Mitrval valve repair for degenerative mitral valve disease: surgical approach, patient selection and long-term outcomes

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ABSTRACT
Mitrval valve repair (MVRepair) has become the procedure of choice to correct severe degenerative mitral regurgitation (MR), due to its documented superiority to valve replacement regarding long-term survival, freedom from valve-related adverse events and preservation of left ventricular (LV) function. The refinement of MVRepair techniques has rendered almost all valves (more than 95%) amenable to repair with a 15-year freedom from reoperation of 90%. The concept of ‘centres of excellence for MVRepair’ has emerged, encouraging referring doctors to select the most experienced institutions or individual surgeons to deal with the most complex cases, based on repair volume, appropriate peri-procedural imaging and data regarding expected outcomes (repair, mortality and durability of repair). Based on the good results, operating on asymptomatic patients with severe MR is now widely accepted, prophylactically avoiding the dire consequences of chronic MR, such as LV function deterioration/enlargement, and development of atrial fibrillation and pulmonary hypertension. In reference centres, where the repair rate is over 95% for all types of disease with <1% mortality, it has become standard practice in nearly 50%–60% of all patients submitted to MVRepair. Finally, recent advances in the surgical treatment with the purpose of reducing invasiveness and surgical trauma, through partial sternotomy or mini-thoracotomy (video-assisted with or without robotics), are now being increasingly performed in 20%–30% of centres, claiming comparable results to conventional surgery. In addition, transcatheter technology, particularly the MitraClip, is evolving and treading its way in the treatment of high-risk patients with severe MR, but the results are still short of ideal.

INTRODUCTION
Mitrval valve repair (MVRepair) has become the gold standard for the correction of significant organic mitral regurgitation (MR), whenever is it is expected to be durable and associated with low morbidity and mortality and is recommended (class I) by current guidelines.1,2 Its superiority, by comparison with mitral valve replacement (MVR), has been demonstrated by many groups.3-11 The MIDA (Mitr regurgitation International DAta-base) investigators recently concluded that, among patients with degenerative MR with a flail leaflet, MVRepair was associated with lower operative mortality, better long-term survival and fewer valve-related complications compared with MVR.12

Since its introduction in the late 1960s, the evolution of the procedure has been remarkable. Early, Carpenter described, in a systematic fashion, the structural changes that ultimately lead to regurgitation and set up the universally embraced ‘functional classification of Carpentier’.13 This concept served as the framework of modern reconstructive mitral valve (MV) surgery, where all the components of the valve complex (annulus, leaflets, chordae tendineae and papillary muscles) were integrated and analysed, in order to provide not only a functional approach but also an anatomical approach. This is settled in three basic principles: to restore or preserve appropriate leaflet mobility; to ensure good leaflet coaptation; and to remodel and stabilise the annulus.

In this work, we review current concepts on surgical management, patient selection and long-term results of MVRepair, with the aim of setting the benchmark from where new technologies, such as transcatheter procedures, should be subjected to comparison.

RECONSTRUCTIVE VALVE SURGERY PARADIGM: FIRST BEGIN WITH AETIOLOGY
Primary (organic) MR and secondary (functional) MR represent distinct entities with regard to pathophysiology, clinical presentation, management and prognosis. Primary MR is a true valvular disease, where any change of one of the valve components may be responsible for regurgitation. In developing countries, rheumatic disease is still most prevalent, with nearly endemic proportions.13 By contrast, the most frequent form of presentation in western countries is degenerative disease, usually classified as fibroelastic deficiency or myxomatous.

On the other hand, in secondary MR, the valve constituents are structurally normal, regurgitation resulting from geometric distortion of the subvalvular apparatus, secondary to left ventricular (LV) remodelling and dilatation, as a consequence of ischaemic disease or dilated cardiomyopathy. This pathology will not be further discussed in this work.

