REVIEW ARTICLE

Percutaneous and Surgical Treatment of Mitral Valve Regurgitation

Joerg Seeburger, Hugo A. Katus, Sven T. Pleger, Ulrike Krumdsdorf, Friedrich-Wilhelm Mohr, Raffi Bekeredjian

SUMMARY

Background: Mitral valve regurgitation is the second most common clinically relevant valvular heart disease in adults, with an incidence of about 2% to 3% per year. Surgical mitral valve repair is the treatment of choice. Recent years have seen major advances in minimally invasive mitral valve surgery. Several new catheter-based techniques are now being clinically evaluated, including percutaneous endovascular mitral valve repair with a mitral clip.

Method: This review is based on a selective review of the literature and on the authors' clinical experience.

Results: Minimally invasive and reconstructive techniques for mitral valve surgery have come into more common use in recent years. In Germany, more than 50% of all mitral valve defects are now treated with a valve-preserving repair procedure. At the same time, percutaneous techniques have been developed that enable reduction of mitral regurgitation in the cardiac catheterization laboratory, without surgery. The implantation of a mitral clip is the sole currently approved technique of this type. In a recently published, randomized comparative clinical trial (EVEREST II), it was found to be safer, but less effective, than surgery.

Conclusion: Mitral valve surgery remains the treatment of choice for severe mitral regurgitation. For patients at high risk from surgery, and particularly those with severe heart failure, the implantation of a mitral clip is a safe and feasible treatment option.

► **Cite this as:**

Seeburger J, Katus HA, Pleger ST, Krumdsdorf U, Mohr FW, Bekeredjian R: Percutaneous and surgical treatment of mitral valve regurgitation. *Dtsch Arztebl Int* 2011; 108(48): 816–21. DOI: 10.3238/arztebl.2011.0816

Diseases of the mitral valve are the second-most common clinically significant form of valvular defect in adults. Mitral valve regurgitation in particular occurs with increasing frequency as part of degenerative changes in the course of aging. The annual incidence of degenerative mitral valve disease in industrialized nations is estimated at around 2% to 3% (1, 2), although there are no data as to the relative percentages of symptomatic and asymptomatic patients with mitral valve regurgitation. In addition to degenerative changes, other causes of clinically significant mitral valve regurgitation include cardiac ischemia, spontaneous detachment of the chordae tendineae, and widening of the mitral valve annulus in the setting of a dilated left ventricle with severely restricted left ventricular pump function (2, 3).

Severe insufficiency of the mitral valve leads to exertional dyspnea and may be accompanied by left atrial dilation, atrial fibrillation, and raised pulmonary arterial pressure. Medication alone in symptomatic mitral valve disease typically does not result in adequate or lasting improvement of clinical symptoms, and in patients with high-grade mitral valve regurgitation it is associated with an annual mortality of about 6% to 7%. Data on the disease course with purely conservative treatment exist mainly in relation to asymptomatic patients with high-grade mitral regurgitation. In this group, during a 5-year study period a cardiac-related mortality of 22% was seen and 51% of patients required mitral valve surgery (4).

The treatment of choice is surgical reconstruction of the mitral valve, for which a minimally invasive technique may be used (5–7). The percentage of reconstructions among mitral valve operations in Germany has markedly increased and they are now performed more frequently than mitral valve replacement operations (8). The recommendations relating to mitral valve surgery are subdivided according to patient symptoms (Table) (9). Unfortunately no data exist as to how many patients with mitral valve regurgitation actually have an indication for surgery. Likewise, there are no large, randomized, controlled studies on the operative treatment of mitral regurgitation.

In recent years, however, new interventional techniques have been developed in the cardiac catheterization

Abteilung für Herzchirurgie, Herzzentrum Universität Leipzig: Dr. med. Seeburger, Prof. Dr. med. Mohr

Abteilung für Kardiologie, Angiologie und Pneumologie; Universitätsklinik Heidelberg: Prof. Dr. med. Katus, Dr. med. Pleger, Dr. med. Krumdsdorf, Prof. Dr. med. Bekeredjian

laboratory that result in a reduction in mitral valve regurgitation. These techniques are based either on direct reconstruction of the mitral valve or on modification of the mitral valve annulus. The mitral clip technique in particular is becoming increasingly well regarded among interventional cardiologists.

