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Mitral Valve Repair With Artificial Chordae: A Review of Its History, Technical Details, Long-Term Results, and Pathology

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Mitral valve repair is considered the procedure of choice for correcting mitral regurgitation in myxomatous disease, providing long-term results that are superior to those with valve replacement. The use of artificial chordae to replace elongated or ruptured chordae responsible for mitral valve prolapse and severe mitral regurgitation has been the subject of extensive experimental work to define feasibility, reproducibility, and effectiveness of this procedure. Artificial chordae made of autologous or xenograft pericardium have been replaced by chordae made of expanded polytetrafluoroethylene (PTFE), a ma-

terial with the unique property of becoming covered by host fibrosa and endothelium. The use of artificial chordae made of PTFE has been validated clinically over the past 2 decades and has been an increasing component of the surgical armamentarium for mitral valve repair. This article reviews the history, details of the relevant surgical techniques, long-term results, and fate of artificial chordae in mitral reconstructive surgery.

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There is strong evidence that mitral valve repair for degenerative valve disease is superior to mitral valve replacement [1, 2]. Very long-term results of mitral valve repair have shown that this procedure, maintaining both valvular tissue and the subvalvular apparatus, has a lower operative mortality, with better preservation of left ventricular function and superior survival rates, than does prosthetic valve replacement [3]. These results suggest an indication for early mitral valve repair in asymptomatic patients and in patients without signs of left ventricular dysfunction [4]. Techniques for mitral valve repair have been popularized by the pioneering work of Carpentier [5], who described various methods of mitral valve reconstruction based on a new pathophysiologic classification. Among these methods, particular attention was given to the treatment of elongated or ruptured chordae, which is a common pathologic finding in patients with both fibroelastic deficiency and those with more complex Barlow disease of the mitral valve [6]. The techniques of leaflet fixation on secondary chordae, chordal transposition, and chordal shortening that Carpentier proposed [5] were undoubtedly appealing, but also technically quite demanding and not easily reproducible. Furthermore the reported results generated conflicting opinions about the effectiveness of these techniques [7, 8], particularly because the repaired chordae are still diseased and may again elongate or rupture with

time, leading to recurrent mitral regurgitation. For this reason, there has been recent renewed interest in the use of artificial sutures to replace diseased native mitral chordae. This paper reviews the history, surgical techniques, and long-term results for such chordal replacement, and discusses the fate of artificial chordae on the basis of available pathologic data.

Material and Methods

A search of the Medline and PubMed databases was conducted for articles in the English language, supplemented by information obtained from archives of the journals available on the CTSNet website and from personal files. Pertinent articles were selected on the basis of the following keywords: mitral valve repair, mitral valvuloplasty, mitral chordae replacement, artificial chordae, expanded polytetrafluoroethylene sutures, and Gore-Tex sutures. Articles containing information on the use of artificial chordae, in terms of technical details, pathology, and results of their use, were considered in this review; also included, for comparison, were articles reporting the long-term results of mitral valve repair using various techniques, with or without chordal replacement.

History

The Use of Pericardium

In patients with degenerative mitral valve disease, mitral incompetence is most often a consequence of the elongation or rupture of chordae tendineae, or both [9, 10].

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Successful repair in this condition was occasionally achieved by direct suture of the affected chorda or leaflet to the papillary muscle, or by chordal replacement with various types of sutures (silk, nylon, mersilene, or other, unspecified materials) as shown by scattered case reports or small clinical series in the early or mid-1960s [11–19]. It is unclear why such suture materials were not effective for chordal replacement. Some of the patients treated with such sutures did not survive operation and others underwent reoperation because of technical failures. Indeed, the reported follow-up of patients who survived has been quite limited, and information about the fate of the various suture materials used in repairing their chordae is lacking. In 1949, Templeton and colleagues reported the use of pericardial tissue to reconstruct cardiac valves [20]. They replaced a cusp of the tricuspid valve in dogs with a graft of fresh, autologous pericardium shaped to contain a rudimentary chorda that was attached to a stump of a papillary muscle. Early results showed that this type of graft maintained function and flexibility in most animals. Other investigators demonstrated the feasibility of mitral valve repair, both experimentally and clinically, done with various techniques and differently shaped pericardial grafts [21–23]; however, in the oldest specimens the grafts appeared almost invariably thickened, fibrosed, and shrunken.

