Advances in Mitral Valve Repair for Degenerative Mitral Regurgitation

Philosophy, Technical Details, and Long-Term Results

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KEYWORDS

• Mitral regurgitation • Degenerative mitral valve disease • Barlow disease
• Myxomatous degeneration • Fibroelastic deficiency • Mitral valve repair • Centers of excellence
• Heart team

KEY POINTS

- Surgical mitral valve repair is the gold-standard treatment in severe degenerative mitral regurgitation.
- In patients with severe degenerative mitral regurgitation, timely surgical referral is crucial to achieve the best clinical outcome.
- A timely surgical indication and an accurate application of the reparative techniques restore normal life expectancy and quality of life.
- Particularly in presence of complex lesions, patients should be referred to centers of excellence in order to maximize the likelihood as well as the durability of the repair.

INTRODUCTION

Mitral regurgitation (MR) is the second most frequent indication for heart valve surgery in the general population.[1–3]

In industrialized countries, myxomatous degeneration of the mitral leaflets[4] or fibroelastic deficiency[5] represent together the most common causes of primary MR reaching the 60% to 70% of all causes.[6]

In the first case, also known as Barlow disease, the valve surface is large, the leaflets are diffusely thick and distended resulting in a "floppy" aspect, and the chordae tendineae are elongated and occasionally broken. In addition, annular calcification of varying degrees as well as fibrosis and calcification of the papillary muscles may be observed. Those alterations are genetically transmitted.[7,8] Patients with Barlow disease are typically younger than 60 years with a long history of a regurgitant murmur.[9]

On the contrary, in case of "fibroelastic deficiency" the mitral valve is characterized by thin and translucent leaflets and the rupture of one or more chordae tendineae, usually those underlying the central portion of the posterior leaflet.[10] In many patients, an isolated myxomatous change of the prolapsing scallop may be observed. Patients with fibroelastic deficiency disease are typically older (>60 years) and present a short clinical

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history at the clinical presentation. Of note, the spectrum of variants between these 2 typical phenotypes is wide.

When left untreated, severe degenerative MR is associated with a high yearly mortality and incidence of cardiac events.[11,12] Conversely, a timely mitral valve repair is able to modify the poor natural history of these patients restoring a normal life expectancy, comparable to that of the age- and sex-matched general population.[13,14]

Alain Carpentier[15] developed and popularized reproducible mitral valve repair techniques, mostly based on resectional approaches, which have been adopted worldwide in the last 40 years. Likewise, Robert Frater[16] established the basis of a different way to repair the mitral valve by replacing native elongated or ruptured chordae tendineae, thus respecting the anatomy of the leaflets. In the recent years, both those methodologies have been increasingly used along with minimally invasive approaches and have confirmed their durability at long-term follow-up.

Particularly in Centers of Excellence for mitral valve repair, the innovations in cardiac imaging and the introduction of the Heart Team have further contributed to the refinement of the results based on a patient-tailored approach.

ECHOCARDIOGRAPHY: THE ESSENTIAL DIAGNOSTIC TOOL FOR MITRAL VALVE REPAIR

Transthoracic echocardiography is the most important diagnostic tool routinely used to evaluate the mitral valve anatomy, the mechanism, and the degree of MR as well as the dimensions and function of the cardiac chambers. Transesophageal echocardiography becomes essential whenever more accurate information is needed, especially for the planning of surgical or percutaneous interventions. The anatomy of the mitral valve apparatus, including leaflet, annulus, and subvalvular structures, should be always completely evaluated with the purpose to enable the detection of leaflet abnormalities (eg, thickness, redundancy, calcification), the presence of clefts, and/or annular calcifications.[17]

To further improve the diagnostic accuracy, a more realistic representation of the mitral valve complex is obtained by using 3-dimensional technology, which allows infinite possibilities of multiplanar reconstructions. Extremely precise details on clefts, gaps, and perforations of the leaflets or tissue deficiency are provided. In addition, acquirement of location of the flail, height of the prolapsing segment, length of the leaflets, precise position of the regurgitant jet, and distribution of calcifications contribute to correctly plan the surgical procedure and decide on the repair technique. Finally, 3-dimensional echocardiography represents the gold standard to assess the mitral valve annular dimensions, guiding the selection of the prosthetic ring.

