

**Mitral valve repair for endocarditis.**

S. Solari<sup>1</sup> and E. Navarra<sup>1</sup> (co-first author), L. De Kerchove<sup>1</sup>, G. El Khoury<sup>1</sup>.

<sup>1</sup>Cardiovascular and thoracic surgery Department. Saint Luc University Clinic. Av Hippocrate 10, 1200 Brussels. Belgium.

Corresponding Author

Silvia Solari

Cardiovascular and thoracic surgery Department

Saint Luc University Clinic

Av Hippocrate 10, 1200 Brussels. Belgium.

## Introduction

Many authors have reported their results of mitral valve (MV) repair<sup>1,2</sup> in acute and healed endocarditis. However, the results published from different authors highlight the fact that the reparability rate for this indication remains low. In fact, in a meta-analysis published in 2007, Feringa et al.<sup>3</sup> showed that the rate of MV repair (MVr) for endocarditis was only 40%, compared to 90% for degenerative disease<sup>4</sup>. The reason could be related to the serious preoperative clinical condition of those patients from one side, and to the complexity of the MV lesions observed in active infective endocarditis (IE), that can probably entice many surgeons to replace rather than repair. Over the last 3 decades our group has adopted an early and repair-oriented approach to the infective endocarditis with the objective to improve the repair rate and the long-term results. In this paper we describe our institutional experience on MVr for IE.

## Material and methods

From 1991 to 2015, 160 consecutive patients in our institution underwent MV surgery for active IE on native MV. The median follow-up was 122 months. Demographical and clinical preoperative characteristics of the whole population are described in Tables 1 and 2. This study was approved by the institutional ethics review board, and written informed consent was waived for this study given its retrospective design.

## *Epidemiology*

Heart valve infections are a quite uncommon pathology with an estimated annual incidence of 3–10 cases in 100,000 in a normal population. With a mortality standing between 15 and

30% (according to clinical circumstances and to the infective organism)<sup>5,6</sup>, this pathology still remains a life-threatening disease that causes also significant morbidity.

As a result of the enormous progress made in terms of diagnosis and treatment, the epidemiological profile of IE has changed in recent decades, as shown by the EURO-ENDO Registry. According to the paper published by EURO-ENDO Investigators in 2019<sup>7</sup>, nowadays IE more frequently affects male patients (around 60 years of age); prosthetic valve IE, intracardiac device-related IE, nosocomial, staphylococcal, and enterococcal endocarditis are more frequent. Moreover, oral streptococcal endocarditis is less frequent, and its frequency has not increased since implementation of the 2009 and 2015 recommendations restricting indications for antibiotic prophylaxis. These considerations help to draw the contemporary profile of patients suffering IE.

#### *Endocarditis Team*

As described in 2015 Guidelines, the implementation of an Endocarditis Team is strongly recommended in order to manage the complexity of this pathology<sup>8</sup>. . In our center we introduced the concept of endocarditis team in 2018 . Besides the intra-hospital management of the patients, the Endocarditis Team provide a correct follow-up in line with the very latest recommendations and participate in patient education program. As shown in the 2019 by Davierwala and colleagues, the Endocarditis Team approach provide a multidisciplinary approach to the patient, enhance the early diagnosis, implement of comprehensive therapeutic strategies and appropriate decision-making, which play an important role in reducing the high morbidity and mortality associated with this disease<sup>9</sup>.

72 *Time of surgery and deal with complication*

73 It's experts' opinion that surgical treatment is necessary in approximately half of the patients  
74 suffering from IE, in order to prevent severe complications such as heart failure, uncontrolled  
75 infection and embolism<sup>10</sup>. In this context, all US and European guidelines are aligned on the  
76 indication of early intervention when surgery is needed.<sup>8,11,12</sup>

77 Early surgery means a surgery "during initial hospitalization before completion of a full  
78 therapeutic course of antibiotics"<sup>11</sup>. Early surgery should be performed in all IE with severe  
79 valve dysfunction to prevent heart failure (and prevent the complete valve destruction, that  
80 could preclude a valve repair), in case of infection due by multi-resistant microorganisms (S.  
81 Aureus, fungal or others), in presence of abscess, heart block, deep tissues destruction, and  
82 in case of a persistent bacteremia and/or fever longer than 5-7 days after onset of an  
83 appropriate antibiotic therapy. Other indications to apply for early surgery are the presence  
84 of large vegetations (larger than 1 cm) and recurrent emboli. In some patient with large and  
85 unstable vegetations, an emergency (in 48 hours) surgery should be considered to avoid  
86 catastrophic emboli. In case of cardiogenic shock, an emergency surgery (in 24 hours) should  
87 be performed <sup>8</sup>.

