A 25-year study of chordal replacement with expanded polytetrafluoroethylene in mitral valve repair

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Abstract

OBJECTIVES: This study examines the outcome of mitral valve repair with chordal replacement using expanded polytetrafluoroethylene over the past 25 years.

METHODS: From July 1988 to February 2013, 224 consecutive patients (mean age 57 years, 34% women) underwent mitral valve repair with chordal replacement using expanded polytetrafluoroethylene sutures at our institution. Isolated anterior leaflet prolapse was observed in 134 patients (60%), isolated posterior leaflet prolapse was observed in 13 patients (6%) and bileaflet prolapse was observed in 77 patients (34%). The number of replaced artificial chordae ranged from 2 to 12 (mean 3.7) per patient. Transthoracic echocardiography was performed pre- and postoperatively and in the follow-up period. The follow-up period ranged from 0.3 to 25.3 years (mean 7.4, median 6.2).

RESULTS: There was 1 early death and 15 late deaths, of which 7 were cardiac related. The actuarial survival rates at 10 and 20 years were 92 and 81%, respectively. Thirty-three patients (15%) developed recurrent moderate or severe mitral regurgitation during the follow-up period and 30 patients (13%) required reoperation on the mitral valve. Rates of freedom from reoperation and freedom from recurrent moderate or severe mitral regurgitation were 84 and 82% at 10 years, and 74 and 59% at 20 years, respectively. Multivariate analysis revealed that the independent predictors of recurrent mitral regurgitation were mitral valve repair without annuloplasty ring and greater than mild postoperative mitral regurgitation; and the independent predictors of mitral reoperation were previous cardiac surgery and greater than two decades have not been well described.

CONCLUSIONS: Our 25-year follow-up demonstrated reliable long-term outcomes of chordal replacement with expanded polytetrafluoroethylene sutures.

Keywords: Chordal replacement • Mitral valve repair • Expanded polytetrafluoroethylene

INTRODUCTION

In recent years, mitral valve (MV) repair has been the preferred procedure for degenerative disease. Data from various registries show that MV repair has increased in frequency over the past decade, with superior results relative to MV replacement [1-3].

The techniques for repairing a prolapsing posterior leaflet have been well established and a great number of excellent outcomes have been reported [4, 5]. With regard to anterior leaflet prolapse, several repair techniques have been reported including triangular resection, chordal shortening, chordal transfer and edge-to-edge suturing. However, some of these techniques are considered technically demanding and not easily reproducible, with less durability than that for posterior leaflet prolapse [6, 7].

Chordal replacement with expanded polytetrafluoroethylene (ePTFE) sutures (Gore-Tex sutures; W.L. Gore & Associates, Inc., Flagstaff, AZ, USA) has been widely adopted as it is considered to increase the probability of successful MV repair [8, 9]. However, the outcomes of this technique with long-term follow-up of more than two decades have not been well described.

The objective of this study was to examine the outcomes of MV repair with chordal replacement using ePTFE sutures over the past 25 years, including histopathological analysis.
MATERIALS AND METHODS

From July 1988 to February 2013, a total of 224 patients underwent MV repair with chordal replacement using ePTFE sutures at the National Cerebral and Cardiovascular Center in Osaka, Japan. The institutional review board approved the present retrospective study and waived the need for written consent. Clinical and echocardiographic data were collected and analysed retrospectively. Echocardiography was performed preoperatively, 1 week after the operation and during the follow-up period. All studies were analysed by the cardiologists at the National Cerebral and Cardiovascular Center using standard criteria to assess the degree of mitral regurgitation (MR), which was graded on a scale of 0–4 (0: none; 1: trivial; 2: mild; 3: moderate; 4: severe).

The preoperative patient characteristics are summarized in Table 1. The patients’ ages ranged from 16 to 84 years (mean 56.5 ± 14.7 years). Thirty-four percent of the patients were female (34%) (Table 2).

The operative technique

Full median sternotomy was performed and cardiopulmonary bypass was established between the ascending aorta and both venae cavae at mild systemic hypothermia. Tepid blood cardioplegia was administered in antegrade and/or retrograde fashion every 25–30 min. All valves were assessed through a left atriotomy in the interatrial groove. As intraoperative findings, isolated anterior leaflet prolapse was seen in 134 patients (60%), isolated posterior leaflet prolapse in 13 patients (6%) and bileaflet prolapse in 91 patients (41%). The cause of MR was degenerative in 197 patients (88%) and infective endocarditis in 27 patients (12%).

