EXPERT REVIEWS

# Current surgical management of mitral regurgitation

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From Walton Lillehei, who performed the first successful open mitral valve surgery in 1956, until the advent of robotic surgery in the 21st Century, only 50 years have passed. The introduction of the first heart valve prosthesis, in 1960, was the next major step forward. However, correction of mitral disease by valvuloplasty results in better survival and ventricular performance than mitral valve replacement. However, the European Heart Survey demonstrated that only 40% of the valves are repaired. The standard procedures (Carpentier's techniques and Alfieri's edge-to-edge suture) are the surgical basis for the new technical approaches. Minimally invasive surgery led to the development of video-assisted and robotic surgery and interventional cardiology is already making the first steps on endovascular procedures, using the classical concepts in highly differentiated approaches. Correction of mitral regurgitation is a complex field that is still growing, whereas classic surgery is still under debate as the new era arises.

**Keywords:** less invasive surgery • mitral valve • percutaneous valve intervention • regurgitation • robotic surgery • valve replacement • valvuloplasty

## Historical notes

Mitral valve (MV) surgery was first suggested by Samways in 1898 as a treatment for mitral stenosis, then the most prevalent mitral pathology [1]. In 1902, Sir Lauder Burton initiated experiments on diseased valves of cadavers and on normal mitral valves of dead cats using a transventricular tenotomy knife [2]. Cushing and Branchused a modification of the Burton procedure and attempted surgery on living dogs, but the experiment resulted in the animals' deaths due to respiratory failure [3]. Finally, in May 1923, Elliot Cutler and his associates, at Peter Brigham Hospital in Boston (MA, USA), performed the first successful mitral valvulotomy in an 11-year old girl who survived 4.5 years after surgery [4,5]. Unfortunately, this was the only successful attempt, with six other patient mortalities.

Bailey from Philadelphia (USA) Harke from Boston (MA, USA) and Sir Brock from England (UK) started performing programmed surgery on stenotic mitral valves in the 1940s and further refined the technique, launching closed mitral valvulotomy [6], which was used extensively from the 1950s to the 1980s, mostly using a mechanical transventricular dilator developed by Andrew Logan from Edinburgh [7].

In 1910, Alexis Carrel tried to develop an operation to correct mitral regurgitation without opening the heart, which consisted in creating a slight stenosis of the basal portion of the left ventricle (LV) through a partial cuneiform resection of the ventricle wall of a dog [8]. Later, Murray and coworkers used an ingenious method of transventricular placement of autologous tissue to occlude the mitral valve during the systole [9]. Ellison and coworkers and others proposed and developed a technique of narrowing the mitral ring, from outside the heart [10]. Finally, in 1958, Davila and his associates published a paper where they describe how to place a circumferential suture around the atrioventricular groove [11].

However, it was the invention of the heart–lung machine by Gibbon in 1953 that led to the development of open mitral surgery and allowed a further advance in the understanding of the importance of mitral insufficiency (mitral regurgitation was then commonly believed to be a less serious lesion and well tolerated) [12].

Extracorporeal circulation permitted Walton Lillehei to perform the first successful open correction of a mitral insufficiency in 1956 at the University of Minnesota. Subsequently, a number of new approaches appeared and

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brought the repair of the insufficient mitral valve into reality. Since then, hundreds of thousands of mitral valve surgeries have been performed [13].

A further major advance was the introduction of the prosthetic heart valve by Starr in the early 1960s [14]. Mitral valve replacement has yielded excellent results, but mitral valvuloplasty lately gradually imposed itself as a preferable alternative. In the early 1970s, Carpentier [15] and Duran [16] laid the foundations of modern mitral valvuloplasty. Over the past 30 years, many surgeons around the world have adopted these techniques and have been able to repair up to 90% of mitral valves with excellent and durable results [17].

## Mitral valve surgery

Mitral valve surgery has dramatically evolved between the first open annuloplasty performed by Lillehei and the recent and novel endoscopic and robotic procedures [18,19]. It is almost intuitive that repair of the mitral valve has important advantages over replacement, and it is now widely held to be true that the mitral valve should be repaired whenever possible. Indeed, most large surgical centers now elect to repair rather than replace the the mitral valves. In our department, we now reconstruct around 88% of insufficient mitral valves (Figure 1) with a mortality of 0.8% for valvuloplasty and of 1.3% for replacement, which is statistically significant for this group of patients, with a higher incidence of postoperative use of inotropics. Countless series were published which proved that the advantages of mitral valvuloplasty parallel the disadvantages of prosthetic valve replacement. Valvuloplasty does not require lifelong anticoagulation, by comparison with mechanical prostheses, especially in patients who have no other reason, such as atrial fibrillation, for anticoagulation. And it is essential to keep in mind that the incidence of thromboembolic complications of mechanical prostheses and of degradation of bioprostheses, another important complication of valve replacement, is more frequent in the mitral than in the aortic position.