At the end of surgery, transesophageal echocardiography is key to assess the repair, detect any residual MR, and provide helpful details to refine the repair whenever necessary.[18]

EARLY REPAIR OR WATCHFUL WAITING: THE ROLE OF CENTERS OF EXCELLENCE

In the last few years, a significant increase in the number of patients submitted to mitral valve repair has been observed with a marked improvement of the outcomes and long-term results. Accordingly, the treatment of severe degenerative MR has been extended to asymptomatic patients in whom a successful and durable repair is very likely to be achieved with a very low operative risk.[19,20] Indeed, in patients with severe MR, symptoms may occur in a relatively advanced stage of the disease, when left ventricular dysfunction is already present and the surgical repair may not be able to restore normal life expectancy anymore.[21] On the other hand, asymptomatic patients without pulmonary hypertension, left ventricular dilatation, or dysfunction do have excellent postoperative outcomes.[11]

Those observations have been endorsed by both the European Society of Cardiology/European Association of Cardiothoracic Surgery and the American College of Cardiology/American Heart Association (ACC/AHA) guidelines, which advise mitral valve repair in asymptomatic patients with degenerative severe MR if the repair is performed in a center in which the likelihood of successful and durable repair exceeds 95% with an operative mortality risk of less than 1%.[22,23]

Nevertheless, it has to be emphasized that also the so called “watchful waiting” approach has been proposed and adopted in asymptomatic patients with severe degenerative MR with good results.[24] This strategy is based on the principle of postponing the operation until the onset of early symptoms or initial left ventricular dysfunction. When managed in an accurate manner, including active surveillance of the patients and serial echocardiographic examinations, this approach can also result in timely referral to surgery, excellent long-term survival, and good surgical outcomes.[25]

Although this matter remains the object of an ongoing debate, several groups have reported better outcomes with the “early repair” policy as compared with the “watchful waiting” approach,

in terms of operative mortality, prevention of secondary atrial and ventricular remodeling, occurrence of atrial fibrillation, and functional tricuspid valve regurgitation.[11,20,26,27] Of course, the benefits of an early operation are completely related to a successful and durable repair. Moreover, an early repair policy has to be considered only if the surgical risk is very low. If those conditions are lacking, an early repair approach cannot be justified and advocated.[28]

The results of mitral valve repair can be highly variable worldwide. Although experienced groups report repair rates greater than 90% with an operative mortality less than 1%,[29,30] in real world practice, up to 50% of the patients still undergo mitral valve replacement, with the related higher operative mortality[31] and the exposure to prosthetic valve complications.[32]

The best outcomes are achieved by the so-called centers of excellence in mitral repair, where focused surgeons, cardiologists interested in mitral valve disease, and dedicated anesthesiologists strictly interact to build up and maintain a successful mitral valve repair program. Three main criteria are crucial to define a center of excellence: first of all, the annual volume of mitral repair procedures; secondly, expert periprocedural imaging capabilities; and finally, transparency regarding outcomes.[33]

The surgeons involved should perform at least 25 repairs per year, considering that an annual surgeon volume less than 25 operations was found to be associated with lower repair rate, higher 1-year mortality, and need of reoperation.[34,35]

Mitral valve repair surgery requires a significant learning curve strictly linked to the case-load of the center. Interestingly, a higher repair rate has been observed when low-volume surgeons work in high-volume centers.[35] This finding strongly confirms the weight of focused centers in which the patients are multidisciplinary managed and low-volume surgeons are mentored by the most experienced ones.

The accuracy of periprocedural imaging is also extremely important. At least one designated cardiologist with interest in mitral valve disease should be present in the team. Echocardiography must be routinely available and the obtained data should be audited for both quality control and education. Intraoperative transesophageal echocardiography performed by accredited anesthesiologists or cardiologists is crucial to guide and evaluate the repair. Finally, at discharge or at the first postoperative outpatient visit, an echocardiography should always be performed.

Core of a mitral valve repair center should be the transparency on the results. The goals of less than 1% mortality for isolated repair, a near 100% repair rate, and less than 5% failure rate at 5 years should be pursued, and the referring cardiologists should be correctly informed.

