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REVIEW

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Artificial chordae for mitral valve repair

Igor Vendramin MD[1] | Aldo D. Milano MD, PhD[2] | Angela Pucci MD[3] | Andrea Lechiancole MD[1] | Sandro Sponga MD, PhD[1] | Uberto Bortolotti MD[1] | Ugolino Livi MD[1]

[1]Cardiothoracic Department, University Hospital, Udine, Italy

[2]Division of Cardiac Surgery, University Hospital, Bari, Italy

[3]Division of Pathology, University Hospital, Pisa, Italy

Correspondence

Prof. Uberto Bortolotti, MD, Largo Traiano, 23, 35036 Montegrotto Terme, Italy.
Email: uberto48@gmail.com

Abstract

Background: Mitral valve repair using expanded polytetrafluoroethylene sutures to replace mitral chordae tendineae is a well-established procedure. However, the incidence of neo-chordae failure causing recurrent mitral regurgitation is not well defined.

Methods: We have reviewed the reported cases of complications after mitral valve repair related to the use of neo-chordae. This study was mainly carried out through PubMed, Medline, and Google Chrome websites.

Results: We have identified a total of 26 patients presenting with rupture of polytetrafluoroethylene neo-chordae, mostly being described as isolated cases. Few other cases of recurrent mitral regurgitation with hemolysis were found, where reoperation was not caused by neo-chordal failure but most likely by technical errors. At pathological investigation the findings were substantially similar in all reported cases. The neo-chordae retained their length and pliability, became covered with host tissue and rupture was mainly related to suture size. Mild calcification was observed not interfering with chordal function; chordal infection did never occur.

Conclusions: The use of artificial neo-chordae provides excellent late results with durable mitral valve repair stability. Chordal rupture may occur late postoperatively leading to reoperation because of recurrent mitral regurgitation. Despite its rarity, this potential complication should not be overlooked during follow-up of patients after mitral valve repair using artificial neo-chordae.

KEYWORDS

cardiovascular pathology, valve repair/replacement

Review of early and late complications

1 | INTRODUCTION

Mitral valve repair (MVr) is the gold standard treatment for patients with degenerative mitral regurgitation (MR). Based on Alain Carpentier's experience and further expanding the principles of the "French correction," MVr has become an increasingly frequent and reproducible procedure.[1] Various techniques and subsequent modifications have been adopted to increase the quality and improve the long-term outcome and durability of MVr in patients with MR. Among these, the use of artificial neo-chordae, made of expanded polytetrafluoroethylene (ePTFE) sutures (Gore-Tex, WL Gore and Associates, Inc.), is recognized as a fundamental tool to be used during MVr particularly in the most complex cases.[2,3] However, some dismal complications have been observed which might be underestimated due to their substantial rarity and an intrinsic difficulty in identifying them from large patient series. Indeed, the real incidence of such complications is unclear and since they may cause significant clinical problems, they should elicit a special attention. This article describes the cases of ePTFE neo-chordae failure reviewing the incidence and causes of this complication.

2 | METHODS

We have performed a research on PubMed, Medline, and Google Chrome to identify articles in the English literature reporting complications related to the use of ePTFE neo-chordae after MVr. Cases described in textbooks or abstracts were excluded as those mentioned in large series with scarce or any clinical and/or pathological details. Further data were obtained analyzing the reference sections of pertinent articles and the archives of the journals on the CTSNet website.

We have entered in the search various terms, alone or in combination, such as MVr, mitral chordal rupture, chordal replacement, artificial neo-chordae, ePTFE sutures, recurrent MR, ePTFE chordal rupture, ePTFE chordal calcification, ePTFE-related complications, pathology of ePTFE neo-chordae. Papers on the use of left ventricular transapical off-pump chordal implantation have not been considered.

For this study, approval by local Ethical Committees was not required as well as informed consent, since patient data were treated anonymously.