In 1964 Frater reported the anatomic rules for repair of a diseased mitral valve [24]. These were based on thorough review of the basic anatomy of normal canine and human mitral valves, with a particular focus on the role played by the chordae tendineae. The essential observation was that although the leaflets had irregular shapes and lengths that varied from one leaflet segment to another, and although the chordae had varied origins and lengths, the free edges of the anterior and posterior leaflets were always parallel wherever they met. If a chorda became too long, the free edge it supported would slide up toward the atrium and normal coaptation would be lost. Knowledge of this made it possible to determine the proper length of a neochorda: the proper length was the length that kept the anterior and posterior free edges parallel when they were in the straight lines they assumed during systole. These rules were validated by replacing the posterior mitral leaflet and chordae with autologous pericardium both experimentally and clinically [25]. The results showed that the pericardium implanted in dogs retained early flexibility but was thickened and contracted in older explants. This technique was applied in 7 patients, who had implantation of a posterior pericardial cusp with chordal sheets with good early hemodynamic results. By 1969, however, it was apparent that the pericardium had lost function because of excessive fibrous healing [26].

Interest in the use of pericardium in replacing ruptured mitral chordae was renewed by the work of Rittenhouse and coworkers in 1978 [27]. This technique was applied clinically in 10 patients with severe mitral regurgitation, in whom strips of autologous pericardium were attached to the papillary muscles and then to the free margin of the mural mitral leaflet, yielding in most cases

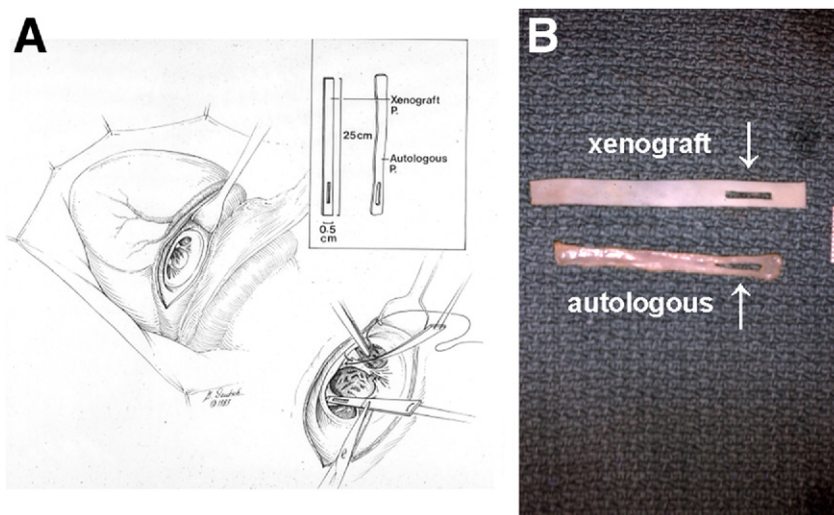
chordae of approximately 2 cm in length. Rittenhouse and coworkers' early results were excellent, with almost complete resolution of mitral regurgitation in all 10 patients and with improved clinical status (to New York Heart Association class I) for up to 3 years in the 9 patients who survived hospitalization. Encouraged by these results, Frater and associates, now at the Albert Einstein College of Medicine in New York City, resumed both their animal experiments and clinical applications. The implantation in dogs of chordae of xenograft pericardium showed that pliability was retained in early explants, with various degrees of fibrosis and calcification at 12 months [28]. When implanted in a series of 11 patients, pericardial neochordae gave satisfactory results, allowing the conclusion that this technique was reproducible and maintained valve competence for up to 3 years [28]. Further experiments were then conducted at the Albert Einstein College of Medicine to test the difference between untreated and glutaraldehyde-treated autologous pericardium and glutaraldehyde-treated xenograft pericardium in dogs and sheep [29, 30]. In these experiments, strips of pericardium were shaped to replicate the intercaval spaces, and were attached to papillary muscles and both the anterior and posterior mitral leaflets (Fig 1). All neochordae showed good healing at both ends, retaining their original length (Fig 2). Untreated autologous pericardium became uniformly fibrosed and stiff, treated autologous pericardium had a marked fibrous reaction at the healing ends but retained its pliability, and xenograft pericardium became stiffened; calcification was observed in all long-term explants [29, 30].

