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ORIGINAL ARTICLE

Intermediate-term outcomes of our original multiple-knot technique using ePTFE sutures for anterior mitral leaflet prolapse

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Abstract

Purpose To define the outcomes of our original simple chordal replacement technique using ePTFE sutures for mitral regurgitation.

Methods Between January, 2004 and March, 2014, 38 patients underwent mitral valve repair using our chordal replacement technique for anterior leaflet prolapse. The mitral regurgitation was caused by degenerative disease in 34 patients and infective endocarditis in 4 patients.

Results The follow-up period was 66 ± 37 months and the 5-year survival rate was 95 ± 4%. Two patients had recurrent mitral regurgitation, caused by degenerative change not associated with the procedure. The 5-year rate of freedom from recurrent mitral regurgitation was 94 ± 4%. In the late postoperative period, 15 (42%) patients had a mean pressure gradient > 5 mmHg. Stepwise logistic regression analysis showed that the use of a full ring (odds ratio 8.9; 95% confidence interval 1.2–64; $p = 0.031$) and a 26 mm annuloplasty (odds ratio 7.5; 95% confidence interval 1.1–50; $p = 0.037$) were significant independent risk factors for a mean pressure gradient > 5 mmHg.

Conclusion The intermediate-term outcomes of our original chordal replacement technique were not inferior to those in previous reports, although a 26 mm annuloplasty was found to be associated with a higher mitral valve gradient at rest.

Keywords Mitral valve · Mitral regurgitation · Mitral valve repair · Artificial chordae · Functional mitral stenosis

Introduction

Chordal replacement with expanded polytetrafluoroethylene (ePTFE) is used widely to correct anterior mitral leaflet prolapse. David et al. [1] described how the technique has evolved to creating multiple new chords with a single suture by successively passing it once through the papillary muscle and twice through the free margin of the leaflet, so that a neochord is made for every 2–3 mm of free margin of the prolapsing leaflet, thus gaining stable valve function in the long-term. Conversely, another recent study described functional mitral stenosis (MS) after annuloplasty for degenerative mitral disease, demonstrated by stress echocardiography [2].

We previously reported our original technique for artificial chordal replacement [3]. With this method, multiple knots are tied until the entire length reaches the free edge of the normal leaflet after placing a suture through the papillary muscle. We named this the "multiple-knot" technique and developed it to overcome the possible disadvantages of artificial chordal replacement, including difficulty with achieving the correct length of the new chordae and ePTFE slippage. Among the various techniques previously described [4–8], we believe that this method is easy to understand and perform in a reproducible manner, even by surgeons with limited experience.

We report the intermediate-term outcomes of mitral valve repair using our original chordal replacement technique. We also report our findings on functional mitral stenosis after mitral annuloplasty using a small size ring.

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Methods

Between January, 2004 and March, 2014, 285 consecutive patients underwent mitral valve surgery for severe mitral regurgitation (MR) at our institution. Of those, 150 were excluded because MR was caused by annular dilatation ($n=31$), rheumatic disease ($n=17$), ischemic heart disease ($n=68$), dilated cardiomyopathy ($n=20$), or other miscellaneous factors ($n=14$). In the remaining patients, MR was caused by degenerative disease in 115 and infectious endocarditis in 20. In those with degenerative disease, the prolapsing leaflet was anterior in 30 (26%), posterior in 73 (64%), and both in 12 (10%). For the 42 patients with anterior leaflet or bileaflet prolapse, mitral valve repair was done using artificial chordae in 34 and using another technique in 8. None received mitral valve replacement. Of 20 patients diagnosed with infectious endocarditis, four with an anterior chordal rupture underwent mitral valve repair using our technique. Thus, the subjects of the present study were 38 patients with anterior leaflet prolapse, who underwent mitral valve repair using our chordal replacement technique. Written informed consent for the procedure was obtained from each patient prior to surgery.

Operative technique

Our original artificial chordal replacement technique was reported previously [3]. Briefly, with our technique, a double-armed 4-0 polytetrafluoroethylene (CV4 [Gore-Tex]) suture is passed twice through the most fibrous portion of the anterior or posterior part of the papillary muscle, and then multiple knots are tied until the whole length reaches the free edges of the normal posterior and anterior leaflets. In this manner, the surgeon can accurately predict the correct length needed to hold the opposing free edges of the posterior and anterior leaflets at the same level. The two arms of the suture are then passed through the thickened free edge of the prolapsed cusp from the ventricular side to the atrial side, thus allowing the ends to be tied together without slippage (Fig. 1). After fluid-testing to confirm the competence of the valve, an annuloplasty with a partial band (Cosgrove ring) or full ring (Physio ring or Saddle ring) was performed in all of the patients. Regardless of the type of ring used, ring selection was based on measurement of the anterior leaflet; however, at our hospital, the surgeon has the option to choose a ring one or two sizes smaller, depending on the cases. During the early stage of the present series, we changed the string from CV5 to CV4, as it was considered that a multiple-knotted CV string might become fragile and lead to chordal rupture in the late stage following the procedure, although no such event has occurred at our institution. To manage postoperative anticoagulation, warfarin potassium was given to achieve an INR of 1.8–2.5 for the first 3 months, then lifelong aspirin 100 mg per day was prescribed thereafter.