This review presents the surgical developments of recent years. In addition, the still relatively young technique of percutaneous clip implantation as a nonsurgical therapeutic option is explained and discussed along with the limited literature that exists to date on this technique. Our account is based on a selective literature search on treatment for mitral valve regurgitation in PubMed and on the personal experiences and data of the authors.

Treatment for mitral valve regurgitation

The treatment of choice for mitral valve regurgitation is surgery (3, 10–12). This is to date the only proven therapeutic option to prevent the development of heart failure and hence significantly reduced survival (13). The surgical options available are replacement of the mitral valve with a biological or mechanical prosthetic valve, or reconstruction of the valve. In recent years the minimally invasive procedure via a right lateral mini-thoracotomy with femoral catheterization (i.e., the heart–lung machine is connected via the femoral vessels) has become established (*Figure 1*) (5). The safety and efficacy of this operation have been shown in large series (5, 14–16). Depending on the surgeon's experience, minimally invasive reconstruction rates for patients with mitral regurgitation as their main disease are over 80%, and for isolated mitral regurgitation they are as high as 97% (5, 17). Long-term survival, at over 82% at 5 years (Kaplan–Meier analysis), is comparable to that of the normal population. These patients also have very low reoperation rates, with nearly 97% success at 5 years (14, 18). In one series the intraoperative rate of conversion to the conservative operation was very low, 0.3% (5). Other large series confirm unequivocally the quality and reproducibility of this operation (15, 19, 20).

To achieve these excellent results, especially in relation to both the high reconstruction rate and the quality of the reconstruction, intraoperative visualization of the mitral valve via a direct perpendicular view at the level of the mitral valve is essential. Femoral catheterization also improves the intraoperative overview and has contributed to this development. In addition, the advantages of this method are the very small wound surface area, rapid recovery, reduced postoperative pain, and better cosmetic result (*Figure 1*) (21).

Based on these results, (minimally invasive) mitral valve reconstruction is the current gold standard in “modern” operative treatment for mitral regurgitation (5, 14, 15, 19). This is true in particular not just for patients undergoing primary operations, but also for those undergoing reoperation, those with special pathologies such as hypertrophic obstructive cardiomyopathy, and older patients (22–25).

TABLE

Guidelines of the German Cardiac Society on the indication for surgery in patients with severe chronic mitral valve regurgitation

Patients	Symptoms	Recommendation grade	Evidence level
Symptomatic patients	Ejection fraction $\geq 30\%$	I	B
	Ejection fraction $< 30\%$, if reconstructable	Ila	C
Asymptomatic patients	Ejection fraction $< 60\%$ and/or end-systolic left ventricular diameter > 45 mm	I	B
	Paroxysmal or newly occurring persistent atrial fibrillation	Ila	C
	Systolic pulmonary artery pressure at rest > 50 mm Hg	Ila	C
	Ejection fraction $> 60\%$ and end-systolic diameter > 45 mm, but no contractile reserve during exercise	Ila	C

Figure 1:

Intraoperative setup for the minimally invasive mitral valve operation with right lateral mini-thoracotomy (upper) and femoral catheterization (middle) for extracorporeal circulation; cosmetic result (lower)

As we mentioned at the beginning, in the past 5 to 10 years several “alternative” procedures were developed such as percutaneous implantation of a clip on the mitral leaflets, implantation of an annuloplasty device in the coronary sinus, or transapical implantation of individual chordae tendineae to treat mitral regurgitation (6, e1–e5). Implantation of a mitral valve clip in particular shows—with correct patient selection—the potential to fill an important niche in the treatment of mitral valve regurgitation in the long term. The concept of treating mitral valve regurgitation percutaneously is among the more recent techniques in invasive cardiology. Despite the excellent results of surgical procedures, there continues to be a great deal of interest in the development of interventional procedures in the cath lab, which would allow a surgical operation, with its use of the heart–lung machine and perhaps general anesthesia, to be avoided or at least delayed. An interventional procedure of this kind should, in our opinion, be evaluated especially for patients with markedly raised surgical risk and/or markedly reduced ejection fraction, if the valvular pathology and morphology are suited to the procedure. Only one system is currently commercially available, a clip placed on the two mitral leaflets in a procedure adapted from the Alfieri operative reconstruction method. The concept developed by the Italian heart surgeon Alfieri is based on suturing together the middle segment of the two mitral leaflets (Alfieri stitch), making a “double orifice” that results in a significant reduction in the mitral regurgitation (e6). The mitral clip imitates this surgical technique and can be applied percutaneously.