The Use of Expanded Polytetrafluoroethylene

Although the work described above clearly demonstrated the feasibility of chordal replacement, the long-term fate of pericardium as a potential chordal substitute was questionable, indicating the need for a longer-lasting material with which to create neochordae. The stimulus for investigating expanded polytetrafluoroethylene (ePTFE) for this purpose came from the observation that although arterial grafts made of GoreTex (Gore-Tex, WL Gore and Associates, Inc., Flagstaff, AZ) did not acquire an inner host covering, the first 1 to 2 mm were seen to have a host covering of fibrous and endothelial tissue. Gaps in the structure of ePTFE, known as "intermodal spaces," had provided attachment of the material to fibroblasts. This led to the belief that an ePTFE suture with the same spaces might gain a covering of host tissue. Vetter tested ePTFE sutures in sheep, and by 5 months the host sheep had grown new chordae over the template provided by the suture [31].

Expanded polytetrafluoroethylene is a thermoplastic polymer used in a wide variety of applications. It has outstanding physical, chemical, mechanical, and thermal properties, and in particular is flexible, with a high tensile strength and resistance to fatigue. The suture material made of ePTFE is a microporous, nonabsorbable, monofilament that, owing to its mechanical and biologic properties, appeared to be an ideal material for constructing

Fig 1. One of the techniques used to replace mitral valve chordae in animal experiments at Albert Einstein College of Medicine in the early 1980s. (A) A drawing of the procedure used to compare autologous and xenograft pericardium. Usually, two pairs of pericardial chordae (approximately 2.5 cm of length and 0.5 cm of width) were first sutured to the tip of each papillary muscle and then to the free margin of the posterior mitral leaflet. (B) The strips of autologous and xenograft pericardium before implantation with creation of intercordal spaces (white arrows).



synthetic neochordae for mitral valve repair surgery. However, in the initial experiments with ePTFE done by Vetter and colleagues [31] in sheep CV2 Gore-Tex (the equivalent of 2-0 conventional sutures) with a host tissue covering showed significantly reduced chordal flexibility. Subsequently, at the same institution, Zussa and associates [32] conducted a study in which CV5 ePTFE sutures

used both in dogs and sheep provided good healing at the papillary muscle level as well as on the cusp side of the mitral valve. On histologic examination for up to 13 months after implantation, the sutures appeared to be progressively and uniformly covered by fibrous tissue with a neointimal cellular sheath and without signs of calcification. All of the chordae made of ePTFE maintained their original length, pliability, and bending properties. These results were replicated by Revuelta and colleagues [33], who confirmed at electron microscopy that ePTFE chordae implanted in sheep were completely covered by tissue with a collagen structure resembling that of a native chorda.

After the provision of experimental evidence that ePTFE sutures could be safely used to replace diseased mitral chordae, clinical application of this technique was begun for treating patients with degenerative mitral valve pathology, and extending to patients with rheumatic disease [32, 34]. Early results of this technique were gratifying, leading to the consideration that it was simpler than chordal transfer and the expectation that it would become the procedure of choice after the durability of ePTFE had been proven [35].