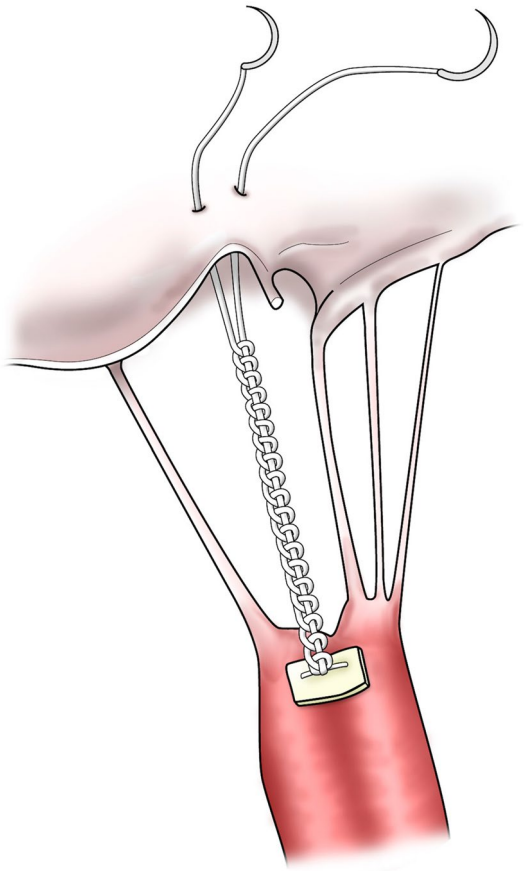

Fig. 1 Our simple chordal replacement technique for anterior mitral leaflet prolapse. A double-armed 4-0 polytetrafluoroethylene (CV4 [Gore-Tex]) suture is passed twice through the most fibrous part of the papillary muscle and multiple knots are tied. The two arms of the suture are then passed through the thickened free edge of the prolapsed cusp from the ventricular side to the atrial side, allowing the ends to be tied together without slippage

Data collection and follow-up

Patient status was assessed by referring to the medical records. Two-dimensional and Doppler transthoracic echocardiographic examinations were performed before and after the operation. All echocardiographic studies were done by expert echocardiographic examiners using commercially available 3.75-MHz transducers (Toshiba, Tokyo, Japan; Hewlett–Packard Sonos). The severity of regurgitation was classified as none (or trivial), mild, moderate, or severe, and recurrent MR was defined as that classified as moderate or severe. The mean pressure gradient (mPG) through the mitral valve was evaluated in all patients. The mitral valve

orifice area (MVA) was identified using a pressure half-time method and/or two-dimensional measurements. Postoperative functional MS was defined as mPG > 5 mmHg in this study. Early postoperative echocardiography was performed 1 week after surgery, then again, at 3 months, and every 12 months thereafter.

Statistical analysis

Patient demographics and outcome variables are expressed as either a percentage of the total or as the mean ± standard deviation. Survival and freedom from reoperation or recurrent MR were analyzed using the Kaplan–Meier method. Pre- and postoperative differences in echocardiographic measures and the B-type natriuretic peptide (BNP) level were analyzed using a paired *t* test. The difference between mPG values for the groups was analyzed using an unpaired *t* test. Associations of preoperative and surgical factors with postoperative functional MS were examined using stepwise logistic regression analysis. Factors with a p value < 0.1 were entered into the multivariate model. Statistical significance was defined as a probability value < 0.05. All statistical analyses were performed using JPM Pro 11 statistical software (SAS Institute, Cary, NC).

Results

Patient characteristics

Table 1 summarizes the patients' clinical characteristics. The mean age of the patients was 63 years (range 37–81 years). Paroxysmal or persistent atrial fibrillation was noted in 20 (53%) patients. Valve abnormality of the anterior leaflet included chordal rupture in 19 (50%) patients. Table 2 summarizes the surgical procedures. In all patients, anterior leaflet prolapse was corrected with chordal replacement. The mean number of artificial chordae (ePTFE sutures) was 2.2 ± 1.0. For the correction of posterior leaflet prolapse or commissural prolapse, resection suturing ($n = 6$), commissuroplasty ($n = 5$), or wedge resection ($n = 1$) were used. 24 (63%) patients received a 26 mm annuloplasty and 10 (26%) received a 28 mm annuloplasty. Annuloplasty was performed with a partial band (Cosgrove ring) in 29 (76%) patients and with a full ring (Physio ring or Saddle ring) in 9 (24%) patients. As a concomitant procedure, pulmonary vein isolation was performed in 9 (24%) patients and 11 (29%) underwent a modified maze procedure [9].