Several reports show that survival is longer after valve repair (Table 1). Moss and coworkers were able to calculate the probability of survival with a hazard ratio for death of 0.46 when compared with MV replacement patients [20]. Enriquez-Sarano and colleagues [21] from the Mayo Clinic, showed that late survival at 5 and 10 years was, respectively, 85 ± 3% and 69 ± 6% after valve repair; similar to the expected survival, and 77 ± 3% and 58 ± 5% after valve replacement ($p < 0.0001$) (Figure 2). Valve repair was an independent predictor of higher postoperative ejection fraction.

One of the reasons why valvuloplasty has better results than valve replacement might be that preservation of the subvalvular apparatus appears to be fundamental for improvement of LV function, especially in the cases of severe dysfunction [22]. Lee and coworkers, from Cambridge (UK) retrospectively studied 612 consecutive patients who underwent MV repair or replacement [23]. Repair was performed in 226 patients, 68 had replacement with subvalvular preservation and 318 had replacement without subvalvular preservation. The authors concluded that MV repair is superior to replacement. If repair was not feasible, preservation of the subvalvular apparatus improved surgical outcome.

MV reconstruction is based on several techniques, of which, the most important are annuloplasty, with or without prosthetic ring, leaflet resection and intervention on the chordae tendinae (all of these developed by Carpentier and together known as the French Correction) and the edge-to-edge correction (the Alfieri technique). Classically, the median sternotomy approach and conventional cardiopulmonary bypass were used. The recent appearance of minimally invasive, endoscopic and robotic-assisted surgeries broadened the therapeutic alternatives. Chitwood postulated that complex mitral repair surgery can be performed endoscopically, using either pure video-assistance or a surgical robot, with results that are similar to those of traditional operations [24]. Currently, several percutaneous approaches to repair the MV are being developed, which use either an annuloplasty ring via the coronary sinus or a modified Alfieri repair.

In the remainder of this text, we shall review the indications, techniques and results of mitral valvuloplasty for the treatment of mitral regurgitation

## Pathology & physiopathology

The 50 years of mitral valve surgery development were marked by the appearance of a tremendous number of new techniques and materials, turning MV reconstruction into a new area of expertise, involving high medical and surgical skills. The choice of the technique that should be used in a particular case is based on the pathophysiology of the regurgitation.

Mitral regurgitation is the result of several types of pathology: congenital, rheumatic, ischemic and degenerative. Congenital mitral regurgitation is relatively rare and requires a special approach and technique. It will not be discussed further in this work. Rheumatic heart disease was predominant in the early decades of cardiac surgery but has almost been eradicated in the developed world, although rheumatic patients from the past still come regularly to our operating theatres. This is still a prevalent disease in the developing world [25].

By contrast, degenerative and ischemic mitral regurgitation appear to be on the increase, fuelled by the ageing of the population.

Mitral regurgitation of whatever cause initiates a vicious circle of atrial and ventricular dilatation, which further distorts the valve mechanism and increases regurgitation. On the other hand, end-stage cardiomyopathy causes mitral annular dilatation and/or papillary muscle dysfunction, leading to MV regurgitation. Increasing volume overload of the dilated LV leads to progression of annular dilatation and worsening of MV regurgitation. It is believed that interruption of this vicious circle, by means of mitral repair, may result in functional and clinical improvement of heart failure [26].

**Table 1. Immediate and long-term results of repair versus replacement for mitral regurgitation.**

| Author (year) | n | | Hospital mortality | | Long-term survival | | Ref. |
|---|---|---|---|---|---|---|---|
| | MVP | MVR | MVP (%) | MVR (%) | MVP (%) | MVR (%) | |
| Antunes *et al.* (1992) | 241 | 386 | 3.3 | 7.8 | 5 years: 90 | 5 years: 76 | [36] |
| Sarrano *et al.* (1995) | 195 | 214 | 2.6 | 10.3 | 10 years: 69 | 10 years: 58 | [21] |
| Braunberger *et al.* (2001) | 162 | – | 1.9 | – | 20 years: 48 | – | [48] |
| Jokinen *et al.*(2007) | 85 | 99 | 4 | 4 | 5 years: 81 | 5 years: 73 | [75] |

MVP: Mitral valvuloplasty; MVR: Mitral valve replacement.

