Impact of MitraClip™ therapy on secondary mitral valve surgery in patients at high surgical risk

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Abstract

Objective: Conventional or minimally invasive surgical mitral valve repair (MVR) is the gold-standard treatment for severe mitral regurgitation (MR) of any etiology. Given its good safety profile, trans-catheter MVR with the MitraClip™ device is used increasingly for high-risk or inoperable patients. We report our experience with failed MitraClip™ therapy and its impact on subsequent surgical strategies, such as the feasibility of MVR in high-risk patients. Methods: During a follow-up of 344 ± 227 days from the first 215 consecutive patients treated with the MitraClip™ device, six patients required surgical re-intervention due to failed repair (n = 3) or recurrent severe MR (n = 3) at 35.8 ± 47.7 (range 0–117) days after trans-catheter MVR. Feasibility of secondary surgical MVR was assessed with regard to prior clip therapy. Results: In three patients, secondary surgical MVR was successfully performed following the surgical strategy deemed optimal before trans-catheter treatment. Injury of the mitral leaflets caused by prior clip treatment was present in three other patients and influenced the surgical strategy toward more complex surgical techniques in one case and MV replacement in two others. One patient died 6 days after MV replacement. All other patients are alive with adequate valve function at the latest follow-up of 12.4 ± 7.4 months (range 4–22). Conclusions: Secondary surgical MVR was feasible in some patients after prior clip treatment, but led to valve replacement in others. At present, patient selection criteria for trans-catheter MVR should not be expanded toward more healthy patients, as primary trans-catheter MVR may complicate secondary surgery in certain cases and may even preclude reconstructive valve surgery.

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Keywords: Mitral regurgitation; Mitral valve repair; Mitral valve replacement; Cardiac catheterization/intervention

1. Introduction

Traditionally, surgical mitral valve repair (MVR) is considered the reference treatment for degenerative disease. In elective patients, it can be carried out with perioperative mortality rates of close to 0% and extremely low complication rates [1]. If performed in a timely fashion, successful valve repair restores both life expectancy and quality of life to normal. Furthermore, at specialized centers, a minimally invasive video-assisted approach via a right-anterior minithoracotomy has been established as the standard of care [2], offering additional benefits in terms of postoperative convalescence, transfusion requirements, or cosmesis.

In functional mitral regurgitation (MR), however, the pathophysiology is more complex and the benefits of surgery more ambiguous. Dilated cardiomyopathy of a given origin causes the morphologically normal valve to leak, and correction of secondary MR will not cure the underlying ventricular disease. Surgery for functional MR mostly in ischemic cardiomyopathy has proven beneficial to some extent, for example, improvement of New York Heart Association (NYHA) functional class [3] or quality of life, but proof of survival benefit is pending. Further, operative risk is elevated as compared with MVR for degenerative MR [4]. It is for this growing population of high-risk patients that less invasive treatment alternatives have been explored, leading to the development and clinical implementation of trans-catheter MVR devices [5]. The MitraClip™ device (Abbott Vascular, Menlo Park, CA, USA) aims to achieve a similar effect as surgical edge-to-edge repair in a beating-heart, catheter-based adaptation. The MitraClip™ achieves approximation of the free edges of the anterior mitral leaflet (AML) and posterior mitral leaflet (PML) by means of a polyester-covered clip that is introduced via the femoral vein and a transseptal route. After antegrade passage of the MV,
the clip is opened and pulled back grasping up to 8 mm of the leaflet margins. Closure of the clip arms then results in a 'double-orifice' valve (Fig. 1) and also induces a cinching effect with tension applied to the mitral annulus. Before detachment of the clip from the deployment catheter, MV function can be assessed under physiological hemodynamic conditions. At this point, the clip can still be reopened and repositioned or it can even be completely retrieved. This feature of the MitraClip™ device has been considered advantageous in that it preserves standard-of-care treatment options, that is, surgical MVR [6]. However, damage to the mitral leaflets has been reported to occur either during the intervention, in the postprocedural period, or during clip removal in cases where secondary surgery became necessary [7]. This issue and its impact on the feasibility and success of secondary surgical MVR are currently under debate.