Surgical Techniques

Each two-armed Gore-Tex suture allows the creation of a pair of neochordae. Recently, techniques have been proposed by which multiple chordae can be obtained by using premeasured Gore-Tex loops [36–38]. In this technique, 4-0 to 6-0 sutures are usually used to construct as many chordae as considered necessary. In the original technique, ePTFE sutures were attached to a papillary muscle in a mattress fashion, with reinforcement by Teflon pledgets on both sides, and were then tied [32]. The two ends of the suture were fixed separately at the free margin of the mitral leaflet, with the stitch brought through the edge and tied around a metal clip or a small ePTFE pledget. Revuelta and associates used a similar technique [33], differing in that both arms of the suture

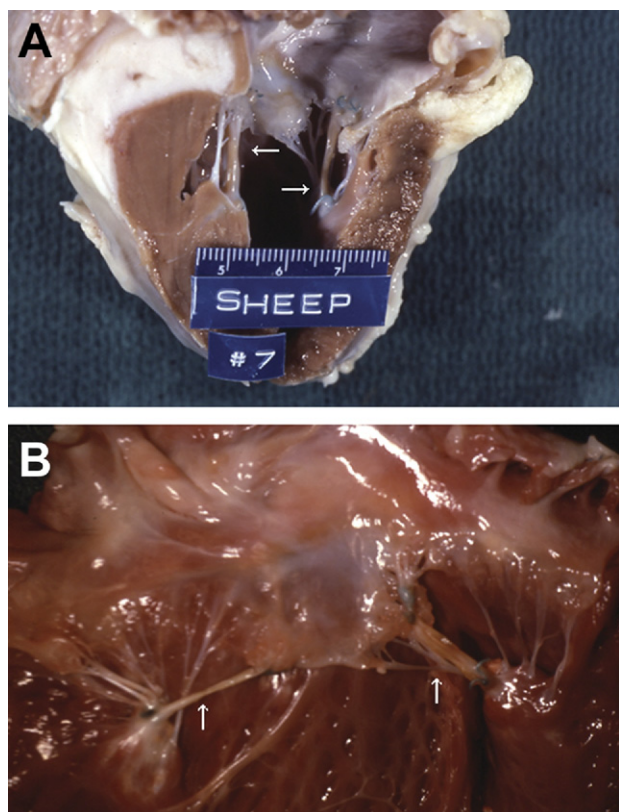


Fig 2. Gross view of explanted hearts after short-term animal sacrifice. (A) The white arrows indicate the pericardial neochordae which retained their original length. (B) Closer view of the anterior mitral leaflet with two pericardial chordae (white arrows).

were brought to the free edge of the leaflet and then woven into the leaflet toward the annulus, where they were tied on a pledget. Many surgeons have adopted such a technique and it has remained fairly standardized. Major variations have included the use of a single pledget at the papillary muscle attachment of the suture, the use of pericardial or ePTFE pledgets instead of Teflon pledgets, and the non-use of pledgets [39–42].

On the leaflet side, sutures are usually passed at least twice on the free margin of the prolapsed leaflet and then tied on the atrial or ventricular side. According to each surgeon's preference, the suture on the leaflet side can be reinforced with small pledgets, particularly if the free margin of the leaflet appears fragile. Prolapsing leaflets commonly have jet lesion-induced thickening of their free edges, which have sufficient strength to hold the sutures well. However, Gore-Tex is slippery, and surgeons have sometimes found that the carefully chosen lengths of ePTFE neochordae have become too short after the suture knot is tied. Some surgeons build multirow knot towers to avoid this problem. There appear to be no consequences of this practice apart from an unaesthetic appearance. The avoidance of this problem is achieved in one of the two following ways: (1) The suture is locked as the knot is begun. There are multiple techniques for doing this, but once locked, the suture can be tied firmly enough to produce the compression of the thread that produces the friction that prevents it from slipping. (2) The free edge of the leaflet is held under tension at the correct height while the knot is tied. Among many methods for achieving this, placement of a nitinol clip has been shown to be effective and safe [43, 44].