The pathoanatomy of mitral regurgitation was first classified by Carpentier in 1983 [27], introducing new concepts in mitral valve repair. Chronic mitral regurgitation is usually the result of pathological involvement of most, or all, components of mitral valve apparatus: annulus, leaflets and chordae tendineae. Carpentier's functional classification of mitral regurgitation is based on the opening and closing motions of the mitral leaflets (TABLE 2).

Frequently, more than one mechanism is present (for example, prolapsing valve with annular dilatation), hence the use of several surgical techniques so the normal physiology of the valve can be re-established.

MV insufficiency is usually well-tolerated for several years, during the compensated phase [28]. In the natural history of this disease there is volume overload of the LV with subsequent dilatation and rise of ventricular filling pressures. There is a decrease in the forward flow and an increase in the backpressure, with pulmonary congestion. Ideally, this late phase should be avoided and surgery performed before the appearance of myocardiopathy.

## Indications for surgery

In a study published in 1996, Ling and colleagues, from the Mayo Clinic, showed that in 10 years without correction there is an incidence of heart failure of 63 and 30% mortality, and that survival is strongly improved with surgery [29]. They proposed that surgery should be performed early in the course of the disease. Several other studies confirm these facts, and the American Heart Association/American College of Cardiology and the European Society of Cardiology guidelines for the management for heart valvular disease, published in 2006 [28] and 2007 [30], respectively, advise surgery in all symptomatic patients (NYHA classes II, III and IV) with moderate or severe mitral regurgitation, and in asymptomatic patients with severe mitral regurgitation and mild-to-moderate LV dysfunction and/or end-systolic dimension greater than 40 mm.

A point for debate regarding surgical indication is in the asymptomatic patient with degenerative severe regurgitation with preserved function of the LV. The ultimate goal of the surgery for MV regurgitation is the preservation of ventricular contractility. Therefore, all patients with no symptoms and with a good LV function in whom the likelihood of a successful repair without residual mitral regurgitation is greater than 90% should be operated (Class IIA indications) [28]. The prediction of a successful repair is based on the morphology of the diseased valve and on the surgeon's skills. Surgery is not indicated for asymptomatic patients in whom significant doubt regarding the feasibility of repair exists [28].

Patients with severe LV dysfunction and dilatated cardiomyopathy have an incidence of functional mitral regurgitation of about 40% [31]. This is a group of patients with poor prognosis, even with optimal medical therapy (patients with severe mitral regurgitation and dilatated cardiomyopathy have a 3-year survival of only approximately 35% [32]). Currently, several indicators demonstrate that mitral surgery under this context can be safely performed, with low mortality [33].

## Surgical technique: 'classical approaches'

### *Annuloplasty*

Annuloplasty is performed to reduce the size and restore the shape of the mitral annulus and to stabilize any repair that involves annular and leaflet resection [34]. Dilatation of the mitral annulus essentially affects the posterior leaflet and the comissures, enlarging the mitral orifice mainly in its anteroposterior diameter. Gillinov and colleagues identified 16% of

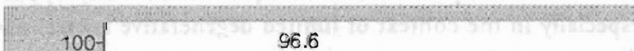


**Figure 1. Feasibility of mitral valvuloplasty according to pathology, in more than 2750 patients in Coimbra, Portugal, during the past 20 years.**

**Table 2. Carpentier's pathophysiological classification of mitral regurgitation.**

| Type | Pathophysiology | Definition |
|---|---|---|
| TYPE I | Normal leaflet motion | The cause for regurgitation is a defect on the leaflet itself (leaflet perforation) or annular dilatation |
| TYPE II | Excessive leaflet motion | This type is essentially constituted by the prolapsing mitral valve. Prolapse happens when, during the systole, the free edge of the leaflet moves above the plane of the annulus without coaptating with the opposite leaflet. Normally, this is due to chordal and/or papillary muscle elongation or rupture |
| TYPE III | Restricted leaflet motion | |
| IIIa | | Thickening of the leaflets and subvalvular apparatus, mostly in rheumatic disease. Restricted movement both in systole and diastole |
| IIIb | | Abnormal movement during systole related to displacement of papillary muscles or chordal shortening. This group appears more in the congenital mitral regurgitation, as with the parachute and the Hammock valves |

the patients with degenerative mitral regurgitation having annular dilatation [35], but this figure can reach 90% in some series [36].