Operative data

The number of artificial chordal replacements has been previously described in detail elsewhere [10]. Briefly, 4–0 double-armed ePTFE suture with a small Teflon pledget was passed through the fibrous portion of the papillary muscle head without tying, and the ends of the suture were passed twice through the free margin of the prolapsing leaflet separately from the left ventricle to the left atrium. After additional procedures for the mitral leaflet and mitral annuloplasty, which was done mostly with a ring, the length of the artificial chordae was determined by comparing with the adjacent normal leaflet or opposing leaflet during distension of the left ventricle with saline solution. The ends of the ePTFE suture were then gently tied on the left atrial side. The number of artificial chordae ranged from 2 to 12, with a mean of 3.7 per patient (Table 2).

Additional procedures done on the mitral leaflet included quadrangular resection of the posterior leaflet in 54 patients (24%), edge-to-edge suture in 33 patients (15%), chordal transfer in 1 patient (0.4%) and so on. Concomitant procedures included Maze procedures (n = 83, 37%), tricuspid annuloplasty (n = 44, 20%), coronary artery bypass grafting (n = 16, 7%), aortic valve replacement (n = 8, 4%) and so on (Table 2).

Histopathological examination

Some ePTFE sutures resected during reoperation were pathologically examined. Microscopic evaluation was performed with haematoxylin and eosin and Masson’s trichrome staining. To label endothelial cells, immunohistochemical staining for factor VIII-related antigen was performed.

Statistical analysis

Continuous values were expressed as mean ± standard deviation or median and interquartile ranges. All data analysis was performed using JMP software (Version 10; SAS Institute, Inc., Cary, NC, USA).

Table 1: Clinical characteristics of 224 patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean ± SD or n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>56.5 ± 14.7</td>
</tr>
<tr>
<td>Sex, female</td>
<td>76 (33.9)</td>
</tr>
<tr>
<td>NYHA functional class</td>
<td></td>
</tr>
<tr>
<td>I and II</td>
<td>80 (35.7)</td>
</tr>
<tr>
<td>III and IV</td>
<td>144 (64.3)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>91 (40.6)</td>
</tr>
<tr>
<td>Infective endocarditis</td>
<td>27 (12.1)</td>
</tr>
<tr>
<td>Associated diseases</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>86 (38.4)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>19 (8.5)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>7 (3.1)</td>
</tr>
<tr>
<td>Previous cardiac surgery</td>
<td>13 (5.8)</td>
</tr>
<tr>
<td>LVEDD &gt;55 mm</td>
<td>44 (19.6)</td>
</tr>
<tr>
<td>LVFS &lt;30%</td>
<td>21 (9.4)</td>
</tr>
<tr>
<td>LAD &gt;60 mm</td>
<td>36 (16.1)</td>
</tr>
</tbody>
</table>

NYHA: New York Heart Association; LVEDD: left ventricular end-diastolic diameter; LVFS: left ventricular fractional shortening; LAD: left atrial diameter; SD: standard deviation.
Kaplan–Meier analysis was used to estimate the rates of survival, freedom from reoperation and freedom from recurrent moderate or severe MR. Univariate Cox regression was used to identify several factors associated with recurrent MR. Tested factors included age over 60, female sex, preoperative New York Heart Association functional class IV, atrial fibrillation, infective endocarditis, associate diseases (hypertension, diabetes mellitus, renal failure), previous cardiac surgery, preoperative echocardiographic data (left ventricular end-diastolic dimension >65 mm, left ventricular fractional shortening <30%, left atrial dimension >60 mm, severe MR), bileaflet lesion, number of artificial chordae <6, surgery without annuloplasty ring and postoperative (before hospital discharge) MR greater than mild. Factors with P-values <0.10 were entered into the stepwise multivariate Cox regression analysis to determine the independent risk factors.

RESULTS

The median follow-up period was 6.2 years (interquartile range 1.5–10.9 years, ranging from 0.3 to 25.3 years). There was one early death of low output syndrome, 6 days after emergency MV repair for acute MR. Fifteen patients died during the follow-up period, of which seven were cardiac-related deaths. Using the Kaplan–Meier estimation, the actuarial survival rates at 1, 10 and 20 years were 99, 92 and 81%, respectively (Fig. 1).