A prerequisite for achieving mitral valve competence is the correct sizing of artificial chordae. The basic principle in this is that during systole, with the chordae in straight lines, the apposing edges of the mitral valve are normally at the same level. Since the chordae are also under tension in diastole [45], it is possible in the arrested heart to insert, under tension, a chorda of normal length opposite a rupture and to choose a new chorda of a length that keeps the edges of the valve leaflets parallel to one another. The ingenuity of surgeons around the world has produced multiple effective solutions for achieving this goal. The simplest method appears to be that used in early experiments or clinical applications [33, 35, 46]. In this method, the chordae have been sutured in place and the left ventricle is filled under pressure until perfect leaflet apposition is obtained. The sutures can then be gently pulled until valve competence is achieved, and can then be tied. This technique has maintained its validity with time, and with certain modifications is still currently successfully used [41, 42, 47–49].

Measurement of the length of artificial chordae may be done preoperatively by means of transesophageal echocardiography. Calafiore suggested such measurement by echographic measurement of the distance between the plane of the mitral annulus and the edge of the prolapsing mitral leaflet. The length of the artificial chorda is obtained by subtracting the length of the elongated

chorda, measured intraoperatively with a ruler, from the initial measurement [50]. Mandegar and coworkers have proposed drawing a line between the base of the anterior and posterior mitral leaflets and calculating the distance between the head of the posterior papillary muscle and the line at the coaptation of the leaflets [51]. Others have favored the intraoperative use of calipers to obtain the correct length of artificial neochordae [36, 37, 52]. More recently, there has been clinical validation of techniques that allow intraoperative adjustment of the length of artificial chordae until perfect coaptation of the mitral leaflet is obtained [53, 54].

There is common agreement that the use of ePTFE chordae should be associated to other repair procedures, particularly in the correction of complex mitral valve disease. Although most surgeons favor the routine use of an annuloplasty ring, excellent midterm results have been obtained with the use of artificial chordae for both anterior and posterior leaflet prolapse without ring annuloplasty [55]. It must, however, be emphasized that the results of this latter approach are at variance with those in most other studies, which suggest a decreased durability of repair when annuloplasty is not done [56, 57]. A further point is the need to emphasize the fundamental role of intraoperative echocardiography in assessing valve pathology, in guiding surgical procedures, and in evaluating the adequacy and effectiveness of mitral valve repair.

Long-Term Results

The results of mitral valve repair have been excellent for periods of up to 20 years both in terms of patient survival and the stability of repair [3, 4]. However, most reports of such repair in the literature present its results as cumulative data, without stratification according to the technique used, which prevents full evaluation of the effect of artificial chordae on the outcomes of such repair. David and associates reported their experience with mitral valve repair with and without chordal replacement [39]. At 10 years there was 75% survival, 96% freedom from reoperation, and 93% freedom from severe recurrent mitral regurgitation. According to David and associates' statistical analysis, chordal replacement had no effect on these endpoints [39].

Although ePTFE chordae have been used in mitral valve repair surgery for more than two decades, data on the long-term clinical results of this technique are limited, with few papers reporting results of 10 or more years of follow-up. Kobayashi and colleagues described 74 patients undergoing mitral valve repair with ePTFE sutures, with an operative mortality of 1.4% [40]. At 12 years they observed an actuarial survival of 89% and an 82% freedom from reoperation. They attributed their higher reoperation rate as compared with that of others to a large number of patients with more complex disease, with bileaflet prolapse, and to the initial lack of adoption of ring annuloplasty. However, none of their cases of recurrent mitral regurgitation were caused by rupture or malfunction of artificial chordae. Kasegawa and associ-