The lack of a universal nomenclature to define degenerative MV disease constitutes one important barrier to the interpretation of studies aimed at evaluating MVRepair results. Hence, the pathophysiological triad of MV disease developed by Carpenter gave an important insight into the genesis and cause of MR, enabling a methodological approach to the treatment. The aetiology (cause of the disease) leads to the appearance of lesions (consequence), which in turn causes dysfunction (effect). Carpenter’s classification of valve dysfunction, with regard to leaflet motion (type I: normal motion; type II:
excessive motion (prolapse); and type III: restricted motion), has now been widely accepted. 14

This analysis has important prognostic implications, since the results of MVRepair (reparability and durability) are different among different aetiologies, type of valve dysfunction and lesions encountered (site of prolapse, presence of calcification, leaflet restriction, etc).

**FIBROELASTIC DEFICIENCY VERSUS BARLOW’S DISEASE**

There is a wide spectrum of degenerative disease, ranging from fibroelastic deficiency to Barlow’s disease (figure 1). 15 The former is characterised by a normal amount of leaflet tissue in a normal-sized annulus. Leaflets are typically thin and chordae are flimsy. Regurgitation is typically caused by elongation/rupture of one or more chordae in a single prolapsing segment, most often P2. In the chronic setting, the prolapsing segment may become distended and thickened by a limited myxomatous process.

At the opposite end of the spectrum, Barlow’s disease is marked by tissue excess, involving multiple segments of both leaflets in a large annulus. Leaflets are thickened and redundant, with elongated, mesh-like chordae which may or may not be ruptured. 16 There is an intermediate form designated ‘forme fruste’, also characterised by excess tissue with myxomatous changes in generally more than one leaflet segment, but usually not in a large valve size. Echocardiographic evaluation is of great importance to discriminate the wide range of degenerative involvement (figure 2).

The repair of valves with fibroelastic deficiency is commonly straightforward because the abnormality is limited to P2 in 75% of patients. Treatment typically consists of resection of the abnormal segment or implantation of artificial chordae, and placement of a ‘normal-sized’ (30–32 mm) prosthetic ring. Repairing myxomatous valves, particularly Barlow’s disease, is far more demanding, usually requiring a vast array of techniques, including leaflet resection, multiple neo-chordal implantation, papillary muscle shortening, commissural closure and use of large (≥34 mm) rings (figure 3).

**REPAIR-ALL’ STRATEGY IN ALL CORNERS OF MITRAL VALVE PROLAPSE**

For many years now, our philosophy has been that all degenerative MV are, by principle, amenable to repair, provided that a thorough and comprehensive pre-operatively and intra-operatively analysis of the whole valve apparatus is made. Accurate identification of all lesions responsible for valve dysfunction is of paramount importance because it allows appropriate selection of the surgical techniques (table 1).

Recent reports show very high rates of MVRepair associated with low mortality in all types of lesions and valve complexity (table 2). 5,8,17–19 We and others have demonstrated that a nearly 100% repair rate of posterior leaflet prolapse (PMLP) can be expected, with long-term durability. 17,20–22 Here, recent experience has shifted towards the philosophy of ‘respect rather than resect’, using artificial chordae to correct the prolapse more
often. However, we still adapt our technique to the type of lesion, applying either resection (for large and bulky posterior leaflet segments) or non-resection techniques (in small leaflets).

Repair rates for anterior leaflet prolapse (AMLPP) or bileaflet prolapse (BLP) are usually slightly lower than that for PMLP, but experienced centres report rates above 90%–95%, with low mortality (<1%). There are several key points that deserve particular attention when repairing Barlow’s valves: (1) reduce the height and volume of a large posterior leaflet by resection (with or without sliding plasty) or chordal implantation (lowering the free margin well into the ventricle) in order to avoid systolic anterior motion; (2) always use large rings (>34 mm); (3) favour artificial chordae, instead of the classical Carpenter shortening/transfer techniques to correct AMLP; (4) in BLP, start by correcting PMLP. We have found that the need for MVR in AMLP/BLP was influenced not only by anatomical issues but also by patient’s characteristics and by the performing surgeon’s experience (table 3).

Recently, the concept of centres of excellence in MVRepair has evolved, to set the standards for best surgical practice in patients with severe MR. These centres should meet several criteria, such as large MV surgery volume (centre and surgeon), appropriate peri-procedural imaging capabilities and willingness to provide data regarding expected outcomes based on the centre’s recent experience, including repair, mortality and stroke rates, and repair durability. However, we still believe that simpler cases (isolated P2 prolapse) are at the reach of any minimally experienced cardiac surgeon.