3 | BACKGROUND

The concept of replacing diseased mitral valve chordae was proposed in the 1960' using various suture materials without being followed by consistent clinical applications.[4] This idea was revitalized by the work of Robert WM Frater and associates, at Albert Einstein College of Medicine in New York, who pioneered the use of autologous and bovine pericardium to replace elongated or ruptured mitral and tricuspid valve chordae, both experimentally and clinically.[5–8] Such neo-chordae showed various degrees of fibrosis and retraction, and although it was demonstrated that replacement of chordae tendineae of the atrioventricular valves was feasible and reproducible, the need for a more durable material as chordal substitute became evident.

ePTFE was tested as material to construct mitral valve neo-chordae,[9] demonstrating great physical, chemical, mechanical, and thermal properties, high flexibility, and tensile strength with consequent resistance to fatigue.[10] ePTFE sutures, made of microporous, nonabsorbable monofilament were considered as ideal material to be used for MVr and were initially tested in sheep showing that the new chordae in a short time became covered by host tissue.[9] Furthermore, it was also demonstrated that ePTFE chordae maintained their original length, pliability, and bending properties.[11,12] Based on such experimental evidence the clinical application of this technique was started with excellent early results.[13]

4 | RESULTS

This review has identified a series of articles reporting complications following the use of artificial neo-chordae for MVr. In some cases, ePTFE sutures were directly responsible for repair failure while in others their contribution was often marginal being failures related to a surgical mistake in many cases. Most of these complications are described in single Case Reports while some of them can be extrapolated from large series.

4.1 | ePTFE chordal rupture

Table 1 summarizes the cases of early and late chordal rupture. The first case of rupture of artificial mitral chordae was described by Yeo et al.,[14] although the suture material was not specified it is very likely that such chordae were made of ePTFE. The first patient with histological evaluation of the ruptured neo-chordae was reported by Butany et al.,[15] followed by 12 further cases.[16–25] In this group there were eight males and six females, with an age range from 44 to 84 years (median, 64 years). Chordal rupture occurred early, 2, 4, and 4 months after MVr, in three cases,[14,18,20] while in the remaining 11 it was observed from 1.4 to 14 years (median, 11 years). At reoperation, a second MVr was reported only in two cases,[14,16] while in all other patients, mitral valve replacement was performed, associated to tricuspid annuloplasty in two and aortic valve replacement in one.[16,19,21] Rupture occurred in chordae attached to the anterior mitral leaflet (AML) in 11 cases and to the posterior leaflet in one; in this last case a CV-4 suture was used while in the others a CV-5 suture was employed in 9, a CV-4 in one and a CV-3 in one. For two patients, incomplete data were available;[13,15] histologic findings were reported in seven cases with ultrastructural data in 3.[20,21,25]

Other cases of ePTFE chordal rupture have been observed in large series of patients undergoing MVr but without providing specific patient information. Lam et al., analyzing the incidence of hemolytic anemia after MVr, reported neo-chordae rupture as cause

TABLE 1 Data of patients with ruptured ePTFE neo-chordae after MVR.

