

The cardiologist's role in increasing the rate of mitral valve repair in degenerative disease

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Purpose of review

To highlight the relevance of preoperative differentiation of degenerative mitral valve disease based on etiology (predominantly Barlow's Disease or fibroelastic deficiency) and severity of lesions with an emphasis on how such differentiation by the cardiologist can result in increased rate of mitral valve repair.

Recent findings

In the hands of reference mitral valve-repair surgeons, 95–100% of degenerative valves are repairable, regardless of etiology; however, in the general cardiac surgical community, the repair rates are around 50%. In contrast to fibroelastic deficiency, Barlow's valves have more complex pathology and require advanced techniques to effect a repair. We present a simple algorithm that enables the cardiologist to stratify degenerative mitral valves into those that are repairable by any experienced cardiac surgeon and those that require reference-center referral to deliver a high probability of repair. Such targeted referral strategy should result in near 100% repair rate for degenerative disease.

Summary

Essentially, all degenerative mitral valves are repairable. By matching echocardiographic findings to the appropriate surgical skill level required to consistently deliver a repair, valve replacement for degenerative mitral valve disease should be infrequent.

Keywords

Barlow's disease, fibroelastic deficiency, mitral valve repair, reference mitral surgeon

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Introduction

Long-standing mitral regurgitation due to mitral valve prolapse is well established as a significant cause of cardiovascular morbidity and mortality [1], with surgical intervention often required in patients with severe regurgitation to preserve life expectancy in affected patients. Mitral valve repair is now well established and is applicable in practically all patients with mitral-valve prolapse due to degenerative mitral-valve disease [2]. Valve repair offers a distinct event-free survival advantage compared with replacement with a bioprosthetic or mechanical valve [3–5,6^{*}]. Despite a consensus in guidelines encouraging mitral valve repair [7^{**},8^{*}], it is interesting to note that a significant number of patients with degenerative mitral-valve disease still undergo planned mitral valve replacement all over the world, including the US. The reasons for this are multifactorial, but one principal issue is a poor match between the complexity of the degenerative mitral process and the expertise and experience of the operating surgeon. Many patients end up with a valve replacement not because the valves are irreparable, but because they are operated on

by surgeons who do not have the specific expertise required to complete a successful repair given the etiology of the degenerative disease and the lesions present in a particular valve. Current practice of widespread valve replacement necessarily results in decreased life expectancy and decreased event-free survival in many patients with mitral valve prolapse. Furthermore, some patients who do have a repair undergo an inadequate repair procedure, and are discovered by their cardiologist to have residual or early recurrence of mitral regurgitation; this may again be related to mismatch between the skill of the surgeon and the complexity of the valve lesions. Patients with residual or recurrent regurgitation have reduced event-free long-term survival and many will require reoperation.

Recent cardiology literature in degenerative mitral valve prolapse has focused on the quantification of the degree of mitral-valve regurgitation, the natural history of the disease, and indications for surgery [9,10^{**},11,12]. It is now imperative that cardiologists additionally become familiar with the classification of the etiology and lesions that underlie the degenerative disease process that results

in the mitral valve prolapse, as lesions and etiology have specific implication in terms of the ‘complexity’ of techniques required to achieve a successful valve repair [13^{*}]. A better understanding of the etiology and lesions in degenerative mitral valve disease will guide optimal referral of patients by cardiologists to an experienced general cardiac surgeon or a mitral valve ‘subspecialist’.

Barlow mitral-valve disease

The syndrome of mid-systolic click accompanying a systolic murmur was first described in the late 1800s, but it was in the early 1960s that its association with mitral regurgitation was demonstrated by Barlow and colleagues using cine-ventriculography [14]. Criley *et al.* [15] correctly identified the mechanism of the regurgitation as posterior leaflet prolapse due to excess leaflet motion, coining the phrase ‘mitral valve prolapse’. Carpentier and co-workers later characterized the surgical lesions resulting from the myxoid degeneration present in Barlow’s disease, which included leaflet thickening, large redundant leaflets, chordal elongation or rupture, and annular dilatation. As the myxoid degenerative process often affects the entire valve, patients with Barlow’s disease generally have complex valve pathology and dysfunction, which is most often multisegmental (i.e. involves more than one segment of the posterior or anterior leaflet).