Our approach when dealing with severe MR due to flail leaflet is detailed in figure 4.

**LONG-TERM SURVIVAL AND DURABILITY AFTER MVREPAIR**

Several groups have published their long-term outcomes after MVRepair, and proved that the procedure is predictably associated with a survival similar to that of the age- and sex-matched general population (figure 5). This benefit has been observed even in elderly patients. The best outcomes regarding durability of the repair are obtained with isolated PMLP, but the results are also gratifying with AMLP or BLP, particularly in young patients (figure 6). It is expected that more than 90% of patients submitted to MVRepair for PMLP will be free from reoperation after 15 years and this figure should be above 75%–80% in other types of prolapse.

However, it is essential to distinguish freedom from reoperation (crude analysis) from freedom from recurrent moderate-to-severe MR (accurate analysis). David et al. assessed the late outcomes of 840 patients with degenerative mitral disease, submitted to MVRepair over a 20-year period. The probability of freedom after MVRepair was low (5.9%) and freedom from recurrent severe MR was 90.7%, but freedom from moderate or moderate-to-severe MR was significantly lower (69.2%). Recently, Suri et al. evaluated the effect of recurrent MR after MVRepair, and they found that it is associated with adverse LV remodelling and late death. Hence, long-standing competence of the MV should be the goal, and close follow-up should be established if recurrent MR is detected.

**CONTROVERSIES SURROUNDING MITRAL VALVE REPAIR**

**Asymptomatic patients**

Early intervention in asymptomatic patients, before the onset of the nefarious consequences of chronic MR, was the natural course in the evolving experience of MVRepair and is now supported by the guidelines. There are several logical assumptions that support this early surgery strategy. First, the natural history of the disease has shown that, if left untreated, the death rate, namely sudden death, can reach 10%–20% per year, once symptoms occur. Second, operating on a patient with significant symptoms (New York Heart Association; NYHA III/IV), or with LV dysfunction or dilatation, implies significantly higher operative mortality and reduced long-term survival. Third, as demonstrated above, MVRepair is possible in the vast majority of patients with degenerative MR, even in those with complex leaflet morphology.

**Table 1: Lesions found in degenerative mitral valve disease and the surgical techniques used to correct them**

<table>
<thead>
<tr>
<th>Lesions</th>
<th>Surgical techniques</th>
<th>Probability of repair</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annular dilatation</td>
<td>Annuloplasty procedure: complete ring* partial ring/band† suture annuloplasty*</td>
<td>&gt;95%</td>
</tr>
<tr>
<td>PMLP</td>
<td>Artificial chordal implantation* Leaflet resection† Sliding plasty† Notch closure between segments† Chordal shortening/transposition†</td>
<td>&gt;98%</td>
</tr>
<tr>
<td>AMLP</td>
<td>Artificial chordal implantation* Chordal shortening/transposition† Suture plication (minor prolapse)† Leaflet resection</td>
<td>&gt;95%</td>
</tr>
<tr>
<td>Commissural leaflet prolapse</td>
<td>Commissural closure (‘magic stitch’)† Papillary muscle shortening† Artificial chordal implantation† Chordal shortening/transposition†</td>
<td>&gt;95%</td>
</tr>
<tr>
<td>Leaflet restriction/small size</td>
<td>Patch augmentation† Leaflet thinning† Secondary chordal resection†</td>
<td>70%–80%</td>
</tr>
<tr>
<td>Annular calcification</td>
<td>Decalcification† Decalcification + patch reconstruction‡</td>
<td>70%–80%</td>
</tr>
</tbody>
</table>

The following options express the authors’ opinions and trends according to their daily experience.

*Techniques frequently used to correct the corresponding lesions.
†Techniques occasionally used.
‡Techniques seldom used.

MV, mitral valve; AMLP, anterior leaflet prolapse; BLP, posterior leaflet prolapse.
majority of patients and it seems that the repair rate in asymptomatic patients is higher than in those presenting with the classical triggers for surgery, probably due to structural valve changes induced by chronic MR.