Transthoracic echocardiogram before hospital discharge was performed in 221 patients (99%) of the enrolled 224 patients. No or trivial MR was found in 186 patients (84%), mild MR in 19 patients (9%) and mild to moderate MR in 16 patients (7%). The median echocardiography follow-up time was 5.5 years (interquartile range 1.8–10.2 years), and 182 patients (82%) had at least one available echocardiogram in the follow-up period. Thirty-three patients (15%) developed recurrent moderate or severe MR during the follow-up period. Ten of 16 patients who had mild-to-moderate MR before discharge developed moderate or severe MR during the follow-up period. Freedom from recurrent moderate or severe MR was 91% at 1 year, 82% at 10 years and 59% at 20 years (Fig. 2).

A total of 30 patients (13%) required reoperation on the MV. The indications for reoperation were recurrence of moderate or severe MR in 23 patients, haemolysis in 6 patients and infective endocarditis in 1 patient. Twenty-nine patients underwent repeat MV replacement and 1 patient underwent repeat valve repair. None of these reoperations were related to rupture or degeneration of implanted artificial chordae or tearing of the mitral leaflet or papillary muscle passed through by the ePTFE sutures. Freedom from reoperation rates at 1, 10 and 20 years were 93, 84 and 74%, respectively (Fig. 3).

Several samples of implanted artificial ePTFE chordae removed during reoperation 1–15 years after MV repair were obtained for pathological examination. Structural examination of the ePTFE sutures demonstrated that they had all retained their length, pliability and strength. Macroscopically, their surface was very smooth without calcification (Fig. 4A). On microscopic examination, the ePTFE suture was totally covered with fibrous tissue and endothelial cells without calcification or microthrombi (Fig. 4B and C). Protein infiltration was observed in the inner layer of the ePTFE suture. There was a mild granulomatous reaction without inflammatory change in the MV leaflet and papillary muscle around the suture (Fig. 4C and D).

Univariate analysis and subsequent multivariate analysis revealed that recurrent MR greater than moderate during the follow-up period was significantly associated with lack of annuloplasty ring (P = 0.022, hazard ratio 2.40) and postoperative MR greater than mild (P < 0.0001, hazard ratio 12.26) (Table 3).

DISCUSSION

Several studies have shown superior outcomes of MV repair for degenerative MR in comparison with MV replacement in terms of operative mortality, quality of life and long-term survival. In MV plasty, both mitral valvular tissue and the sub-valvular apparatus can be maintained and it can result in good preservation of left ventricular function [5].

Although standard techniques to repair posterior mitral leaflet prolapse have been well established since Carpentier proposed various methods of MV repair, correction of the anterior mitral leaflet prolapse with a reproducible and durable technique has remained a challenge [4, 11]. The techniques of leaflet fixation on secondary chordae, chordal transposition and chordal shortening were undoubtedly appealing, but also technically quite demanding [4, 6, 12]. Furthermore, repaired native chordae may
cause re-elongation or rupture in the follow-up period because they are still diseased [6]. For these reasons, the focus has turned to MV repair with artificial chordae.

From the 1960s, several materials have been used as artificial chords including silk, Teflon, nylon, autologous pericardium and ePTFE suture. Chordal replacement with ePTFE sutures was first introduced experimentally during the early 1980s, with David then adopting the technique [8, 9, 13]. After demonstration of its excellent results, many surgeons preferred using the ePTFE suture and it became the dominant material used [9, 14, 15].

We introduced chordal replacement with ePTFE sutures at the National Cerebral and Cardiovascular Center in Osaka, Japan in the 1980s. As our basic strategy, we have applied chordal replacement for anterior leaflet prolapse, and triangular or quadrangular resection for posterior leaflet prolapse. For larger or multiple prolapse of the posterior leaflet, we have adopted chordal replacement. We have also used the edge-to-edge suture for para-commisural lesions. For these reasons, we had fewer patients with isolated posterior leaflet prolapse in this study.

In the authors’ opinion, there are two big concerns regarding the technique and results of chordal replacement using ePTFE sutures. The first is how to determine the optimal length of neochordae. So far, several different techniques to adjust the ePTFE length have been reported, with two broad strategies used to generate neochordae of the correct length [6, 15, 16]. The length of neochordae may be predetermined, or determined after testing the valve function with a leaking test. The predetermined length was estimated by transoesophageal echocardiogram or direct measurement, and could not be changed minutely after securement. We thought that fine adjustment to the length of artificial chordae should be made repeatedly by checking valve coaptation until any regurgitation disappeared. Therefore, we preferred to determine the length of ePTFE sutures after the other associated procedures had been carried out, including ring annuloplasty or quadrangular resection of the posterior leaflet, and repetitive leak test by filling the left ventricle with saline.

Figure 3: Actuarial freedom from reoperation on the MV.