Author	Sex, age	ePTFE sutures size and site	Reoperation	Interval (years)	Findings
Yeo et al.[14]	M, 44	NA	MVr	0.4	Chordae rupture, hemolysis, histology NA
Butany et al.[15]	F,76	NA	MVR	14	Chordae rupture, Ca^{++}, no inflammatory cells
Coutinho et al.[16]	M, 68	CV-5 anterior mitral leaflet (AML)	MVr, new chordae	6	AML CV-5 chordae rupture, pannus formation, collagen infiltration
	F, 67	CV-5, AML	MVR, TAP	11	AML CV-5 chordae rupture, Ca^{++}, fibrosis, no inflammatory cells
Farivar et al.[17]	M, 57	NA, AML	MVR	11	AML chordae rupture, thickening, histology NA
Yamashita et al.[18]	F, 60	CV-3[a], CV-5 AML	MVR	1.4	AML CV-5 chordae rupture, histology NA
	M, 78	CV-3[a], CV-5 AML	MVR	0.2	AML CV-5 chordae rupture, histology NA
Bortolotti et al.[19]	M, 51	CV-5, AML, PML	MVR, AVR	11	AML CV-5 chordae rupture, fibrosis, minimal Ca^{++}
Castillo et al.[20]	M, 55	CV-5[a] CV3[b] AML, CV-3 PML	MVR	0.4	CV-3 and CV-5 chordal loops rupture, fibroblast ingrowth
Kudo et al.[21]	F, 60	CV-5 AML	MVR, TAP	3	AML CV-5 chordae rupture, inflammatory cells, no Ca^{++}
Mori et al.[22]	M, 65	CV-5 AML	MVR	10	AML CV-5 chordae rupture, histology NA
Nakaoka et al.[23]	M, 63	CV-5 AML	MVR	7	AML CV-5 chordae rupture, hemolysis, histology NA
Luthra et al.[24]	F, 84	CV-4 PML	MVR	12	PML CV-4 chordae rupture, Ca^{++}, histology NA
Luthra et al.[25]	F, 76	CV-4 AML	MVR	6	AML CV-4 chordae rupture, Ca^{++} infiltration at fracture point

Abbreviations: AML, anterior mitral leaflet; ePTFE, expanded polytetrafluoroethylene; F, female; M, male; MVr, mitral valve repair; MVR, mitral valve replacement; NA, not available; PML, posterior mitral leaflet; TAP, tricuspid annuloplasty.

[a]Anchoring loop to papillary muscle tip.

[b]Loop-in-loop technique.

of recurrent MR among 32 patients of their series;[26] the incidence of this complication was not specified and this issue not commented. Tabata et al., in 700 patients with MVr found that three required reoperation 4, 7, and 84 months due to ruptured neo-chordae;[27] in all cases rupture had occurred at their middle portion. David et al., in analyzing their experience spanning two decades observed only two cases of ruptured neo-chordae as cause of recurrent MR and reoperation.[28]

Recently, Mutsuga et al., reported a total of 16 ePTFE chordal ruptures which caused recurrent MR in seven patients.[29] In five the neo-chordae were attached to the PML and in two to the AML, but the total number of ruptured chordae was similar (8 vs. 7); except in one case sutures were size CV-5. Most importantly, suture rupture was identified as a predictor of risk of reoperation at univariate analysis.[29]

4.2 | ePTFE-related complications without rupture

As shown in Table 2, five patients have been reported in whom reoperation was required after MVr, the cause being referred to the presence of unbroken ePTFE neo-chordae.[30–34] There were 4 males and one female aged 49–74 years (median, 63). In all of them, the neo-chordae had been attached to the AML but only in two cases the chordal size (CV-4 and CV-5) was specified.[30,32] The indication for reoperation was hemolysis in three patients and recurrent MR in two. At reoperation, calcification of ePTFE chordae was found in two cases[31,32] and absence of chordal endothelialization in one.[33] In one patient the neo-chordae were found to be too long at reoperation[30] while in another patient two pairs of chordae attached to the AML had been incorrectly inserted at initial repair;[34] in this patient, reoperated because of early severe hemolysis, two pairs of neo-chordae were overlapping each other with AML retraction causing relevant MR.[34] In the reported cases reoperation occurred 0.2 months to 7 years, while in one case reoperation was only indicated as "early."[34] In one patient a second MVr was performed while in all others the mitral valve was replaced.

In all these cases either recurrent MR or hemolytic anemia were considered related to the presence of ePTFE sutures.

4.3 | Pathology of failing ePTFE chordae

Information on the pathologic changes in implanted neo-chordae can be obtained from few specific articles[35–37] and from scattered individual case reports;[15,19,29,31,32] furthermore, in three cases also

TABLE 2 Data of patients without rupture of ePTFE chordae requiring reoperation after MVr.