Annuloplasty can be achieved with a suture or with a prosthetic ring. Although the prosthetic ring is the gold standard for remodelling of the mitral annulus, we believe that there is still a place for suture annuloplasty. This may assume two forms, according to the place of the suture: commissural area and mural portion of the annulus [37]. The commissural annuloplasty, developed by Reed [38] and by Wooler [39], tries to reduce the length of the posterior annulus by plication, mostly at the commissural level. The mural (posterior) annuloplasty involves the whole posterior annulus and can be performed with running [36,40] or interrupted sutures [41]. Suture annuloplasty is harder to reproduce and the results difficult to compare. This technique can be safely applied especially in the context of limited degenerative mitral valve disease [37].

Prosthetic ring annuloplasty was established as the procedure of choice for reducing the size and reshaping the form of mitral annulus, and stabilize other repairs. Currently, there are more than 20 types of annuloplasty rings available in the market [42]. For simplicity of analysis, we will divide rings into two categories: complete and incomplete. The latter are based on the principle that only the posterior annulus dilates and that the anterior annulus is unaffected by different pathologies. Recent evidence, however, indicates that this may not be the case [43]

Complete rings can also be categorized into: Rigid rings, typified by the Carpentier-Edwards ring; flexible rings (Duran-Medtronic); and semi-rigid rings. The rigid ring allows for a measured plication of the entire annulus. It essentially immobilizes the posterior leaflet and, theoretically, fixes the MV at the optimal size for the annulus in systole and in a horizontal plane. However, it does not allow movement of the annulus. If, for some reason, the ring is oversized, it can obstruct the outflow tract of the LV by systolic anterior motion of the anterior leaflet.

It had previously been established that the mitral annulus has a 3D movement during the cardiac cycle that stimulated the appearance of flexible rings in an attempt to preserve the physiology of the annulus. However, although hemodynamic parameters and ventricular function appear to be greatly improved in the short-term, using the flexible rings, there is no clear survival advantage of flexible over rigid rings.

Several studies defend one or the other type of ring, but absolute consensus does not exist [42]. Chang and collaborators, from Korea, reviewed 363 patients in order to establish differences in the performance of rigid and flexible rings [44]. They studied hospital and long-term survival, LV function, recurrence of significant mitral regurgitation, reoperation and infective endocarditis and did not find any statistical difference between the two groups. Spoor *et al.* found that patients with congestive heart failure with ischemia and dilatated cardiomyopathy in whom a flexible ring was applied had a higher likelihood of developing recurrent regurgitation requiring reoperation [45].

Other types of rings, recently introduced, include partially flexible rings and adjustable flexible rings, many of which are still under evaluation and struggling for a definitive place in the surgical armamentarium.

### *Correction of leaflet prolapse*

Prolapse represents the most common dysfunction of degenerative mitral regurgitation [46]. The two leaflets can prolapse individually or simultaneously, due to elongation and/or rupture of the chordae tendineae [47]. Posterior leaflet prolapse usually involves the middle scallop (P2). Anterior leaflet prolapse normally also involves the central free edge and has an incidence of approximately 17% [48]. Posterior chordal rupture is a frequent pathological finding in this clinical subset (about half the patients with degenerative disease) [47].

Quadrangular resection is the gold standard surgery for correction of posterior leaflet prolapse, with or without a sliding plasty [49] or an annular plicature [50], to obliterate the gap created at the base of the resection. This is a relatively simple and easy procedure, but there is still a ratio of only 40% repairs worldwide [51]. A study published by Perier *et al.* demonstrates that durability was greatest after quadrangular resection and annuloplasty for posterior leaflet prolapse [47]. Gazoni *et al.* described a correction of both anterior and/or posterior flail leaflets using a triangular resection in 154 patients, with good short and long-term results [52].