![Figure 4: (A) Representative macroscopic appearance of removed expanded polytetrafluoroethylene (ePTFE) artificial chordae. The patient underwent reoperation 7.5 years after MV repair. Arrows indicate implanted ePTFE sutures, six in total. (B–D) Microscopic appearance of extracted ePTFE suture and ambient tissue. Protein infiltration is observed in the inner layer and the surface of the ePTFE suture is completely endothelialized without calcification or microthrombi. No inflammatory reaction is observed in the surrounding MV tissue (B: staining for factor VIII-related antigen; C: haematoxylin and eosin staining; D: Masson’s trichrome staining). Scale bars: 100 μm (B), 200 μm (C and D).](https://academic.oup.com/icvts/article-abstract/20/4/463/653720)
Table 3: Predictors of recurrent mitral regurgitation greater than moderate

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Univariate P-value</th>
<th>Hazard ratio</th>
<th>95% CI</th>
<th>Multivariate P-value</th>
<th>Hazard ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Old age (&gt;60 years)</td>
<td>0.27</td>
<td>1.48</td>
<td>0.74–2.96</td>
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<tr>
<td>Female</td>
<td>0.20</td>
<td>1.58</td>
<td>0.77–3.15</td>
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<tr>
<td>NYHA class IV</td>
<td>0.54</td>
<td>1.41</td>
<td>0.42–3.59</td>
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<td></td>
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<tr>
<td>Diabetes mellitus</td>
<td>0.11</td>
<td>2.23</td>
<td>0.83–5.07</td>
<td></td>
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<tr>
<td>Hypertension</td>
<td>0.87</td>
<td>1.06</td>
<td>0.49–2.23</td>
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<tr>
<td>Endocarditis</td>
<td>0.77</td>
<td>1.16</td>
<td>0.39–2.77</td>
<td></td>
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<tr>
<td>Prior cardiac surgery</td>
<td>0.24</td>
<td>2.20</td>
<td>0.53–6.26</td>
<td></td>
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<td></td>
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<tr>
<td>Renal failure</td>
<td>0.58</td>
<td>1.85</td>
<td>0.10–8.66</td>
<td></td>
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<td></td>
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<tr>
<td>Atrial fibrillation</td>
<td>0.23</td>
<td>0.64</td>
<td>0.29–1.31</td>
<td></td>
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<tr>
<td>Bileaflet lesion</td>
<td>0.48</td>
<td>1.29</td>
<td>0.64–2.77</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Artificial chordae &lt;6</td>
<td>0.21</td>
<td>2.00</td>
<td>0.71–8.36</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Without ring</td>
<td>0.013</td>
<td>2.60</td>
<td>1.23–5.31</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative severe MR</td>
<td>0.75</td>
<td>1.13</td>
<td>0.56–2.42</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEDD &gt;65 mm</td>
<td>0.94</td>
<td>1.03</td>
<td>0.43–2.21</td>
<td>0.022</td>
<td>2.40</td>
<td>1.14–4.88</td>
</tr>
<tr>
<td>LVFS &lt;30%</td>
<td>0.22</td>
<td>1.80</td>
<td>0.67–4.11</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD &gt;60 mm</td>
<td>0.60</td>
<td>1.26</td>
<td>0.50–2.77</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-MR &gt; mild</td>
<td>&lt;0.0001</td>
<td>12.57</td>
<td>5.70–26.45</td>
<td>&lt;0.0001</td>
<td>12.26</td>
<td>5.51–26.04</td>
</tr>
</tbody>
</table>

NYHA: New York Heart Association; MR: mitral regurgitation; LVEDD: left ventricular end-diastolic diameter; LVFS: left ventricular fractional shortening; LAD: left atrial diameter; CI: confidence interval.

Second, the long-term outcomes of MV repair with artificial ePTFE chordae have not been well described, although mid-term results have proved to be excellent and durable [9, 10, 14, 17]. Regarding late complications, there were some documents reporting rupture of the ePTFE chordae related to the calcification of ePTFE suture or ePTFE fatigue-induced lesion [18, 19]. In the present study and in our previous studies, pathological examination revealed no structural failures of ePTFE chordae including rupture or calcification in patients with reoperation 6–9 years after MV repair [10, 20]. Although rare, calcification and rupture of the artificial chordae may cause recurrent MR. Therefore, continuous close follow-up including detailed echocardiography is mandatory.