We therefore hypothesise that early surgery can, at least, prevent some degree of leaflet degeneration caused by chronic MR, but there are authors that favour a more conservative approach (“watchful waiting”), to intervene only when symptoms or LV dysfunction occurs.

In our experience, the overall repair rate in asymptomatic patients with severe degenerative MR and preserved LV function, including all types of prolapse, was 98.2% with a 30-day mortality of 0.8%. Interestingly, in the subgroup of patients with AMLP/BLP, the repair rate increased from 94.8% to 98.4% in asymptomatic or mildly symptomatic patients. Moreover, these patients had increased late survival in comparison to those with pre-operative NYHA class III/IV symptoms, and similar survival to the age- and sex-matched population (figure 6).

Therefore, as the guidelines recommend, asymptomatic patients with severe MR should be offered surgery if MVR repair is likely (>95%) with low mortality (<1%), and, when possible, patients should be referred to centres/surgeons with large experience.

### Atrial fibrillation

Atrial fibrillation (AF) is present in 30%–50% of patients undergoing MV surgery and has been identified as a prognostic marker of poorer outcome. Even after successful MVRepair or MVR, a non-negligible percentage of patients will remain in AF. Grigioni et al. analysed the occurrence of AF in patients with degenerative MR under conservative management and in sinus rhythm at diagnosis, and they found that the incidence at 5 and 10 years was 18±3% and 48±6%, respectively, with a linearised rate of 5.0±0.7% per year, and it was associated to increased cardiac mortality and morbidity.

We have recently evaluated the impact of pre-operative AF and of pulmonary hypertension (PHT) in the long-term outcomes of asymptomatic patients with severe degenerative MR (preserved LV function) after MVRepair. Patients with AF/PHT had poorer long-term survival and event-free survival even after successful surgery. The durability of MV repair was also compromised in these patients, which probably indicates that they should have been operated on earlier. On the other hand, the Mayo Clinic group found that post-operative AF occurred after surgery for MR in 24% of patients previously in sinus rhythm and was associated with increased subsequent morbidity. Left atrial enlargement was a powerful predictor of post-operative AF.

In recent years, there has been a trend to perform surgical ablation of AF during MV surgery. Recent data from the STS Database showed that 32.2% of patients presented to MV surgery have AF and concomitant AF ablation in this setting is performed in 61.5% of patients. Rates of post-ablation freedom from AF of 80% or higher have been described. Gillinov and associates have recently evaluated the safety and effectiveness of surgical AF ablation during mitral surgery. They randomly assigned 260 patients with persistent or long-standing AF who required MV surgery to undergo either surgical ablation or no ablation (control). The addition of ablation to MV surgery significantly increased the rate of freedom from AF at 1 year (63.2% vs 29.4%), with similar early mortality in the two groups, but implantation of a permanent pacemaker was increased after ablation.

### Tricuspid valve repair

Functional tricuspid regurgitation (FTR) is commonly associated to left-sided heart valve disease. Persistent PHT leads to increased right ventricular (RV) afterload, which ultimately results in ventricular enlargement and geometric distortion, and tricuspid annular dilatation and flattening, leading to tricuspid regurgitation (TR). Until recently, the tricuspid valve (TV) was the ‘forgotten valve’, not entered in the surgical algorithm, due to the erroneous concept that it played a passive role in the evolution of the disease. It was then thought that FTR would disappear after correction of the mitral or aortic pathology. However, experience has shown that this does not always happen and TR may actually increase when the primary left-sided valve disease is repaired.