Techniques to correct anterior leaflet prolapse are more demanding and often less successful than quadrangular resection for posterior leaflet prolapse. Hence, correction of anterior leaflet prolapse is preferably performed by chordal surgery. Several techniques have been used (elongation, shortening, transposition and implantation), but there is consensus that chordal implantation or transposition is superior to elongation and shortening. Smedira *et al.* have demonstrated that, after reconstruction, residual or recurrent mitral regurgitation was significantly more prevalent in the shortening group (22% with grade 2 to 3+ MR) than in the transfer group (4%; $p = 0.01$) [53]. Nonetheless, most surgeons have evolved to a technique of chordal replacement, which consists of the creation of artificial chordae from polytetrafluoroethylene sutures. This technique has been used mainly in anterior leaflet prolapse but can also be used for the posterior leaflet. It has consistently produced better and long-lasting results [54]

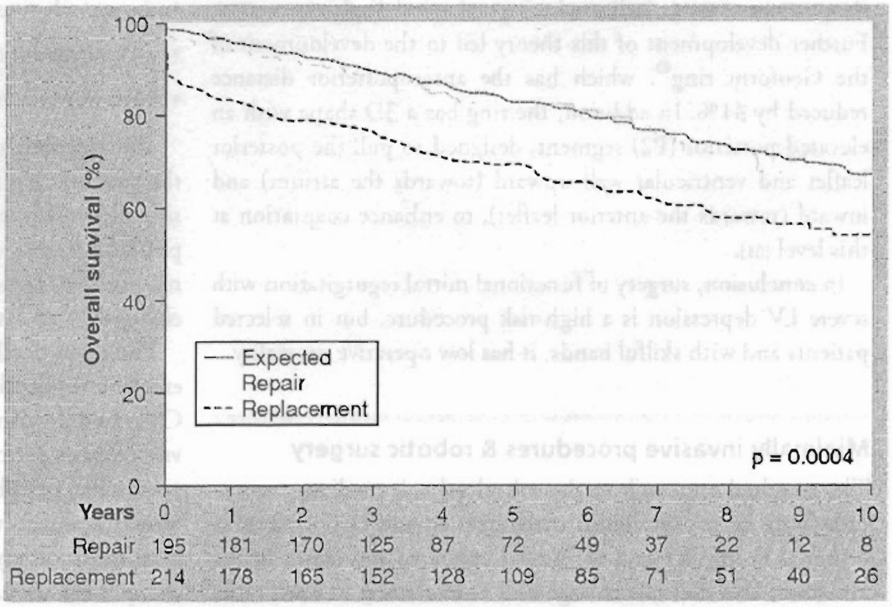


**Figure 2. Survival after mitral valve replacement and repair, compared to that of expected survival of the population.** Reproduced from [21].

Overall results of anterior mitral prolapse correction, compared with posterior prolapse, were presented by Mohty *et al.* [55] who concluded that there is a higher reoperation rate in patients with anterior prolapse and in patients in whom residual mitral regurgitation, even mild, is noted during surgery. However, there has recently been a marked improvement in long-term durability of repair for all types of mitral valve prolapse.

Alfieri, from Milan, described a simple method of correction of prolapse, especially of complex anterior leaflet prolapse and of the bileaflet type, which consists of an edge-to-edge suture approximation of the posterior and anterior leaflets in order to restore coaptation. This is a simple and reproducible but nonphysiological technique, resulting in a double-orifice valve, which generates some concern related to the creation of stenosis. This group built a 3D computational model for the evaluation of the hemodynamics of this type of repair and concluded that the double orifice mitral valve does not differ from a normal valve of the same total area and that Echo Doppler estimation of the maximum velocities is a reliable method for the calculation of pressure gradients across the repaired valve [56]. Nonetheless, this technique achieved only a limited degree of acceptance by the surgical fraternity and is accepted by most as a bailout procedure, when everything else fails. The Milan group now uses it in only less than one quarter of their cases [ALFIERI, PERS. COMM.].

## Mitral repair in severe LV dysfunction

Mitral regurgitation may occur with a structurally normal valve as a complication of LV dysfunction and almost half the patients with severe LV dysfunction have at least moderate mitral insufficiency [57]. This complication of end-stage cardiomyopathy results from dilatation of the annular–ventricular apparatus, altered ventricular geometry (ventricle with a more spherical shape), or papillary muscle dysfunction. Several surgical strategies are used to treat the resulting heart failure or postpone heart transplantation, including mitral valve surgery.

Mohr *et al.* described their experience with 66 patients with significant mitral regurgitation and LV ejection fraction (EF) below 30% who were operated on with a 30-day mortality of 6.1% [58]. Actuarial survival after 1 and 5 years was 86 ± 4 and 66 ± 8%, respectively. The Mayo Clinic group operated on 43 patients with functional mitral regurgitation in a setting of nonischemic myocardiopathy, with a mean EF of 29 + 5%, 63% of whom had MV repair [33]. The 30-day mortality was 2.3% and 1- and 3-year survival rates were 84 and 80%, respectively, but survival beyond 5 years is less than 50%.