Clinical presentation

Patients with Barlow mitral-valve disease are generally adults around the age of 50 years who have known for a long period of time, often decades, that they ‘have a murmur’. Often asymptomatic, patients may have been followed by an internist for years, and referral to a cardiologist and subsequently to a cardiac surgeon is usually triggered by the development of symptoms or signs such as atrial fibrillation, shortness of breath and fatigue, or echocardiographic

documentation of ventricular or atrial enlargement, or a decline in ventricular function, often accompanied by varying degrees of pulmonary hypertension. Physical examination most often reveals the presence of a mid-systolic click and a mid to late systolic murmur, which reflects the timing of prolapse in the setting of excess tissue and chordal elongation without chordal rupture (i.e. flail leaflet) [15].

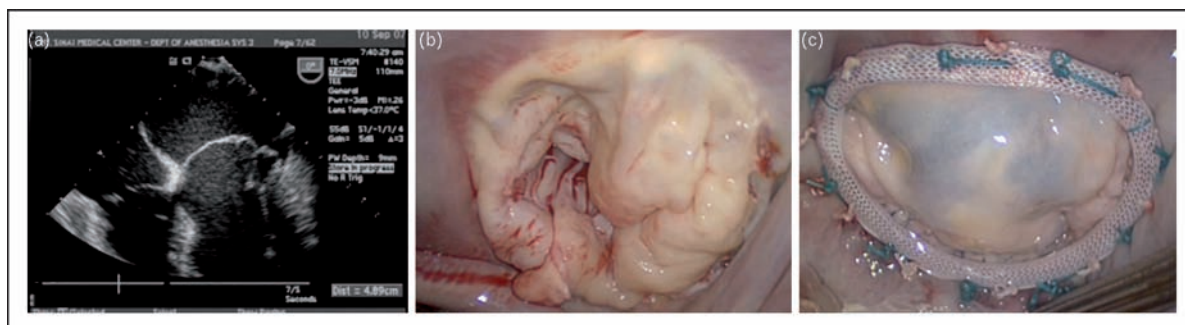
Echocardiographic findings

Echocardiography is a sensitive tool in the differentiation of degenerative mitral valve disease. A striking feature of the patient with Barlow’s disease is the size of the valve apparatus – the leaflets are usually thick, bulky, elongated, and distended; the chords thickened and elongated, often mesh-like in nature; and the annulus dilated and enlarged, often times greater than 36 mm in the intercommissural distance (Fig. 1). The prolapse is often multisegmental, and involves both leaflets in up to 40% of patients [16^{**}]. The insertion of the posterior leaflet is often displaced toward the left atrium away from its normal insertion in the atrio-ventricular groove, creating a cul-de-sac at the base of the leaflet. The bodies of distended leaflet segments often billow above the plane of the annulus, and the margin of the leaflet segments prolapse in mid-systole in the setting of chordal elongation, or in early systole if chordal rupture has occurred. Calcification of the annulus and papillary muscles may be present. Real time three-dimensional echocardiography is allowing additional clarity of the segmental nature of the billowing, as well as prolapse, in Barlow’s disease [17,18^{*},19] and may play a critical role in the preoperative work up of these patients in the future.

Surgical considerations

The complexity of surgical lesions in Barlow mitral-valve disease is consistent with the echocardiographic findings (Fig. 1). Lesions include excessively thick and billowing

Figure 1 Barlow’s disease



(a) Transesophageal echocardiography 4 chamber view showing bileaflet billowing with prolapse, large valve size, and thickened leaflet, all hallmarks of Barlow’s disease. (b) Surgical view of the same valve shows tall prolapsing leaflets with excess tissue. (c) Valve has been successfully repaired after ‘complex’ bi-leaflet plasty. Repairs of this nature can only be reproducibly undertaken by reference mitral surgeons – in nonreference settings this valve would generally be replaced.