Author	Sex, Age	ePTFE sutures size and site	Reoperation	Cause	Interval (years)	Findings
Kihara et al.[30]	M, 49	CV-4, AML	MVr	Hemolysis	0.4	Chordae too long
Di Gioia et al.[31]	M, 49	NA, AML	MVR	Recurrent MR	7	Chordae fibrosis, Ca^{++}, no inflammatory cells
Fukunaga et al.[32]	F, 63	CV-5, AML	MVR	Recurrent MR	7	Chordae calcification and sclerosis
LI et al.[33]	M, 74	NA, AML	MVR	Hemolysis	0.2	Absence of chordae endothelialization
Ceresa et al.[34]	M, 65	NA, AML	MVR	Hemolysis	NA	Incorrect chordae placement

Abbreviations: AML, anterior mitral leaflet; ePTFE, expanded polytetrafluoroethylene; F, female; M, male; MR, mitral regurgitation; MVr, mitral valve repair; MVR, mitral valve replacement; NA, not available; PML, posterior mitral leaflet.

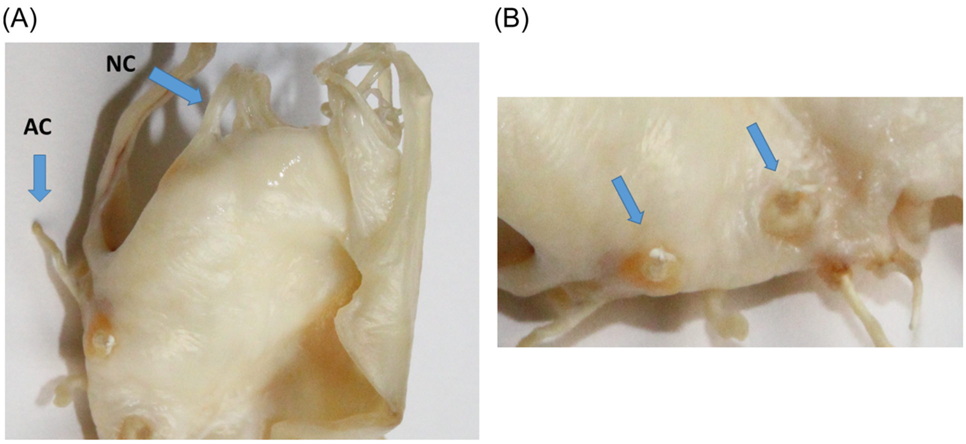

FIGURE 1 (A) Gross appearance of the anterior mitral leaflet excised at reoperation because of late expanded polytetrafluoroethylene (ePTFE) neo-chordae rupture. Remnant of an artificial chorda (AC) is barely recognizable from the natural chordae (NC) (arrows). (B) Arrows indicate the suture knots, fixing the artificial chordae to the free margin of the anterior mitral leaflet, which are still visible despite the host tissue reaction.

ultrastructural studies with electron microscopy of the explanted ePTFE chordae have been performed.[20,21,25]

From the available data, it appears that changes in ePTFE neo-chordae are quite common among all studies. In fact, rupture of ePTFE chordae generally has occurred at their mid-point or at one of their extremities. Detachment of a neo-chorda from a papillary muscle tip of from its insertion on a leaflet has been exceedingly rare.[35]

From gross appearance, ePTFE neo-chordae are generally well preserved, they maintain their flexibility and original length and with time may be difficult to differentiate from natural chordae tendineae (Figure 1A). At the attachment site on the free margin of the mitral leaflets they become incorporated by the host reaction although suture knots may still be visible (Figure 1B). Depending on the time of function they get progressively covered, usually starting from the leaflet attachment and then progressing towards their midline. Complete absence of neo-endothelialization is extremely rare and observed usually only in early explants.[33,35,38] Late postoperatively, neo-chordae have been found to have an increased thickness with at times some calcific infiltrates, extensive calcification being very uncommon.[32]

Histologically, the host tissue covering the sutures was mainly formed by collagen while the microporous structure of ePTFE became often filled by plasmaprotein insudation which could convey calcium deposition (Figure 2). Inflammatory cells were rarely seen and considered as a foreign body reaction process;[21] in particular no cases of endocarditis on artificial neo-chordae have been reported.