<table>
<thead>
<tr>
<th>Authors</th>
<th>n</th>
<th>Repair rate</th>
<th>Early mortality</th>
<th>Long term survival</th>
<th>Reoperation</th>
</tr>
</thead>
<tbody>
<tr>
<td>PMLP</td>
<td></td>
<td>556</td>
<td>100%</td>
<td>0.8%</td>
<td>5 years – 97%</td>
</tr>
<tr>
<td>David et al.</td>
<td></td>
<td>359</td>
<td>95%</td>
<td>0.6%</td>
<td>12 years – 75%</td>
</tr>
<tr>
<td>Johnston et al.</td>
<td></td>
<td>3383</td>
<td>97%</td>
<td>1.1%</td>
<td>15 years – 76%</td>
</tr>
<tr>
<td>Suri et al.</td>
<td></td>
<td>736</td>
<td>92%</td>
<td>0.7%</td>
<td>15 years – 58%</td>
</tr>
<tr>
<td>Correia et al.</td>
<td></td>
<td>492</td>
<td>98.4%</td>
<td>0.2%</td>
<td>15 years – 65%</td>
</tr>
<tr>
<td>AMLP/BLP</td>
<td></td>
<td>42/146</td>
<td>100%/99%</td>
<td>4.8%/10%</td>
<td>7 years – 86%/89%</td>
</tr>
<tr>
<td>Castle et al.</td>
<td></td>
<td>93/316</td>
<td>95%</td>
<td>0.6%</td>
<td>12 years – 73%/78%</td>
</tr>
<tr>
<td>De Bonis et al.</td>
<td></td>
<td>139</td>
<td>Nd</td>
<td>0%</td>
<td>17 years – 72%</td>
</tr>
<tr>
<td>Goldstone et al.</td>
<td></td>
<td>131</td>
<td>98.5%</td>
<td>0.2%</td>
<td>8 years – 92%</td>
</tr>
<tr>
<td>Seeberger et al.</td>
<td></td>
<td>156/402</td>
<td>91%/90.3%</td>
<td>2.6%/2.2%</td>
<td>5 years – 87.3%</td>
</tr>
<tr>
<td>Coutinho et al.</td>
<td></td>
<td>274/227</td>
<td>94.5%</td>
<td>1.2%</td>
<td>20 years – 43%</td>
</tr>
</tbody>
</table>

AML, anterior mitral leaflet prolapse; BLP, bileaflet prolapse; N, number of patients; Nd, not documented; PMLP, posterior mitral leaflet prolapse.

### Table 3 Factors predisposing to mitral valve replacement rather than repair in anterior or bileaflet prolapse

<table>
<thead>
<tr>
<th>Variables</th>
<th>HR</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per year)</td>
<td>1.098</td>
<td>1.037 to 1.163</td>
<td>0.001</td>
</tr>
<tr>
<td>Previous cardiac surgery</td>
<td>4.083</td>
<td>1.489 to 9.046</td>
<td>0.002</td>
</tr>
<tr>
<td>LV dysfunction (EF &lt;45%)</td>
<td>5.504</td>
<td>1.209 to 25.064</td>
<td>0.027</td>
</tr>
<tr>
<td>Mitral calcification</td>
<td>3.703</td>
<td>2.093 to 6.352</td>
<td>0.001</td>
</tr>
<tr>
<td>Restriction/surgery of PL</td>
<td>2.341</td>
<td>0.075 to 5.169</td>
<td>0.018</td>
</tr>
<tr>
<td>AMLP (2 segments)/Barlow’s</td>
<td>3.983</td>
<td>2.966 to 7.163</td>
<td>0.002</td>
</tr>
<tr>
<td>Surgeon*</td>
<td>1.525</td>
<td>1.047 to 2.222</td>
<td>0.028</td>
</tr>
</tbody>
</table>

*The surgeon variable was transformed into a dichotomous variable, with the most experienced surgeon in comparison with other surgeons.

AML, anterior mitral leaflet prolapse; EF, ejection fraction; LV, left ventricle; PL, posterior leaflet.
is not completely resolved during surgery, as in the case of a less than perfect valve repair. Furthermore, isolated severe TR is now increasingly observed in patients with normal left heart valve function after either mitral valvuloplasty or replacement. This is an important issue because reoperation carries high hospital mortality, particularly in the presence of RV dysfunction.

Hence, current guidelines recommend a more aggressive approach with regard to performing TV surgery whenever there is significant annular dilatation (>40 mm or 21 mm/m²), even when there is only mild-to-moderate TR. The procedure does not usually increase operative risk. Since in FTR the valve is structurally normal, correction is relatively straightforward by annuloplasty alone. Most reports attribute superiority to rigid annuloplasty rings over suture-based or flexible-band annuloplasty for the treatment of FTR. However, due to a favourable past experience with a modified DeVega annuloplasty in well over a thousand patients, we still use this approach in the majority of cases, reserving use of rings for organic TV disease. Desai et al recently assessed the behaviour of FTR in 1833 patients with degenerative MR who underwent MVRepair. Notably, TR grade and RV function improved after surgery in all patients undergoing MVRepair alone, but the improvement was temporary and, by 3 years, both parameters returned to preoperative levels. By contrast, concomitant annuloplasty in patients with moderate-to-severe TR durably eliminated regurgitation and RV function improved up to 3 years.