Table 1 Targeting referral pattern to optimize repair rates

	Likelihood of successful repair	
	Experienced cardiac surgeon	Reference mitral valve surgeon
FED: posterior leaflet prolapse	Almost certain	Certain
FED: anterior leaflet prolapse	Possible	Certain
Barlow's disease: posterior leaflet	Possible	Certain
Barlow's disease: anterior or bi-leaflet	Unlikely	Almost certain

FED, fibroelastic deficiency.

leaflet segments, chordal elongation and chordal rupture, calcification of the papillary muscles and/or annulus with chordae restriction, and severe annular dilatation with giant valve size. It is important that the cardiologist as well as the surgeon has an appreciation for these lesions, as the complexity of techniques required to achieve a successful repair then becomes obvious in this subset of degenerative mitral-disease patients. Dealing with excess tissue height is an important consideration to reduce the likelihood of postoperative systolic anterior motion. Repair of Barlow valves is thus more complicated and, in our experience, often requires multiple different techniques and 2–3 h to remove all of the diseased tissue, and reconstruct the leaflets to a normal configuration [16**]. To achieve a Barlow repair, the surgeon therefore needs to be well versed with various advanced mitral repair techniques, such as extensive leaflet resection, sliding leaflet plasty, chordal transfer, neochordoplasty, commissuroplasty, annular decalcification and use of large annuloplasty rings. Patients with advanced forms of Barlow's disease will therefore likely have a high probability of successful valve repair only if done in reference centers by mitral subspecialists (Table 1).

Fibroelastic deficiency

In contrast to Barlow's disease, patients with mitral regurgitation due to fibroelastic deficiency have a lack

of connective tissue as the pathological mechanism that triggers leaflet and chordal thinning and eventual chordal rupture [13*]. Carpentier's group characterized the typical findings in fibroelastic deficiency, noting that the chordal rupture resulting in mitral valve prolapse was often isolated, usually leading to prolapse of a single leaflet segment [20].

Clinical presentation

The typical patient with fibroelastic deficiency is over the age of 60 years, and does not have a long history of a heart murmur. Often asymptomatic until the time of chordal rupture, the patient often presents with palpitations or shortness of breath of limited duration. Patients may remain asymptomatic after chordal rupture, and present as a new-onset murmur or abnormal echocardiogram, but this is less frequent than in the setting of Barlow's disease. Physical examination is remarkable for a holosystolic murmur, often harsh in nature.

Echocardiographic findings

In contrast to Barlow's disease, echocardiographic signatures of fibroelastic deficiency include normal or near-normal valve size, thin leaflets and chordae, and typically single segment prolapse, most commonly of the middle scallop of the posterior leaflet (P2) (Fig. 2). The prolapsing segment may appear to be distended, thickened, and elongated, while the adjacent segments appear normal in height and consistency. Billowing of nonprolapsing segments is not observed, and bi-leaflet dysfunction is uncommon.

Surgical considerations

In contradistinction to Barlow's disease, patients with fibroelastic deficiency often present with minimal, as opposed to excess, tissue (Fig. 2), so extensive leaflet resection or complex leaflet remodeling procedures are rarely indicated. In general, a limited quadrangular or triangular resection, or simple leaflet resuspension with a

Figure 2 Fibroelastic deficiency



(a) Transesophageal echocardiography 4 chamber view shows single segment prolapse in a normal sized valve with isolated ruptured chord. The leaflets do not billow. (b) Valve analysis shows an otherwise normal-looking valve with a single chordal rupture to the P2 segment. (c) This valve was easily repaired with a limited triangular resection and ring annuloplasty, techniques that can be reproducibly performed by most experienced cardiac surgeons.

chordal transfer or artificial chord, is all that is required to correct leaflet prolapse. For posterior leaflet prolapse, although the prolapsing segment may look very abnormal, the remainder of the valve is relatively unaffected, so that the surgeon does not usually require advanced techniques to achieve a successful mitral valve reconstruction. It should, however, be noted that ‘complex’ prolapse can occur in fibroelastic deficiency, usually involving an anterior leaflet segment or a commissural segment, and in this setting more advanced techniques and surgical skill are generally required to perform a successful reconstruction. Otherwise, simple fibroelastic deficiency with P2 prolapse is a condition associated with high repair rates in most experienced surgeons’ hands, and a virtually 100% repair rate within a reference center setting with a mitral repair subspecialist (Table 1).