In the initial multicenter approval study (EVEREST I) this technique was used in over 100 patients who would also have been candidates for surgical mitral valve reconstruction (e1). This study showed a low periprocedural risk (hemorrhage, stroke, pericardial effusion, emergency operation, 30-day mortality, clip embolization) and an initial success rate of 74%. The successor study (EVEREST II) had 279 patients randomized into a mitral clip arm and a surgical arm (in a ratio of 2:1) and compared in particular safety and therapeutic outcome (e7). This study showed that periprocedural safety was significantly superior with the mitral clip (severe complications—including administration of more than one red blood cell concentrate transfusion—in the first 30 days: 15% for clip patients, 48% for surgical patients; $p < 0.001$) and clinical effectiveness after 12 months was significantly higher in the surgical arm (73% compared with 55% in the mitral clip arm; $p = 0.007$) (e7). This study defined the primary end point as the combination of absence of death, absence of need for a mitral valve operation or repeat operation, and absence of severe mitral valve regurgitation (3+ or 4+) after 12 months. At the end of 12 months patients’ quality of life was significantly improved in both groups (no difference between groups), but with a statistically significant advantage in terms of symptoms of heart failure in the mitral clip group. The EVEREST II data also provide indications that even a

Figure 2: Mitral clip implantation: transesophageal echocardiography visualizes capture and fixation of the mitral leaflets. Upper left: the open clip is seen in the left ventricle. Upper right: the open clip is pulled back towards the mitral leaflets. Lower left: having grasped the leaflets, the clip is closed. Lower right: schematic representation of endovascular mitral valve reconstruction (view of the mitral valve from the left atrium). LA, left atrium; LV, left ventricle; AV, aortic valve; arrow, clip arm

small reduction of mitral regurgitation can improve the patient's strength and clinical condition. A prospective study of 51 high-risk patients (defined as patients with a logistic EuroSCORE >20% or a Society of Thoracic Surgeons Score >12) also showed high periprocedural safety of the interventional procedure (no hospital mortality, no severe complications) and successful clip implantation in 96% of patients (e8). In Heidelberg and Leipzig, we can confirm this experience in our own patients with severe heart failure. In our opinion, this reflects the applicability of this method in high-risk patients—in these patients, we regard this procedure as appropriate given suitable leaflet morphology.

Technique of percutaneous mitral clip implantation

Because continuous transesophageal echocardiography (TEE) is needed to guide this procedure, mitral clip implantation is carried out with the patient under general anesthesia. Once anesthesia has been induced, venous access via the right femoral vein is chosen. After puncture, the vein is probed with a wire and a trans-septal puncture catheter advanced to the heart. Via a puncture in the atrial septum, a catheter can be introduced from the right into the left atrium. After changing to a harder wire, a 24-French guide catheter with a dilator is placed

in the left atrium. The dilator and wire are removed and a catheter with the mitral clip is advanced into the left atrium. There, the mitral clip is first aligned over the site of maximum regurgitation, then introduced in the open position into the left ventricle. By pulling the clip back, the mitral leaflets can be caught and fixed with the clip arms. Closing the clip fixes the clip further and the leaflets are pulled together (Figure 2). Immediately after the clip is closed, TEE can be used to check and quantify the reduction of the regurgitation, and to rule out a potential mitral valve stenosis, which can occur due to the mitral clip. In some patients with very wide regurgitation surfaces, placement of a second clip may be necessary. If no significant reduction in regurgitation is visualized after clip implantation, the clip can be removed. If the result is good, the catheter is disconnected from the clip and the clip remains on the mitral valve.

Future perspective

We believe the percutaneous interventional treatments for mitral valve disease should be carried out in patients at high risk from surgery. This means in particular patients with an ejection fraction below 30% and those with a logistic EuroSCORE above 20%.