88 While in in the abovementioned cases the recommendations are quite intuitive, there are  
89 different challenging situations that the surgeon has to deal with. In fact, symptomatic  
90 neurological events develop in 15–30% of all patients with IE and additional silent events are  
91 frequent. How to handle these situations? Evidence regarding the ideal time interval between  
92 stroke and cardiac surgery is inconsistent, but most recent data favor early surgery. If any  
93 cerebral hemorrhage has been excluded by radiological and clinical assessment and if  
94 neurological clinical state is not severely compromised, surgery should not be delayed and  
95 can be performed with a low neurological risk (3–6%) and good probability of complete

neurological recovery<sup>13,14</sup>. In contrast, patients with intracranial hemorrhage, have worse neurological prognosis and surgery should generally be postponed for 2-4 weeks<sup>15,16</sup> .

With increasing experience in MV repair for active IE, we progressively expanded the indication for “early” surgery to include patients presenting with severe mitral regurgitation (MR) but no other complications. In those patients, surgery can be performed electively, even before completion of antibiotic therapy. As previously reported, in our institution the median delay between diagnosis and surgery has decreased over the time and during the last 5 years, the median delay was 9 days and 75% of the patients underwent operation within 2 weeks after diagnosis. Primary indication to surgery in our Institution are listed in table 1.

### **Surgical Techniques**

The surgical approach to the IE can be very challenging for the surgeon who is not familiar with this kind of valve lesion and a strict approach is required. In our institution most of the MV repair for IE are performed through a median sternotomy, standard cardiopulmonary bypass and a warm blood cardioplegia. The mitral valve is exposed through a left atriotomy and usually two U stitch are placed on the posterior mitral annulus at level of P1 and P3 enhance the optimal visualization of the valve. This exposition should allow to perform a careful valve analysis and a fine examination on the leaflets, commissures, and sub-valvular structures to highlight any valve lesion as vegetations, abscess or perforations. In addition, we should identify the presence of concomitant degenerative or rheumatic lesions that have to be addressed. After careful examination of the valve, the infected tissue must be completely resected. Vegetations should be resected with caution to preserve non-infected surrounding tissues and maximize the possibility of valve repair. The leaflet free margin and normal native chordae should be preserved whenever possible.

After the complete resection of infected tissue and abundant washing, the feasibility of MV repair is evaluated. Extensive destruction of a single leaflet or the presence of abscess do not contraindicate MV repair. However, the extensive destruction of both leaflets or the poor quality of the remaining tissues (through calcification, retraction or thickening) are usually a good reason to replace the valve. Repair techniques are listed in table 2.

#### *No patch techniques*

Small posterior and commissural valve defects can generally be primarily closed like usually done with triangular resection or quadrangular resection and sliding techniques. In those cases, usually, the use of artificial chordae or patch is not required to restore the valve function.

#### *Patch techniques*

In case of a large defect or in case of annular abscess or calcification, the posterior leaflet and commissures should be repaired with patch techniques. Anterior leaflet defects generally are repaired using patch techniques to avoid the reduction of its surface that could compromise the coaptation. A variety of patches are used for leaflet and annulus repair, each type having a specific indication. Autologous and bovine pericardium are the most frequently used patches. Untreated autologous pericardium is, typically used to repair leaflet perforations. It has the advantage to be cheap, but is not ease to manipulate. Glutaraldehyde-treated autologous pericardium and bovine pericardium, both offering the advantage of easier manipulation, and are used for more complex repair, such as free margin destruction repair. In those cases, the neo free margin must be suspended with native chordae transfer or

artificial chordae. Bovine pericardium is usually used when autologous pericardium is not readily available, such as re-operative surgery.

In case of large mitral annulus calcification or abscess, the atrioventricular groove should be addressed. The resection should be carefully performed to spare the maximum of healthy tissue. After the resection of the posterior annulus for, atrioventricular junction can be repaired by multiple Teflon-reinforced U-stitch or using a bovine pericardial patch covering the area of resection. When necessary, this pericardial patch can be folded on its atrial side and used to reinsert and extend the posterior leaflet. Bovine pericardium is also generally used to reconstruct the mitral-aortic curtain after abscess resection in case of mitral or aortic endocarditis.

Three other types of patch technique are currently used in our institution for specific lesions. The tricuspid valve autograft patch is used to repair large commissural defects. The original technique was modified by adding 2 artificial chordae on the tricuspid autograft free margin to partially relieve the tension on the tricuspid papillary muscle suture<sup>18</sup>. Usually, the posterior leaflet of the tricuspid valve is harvested with a tiny layer of tricuspid annulus and the head of the papillary muscles. The tricuspid valve defect can usually be closed with a direct suture and an annuloplasty is performed as well. The flip-over technique, the transfer of part of P2 with the corresponding marginal chordae on A2, is used to repair anterior leaflet defects. This technique allows to fill the gap on the anterior leaflet without the need to add any artificial chordae. Finally, parts of MV homografts have been used to reconstruct large posterior valve defects or to repair the mitral-aortic curtain. For posterior leaflet reconstruction, the posterior part of a MV homograft inserted by first implanting its anterior and posterior papillary muscle onto the corresponding native papillary muscle and then suturing the leaflet tissue in place. Commissures were closed by a few millimeters to initiate

coaptation. After resection of the mitral-aortic continuity due to an abscess complicating aortic valve endocarditis, the aortic valve was replaced with an aortic valve homograft. The mitral-aortic continuity was reconstructed using the anterior mitral leaflet of the aortic valve homograft. The anterior mitral homograft valve was sutured with a running 4-0 polypropylene suture to the base or body of the native anterior MV.