In addition, a reference center for mitral valve repair should be scientifically productive. A minimum number of 10 papers per year should be published on peer reviewed journals, and all the players of the center should be present as speakers at international meetings. Finally, the entire team should be always up-to-date on any new topic regarding this field,[34] and every innovative technique should be explored.[36]

SURGICAL MITRAL VALVE REPAIR

Objective

Mitral repair for degenerative MR aims to obtain a "neutralization" of the disease. A well-timed operation made before the onset of symptoms, atrial fibrillation, left ventricular dysfunction, or pulmonary hypertension can ensure a competent valve without stenosis, a preserved left ventricular function, the absence of arrhythmias, or significant concomitant tricuspid regurgitation. Once reached this goal, the patients will experience a survival expectancy similar to that of the general population.[13,37]

Timing of Mitral Regurgitation Correction

According to current European[22] and US[23] guidelines, mitral valve repair for primary MR is recommended in symptomatic patients or in those with left ventricular dysfunction. In asymptomatic patients with preserved left ventricular function, surgery should be considered in presence of pulmonary hypertension or atrial fibrillation. Surgery should also be considered in asymptomatic patients with preserved left ventricular ejection fraction ($\geq$60%) who are in sinus rhythm when left ventricular end-systolic diameter is greater than 40 mm according to the US guidelines or 40 to 44 mm for the European guidelines, when a durable mitral valve repair is likely and performed in a center of excellence and operative risk is low.

In the remaining asymptomatic patients, without other indication for surgery, the most appropriate management (early repair vs watchful waiting) remains controversial. However, in elderly patients with considerable comorbidities and/or complex valve lesions a "watchful waiting" approach seems more appropriate.[24]

Surgical Technique

In the last 20 years, an evolution of the reparative techniques and the surgical approaches has been progressively observed. As alternatives to

conventional full median sternotomy, several mini-invasive approaches such as right minithoracotomy or totally endoscopic approach, with or without robotic assistance, have been increasingly used and preferred by many surgeons.

During mitral valve repair, an accurate exposure is key to perform the procedure. Left atriotomy through Waterstones groove remains the favorite approach to the mitral valve, although a transseptal incision or a superior approach through the roof of the left atrium may be adopted.

Once the mitral valve has been exposed, an in-depth analysis must be performed. In first instance, it is critical to discriminate between myxomatous degeneration and fibroelastic deficiency, and it is important to consider the possibilities of intermediate degrees between these 2 extreme forms. The mitral leaflets are gently pulled to assess their mobility and to identify chordal elongation or rupture. Because the anterior scallop of the posterior leaflet (P1) does not prolapse in most of the cases, it is commonly used as reference point to evaluate the presence and degree of prolapse of the other scallops of both leaflets. Subsequently, the subvalvular apparatus and the commissural area are assessed. Finally, the mitral annulus is checked to identify dilatation and calcification.

According to the classification proposed by Carpentier,[15] type II lesions are usually present in degenerative mitral valve pathology. The proper identification of those lesions will guide the choice of the reparative technique.

Aim of the repair approach, firstly described by Carpentier[15] and still largely adopted in the contemporary worldwide practice, is to restore the physiologic leaflets motion, to establish an adequate line of leaflets coaptation, and to stabilize the annulus.

Beside these concepts, new procedures have been proposed over the last years, including the use of artificial chordae[38] and the edge-to-edge technique.[39]

In the present days, greater than 95% of degenerative lesions can be successfully repaired in centers of excellence (**Table 1**).

PROSTHETIC ANNULAR RING

Prosthetic annuloplasty plays a key role in modern mitral valve repair and is routinely carried out using a ring or a band.

Table 1
Surgical mitral valve repair feasibility

	Easily Repairable Valve	Tough Anatomy	Relative Contraindications to Mitral Valve Repair
Involved leaflet	Posterior	Anterior or bileaflet	None
Leaflet calcifications	None	Mild	Moderate to severe
Annular calcifications	None	Mild to moderate	Severe or with significative leaflet involvement
Chordae tendineae and papillary muscles	Thin	Mild diffuse thickening	Severe and diffuse thickening with leaflet involvement
MR mechanism	Fibroelastic deficiency or focal myxomatous prolapse or flail	Forme fruste or bileaflet myxomatous disease. (Barlow); active or healed endocarditis with minimum leaflet destruction; mild leaflet fibrosis or thickening	Severe leaflet tethering or fibrosis; active or healed endocarditis with severe leaflet or annular tissue destruction
Adjunctive features	None	Mitral re-repair; anatomic context with high risk of systolic anterior motion; adult congenital pathologies	Mitral valve re-repair with little native leaflet tissue left; radiation-induced MR; papillary muscle rupture

The aim of prosthetic annuloplasty is to restore the normal shape of the annulus, the physiologic ratio between the anteroposterior and intercommissural annular diameters, to prevent further dilatation, and to increase the coaptation of the leaflets. All those effects strongly contribute to the long-term durability of the repair.[40–42]

POSTERIOR LEAFLET PROLAPSE

Triangular/Quadrangular Resection

The most frequent cause of degenerative MR is represented by the prolapse or flail of the central scallop (P2) of the posterior leaflet. When the lesion is very limited, a triangular resection of the prolapsing portion may be used (**Fig. 1**). Conversely, when the prolapse is relatively large, a quadrangular resection represents the technique of choice, eventually followed by plication of the annulus at the base of the resected portion.