The most common procedure in the correction of functional mitral regurgitation is the implantation of a prosthetic ring [59]. The procedure is usually performed using undersized rings to enhance coaptation of the tethered leaflets, which are displaced toward the apex of the remodeled and dysfunctioning LV. In severely dilatated and hypokinetic ventricles, it has been suggested that when coaptation depth is greater than 10 mm below the annular plane, simple annuloplasty is not enough to address the problem.

Maisano and colleagues hypothesized that the use of a specifically designed annular prosthesis with a modified shape could improve the capability of annuloplasty to force coaptation in the presence of severe leaflet tethering and apical displacements [60]. Further development of this theory led to the development of the Geoform ring©, which has the anteroposterior distance reduced by 41%. In addition, the ring has a 3D shape with an elevated posterior (P2) segment, designed to pull the posterior leaflet and ventricular wall upward (towards the atrium) and inward (towards the anterior leaflet), to enhance coaptation at this level [61].

In conclusion, surgery of functional mitral regurgitation with severe LV depression is a high-risk procedure, but in selected patients and with skilful hands, it has low operative mortality.

## Minimally invasive procedures & robotic surgery

The standard approach to the mitral valve is median sternotomy, because the incision is easily opened and closed, there is minimal morbidity and facilitated access to the entire heart. However, this incision is large and cosmetically unacceptable to some patients, and surgeons have been looking for less invasive approaches. One of the first minimally invasive procedures was described by Navia *et al.*, from the Cleveland Clinic, in 1996, whereby a 10-cm incision was made extending from the inferior border of the right second costal cartilage to the superior edge of the fifth costal cartilage, 3 cm lateral to the sternum [62]. The third and fourth cartilages were completely resected. Extracorporeal perfusion was performed through femoral cannulation.

Cosgrove and colleagues approached the MV through a right minithoracotomy, cannulating the femoral artery in about 85% of the cases [63]. Between 1996 and 2002, the Cleveland Clinic group had performed 1427 minimally invasive mitral operations, under direct vision [64]. This series had low mortality (0.3%) and complication rates (bleeding [3.1%], strokes [1.8 %], and respiratory insufficiency ([0.8%]). Chitwood and Nifong reported similar results [64]. Complex repairs were performed in operating times similar to those of conventional surgery, and the results of the repair were excellent [64].

These experiences placed emphasis mainly on the size and location of the incision, essentially for cosmetic reasons. However, the ultimate aim is endoscopic surgery with skin incisions limited to small 1–2 cm ports, as has been performed in abdominal surgery for more than a decade. The initial steps to fully endoscopic mitral surgery were taken as soon as the technology became available. With training and practice, results comparable to classic surgery were reported and, progressively, surgeons advanced to more challenging procedures. However, instrumentation is more difficult and newer instruments had to be developed for this specific use. However, long-shafted instruments amplify the natural human hand tremor, making the maneuvers less accurate. More recently, robotic-enhanced or -assisted surgery has entered the field and permitted firmer handling of specially designed instruments. The Da Vinci surgical system (Intuitive Surgical, Inc.) has three components:

- a surgeon's console
- an instrument cart
- a vision platform

The surgeon's operative console is physically separated from the patient, even the operating room, and allows the surgeon to sit comfortably, resting the arms ergonomically with the head positioned in a 3D vision window, while commanding the robotic arms handling the instruments, which are sequentially changed by an assistant at the patient's side.

The main challenge of these procedures is to reproduce the excellent results that conventional mitral repair surgery offered. Chitwood described 249 video-assisted and 100 robotic mitral valve repairs performed between 1996 and 2004 [24]. For these operations, peripheral arterial and venous cannulation, kinetic venous drainage, thin-walled high-flow cannula, a 4/5 cm right mini thoracotomy, and a newly developed transthoracic aortic clamp were used. An endoscopic camera either assisted with vision in difficult-access areas or was the sole image source during completely endoscopic repairs. The 30-day mortality was 2.2 and 1% for the video-assisted and robotic series, respectively. For the video-assisted group, cardiopulmonary bypass and aortic cross-clamp times averaged 139.7 ± 2.7 and 86.8 ± 2.4 min, respectively, 4.4% of the patients required reoperation for bleeding, and 29.6% received a blood product transfusion. Six patients who had video-assisted repairs, (2.4%) required reoperation for residual or recurrent mitral regurgitation. For the robotic group, cardiopulmonary bypass and aortic cross-clamp times averaged 162 ± 4.2 and 126.0 ± 3.0 min, respectively, two patients required reoperation for bleeding, and only 15% received a blood product transfusion. In this group, two patients required reoperation for a failed valve repair. Complex repair procedures were performed by both approaches.