The short- and long-term outcome of catheter-based percutaneous reconstruction of the mitral valve needs

KEY MESSAGES

- The treatment of choice for mitral valve regurgitation is surgical valvular reconstruction. Because of its very good results, the minimally invasive procedure is becoming more widely accepted.
- The more recent, interventional procedure of percutaneous implantation of a mitral clip offers the possibility of achieving significant reduction of mitral valve regurgitation in high-risk patients.
- The further development of surgical and percutaneous treatment of the mitral valve must be done by means of close collaboration between cardiologists and heart surgeons.

to be demonstrated in prospective controlled clinical studies. Existing data indicate that for patients with markedly reduced left ventricular pump function, mitral clip implantation can be another tool in the treatment of heart failure. To date, however, no long-term results of the mitral clip have been reported.

Other techniques for interventional treatment of mitral regurgitation are undergoing clinical trials, e.g., left ventricular annuloplasty (6, e1–e5). It is important that these continuing developments are pursued in intensive, comprehensive collaboration between interventional cardiologists and heart surgeons. We believe that intensive cooperation is essential if continued optimal patient care is to be guaranteed.

Conflict of interest statement

Professor Katus has received funding for an initiated research project from Abbott for the Biobank.

Dr. Pleger has had attendance fees reimbursed by Abbott for TCT, Washington.

Professor Mohr has received third-party funding carrying out commissioned clinical studies as part of the Sapien and Partner studies.

Professor Bekerredjian has received payment from Abbott for the preparation of scientific educational events.

Dr. Seeburger and Dr. Krumdordf declare that no conflict of interest exists.

Manuscript received on 26 January 2011, revised version accepted on 18 April 2011.

Translated from the original German by Kersti Wagstaff, MA.

REFERENCES

1. Freed LA, et al.: Prevalence and clinical outcome of mitral-valve prolapse. *N Engl J Med* 1999; 341: 1–7.
2. Devereux RB, et al.: Prevalence and correlates of mitral valve prolapse in a population-based sample of American Indians: the Strong Heart Study. *Am J Med* 2001; 111: 679–85.
3. Adams DH, Rosenhek R, Falk V: Degenerative mitral valve regurgitation: best practice revolution. *Eur Heart J* 2010; 31: 1958–66.
4. Enriquez-Sarano M, et al.: Quantitative determinants of the outcome of asymptomatic mitral regurgitation. *N Engl J Med* 2005; 352: 875–83.
5. Seeburger J, et al.: Minimal invasive mitral valve repair for mitral regurgitation: results of 1339 consecutive patients. *Eur J Cardiothorac Surg* 2008; 34: 760–5.
6. Seeburger J, Borger MA, and Mohr FW: EHJ Transcatheter mitral valve repair: a high mountain to climb. *European Heart Journal* 2010; 12: 46–51.
7. Enriquez-Sarano M, Sundt TM 3rd.: Early surgery is recommended for mitral regurgitation. *Circulation* 2010; 121: 804–11; discussion 812.
8. Gummert JF, et al.: Cardiac surgery in Germany during 2008. A report on behalf of the German Society for Thoracic and Cardiovascular Surgery. *Thorac Cardiovasc Surg* 2009; 57: 315–23.
9. Daniel WG, et al.: Aortic stenosis. *Clin Res Cardiol* 2006; 95: 620–41.
10. Braunberger E, et al.: Very long-term results (more than 20 years) of valve repair with carpentier's techniques in nonrheumatic mitral valve insufficiency. *Circulation* 2001; 104 (Suppl 1): 8–11.
11. Mohr D, et al.: Very long-term survival and durability of mitral valve repair for mitral valve prolapse. *Circulation* 2001; 104 (Suppl 1): 1–7.
12. Bonow RO, et al.: ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to revise the 1998 Guidelines for the Management of Patients With Valvular Heart Disease): developed in collaboration with the Society of Cardiovascular Anesthesiologists: endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. *Circulation* 2006; 114: 84–231.
13. Ling LH, et al.: Clinical outcome of mitral regurgitation due to flail leaflet. *N Engl J Med* 1996; 335: 1417–23.
14. Seeburger J, et al.: Comparison of outcomes of minimally invasive mitral valve surgery for posterior, anterior and bileaflet prolapse. *Eur J Cardiothorac Surg* 2009; 36: 532–8.
15. Modi P, et al.: Minimally invasive video-assisted mitral valve surgery: a 12-year, 2-center experience in 1178 patients. *J Thorac Cardiovasc Surg* 2009; 137: 1481–7.
16. Woo YJ, Seeburger J, Mohr FW: Minimally invasive valve surgery. *Semin Thorac Cardiovasc Surg* 2007; 19: 289–98.
17. Seeburger J, et al.: Chordae replacement versus resection for repair of isolated posterior mitral leaflet prolapse: à égalité. *Ann Thorac Surg* 2009; 87: 1715–20.
18. David TE, et al.: A comparison of outcomes of mitral valve repair for degenerative disease with posterior, anterior, and bileaflet prolapse. *J Thorac Cardiovasc Surg* 2005; 130: 1242–9.
19. McClure RS, et al.: Early and late outcomes in minimally invasive mitral valve repair: an eleven-year experience in 707 patients. *J Thorac Cardiovasc Surg* 2009; 137: 70–5.
20. Casselman FP, et al.: From classical sternotomy to truly endoscopic mitral valve surgery: a step by step procedure. *Heart Lung Circ* 2003; 12: 172–7.
21. Modi P, Hassan A, Chitwood WR Jr.: Minimally invasive mitral valve surgery: a systematic review and meta-analysis. *Eur J Cardiothorac Surg* 2008; 34: 943–52.
22. Meyer SR, et al.: Reoperative mitral valve surgery by the port access minithoracotomy approach is safe and effective. *Ann Thorac Surg* 2009; 87: 1426–30.
23. Casselman FP, et al.: Endoscopic mitral and tricuspid valve surgery after previous cardiac surgery. *Circulation* 2007; 116 (Suppl 11): 270–5.