However, annular plication may expose to the risk of kinking of the circumflex artery. A sliding or folding plasty can be alternatively adopted to avoid this complication and prevent a systolic anterior motion of the anterior leaflet by decreasing the height of the posterior mitral leaflet.

Artificial Chordae Implantation

Polytetrafluorethylene (PTFE) chordal implantation has become a popular technique for the treatment of the prolapse or flail of the posterior leaflet. PTFE neochordae can be implanted in either anterior or posterior papillary muscles and then sutured to the free margin of the leaflet.

For the proper application of this technique, it is crucial to establish the correct length of PTFE neochordae. Different methods have been proposed, mostly consisting in adjusting the length of the neochordae after filling the left ventricle with saline or cardioplegia solution and then pushing the redundant leaflet tissue into the ventricle to obtain a good coaptation surface. Several years ago, modified artificial chordae with premeasured loops have been introduced to facilitate the use of this method. The proper length of the loop may be chosen preoperatively based on transesophageal echocardiography measurements or intraoperatively by using a dedicated caliper.

ANTERIOR LEAFLET PROLAPSE

The repair of anterior leaflet prolapse is more complex than the repair of the posterior one. Different techniques may be used.

Chordal Transfer

Chordal transfer consists in selecting the normal looking secondary chordae, detaching their insertion on the leaflet, and reattaching them to the margin of the anterior leaflet with 5.0 polypropylene suture. A limitation of this technique is the number of the normal chordae available in valves affected by extensive disease.

Chordal Transposition

Native normal chordae attached to the posterior leaflet can be transferred to the anterior one to correct a prolapsing segment.

The chosen chordae are resected from the posterior leaflet with a portion of the surrounding tissue and transposed on the free margin of the anterior leaflet.

A major advantage of this technique is that the transferred native chordae already have the correct length. Conversely, the main disadvantage is

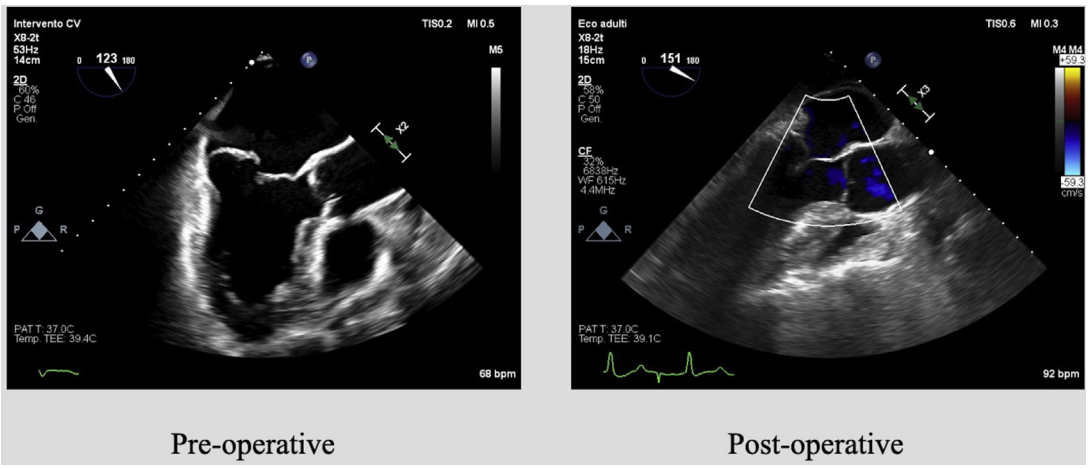

Fig. 1. Posterior leaflet prolapse treated by triangular resection.