Folliguet and colleagues compared, in a nonrandomized study, the safety and efficacy of 25 cases of posterior leaflet prolapse corrected trough robotic technology retrospectively with another 25 patients who underwent the same repair via a median sternotomy [65]. They found no difference between the two techniques, but state that long-term follow-up is still required to determine the durability of the mini-invasive repair.

The advantages of minimally invasive surgery are intuitive: much smaller incisions, less bleeding, rapid recovery and more 'appealing' scars, but there remain major concerns about the specific complications of these procedures and it will take some time before these advantages overcome the results of conventional surgery. In addition, the robotic systems are extremely expensive and out of reach of most institutions.

## Percutaneous mitral valve repair

As discussed above, surgical treatment of mitral insufficiency requires unsightly incisions, extracorporeal circulation and cardiac arrest, and has long recovery times, limiting the candidates to this procedure and pushing the surgical indications to more advanced phases of mitral regurgitation. These problems have not been completely overcome by the less invasive procedures, including video and robotic-assisted surgery. The ultimate minimally invasive valve intervention should avoid skin incisions and cardiopulmonary bypass. On the other hand, although surgical mitral repair may be sophisticated and complex, many repairs currently consist of simple annuloplasty [66].

In recent years, interventional cardiology, performed in the catheter laboratory, greatly evolved, with percutaneous coronary procedures, mitral and aortic valve dilatations, atrial and ventricular septal defect closure, and, more recently, pulmonary and aortic valve implantations being performed. Hence, the natural extension to mitral valve procedures, which have been developed in the past couple of years.

The percutaneous approach to MR repair consists mainly in endovascular correction of leaflet prolapse and annuloplasty. Bearing in mind the relative efficacy and simplicity of the surgical Alfieri technique for the treatment of MR caused by leaflet prolapse, researchers have developed a percutaneous method by which the free edge of the mitral valve leaflets are grasped together with a clip, thus obtaining an edge-to-edge repair [25]. In December 2005, Feldman and collaborators published the first results of the Everest Phase-1 clinical trial [67]. Clips were implanted in 24 patients without procedural complications but with partial clip detachment in three patients and one postprocedure stroke during 30-day follow-up. The approach involves venous access and a transseptal approach to the mitral leaflets. Under fluoroscopic and/or echocardiographic guidance, timing the systolic coaptation of the leaflets, the clip is closed in the center of the free edge of the anterior and posterior mitral leaflets. If the repair is not adequate, the leaflets can be released and the approximation reattempted [25]. This study concludes that percutaneous edge-to-edge mitral valve repair can be performed safely and that a reduction in mitral regurgitation can be achieved in a significant proportion of patients. One year after the application of the device, the patients maintained mitral insufficiency less than grade 2 [68].

In 2006, Webb and collaborators published the first paper describing percutaneous transvenous mitral valve annuloplasty in humans using the Percutaneous Mitral Annuloplasty System (Viking, Edwards Lifesciences Inc) [69]. This procedure is based on the anatomical relationship between the coronary sinus and the posterior mitral annulus. The implant is made of three sections: a distal self-expanding anchor, deployed in the great cardiac vein, a spring-like 'bridge', which is the annuloplasty component, and a proximal self-expanding anchor deployed in the distal coronary sinus. The bridge has shape-memory properties that result in shortening forces at body temperature. The procedure was performed successfully in four out of the five patients enrolled in two different clinical sites, some difficulty having been experienced in orientating the guide in one patient. The authors accomplished a reduction of mitral regurgitation grade 3.0 + 0.7 to a grade 1.6 + 1.0, thus 'demonstrating' that percutaneous mitral annuloplasty is feasible.

This trial, together with several animal models, stimulated the *in vivo* evaluation of the anatomy of the coronary sinus that could help to predict the success of percutaneous procedures [70]. Tops *et al.* found that the coronary sinus is in a plane superior to the mitral annulus in 90% of the patients studied and that the minimal distance between the mitral annulus and the coronary sinus is greater in patients with dilatated myocardiopathy and mitral regurgitation [71]. These authors also demonstrated that in 68% of the patients the circumflex artery runs between the coronary sinus and the mitral annulus. This was confirmed by the studies of Maselli *et al.* who found that the main circumflex coronary artery or its branches were located between the coronary sinus and mitral annulus in 64% and a diagonal or ramus intermedius branch in 16% of the cases [72]. This obviously raises the question of eventual myocardial ischemia being produced by placement of the device.

