 2 years. Multivariate analysis identified APS failure (HR 2.13, p = 0.02), NYHA Class IV
at baseline (HR 2.11, p = 0.01) and Society of Thoracic Surgeons (STS) score greater than or equal to 12 (HR 2.20, p < 0.0001) as significant independent predictors of all-cause mortality, and APS failure (HR 2.31, p = 0.01) and NYHA Class IV at baseline (HR 1.89, p = 0.03) as significant independent predictors of heart failure rehospitalisation. Also, a post-procedural significant decrease in hospitalisation rate could only be observed after successful interventions (0.89 ± 1.07 per year before versus 0.54 ± 0.96 after implantation, p = 0.01). Patients with severely dilated and overloaded ventricles who did not meet EVEREST II eligibility criteria were at higher risk of APS failure. The authors concluded that failure of acute procedural success proved to have the most important impact on outcome after MitraClip implantation.

Gonzalez et al (2015) stated that in recent years, MitraClip has become available as a treatment option for MR in high-risk surgical patients. Focusing on the incremental effectiveness of MitraClip versus the current standard of care, these investigators provided a comparative review of the evidence on MitraClip and standard medical therapy (MT) in high-risk MR patients. Evidence was retrieved from 7 major databases. Results suggested that MitraClip presented a high safety profile and a good middle-term effectiveness performance. Evidence on long-term effectiveness is limited both for MitraClip and MT. Few studies allowed a comparison with MT and comparative results on different endpoints were mixed. Therefore, the available evidence does not conclusively inform whether or under which circumstances MitraClip should be preferred over MT in the treatment of high-risk patients. The authors concluded that head-to-head real-world studies would be needed, as they would provide great and timely insights to support policy decisions when medical devices are at stake.

Severe Heart Failure:

heart failure (HF) in comparison to mortality predicted by the Seattle Heart Failure Model (SHFM) and the HF calculator of the meta-analysis global group in chronic HF (MAGGIC). This retrospective study included 194 consecutive patients, who received a MC implantation between 2009 and 2013 at the authors’ institution. The observed mortality was compared with that predicted by the SHFM and the MAGGIC after 1 year: 24 % observed, 18 % by SHFM (p = 0.185) and 20.9 % by MAGGIC (p = 0.542). At 2 years: 32 % observed versus 33 % by SHFM (p = 0.919). The subgroup of patients with end-stage HF and N-terminal pro-B-type natriuretic peptide (NTproBNP) greater than 10,000 pg/ml (n = 41) had significantly worse mortality after 1 year (49 %) than predicted by SHFM (24 %, p = 0.034) and MAGGIC (24.8 %, p = 0.041). The authors concluded that in the overall patient cohort defined by 3+ to 4+ mitral valve regurgitation with NYHA III and IV symptomatic HF, mortality following MC is consistent with that predicted by SHFM and MAGGIC for patients that are not at high risk. However, the subset of patients with severe HF defined by NTproBNP greater than 10,000 pg/ml had worse than predicted mortality and may not benefit from MC therapy, mainly due to a high 30-day mortality.

Guerrero et al (2016) conducted a study to evaluate the early experience of TMVR with balloon-expandable valves in patients with severe mitral annular calcification (MAC). These investigators presented the first large retrospective series from a multicenter global registry. The investigators noted that there are isolated reports of successful TMVR with balloon-expandable valves in this patient population. From September 2012 to July of 2015, 64 patients in 32 centers underwent TMVR with compassionate use of balloon-expandable valves. The mean age of patients was 73 ± 13 years, 34% were male, and the mean Society of Thoracic Surgeons score was 14.4 ± 9.5%. They reported that the mean mitral gradient was 11.45 ± 4.4 mm Hg and the mean mitral area was 1.18 ± 0.5 cm². SAPIEN valves (Edwards Lifesciences, Irvine, California) were used in 7.8%, SAPIEN XT in 59.4%, SAPIEN 3 in 28.1%, and Inovare (Braile Biomedica, Brazil) in 4.7%. The patient
population access was transatrial in 15.6%, transapical in 43.8%, and transseptal in 40.6%. The Mitral Valve Academic Research Consortium criteria indicated success was achieved in 46 (72%) patients, primarily limited by the need for a second valve in 11 (17.2%). Six study participants (9.3%) had left ventricular tract obstruction with hemodynamic compromise. Mean mitral gradient post-procedure was 4 ± 2.2 mm Hg, paravalvular regurgitation was mild or absent in all. Study results showed that thirty-day all-cause mortality was 29.7% (cardiovascular = 12.5% and noncardiac = 17.2%) and that 84% of the survivors with follow-up data available were in New York Heart Association functional class I or II at 30 days (n = 25). The authors concluded that TMVR with balloon-expandable valves in patients with severe MAC is feasible but may be associated with significant adverse events. This strategy might be an alternative for selected high-risk patients with limited treatment options.

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

ICD-10 codes will become effective as of October 1, 2015:

CPT codes covered if selection criteria are met:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0345T</td>
<td>Transcatheter mitral valve repair percutaneous approach via the coronary sinus [MitraClip]</td>
</tr>
<tr>
<td>33418</td>
<td>Transcatheter mitral valve repair, percutaneous approach, including transseptal puncture when performed</td>
</tr>
<tr>
<td>33419</td>
<td></td>
</tr>
</tbody>
</table>

ICD-10 codes covered if selection criteria are met:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I34.0 - I34.9</td>
<td>Mitral valve disorders [symptomatic degenerative mitral regurgitation]</td>
</tr>
</tbody>
</table>

ICD-10 codes not covered for indications listed in the CPB (not all-inclusive):

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I01.1</td>
<td>Acute rheumatic endocarditis</td>
</tr>
<tr>
<td>I33.0 - I33.9</td>
<td>Acute and subacute endocarditis</td>
</tr>
</tbody>
</table>
The above policy is based on the following references:


Amendment to
Aetna Clinical Policy Bulletin Number: 0880
Percutaneous Mitral Valve Repair

There are no amendments for Medicaid.