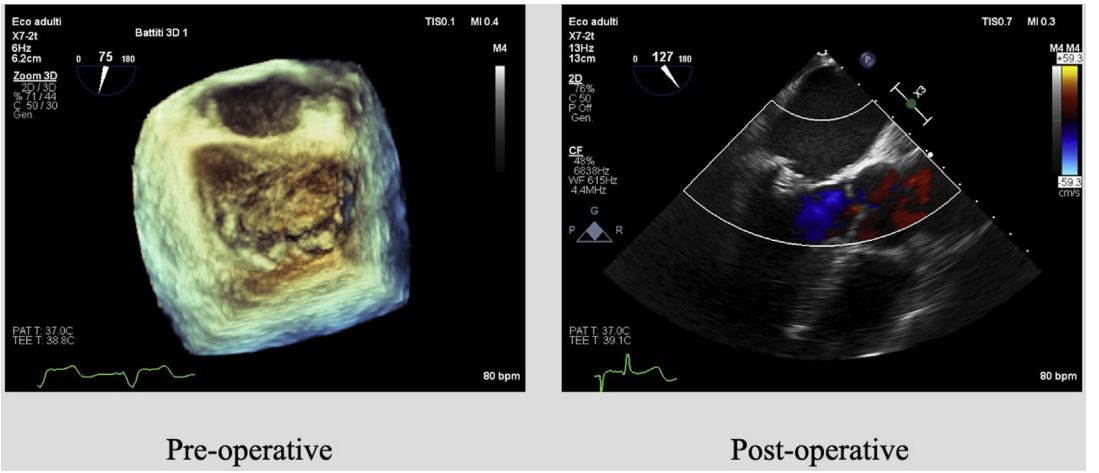

Fig. 2. Anterior leaflet prolapse treated by neochordal implantation.

represented by the fact that a portion of the posterior leaflet not affected by the pathology will be resected.

Implantation of Artificial Chordae

The use of artificial PTFE neochordae is also indicated for the treatment of anterior leaflet prolapse (Fig. 2). The implantation technique, the measurement methods as well as the potential employment of preformed loops follow the same rules discussed for the disease of the posterior leaflet.

Edge-to-Edge Technique

A segmental prolapse of the anterior mitral valve leaflet can be effectively treated with the edge-to-edge technique. This technique consists of suturing together the matching edges of both leaflets at the site of MR. When the prolapse involves the central scallop of the anterior leaflet (A2), this correction creates a double orifice valve. On the other hand, when the lateral (A1) or medial (A3) scallops of the anterior leaflet are affected by the prolapse, the edge-to-edge suture results in a single orifice valve with a relatively smaller area.

This approach allows a "functional" rather than an "anatomic" repair, which has nevertheless demonstrated an effectiveness and durability not inferior to conventional "anatomic repairs" at long-term.

BILEAFLET PROLAPSE

Simultaneous prolapse of both leaflets is typically observed in patients affected by global myxomatous degeneration of the mitral valve (Barlow disease). A combination of the surgical techniques previously described in the context of posterior

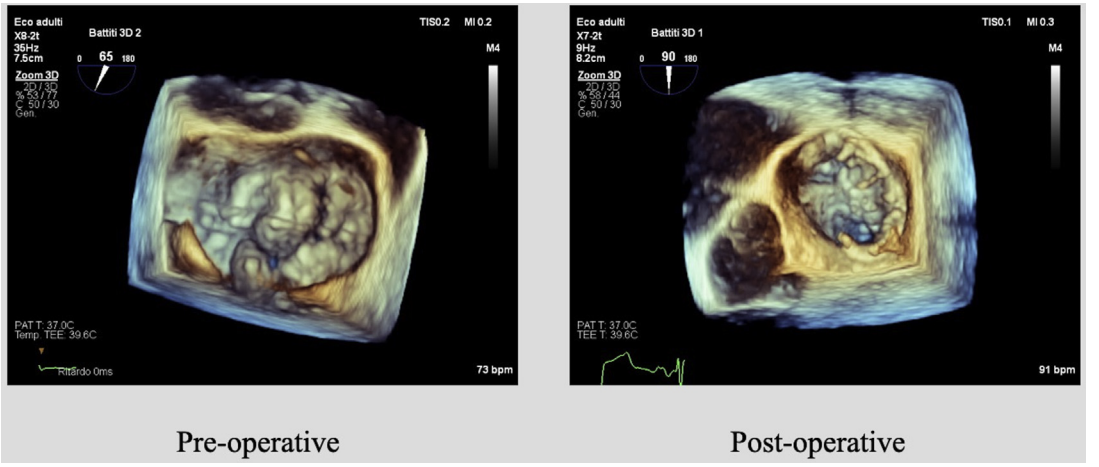

Fig. 3. Bileaflet prolapse treated by edge-to-edge technique.