At the site of rupture disruption of the chord architecture was described and confirmed, as all other findings, at electron microscopy.

5 | COMMENT

The use of ePTFE neo-chordae in MVr procedures provides excellent long-term results in term of repair durability and survival.[27,28,39] The incidence of recurrent MR after MVr with the use of neo-chordae is low and generally ascribed to progression of the mitral degenerative disease or incomplete initial repair. Reoperation due to intrinsic

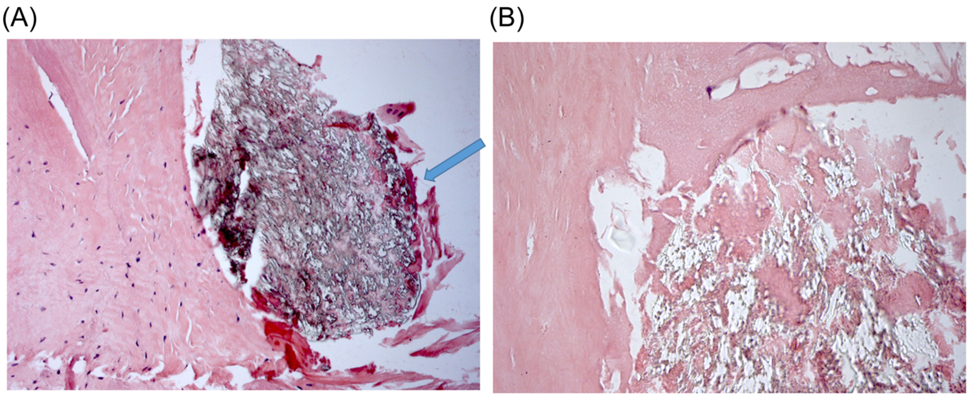

FIGURE 2 (A) Histologic section of a ruptured expanded polytetrafluoroethylene (ePTFE) chorda remnant that is partially covered by collagenous tissue which infiltrates the fibers of the chorda (arrow). (Hematoxylin—eosin staining; original magnification 20x). (B) Higher magnification of the dense, acellular or pauci-cellular connective tissue at the periphery of the ePTFE chorda. (Hematoxylin—eosin staining; original magnification 40x).

failure of ePTFE chordae is quite uncommon, as confirmed by the present review.

Postoperative rupture is the major complication related to the use of neo-chordae and it is generally reported as isolated cases or may be found as rare cause of reoperation in large patient series with extended follow-up. David et al., reviewing their 25-year experience of MVr with chordal replacement using ePTFE sutures in over 600 patients, reported 35 reoperations, only two of them being related to neo-chordal rupture.[28] Hata et al., during a follow-up of more than 20 years, did not observe instances of rupture or degeneration of neo-chordae in reoperated patients.[3] Similar results are reported by Salvador et al., in over 600 patients with a freedom from reoperation of 92% at 15 years, with no cases of ePTFE chordae failure.[40]

We have identified a total of 26 cases of rupture of artificial neo-chordae.[14–25,27–29] However, the real incidence of this complication is difficult to verify since in some reports the number of cases is not specified or the pairs of chordae implanted in each patient is extremely variable. We have estimated that in the present series of patients over 60 ePTFE neo-chordae rupture have been reported; however, it is not always clear how many neo-chordae were implanted at initial MVr. Furthermore, from a single Gore-Tex suture a pair of neo-chordae is obtained but in most articles the term "neo-chorda" or "pair of neochordae" is often used indifferently.