Early referral or watchful waiting

It is interesting to note that longitudinal studies of the natural history of mitral valve prolapse have not taken into account the underlying etiology – Barlow’s disease or fibroelastic deficiency. On the basis of natural history, typical lesions, and typical regurgitation patterns, one can, however, make the assumption that patients with Barlow’s disease are more likely to undergo a longer period of event-free survival before developing typically accepted indications for surgery, such as symptoms, depressed left ventricular function, moderate pulmonary hypertension, or atrial fibrillation. Fibroelastic deficiency, on the other hand, often presents with holo-systolic regurgitation, in older individuals, and may require closer follow-up in anticipation of a shorter event-free period prior to surgical referral.

This logic is highlighted in two recent articles assessing event-free survival in asymptomatic patients with severe mitral regurgitation. Enriquez-Sarano and colleagues [21] reported on a cohort of patients with quantitatively graded severe mitral regurgitation with a mean age of 63 years (typical of fibroelastic deficiency), and concluded that early referral should be considered because of high event rates, including increased cardiac mortality, over 5 years of follow-up. In contrast, Rosenhek and colleagues [22] presented good results with a policy of watchful waiting in patients with semi-quantitatively graded severe mitral regurgitation with a mean age of 55 years, which is more typical of Barlow’s disease (although by 8 years of follow-up many patients developed an indication for surgery, also typical of Barlow’s disease). Interestingly, when Rosenhek *et al.* [22] looked at the subgroup with flail leaflets (i.e. ruptured chordae), the event-free survival rate diminished, although the numbers were too small to make any significant conclusions. Nonetheless, until future reports take into account specific lesions and presumed etiology in terms

of the impact on the natural history, it is logical to counsel asymptomatic patients with Barlow’s disease and chordal elongation (mid-systolic regurgitation) that continued close follow-up is a reasonable alternative to early surgery, emphasizing most will require elective valve reconstruction within several years of follow-up. On the other hand, patients with fibroelastic deficiency and severe regurgitation should be made aware that events are common early during follow-up so early surgery is advisable.

Reference center referral

The new ACC-AHA Guidelines for Management of Patients with Valvular Heart Disease [7**] have introduced the concept of ‘reference center’ referral to ensure patients who have complex degenerative valve disease requiring surgery have the best possible chance of avoiding a valve replacement, particularly in the asymptomatic setting. Criteria to define a ‘reference center’ for mitral valve repair were not given, but phrases such as high likelihood of repair depends on the ‘skill and experience of the surgeon’ are inferential to reference centers. The United Kingdom is also starting to explore the concept of best-practice standards for patients with degenerative mitral valve disease, suggesting a surgeon undertaking such procedures should perform a minimum of 25 mitral valve repairs a year, and a center 50 repairs a year, to be part of a network of mitral valve repair centers [23*]. Perhaps of more significance, it was explicitly recognized that patients with Barlow’s disease should ideally be referred to ‘super-specialists’ to increase the likelihood of valve repair. Although healthcare purchasers have not yet become involved, it is significant that Dr Bernadine Healy, former head of the National Institutes of Health and the American Red Cross, wrote a recent article in a major US news magazine entitled ‘The Mitral Valve Question’ [24], which highlighted in clear layman’s terms that too many patients undergo inappropriate mitral valve replacement. The relevance of reference center referral is summarized in the advice she gave to a patient with mitral regurgitation a decade earlier – ‘someday he would likely need an operation, and wherever he was, whoever his doctor was, he must go to a place skilled at repair’. Such counseling should also apply today to most of our patients requiring elective surgery for mitral regurgitation. With the new attention being brought to bear from various directions, it would be surprising not to see the field of mitral valve repair evolve toward a reference center model, already commonplace in subspecialties like heart transplantation and congenital heart surgery. Healthcare purchasers and health authorities may also mandate certain requirements for hospitals and surgeons to be credentialed in mitral valve repair. In the meantime, practicing cardiologists and internists should carefully counsel patients regarding the issue of outside reference referral, particularly in younger

patients where an unnecessary mechanical valve replacement could result in substantial reduction in overall life expectancy and event-free survival.