Table 2
Outcomes of mitral valve repair

	N. pts	30-d Mortality	Overall Survival	Freedom From/CI REDO	Freedom From/CI MR ≥3
Seeburger et al,[53] 2008	1339	2.4%	82.6% at 5 y	96.4% at 5 y	-
Di Bardino et al,[52] 2010	1042	0.6%	62% at 20 y	82% at 20 y	-
David et al,[50] 2013	606	0.8%	66.8 at 18 y	90.2 ± 2.4% at 18 y	67.5 ± 4.2% at 18 y
Yaffee et al,[49] 2014	1612	1.3%	77% (PB) 83% (CR)	95% (PB) 92% (CR)	91% (PB) 92% (CR)
Tabata et al,[48] 2014	700	1.3%	85.9% at 12 y	88.7% at 12 y	72.3% at 12 y
Coutinho et al,[37] 2016	475	1.2%	61 ± 3.7% at 15 y	88 ± 2.7 at 20 y	-
Suri et al,[42] 2016	1218	-	-	6.9 ± 1% at 15 y	13.3 ± 1.2% at 15 y
Li et al,[54] 2020	322	1.6%	96.9%	91.2	73.4%

Abbreviations: CI, cumulative incidence; CR, complete ring; PB, posterior band.

and anterior leaflet prolapse can be used to address the multiple lesions characteristic of this etiology. Alternatively, the edge-to-edge technique dose have one of its best indications in this difficult setting (**Fig. 3**).

RESULTS OF SURGERY

Despite the absence of randomized trials, all the observational data accumulated so far have demonstrated that mitral valve repair is associated with lower hospital mortality, better survival, and lower morbidity at long-term as compared with mitral valve replacement.[43] Remarkably, in degenerative mitral valve disease, hospital mortality after isolated mitral valve repair is less than 1% in high-volume centers.[44–46]

Patients undergoing mitral valve repair before the onset of symptoms and left ventricular dysfunction will experience survival and quality of life similar to that of the same-age healthy general population.[13,37] Conversely, life expectancy will be significantly decreased if the procedure is carried out in patients with reduced LVEF or with symptoms of congestive heart failure.[47]

The long-term durability of mitral valve repair depends on the lesions causing the regurgitation, the surgical technique, and the experience of the center. The presence of residual MR greater than mild immediately after surgery is a strong predictor of repair failure at long term.

In many studies, the long-term durability of mitral repair is still evaluated by using the freedom from reoperation. Nowadays this cannot be considered an accurate parameter because the reoperation rate underscores the true recurrence of MR, which should represent the only endpoint to assess the validity of the repair technique[42,46,48–50] (**Table 2**).

Different results have been observed according to the involved leaflet. For the isolated prolapse of the posterior leaflet, both freedom from reoperation and freedom from recurrence of moderate or severe MR are excellent, especially when surgery is performed in high-volume center.

Conversely, for anterior and in bileaflet prolapse, the outcomes in terms of rate of recurrence of moderate or severe MR are less favorable, with this risk approaching 1% to 2% per year.[48–53]

The presence of annular calcification, large leaflets prolapse in the context of severe myxomatous degeneration, and subvalvular involvement are some of the conditions that make the repair particularly challenging.

Specifically, in these complex cases, patients should be referred to experienced centers with a multidisciplinary heart team to maximize the likelihood of a durable reconstruction.[34]

SUMMARY

Surgical mitral valve repair represents the standard of care for patients with severe degenerative MR. This approach is safe and almost invariably feasible, especially when performed in high-volume centers. A timely surgical referral is crucial to carry out the operation with a very low operative risk. In addition, using the appropriate techniques,

the durability of mitral valve repair is excellent, and normal life expectancy combined with good quality of life is restored.

CLINICS CARE POINTS

- Patients with severe degenerative mitral regurgitation left untreated show a poor clinical outcome.
- Appropriate surgical correction of mitral regurgitation provides a restored life expectancy and quality of life.
- Heart Team approach and centers of excellence for mitral valve repair are important to obtain a durable valve repair with low surgical risk.

COMPETING INTERESTS

The authors declare no competing interests.

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