ates, in 2006, reported a 12-year follow-up of the repair of anterior mitral leaflet prolapse with ePTFE chordae [41]. Among 236 patients with severe mitral regurgitation, ePTFE chordae were used in 204 patients, with a 1.4% 30-day mortality. At 12 years, survival and freedom from reoperation were 85% and 90%, respectively. The longest follow-up so far available, and the one involving the largest series of patients, is that conducted by Salvador and coworkers [42], who reported a 20-year experience with mitral valve repair using artificial chordae in 608 patients. In their series, chordae made of ePTFE were used in the repair of a wide variety of mitral valve pathologies, most of which were degenerative, with an operative mortality below 1%. Data at 15 years of follow-up indicate an 84% actuarial survival, a 92% freedom from reoperation, and an 85% freedom from severe mitral regurgitation. Again no cases of primary failure of ePTFE chords were observed.

All these excellent results clearly indicate that chordal replacement can be successfully applied to a variety of anatomic situations and provides effective and stable mitral repair. Recently, Perier and coworkers presented the results of a more conservative approach to the reconstruction of posterior mitral leaflet prolapse, using artificial chordae without tissue resection [58]. At 10 years of follow-up, they reported an 87% survival, which was the same as that for the general population matched for age and sex, and a 93% freedom from reoperation. Various studies have shown that the midterm results of the repair of prolapse of the posterior mitral leaflet with either quadrangular resection or the use of artificial chordae are equivalent [59–61]. However, in a randomized prospective trial, Falk and coworkers [59] could demonstrate a significantly longer line of leaflet coaptation after the implantation of ePTFE loops than after leaflet resection. Early and midterm echocardiographic follow-up revealed excellent valve function in the majority of their patients, with no significant difference in mitral orifice area from that with leaflet resection [59].

Satisfactory results were also obtained with the use of artificial chordae in children, although the experience in this patient population is much more limited than that with adults. Early data supported the use of Gore-Tex sutures for repairing various mitral valve malformations in children [62, 63]. Over the long range, freedom from reoperation at 15 years was as low as 80%, probably owing to the severity of mitral disease and complexity of repair in children, although no reoperation was necessitated by chordal malfunction [64].

The extended experience acquired with artificial chordae made of ePTFE for mitral valve repair has allowed its use for different purposes. Thus, for example, Sintek and Khonsari reported the use of ePTFE chordae to re-establish annular papillary connection after complete valve excision during mitral valve replacement, demonstrating the versatility of ePTFE in addition to its other properties [65].

Pathology Associated With the Use of ePTFE Chordae

Because of the excellent long-term durability of mitral valve repair with ePTFE sutures, little is known about the structural changes observed in artificial chordae implanted in patients, although some information about this can be obtained from a few reports of clinical and pathologic findings. The early changes observed in ePTFE sutures are similar to those observed in animal experiments, indicating that artificial chordae made of ePTFE soon become covered by fibrous tissue, although with a slower rate of host tissue overgrowth [32]. Others observed an early proliferation of fibroblasts without a detectable endothelial layer [66]. In intermediate-term observations, made from 6 to 9 years after implantation, ePTFE chordae usually kept their flexibility, being encapsulated with fibrous tissue covered with endothelium, but without calcification [67, 68]. Although there are data to the effect that even after 10 years ePTFE chordae are still flexible and pliable, or have extensive fibrosis that makes them indistinguishable from native chordae [42], there is evidence that with the progression of time, artificial chordae may degenerate, calcify, and eventually rupture (Fig 3). The first case of ruptured ePTFE chordae as cause of recurrent mitral regurgitation was described by the Toronto group in 2004 [68]. In this case, calcification led to chordal rupture 14 years after the repair of damage from rheumatic mitral valve disease. Subsequently, Coutinho and associates reported two similar cases, occurring 6 and 11 years after the repair of myxomatous mitral incompetence [69]; in the one case in which histologic findings were available, calcification of the synthetic material was observed. Farivar and colleagues reported the case of a patient in whom severe hemoglobinuria was caused by recurrent mitral regurgitation from a ruptured artificial chorda 11 years after its insertion; unfortunately, no pathologic data were provided in this case [70]. Fukunaga and coworkers presented the case of a patient with dystrophic calcification of ePTFE sutures causing chordal shortening and recur-