Solving the mitral valve repair quandary

While the overall mitral valve repair rate continues to increase in the United States, the rate of progress is too slow for many patients, as current estimates suggest that repair rates now approach 50% in patients with degenerative disease. Most simple prolapses due to fibroelastic deficiency can be repaired by experienced cardiac surgeons, while most complex valves can be repaired in the hands of mitral valve subspecialists [16^{**}]. There should therefore be sufficient surgical skill in most health systems to achieve a high repair rate provided patients are appropriately matched to the level of surgical expertise required to repair their valves (Table 1). This will, however, often require referral of patients with complex disease to reference centers that have mitral valve subspecialists.

It is imperative that all cardiovascular physicians re-dedicate themselves to increase the mitral valve repair rate for degenerative disease to at least 90% in the next 5 years. This is an attainable goal but will require a change in referral patterns and a commitment for active assessment of clinical activity. Table 2 summarizes our recommendations to increase the rate of mitral valve repair. Cardiologists should become more familiar with the causes of degenerative mitral regurgitation and specifically the lesions that lead to the valve dysfunction. The introduction of real-time 3D echocardiography should facilitate both lesion identification and localization, when it becomes integrated into everyday practice. Once the lesions and etiology are distinguished, the cardiologist will then be in a position to select a surgeon based on the surgeon's expertise with the particular lesions present in the patient. Concentrating referral to a specific local surgeon interested in mitral repair (rather than to all local experienced cardiac surgeons) will ultimately help grow local expertise and, with time, such surgeons would acquire expertise to take on more complex cases, thus negating the need to travel to reference centers for any but the most complex of cases. During consultation, the surgeon must be honest about his own personal experi-

ence with valve repair for the specific mitral lesions and etiology that have been identified, and not hesitate to discuss referral of a specific patient to a mitral subspecialist. Specifically, their own personal repair rate for the condition presented (for example, bi-leaflet prolapse with presumed Barlow's disease) should be part of the informed consent provided to the patient.

Combining this strategy with a regular audit of clinical activity by both the cardiologist and surgeon should increase the uptake and quality of mitral valve repair.

Conclusion

No patient should be referred or accepted for surgery without a careful review of the echocardiographic lesions by the cardiologist and surgeon. Repair rates below 90% or residual or early recurrent 2+ or greater mitral regurgitation rates above 5% in patients separated by etiology (i.e. Barlow's or fibroelastic deficiency) or leaflet involvement (posterior compared with anterior or bi-leaflet) suggest the need for continued education and more reference-center referral. The mitral valve repair quandary is solvable; by targeted referral practice, cardiologists will play a pivotal role moving the field forward.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 156–157).

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Recently updated guidelines on management of valvular heart disease introduces the concept of reference center referral for mitral valve repair.

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European consensus guidelines note that the results of mitral valve repair are highly dependent on the experience of the surgeon, especially for valves with complex lesions. These guidelines recommend that surgery on asymptomatic patients be considered only where there is high likelihood of a durable repair.

Table 2 How cardiologists can improve the rate of degenerative mitral valve repair

1. Identify the etiology and the specific lesions
2. Refer to a mitral subspecialist if there is any doubt about reparability
3. Anticipated local repair rate <90% suggests the need for reference center referral
4. Early recurrent MR ($\geq 2+$) rate >5% suggests the need for more reference referral
5. Develop local expertise for simple lesions through targeted referral

MR, mitral regurgitation.

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