2. Patients and methods

Of the first consecutive 215 patients treated with the MitraClip™ device, surgical revision became necessary in six cases for failed clip placement (n = 3) or recurrent severe MR (n = 3; 6 of 215, freedom from surgery 97.2%) within a mean follow-up of 344 ± 227 days after trans-catheter MVR. Surgical revision was performed at a mean of 35.8 ± 47.7 (range 0–117) days after trans-catheter MVR. Detailed demographic and intraprocedural data of all cases are provided in Table 1.

3. Results

3.1. Case report #1

A 47-year-old male patient with advanced dilated cardiomyopathy was evaluated for treatment. Pre-procedural echocardiography revealed MR grade 4+ due to annular dilatation and restrictive PML. Interventional treatment was initiated with the clip delivery system advanced into the left atrium. However, due to severe dilatation of the mitral annulus, grasping of both leaflet margins was not achieved and the procedure aborted. As the patient continued to be in a state of marked hemodynamic compromise, decision was made for elective surgical MVR 4 days later. Standard bicaval and aortic cannulation were performed and access to the MV was gained via a transeptal approach. The mitral annulus diameter was measured at >5 cm with restrictive PML. Downsizing annuloplasty was performed using a 30-mm IMR ring (Edwards Lifesciences, Inc., Irvine, CA, USA). In addition, resection of the left-atrial appendage and tricuspid valve repair with an Edwards Classic 32-mm ring (Edwards Lifesciences, Inc.) were carried out. In the further course of his hospitalization, the patient developed hemodynamically relevant pericardial effusion, necessitating drainage on postoperative day 5. Prior to discharge, transthoracic echocardiography demonstrated residual MR 1+ with no residual tricuspid regurgitation. At the latest follow-up 18 months after surgery, the patient was well with only trace residual MR, no tricuspid regurgitation, and stable left-ventricular function at 35–40% ejection fraction under intensified heart-failure medication.

3.2. Case report #2

A 58-year-old male patient was referred to our center with severe MR due to Barlow’s disease with ruptured PML chords. In addition, he had an ischemic cardiomyopathy with markedly reduced left-ventricular function and had undergone all-arterial triple coronary artery bypass grafting 6 years earlier with patent grafts. MitraClip™ treatment was performed using two clips and acutely resulted in marked reduction of MR severity (residual MR 1+). Two months later, however, the patient was re-admitted with recurrent severe MR and P2/P3 prolapse presumably due to partial clip detachment, as suspected from transthoracic echocardio- graphic. The patient underwent re-entry sternotomy and conventional surgical MVR with triangular resection of prolapsing P2/P3 tissue and annuloplasty using a 38-mm Physio II ring (Edwards Lifesciences, Inc.). The procedure was complicated by pronounced calcification of the posterior mitral annulus. Intra-operatively, one clip was found to be detached from the P3 segment and adherent to the A3 segment only. The second clip was still in correct position adapting P2/A2 segments (Fig. 2). Both clips were removed.
Table 1. Patient demographics, procedural data and follow-up. logEuroSCORE, logistic EuroSCORE; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; PML, posterior mitral leaflet; ICM, ischemic cardiomyopathy; CABG, coronary artery bypass grafting; LIMA, left internal mammary artery; LAD, left anterior descending; RIMA, right internal mammary artery; OM1, first obtuse marginal branch; D1, first diagonal branch; SVG, saphenous vein graft; RIVP, ramus interventricularis posterior; ASD, atrial septal defect; AHT, arterial hypertension; LAA, left atrial appendage; CM, cardiomyopathy; TR, tricuspid regurgitation; PHT, pulmonary hypertension; COPD, chronic obstructive pulmonary disease; VF, ventricular fibrillation; Afib, atrial fibrillation; IDDM, insulin-dependent diabetes mellitus; CAD, coronary artery disease; ICD, implantable cardioverter defibrillator.