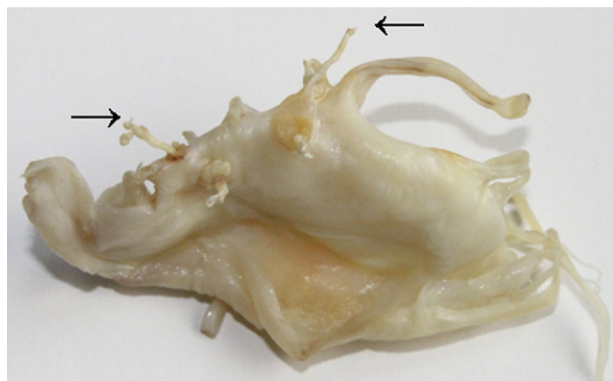


Fig 3. Rupture of an ePTFE chorda, causing severe recurrent mitral regurgitation in a patient approximately 11 years after mitral valve repair. Arrows indicate the torn chordae, which connected to the anterior mitral leaflet.

rent mitral incompetence from loss of coaptation of the mitral leaflets [71]. Features common to the reported cases of ePTFE-related pathology indicate that with time, a fibrous reaction may be a potential site of dystrophic calcification that weakens the ePTFE, causing chordal failure. Interestingly enough, no cases of calcification of Gore-Tex chordae have so far been reported in the pediatric population.

Available clinical data and the limited number of pathology reports related to their use have documented excellent durability and a low rate of structural deterioration of ePTFE chordae. However, it must be recognized that many patients with valve failure following mitral valve repair may not undergo reoperation, and the true incidence of artificial chordae failure may therefore be underestimated. On the other hand, it must be also emphasized that recurrent mitral regurgitation from chordae that are too long or inappropriately placed must not be considered as failures of ePTFE but essentially as technical errors.

Conclusion

Mitral valve repair is the procedure of choice to correct mitral regurgitation for myxomatous disease, yielding long-term results that are superior to those with valve replacement. The use of artificial ePTFE chordae is an established method for addressing the problem of elongated or ruptured chordae causing mitral valve prolapse. This technique appears to be safe, effective, and reproducible, and has become a useful additional tool among the many tools needed for the repair of most cases of degenerative mitral valve disease. However, the use of artificial ePTFE chordae requires a learning curve that is difficult to quantify and can be extremely variable. Indeed, learning curves, particularly in the field of mitral valve repair, depend not only on each surgeon's experience and case exposure but also on the complexity of the disease.

Review of the experimental and clinical experience acquired with the use of ePTFE in mitral valve repair allows the following conclusions:

- Classical techniques led the way in establishing repair as the optimal mode of handling degenerative mitral valve disease.
- The use of ePTFE chordae is by now securely established as reproducible and durable. It has enabled some surgeons to increase the number of effective repairs of mitral valve disease, and is now an essential part of the wide array of techniques needed for the conservative treatment of a greater number of cases of even extremely complex mitral valve disease. In fact, according to David and associates [72] the use of artificial chordae was the single most important factor in making mitral valve repair feasible in most patients with mitral insufficiency caused by leaflet degeneration, ranging from degeneration caused by fibroelastic deficiency to that caused by severe Barlow disease.
- A wide variety of technical solutions have been adopted for mitral valve repair with the use of artificial chordae, with particular attention directed at defining their correct length.
- It can be foreseen that the use of artificial chordae for mitral valve repair will have wide future adoption should a "nonresectional approach" to mitral valve repair [54] become widely accepted.
- It has been documented that ePTFE can occasionally fail over the long-term because of calcification. Thus, as follow-up of such patients increases. Consequently, the careful and continuous echocardiographic surveillance of patients with ePTFE chordae appears justified and mandatory as the duration of their follow-up increases.

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