In some patients, recurrent MR presented with hemolytic anemia which is a well-recognized consequence of a failing MVr.[26] The degree of hemolysis depends on the regurgitant jet velocity and some distinct patterns of flow disturbance have been associated to shear stresses.[14] In some cases, hemolysis was considered the result of blood cell trauma by the contact of the regurgitant jet with the mitral prosthetic ring or the uncovered neo-chordae.[33] In two cases it was considered the consequence of excessive chordae length or incorrect insertion,[30,34] but in such cases it was an evident technical mistake.

ePTFE chordal strength much depends from the size of the sutures used for MVr. In the reported cases, CV-5 sutures were more prone to rupture compared to CV-4 or CV-3 ones. Sizing of ePTFE sutures differs from that of other traditional suturing material commonly used; Gore-Tex CV-5 corresponds to 4/0 and CV-6 to 5/0 polypropylene monofilament sutures, which should be considered when selecting the type of neo-chorda.[41] In some papers, both sizing criteria are indifferently used and this may generate some confusion. Furthermore, incorrect suture handling, using clips, forceps or other instruments, may have weakened the neo-chorda favoring rupture regardless from its initial size.[29] A point that it is important to emphasize is that instrumental manipulation of ePTFE sutures during the repair must therefore be avoided since this it is, probably, the only other aspect in which the surgeons can act to decrease the possibility of this complication to happen.

Different techniques of neo-chordae length sizing have been used, most of which have been demonstrated to be equally effective. In this study, chordal rupture did not appear to be related to any specific technique and indeed this complication involved also use of premeasured chordal loops.[18,20] Neo-chordae rupture occurred only in one suture inserted to the PML;[22] this is likely to be due to the fact that ePTFE sutures have been mostly used to repair AML prolapse. The growing experience with nonresectional approaches in MVr will certainly increase the number of ePTFE chordae inserted to the PML and their durability in this position will have to be tested with time.[42]

A recent experimental study has shown that suboptimal MVr can be caused by alterations in chordal forces and leaflet stresses, being increasingly relevant as more complex prolapse forms were considered being worst when simulating implantation of a single neo-chorda.[43] Use of multiple chordae was associated to less errors in neo-chordae length tuning and a suboptimal suture length significantly altered chordal forces and leaflet stresses, possibly influencing the long-term outcome of MVr. Other have suggested that use of a greater number of chordae would provide a more durable MVr.[39]

Unfortunately, in this study, limited information on the pathological features of failing ePTFE chordae could be found. However, in most cases uniform data were reported, indicating that even after many years neo-chordae maintain their initial size and flexibility becoming covered with host tissue rendering them unrecognizable from native chordae tendineae. At the site of rupture, ePTFE showed signs of structural deterioration owing to friction and traction forces, expression of fatigue-induced lesions;[19,20] nevertheless, due to the rare cases of suture fracture reported, ePTFE seems to maintain its structural integrity in most cases for many years.[15] It has been postulated that chordal calcification may lead to subsequent rupture.[29] Small calcific deposits within neo-chordae structure, probably favored by plasmaprotein insudation, have been occasionally observed and interestingly, only in one case diffuse neo-chordae calcification without rupture was considered responsible for MVr failure.[32] Inflammatory infiltrates were seldom found and no cases of chordal endocarditis have been reported, indicating resistance of ePTFE sutures to infection.

6 | STUDY LIMITATIONS

This study has some limitations. Most complications related to the use of ePTFE neo-chordae for MVr have been found in the description of isolated cases; in large series of patients undergoing MVr the cause of recurrent MR was not always specified which renders the real incidence of neo-chordal failure difficult to establish. Nevertheless, even if extremely rare, considering the extensive use of ePTFE sutures to treat MR through over three decades, neo-chordae rupture might be still underestimated. Furthermore, incomplete data in each reported case may allow only some speculations on the real influence of specific surgical techniques, suture sizes and site of implant on early and long-term fate of MVr.

7 | CONCLUSIONS

ePTFE sutures are excellent substitutes for ruptured or elongated mitral valve chordae causing prolapse of both AML and PML. Recurrent MR may be ascribed to neo-chordae failure in an extremely limited number of cases although the real incidence of this complication is unknown and probably underestimated. Increasing the number of neo-chordae, a correct length sizing and the use of thicker sutures seem to be prerequisites for a more durable MVr. Patients having MVr with implant of ePTFE neo-chordae should benefit from continuous follow-up and echocardiographic assessment of repair stability.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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