<table>
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<tr>
<th></th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
<th>Patient 5</th>
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<td>Etiology of MR</td>
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<td>Functional MR w. PML restriction, annular sclerosis</td>
<td>Functional MR w. annular dilatation</td>
<td>Functional MR w. annular dilatation</td>
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<td>ICM, history of CABG w. patent grafts (LIMA/LAD, RIMA/OM1, radial artery/D1), ICM, PHT, history of heart failure, history of myocardial infarction, AHT, renal insufficiency, IDDM, cirrhosis (Child-Pugh B)</td>
<td>ICM, history of CABG w. patent grafts (LIMA/LAD, sequential SVG/D1/OM1, SVG/RIVP), history of heart failure, permanent AFib, IDDM, renal insufficiency</td>
<td>ICM, PHT, history of heart failure, AHT, renal insufficiency</td>
<td>History of type A aortic dissection and replacement of ascending aorta and aortic arch, renal insufficiency, cirrhosis (Child-Pugh A), permanent AFib, status post ICD implantation for ventricular tachycardia</td>
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<td>None</td>
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<td>Fatal cerebral stroke on postoperative day 6</td>
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<td>10 months MR 0 NYHA class I</td>
<td>4 months MR trace NYHA class II</td>
<td>22 months MR 1 NYHA class I</td>
<td>8 months MR 0 NYHA class II</td>
<td>n/a</td>
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without damage to the leaflets. Additional cooled radiofrequency MAZE procedure was performed for atrial fibrillation. The patient made an uneventful recovery and was discharged on day 8 after surgery in sinus rhythm. Follow-up echocardiography 10 months after surgical MVR demonstrated no residual MR and sustained sinus rhythm.

### 3.3. Case report #3

A 57-year-old male patient was admitted with ischemic cardiomyopathy and markedly reduced left-ventricular function. Transthoracic echocardiography revealed severe MR due to bileaflet prolapse. The patient underwent transcatheter MVR with placement of one clip and initial successful reduction to MR grade 1, and a second clipping procedure 11 months later for recurrent MR 3. As the second procedure did not achieve relevant reduction of MR, surgery was planned. Intra-operatively, detachment of one clip from the PML with adherence to the AML only became apparent. Clip removal resulted in a 5 × 10 mm AML defect as well as a P2/P3 cleft, which was repaired by a Cardionyl 5/0 running suture. Three and two polytetrafluoroethylene (PTFE) Goretex neochords were used to correct AML and PML prolapse, respectively. A 28-mm IMR ring (Edwards Lifesciences, Inc.) was implanted and repaired completed by a commissural P3/A3 Alfieri stitch.

In addition, aortic valve replacement was performed for severe regurgitation of the sclerotic aortic valve, using a Solo Freedom 23-mm valve (Sorin Biomedica Cardio, Saluggia, Italy) and tricuspid valve repair due to severe tricuspid regurgitation using a 32-mm Edwards Classic (Edwards Lifesciences, Inc.) annuloplasty ring on the fibrillating heart.

The patient was discharged to a rehabilitation facility 9 days after surgery and is in good condition at the latest follow-up 4 months postoperatively, with no residual MR or TR as well as adequate function of the aortic-valve prosthesis.