Other types of devices have been used however, the results have yet to meet initial expectations. As opposed to surgical annuloplasty, in which the ring is firmly anchored in the fibrous skeleton of the mitral annulus to achieve optimal correction, clinical efficacy of percutaneous devices will instead need to rely on traction of the left atrial wall to decrease the septal-lateral diameter of the mitral orifice [73]. On the other hand, only partial annuloplasty is possible with these devices, in contrast with surgically implanted rings. Randomized clinical trials are required in order to establish the groups of patients that might benefit from this technique and what studies need to be performed before the procedure in order to select the best candidates.

Finally, following on the past 2 years' success with percutaneous aortic valve implantation, it is likely that these prostheses and respective implantation systems will be adapted for use in the mitral position. Experimental work has begun and it will be only a couple years before clinical use is initiated, especially in compassionate cases, that is to say, nonoperable patients or those thought to constitute an extremely high risk for surgery.

## Expert commentary

Surgical mitral valvuloplasty has achieved wide acceptance and is, today, considered the preferred method by comparison with prosthetic valve replacement. The techniques have evolved, but the original concepts established more than 30 years ago by Carpentier remain. There is little if any space for new breakthroughs. However, less invasive procedures have attracted much attention, more for their cosmetic advantages than for any other reason, certainly not for better results. And they are probably less reproducible and teachable.

Mack and coworkers stated that there are three barriers to the adoption of any new technology: first, demonstration of value; second, user-friendliness; and last, teachability [74]. All of these barriers are yet to be transposed. We do not have many doubts that, in the future, near or not, minimally invasive

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surgery may reproduce the long-term surgical results that we are accustomed with conventional approaches, especially in highly complex pathology.

Gibbon, the father of open heart surgery, would not recognize today's heart surgery. We believe that, in time, technology will present us with highly user-friendly instruments. But how many surgeons are going to have the possibility to work in countries or centers that will have the economical capacity to pay for these highly advanced technologies? An important drawback for the development of these techniques is that they will be limited to a few major centers and the training programs restricted to a few physicians.

We strongly believe that before general application of percutaneous procedures to correct MV regurgitation, randomized clinical trials with reasonable follow-up are required, defining which patients may really benefit from these novel technologies.

## Five-year view

Surgery of mitral regurgitation is now well-standardized and, most likely, will not change much in the next 5 years, except for a momentum in the enthusiasm of cardiac surgeons favoring valvuloplasty over replacement of the mitral valve. Minimal access surgical procedures have, most likely, already established their definitive ground and robotic technology still requires major advances before obtaining generalized utilization, which, in our view, will take another decade and is unlikely to occur until the costs of the systems are significantly reduced. Nevertheless, advances in technology are occurring at an extremely fast speed and in the next 5 years new techniques and new instruments will challenge currently accepted methods.

On the other hand, percutaneous intervention on the MV is just beginning and presenting the preliminary results of limited clinical trials. These very early experiences have, so far, fallen short of expectations. Unlike other percutaneous procedures, including prosthetic valve implantations, they are based on completely different concepts and devices, which will take some time before they can be mastered to match those used in conventional surgery. In terms of MV repair, it is unlikely that the next 5 years will witness significant evolution, but catheter-based prosthetic valve implantation will, almost surely, be feasible for use in otherwise nonoperable patients.


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*The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.*

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## Key issues

- Mitral valve regurgitation, caused by different types of pathology, is one of the most common forms of heart valve disease.
- Mitral valve repair (valvuloplasty) is better than replacement, resulting in less morbidity and mortality, both perioperative and in the long-term.
- Valvuloplasty may be possible in up to 90% of the cases, depending on the pathology.
- The classical (Carpentier) approach has excellent immediate and long-term results (low recurrence of regurgitation and good survival).
- Less invasive (including vide-assisted) procedures, have yielded good results in experienced hands but are more difficult to master and to reproduce.
- Robotic-enhanced techniques are used only by a handful of units in the world and have not yet been able to achieve wide acceptance. The systems are extremely expensive and out of the reach of many institutions.
- Percutaneous (interventional cardiology) approaches are in their infancy and have not been able to meet expectations.

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