In addition to repair of the IE lesion, any degenerative rheumatic lesion was addressed with resection techniques, commissurotomy, chordal transfer, or artificial chordae. A prosthetic ring or pericardial band annuloplasty can be used in case of annulus dilatation to increase valve coaptation and stabilize the repair.

## Results

Hospital mortality was 11.6 % ( $n = 18$ ). Early MV reoperation before hospital discharge was required in 5 (3.1%) patients. The repair failure was due to a recurrent MR on suture dehiscence in 3 patients, recurrent endocarditis in 1 patient and systolic anterior motion in 1 patient. In 4 patients the MV were replaced and in 1 patient re-repaired. Of those 5 patients, 2 died within 30 days, 1 from traumatic cerebral hemorrhage and the other from *S. aureus* sepsis (the patient with early recurrent endocarditis)<sup>17</sup>.

At 5, 10 and 15 years, overall survival in the MVr for endocarditis in group was  $79 \pm 4\%$ ,  $65 \pm 5\%$ ,  $57 \pm 6\%$ , respectively. Overall survival was similar in MVr with and without the patch ( $P = 0.57$ ). Freedom from reoperation at 5, 10 and 15 years was  $95 \pm 2\%$ ,  $88 \pm 4\%$  and  $81 \pm 6\%$ , respectively. Twelve patients required MV reoperation, 9 for recurrent MR, 1 for mixed MV disease, 1 for reinfection and 1 for MV stenosis. Of these 12 patients, 4 had re-repair and 7 had replacement. One patient died after the reoperation. Freedom from MV reoperation was



not significantly different in patient undergoing MVr with or without the patch (15 years,  $75.4 \pm 8.6\%$  vs  $92 \pm 4.5\%$ ,  $P = 0.33$ )<sup>17</sup>.

## Discussion

MV repair in IE is the gold standard treatment for patients needing surgery. As previously reported, since early 90s our group has adopted a repair-oriented surgical approach to the IE. This attitude allows us to achieves a repair rate of 80% with acceptable morbidity and good long-term results. In almost 60% of the cases, patch repairs were used to restore MV function, and the durability of those techniques approximates the durability obtained with no-patch reconstructive techniques. In our Institution MV repairs performed for remain stable over time with freedom from reoperation at 10 and 15 years of 88% and 81% respectively, with a similar rate of reoperation compared to our replacement group. These results show that for patients undergoing repair with the no-patch techniques classically used in degenerative MV disease, the durability is similar to the long-term results reported in MV repair for degenerative disease<sup>4</sup>. The use of a patch for leaflet extension or annulus repair was associated with a somewhat higher long-term failure rate in comparison with the no-patch techniques, but the difference did not reach statistical significance. Reasons for the relatively good outcomes of patch repair techniques may be that we used a patch technique for localized repair only, respecting the native tissue as much as possible, and that we adapted the type of patch to the lesion as described in our surgical techniques. Of note, patch-related durability is also influenced by the type of patch and the way the patch is used. For a pericardial patch, better durability is suggested in patients in whom it was used to treat leaflet perforation. Therefore, leaflet free margin, even a thin band, should be preserved whenever possible. The autologous transfer from posterior to anterior leaflet (the flip-over technique)

has shown no failure; a wider use of this technique may be an option to improve the results of anterior free margin repair. Suture dehiscence observed in early failures is likely related to excessive tension on the sutured tissues. There are 2 potential technical solutions to this problem: to reduce the tension on the suture and to make the suture stronger. For example, a more aggressive annular reduction in addition to quadrangular resection will reduce tension on leaflet approximation. Additional artificial chordae or chordae transfer will reduce tension on a free margin patch or a tricuspid autograft papillary muscle suture. On the other hand, reinforcement of the suture itself can be done by suturing in healthy tissues (ie, non-inflammatory tissues), by taking more tissue in the suture (ie, larger bites), or by adding single stitches over a running suture.

Our specific approach to active IE has apparently not reduced mortality in comparison with a less aggressive reconstructive surgical approach<sup>19,20</sup>. This finding may be explained by the fact that in IE, the potential survival benefit conferred by MV repair is negated by disease-related factors, such as advanced age, associated comorbidities, and perivalvular extension, which are all strong predictors of mortality. However, as already reported by Feringa and colleagues<sup>3</sup> in a meta-analysis comparing MV repair with replacement in IE, we confirm the benefit of MV repair in terms of low rates of cerebrovascular event and recurrent IE.

Concluding, in experienced centers, an early and repair-oriented surgical approach using a wide variety of repair techniques including the pericardial patch can achieve a reparability rate of 80%. These recent encouraging results, are an additional argument to continue to promote MVr in IE whenever possible. In fact, repair surgery in addition to antibiotics therapy seems to provide the best chance for patients to be cured from the infection with an optimal event-free survival.

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