### 3.4. Case report #4

A 71-year-old female patient with severe functional MR due to annular dilatation and restrictive PML was referred for MiraClip™ treatment. Grasping of both AML and PML margins was technically demanding, but eventually successful. However, when closing the clip, rupture of an AML chord occurred, presumably due to calcification of chords and papillary muscle heads. As further attempts at clip placement did not seem promising, the clip was retrieved and the procedure terminated. On the following day, the patient underwent elective surgical MVR. Intra-operatively, a primary chord of the A2 segment proved to be ruptured. In addition, a P2/P3 cleft was apparent, likely caused by the attempted clip placement. To restore valve function, a PTFE Goretex neochord (W.L. Gore & Associates, Inc., AZ, USA) was inserted to re-attach the A2 segment. The PML defect was repaired with a 5/0 Cardionyl (Peters Surgical, Bobigny Cedex, France) running suture. Repair was completed by a coaptation stitch between P3 and A3 segments and annuloplasty using a 28-mm Physio ring (Edwards Lifesciences, Inc.). Concomitant tricuspid regurgitation was corrected by placement of a 36-mm Edwards Classic tricuspid annuloplasty ring (Edwards Lifesciences, Inc.). Postoperative echocardiography confirmed adequate valve function with trace residual MR and no residual tricuspid regurgitation at discharge.

Three months after surgery, the patient was re-admitted with recurring severe MR most likely due to dehiscence of the annuloplasty ring, as suspected from transthoracic echocardiography. As the patient was highly symptomatic, the decision was made for repeat surgery. Intra-operatively, the annuloplasty ring was found detached from the posterior mitral annulus with two clefts near the base of P2. Because of marked valve tissue degeneration and to ensure adequate valve function, valve replacement using a 31-mm Edwards Perimount prosthesis (Edwards Lifesciences, Inc.) was performed. The further intra- and postoperative course was uneventful with discharge 10 days after surgery. The patient is alive and well up to the latest follow-up 22 months after MV replacement.

### 3.5. Case report #5

A 75-year-old female patient was admitted with ischemic cardiomyopathy and severely compromised left-ventricular function after suffering recurrent episodes of acute heart failure. Severe functional MR due to annular dilatation was demonstrated on preoperative echocardiography. Interventional treatment was performed placing two clips, which failed to reduce MR. Intraprocedural TEE suggested injury of the AML. Decision was made for immediate conversion to surgical MVR in the same hybrid operating room. Intra-operatively, the clips were found attached to the P3 segment only. There was a large cleft in A2/A3 segments, presumably caused by clip tear out. Due to this finding, repair was deemed impossible and valve replacement using a 31-mm Edwards Perimount Plus prosthesis (Edwards Lifesciences, Inc.) with concomitant exclusion of the left-atrial appendage was performed. Persistent total atrio-ventricular conduction block necessitated pacemaker implantation on postoperative day 3. The patient was discharged on day 10 with adequate prosthesis function and is in good condition 8 months after surgery.

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**Fig. 2.** Intraoperative findings (case #5). The patient underwent surgical MVR for recurrent MR 2 months after MitraClip™ therapy. In this case, the clip was removed without difficulty and successful repair performed.
To date, most available reports on MV surgery after MitraClip™ therapy stem from the EVEREST experience in low-risk patients. Feasibility of surgical MVR after failed trans-catheter MVR with the MitraClip™ device in elective patients with mostly degenerative MV disease was reported for the majority of patients in these studies. However, as of yet there are no reports on the effect of MitraClip™ therapy on secondary MV surgery in high-risk patients with predominantly functional MR.

Dang and colleagues reported on six patients from the early EVEREST I study experience in whom surgery became necessary after prior trans-catheter MVR [6]. All patients had myxomatous disease with preserved left-ventricular function. Reasons for surgical revision were malpositioning with subsequent partial detachment of clips in four patients and insufficient reduction of MR in two cases. Secondary surgical MVR was successful in five patients, while intended MV replacement was performed in one case. In their experience, removal of clips was unproblematic and did not influence the initial surgical strategy.

In another series, Rogers and colleagues report on four cases of late surgical MVR after prior MitraClip™ therapy [12]. Recurrent MR after interventional treatment necessitated surgical revision, which was successfully carried out after up to 5 years after trans-catheter MVR. Although the clips were described as heavily encapsulated in fibrous tissue in most patients, removal was possible without extensive leaflet damage, allowing for valve repair in all four cases.