In our study, rates of freedom from recurrent MR greater than moderate and freedom from reoperation were 82 and 84% at 10 years, and 59 and 74% at 20 years, respectively. These results are comparable with those of other large and long-term studies [21, 22]. There was a gap between freedom from recurrent MR and freedom from reoperation. One possible explanation is that some patients developed recurrent MR but chose not to undergo reoperation because of their asymptomatic status. These patients are reoperation-free, but should be considered to be at high risk of cardiac events. Therefore, careful, long-term follow-up is essential.

In the present study, univariate and multivariate Cox regression analysis revealed that residual mild or greater MR before discharge was an independent risk factor for recurrent MR. It is well known that mild residual MR that presents immediately after surgery tends to increase in intensity along with the improvement of wall motion, especially in case of anterior leaflet prolapse [23]. Therefore, periodic close echocardiographic examination is very important.

MV repair without annuloplasty ring was another independent risk factor for recurrent MR in our study. Ring annuloplasty is already regarded as a standard technique for MV repair. Our study demonstrated the importance of ring annuloplasty, which could effect complete coaptation of mitral leaflets in MV repair with artificial ePTFE chordae.

Since Perier et al. advocated the concept ‘respect rather than resect’, the mainstream strategy for repairing posterior leaflet prolapse has been shifting from the resection and suture method to techniques preserving the mitral leaflet and the sub-valvular apparatus [24, 25]. Although the resection and suture technique has shown good short-term and long-term outcomes, it results in loss of normal leaflet tissue and the sub-valvular apparatus; this may then affect left ventricular geometry and function or cause mitral stenosis to some extent. Therefore, an increasing number of patients suffering from degenerative isolated posterior leaflet prolapse will likely receive chordal replacement with ePTFE sutures in future.

Concerning the follow-up period, a few reports have demonstrated very long-term results of MV repair with chordal replacement using ePTFE sutures. David et al. [22] presented excellent results of chordal replacement using ePTFE sutures with a mean follow-up period of 10.1 years (range 0–23 years). Salvador et al. [21] reported that, in their 20-year experience, the median follow-up period was 5.7 years. In our study, the median follow-up period was 6.2 years (range 0.3–25.3 years). As our study is one of the longest follow-up studies of this technique, we believe that it should have a big impact on the choice of the MV repair technique.

Our study has some limitations. This is a retrospective, observational study of patients who underwent MV repair with chordal replacement using ePTFE sutures. The technique of additional mitral annuloplasty and use of an annuloplasty ring changed during the study, which may have influenced the incidence of recurrent MR or reoperation on MV. Although almost 99% of patients received a postoperative echocardiogram before discharge, only ~80% of patients underwent echocardiographic examination in the follow-up period. Finally, although our study cohort was probably the largest among the studies carried out in our country, it was relatively small in comparison with studies in other countries.

In conclusion, our study demonstrated excellent long-term outcomes of ePTFE sutures used as artificial chordae to repair degenerative mitral leaflet prolapse. Implanted ePTFE chordae can retain flexibility and durability without calcification for a very long time. Continuous close observation including periodic echocardiography is essential.
Conflict of interest: none declared.

REFERENCES


APPENDIX. CONFERENCE DISCUSSION

Dr H. Vetter (Wuppertal, Germany): The paper presented is an excellent retrospective clinical study because frequent echocardiographic data and histopathological examination of explanted neochords is provided. I myself am strongly interested in such patient data, because in 1984, I did have the privilege of working as a research fellow together with Dr Robert Frater at the Albert Einstein College of Medicine. In January 1984, I implanted the first Gore-Tex suture in a weaning sheep model. When the animals were sacrificed after three to 12 months, the results were very satisfactory with regard to durability and healing.

In your patient study, you did have a rather high percentage of patients in New York Heart Association classification III and IV, and 41% of patients were in atrial fibrillation. This fact would mean that your patients were in advanced mitral valve disease. We appreciate also your histopathological examination of the explanted artificial suture at the time of reoperation. As we did in our experimental study 30 years ago, you found endothelial cells within the neointima of the Gore-Tex surface. This means the neochord surface provides a structure for a real healing process. I have two questions to you.

What is your policy on operating on patients with asymptomatic mitral valve incompetence, and second, did you find elongation of the papillary muscle at the site where the artificial chords were anchored on the papillary muscle side?

Dr Hata: In your patient study, you did have a rather high percentage of patients in New York Heart Association classification III and IV, and 41% of patients were in atrial fibrillation. This fact would mean that your patients were in advanced mitral valve disease. We appreciate also your histopathological examination of the explanted artificial suture at the time of reoperation. As we did in our experimental study 30 years ago, you found endothelial cells within the neointima of the Gore-Tex surface. This means the neochord surface provides a structure for a real healing process. I have two questions to you.

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