24. Seeburger J, et al.: A new concept for correction of systolic anterior motion and mitral valve regurgitation in patients with hypertrophic obstructive cardiomyopathy. *J Thorac Cardiovasc Surg* 2010; 140: 481–3.
25. Chikwe J, et al.: A propensity score-adjusted retrospective comparison of early and mid-term results of mitral valve repair versus replacement in octogenarians. *Eur Heart J* 2011; 32: 618–26.

Corresponding author

Prof. Dr. med. Raffi Bekereditian
Abteilung für Kardiologie, Angiologie und Pneumologie
Universitätsklinik Heidelberg
Im Neuenheimer Feld 410
69120 Heidelberg, Germany
raffi.bekereditian@med.uni-heidelberg.de

For eReferences please refer to:
www.aerzteblatt-international.de/ref4811

REVIEW ARTICLE

Percutaneous and Surgical Treatment of Mitral Valve Regurgitation

Joerg Seeburger, Hugo A. Katus, Sven T. Pleger, Ulrike Krumdorst, Friedrich-Wilhelm Mohr, Raffi Bekeredjian

eReferences

- e1. Feldman T, et al.: Percutaneous mitral repair with the MitraClip system: safety and midterm durability in the initial EVEREST (Endovascular Valve Edge-to-Edge REpair Study) cohort. *J Am Coll Cardiol* 2009; 54(8): 686–94.
- e2. Feldman T, et al.: Percutaneous mitral valve repair using the edge-to-edge technique: six-month results of the EVEREST Phase I Clinical Trial. *J Am Coll Cardiol* 2005; 46(11): 2134–40.
- e3. Schofer J, et al.: Percutaneous mitral annuloplasty for functional mitral regurgitation: results of the CARILLON mitral annuloplasty device european union study. *Circulation* 2009; 120(4): 326–33.
- e4. Bajona P, et al.: Beating-heart, off-pump mitral valve repair by implantation of artificial chordae tendineae: an acute in vivo animal study. *J Thorac Cardiovasc Surg* 2009; 137(1): 188–93.
- e5. Seeburger J, Borger MA, Tschernich H, et al.: Transapical beating heart mitral valve repair. *Circulation: Cardiovascular Interventions*. 2010; 3: 611–2.
- e6. Maisano F, et al.: The edge-to-edge technique: a simplified method to correct mitral insufficiency. *Eur J Cardiothorac Surg* 1998; 13(3): 240–5; discussion 245–6.
- e7. Feldman T, et al.: Percutaneous repair or surgery for mitral regurgitation. *N Engl J Med* 2011; 364: 1395–406.
- e8. Franzen O, et al.: Acute outcomes of MitraClip therapy for mitral regurgitation in high-surgical-risk patients: emphasis on adverse valve morphology and severe left ventricular dysfunction. *Eur Heart J* 2010; 31(11): 1373–81.