In the largest series to date, Argenziano and colleagues recently reported outcomes of 32 patients (19 patients from the EVEREST I trial and 13 EVEREST II roll-in patients) undergoing surgery after previous MitraClip treatment [13]. Of these, 23 patients had at least one clip implanted; the remaining nine patients had not received an implant. The optimal surgical strategy had been assessed retrospectively (EVEREST I) or prospectively (EVEREST II), according to trial requirements. Surgical revision was carried out as initially planned before trans-catheter MVR in 27 of 31 patients (87%). Overall, 67% (21 of 32) of patients had MVR and 33% (11 of 32) had MV replacement. Of the latter, six replacements had been planned preoperatively, four patients were converted from repair to replacement, and, in one patient, the initial surgical strategy was unknown. Only in two patients, damage to MV leaflets was reported, in one case explicitly related to the clip procedure. The authors conclude that surgical options as planned before clip procedures are preserved in the majority of cases.

In contrast to previous series, we report our experience of secondary MV surgery in high-risk patients. In three cases, secondary surgical MVR was feasible without a major change in the surgical strategy deemed optimal before trans-catheter MVR: in case #1, trans-catheter MVR had been aborted before clip placement and therefore did not influence secondary MV surgery and in case #2, clip removal was unproblematic. In case #3, clip removal resulted in a small AML defect as well as a PML cleft, which was however easily repaired by a running suture.

In three other cases, however (cases #4, #5, and #6), prior trans-catheter MVR influenced secondary MV surgery. In case #4, chordal rupture and injury of the PML necessitated more complex surgical MVR with implantation of an AML neochord
and PML cleft repair, as opposed to annuloplasty alone. Although valve repair was initially successful, during the further follow-up, MV replacement became necessary for recurrent severe MR due to partial ring detachment from a calcified posterior annulus but unrelated to prior clip therapy. In case #5, a large defect in segments A2/A3 precluded valve repair and led to MV replacement, where annuloplasty had been the initially proposed surgical strategy. In case #6 a large PML cleft made valve repair impossible and led to prosthetic valve replacement.

5. Conclusions

In our experience, the MitraClip™ system is a promising additional tool for the treatment of high-risk patients with limited surgical options. The favorable risk–benefit ratio of MitraClip™ treatment with low periprocedural complication rates underscores its adequacy for high-risk patients in whom even a result considered suboptimal from a surgeon’s point of view may offer substantial clinical improvement. However, it is our firm belief that trans-catheter MV repair should remain restricted to high-risk patients, especially as secondary surgical MV may not always be feasible after prior MitraClip™ treatment as demonstrated in our series. Furthermore, MV repair may require more complex techniques due to prior MitraClip™ treatment and impact on long-term durability of surgical MV in these patients is unknown. Given the rising caseload of transcatheter MV therapy across European centers, it can be anticipated that surgeons will be confronted with increasing numbers of patients with recurrent MR after MitraClip™ treatment or after failed procedures. In an ideal setting, potential candidates for trans-catheter MV repair should be assessed in an interdisciplinary conference of cardiologists and cardiac surgeons to determine the optimal treatment strategy for each patient — surgical or interventional.

References


Editorial comment

Surgery after MitraClip therapy: you can’t win them all

Keywords: Mitral regurgitation; Mitral repair; Catheterization intervention

MitraClip therapy is a percutaneous mitral valve (MV) repair procedure that has been applied to both degenerative and functional mitral regurgitation (MR) pathologies. It is modeled after the surgical Alfieri technique, which involves generation of a double-orifice valve by approximating the mid-anterior and posterior leaflets with suture, and, in the case of the MitraClip, a cobalt—chromium trans-catheter-delivered clip.

Worldwide experience with the MitraClip now exceeds 2000 patient implants, and this therapy has been studied in a