**FUTURE TRENDS IN MITRAL VALVE REPAIR SURGERY**

Recently, there have been major technological developments in the management of valvular heart disease, which have enabled cardiologists and surgeons to go a step further in the treatment of patients with MV disease. One such development is the use of percutaneous mitral repair devices. These devices are designed to repair or replace the mitral valve without the need for open-heart surgery._disadvantages_. The technique of choice is usually determined by the specific anatomy of the mitral valve and the severity of the regurgitation. The 5-year survival rate for patients undergoing percutaneous mitral repair is approximately 90%, with a low rate of complications. However, further studies are needed to establish the long-term efficacy and safety of these devices.
of high-risk patients, in addition to decreasing invasiveness of the procedures. The MV has not been an exception and percutaneous treatment of severe MR has evolved alongside with surgical treatment.

With regard to surgery, the access for minimally invasive MV surgery (MIMVS) can be subdivided into two groups: partial sternotomy and right thoracotomy, including the open and video-assisted methods, with or without robotic assistance. Thus, MIMVS does not refer to a single procedure but rather to a group of methods aimed at decreasing surgical trauma, by minimising the size of the incisions and avoiding full sternotomy.

In a recent meta-analysis, Sündermann et al.46 showed excellent short-term and mid-term outcomes with MIMVS, by comparison to conventional surgery, with regard to stroke, mortality, MVRepair rate and durability of the repair. MIMVS has also been associated with reduced bleeding and blood transfusion, ventilation time and intensive care stay, as well as with elimination of sternum-related morbidity and more rapid resumption of normal activity.77 Moreover, Iribarne et al.48 have reported that MIMVS was associated with lower hospital costs.

Although robotic-assisted MIMVS has become the least invasive approach, totally endoscopic and without thoracotomy or significant rib spreading, it is associated with high capital investment, resulting in higher per-case operative costs. Still, approximately 10% of all MIMVS procedures in the USA are already performed using this method. The advantages reported are the superb three-dimensional visualisation of the valvular and subvalvular apparatus and the precise movements given by the EndoWrist, which permits complex surgical manoeuvres with high degree of dexterity.37

Finally, along came the transcatheter techniques. Since the feasibility Everest Phase I Clinical Trial, in 2005, the MitraClip technology has ‘forced’ the entry into the MR treatment arena, and its use for inoperable or high-risk patients with degenerative MR has been approved by the Food and Drug Administration. However, there are several key issues that require further attention before this procedure becomes accepted in a large scale.

Most importantly, it is founded on the edge-to-edge operation developed by Alfieri in the early 1990s, not consensus within the surgical community because the procedure only yields functional and not anatomical correction. Of note, the Alfieri group have recently evaluated their long-term results (18 years) with the technique and verified that the isolated procedure, without annuloplasty, was not satisfactory, hence stressed the need for a reliable annuloplasty to improve long-term outcomes.39

However, several methods of percutaneous mitral annuloplasty have, so far, yielded less than optimal results. The early failure of repair is exceedingly higher in the MitraClip patients and the need for MV surgery or reoperation increased by five-fold, and 58% of these patients had significant MR at 4 years compared to 18% in the surgical group in one recent study.40

CONCLUSIONS

The contemporary results of transcatheter MVRepair are still far from optimal, especially in degenerative MR where surgical techniques have demonstrated incomparably better results until this date. In this pathology, valve replacement is exceptionally required. Improved surgical techniques, with particular emphasis on chordal substitution, have played a fundamental role in achieving these results. The techniques are very reproducible and at the reach of the majority of centres and surgeons. Therefore, for the foreseeable future, percutaneous therapy of MR will be limited to patients who would otherwise not be eligible for surgery.

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