Table 1 Patient characteristics

Age (years)	63.2 ± 9.6
Female	10 (26%)
BSA (m^2)	1.68 ± 0.13
NYHA functional class (I, II/III, IV)	30 (79%)/8 (21%)
Atrial fibrillation	20 (53%)
LVESD > 40 mm	6 (16%)
sPAP > 50 mmHg	5 (13%)
Combined posterior leaflet prolapse	10 (26%)
Associated disease	
Tricuspid regurgitation (TR ≥ 3/4)	10 (26%)
Coronary artery disease	6 (16%)
Active IE	4 (11%)
Chordae lesions	
Rupture	16 (42%)
Elongation	9 (24%)
Rupture and elongation	3 (8%)
Leaflet and chordae lesions	
Excess leaflet tissue and elongation	5 (13%)
Perforation and rupture	1 (3%)
Miscellaneous	1 (3%)

Values are expressed as mean values ± standard deviation or *n* (%)

BSA Body surface area, *IE* infectious endocarditis, *LVESD* left ventricular end-systolic diameter, *NYHA* New York Heart Association, *sPAP* systolic pulmonary arterial pressure, *TR* tricuspid regurgitation

Early and late results

All patients for whom chordal replacement was indicated were treated with this technique and none required a second pump run or conversion to valve replacement. The follow-up period after surgery ranged from 1 to 11 years (mean 66 ± 37 months). There was one in-hospital death (3%) and one late death. One patient, who was on hemodialysis for end-stage renal disease and had undergone concomitant coronary bypass grafting for severe coronary artery disease (NYHA functional class II), suffered ventricular arrhythmia 27 days postoperatively and died of multiple organ failure. The 5-year actuarial survival rate was 95 ± 4%. One patient with recurrent MR required a reoperation 28 months after surgery because of hemolysis caused by MR. The 5-year actuarial rate of freedom from reoperation was 96 ± 4%.

Recurrent mitral regurgitation

The echocardiographic follow-up period ranged from 10 days to 11 years (mean 62 ± 36 months). Table 3 lists the pre- and postoperative echocardiographic data. None of the patients were found to have systolic anterior motion on intraoperative transesophageal echocardiography. The MR grade 1 week after surgery was none or trivial in 24 patients and mild in 14 patients, whereas that in the late follow-up period was none or trivial in 13 patients and mild in 21 patients. Two patients suffered recurrent MR in the late follow-up period and the 5-year actuarial rate of freedom from recurrent mitral regurgitation was 94 ± 4% (Fig. 2). One patient

Table 2 Surgical procedures

No. of artificial chordae	
1	9 (24%)
2	16 (42%)
3	9 (24%)
≥4	3 (8%)
Unknown	1 (3%)
Concomitant mitral valve repair	
Resection suture	6 (16%)
Commissuroplasty	5 (13%)
Wedge resection	1 (3%)
Annuloplasty	
Cosgrove ring (26 mm)	17 (45%)
Cosgrove ring (28 mm)	8 (21%)
Cosgrove ring (30 or 32 mm)	4 (11%)
Physio ring (26 mm)	6 (16%)
Physio ring (28 mm)	2 (5%)
Saddle ring (26 mm)	1 (3%)
Concomitant procedure	
Tricuspid annuloplasty	33 (87%)
CABG	5 (13%)
Maze procedure	11 (29%)
PV isolation	9 (24%)
PFO closure	1 (3%)

Values are *n* (%)

CABG Coronary artery bypass grafting, *PFO* patent foramen ovale, *PV* pulmonary vein

with recurrent MR required a reoperation 28 months after surgery for hemolysis caused by MR. During the reoperation, all artificial chordae were found to be intact, but the prolapsed A2 leaflet was fibrotic and thickened. Histological examination revealed degenerative change of the A2 leaflet. Recurrent MR was found 15 months after the operation in another patient, who had undergone artificial chordal reconstruction and resection suturing for an A2 prolapse and P2 perforation caused by infectious endocarditis. The origin of the recurrent MR jet was anterior commissure, which was not associated with the initial operation site. Her last echocardiographic examination showed moderate MR (regurgitant volume: 55 ml/beat), but as she has no cardiac symptoms, she is being followed up regularly.

Functional mitral stenosis

Postoperative MS caused by pannus or calcification of the leaflets [1] was not observed in this series. Moreover, none of the patients were found to have restricted movement of the mitral leaflet on echocardiography. The resting mean pressure gradient was 4.4 ± 1.6 mmHg (range 2.5–9.7 mmHg; $n = 38$) 1 week after surgery, 4.4 ± 1.7 mmHg (range 2.0–11.1 mmHg; $n = 32$) 3 months after surgery, and 4.9 ± 1.7 mmHg (range 1.6–9.7 mmHg; $n = 36$) in the late postoperative follow-up period. The resting MVA was 2.8 ± 0.6 cm^2 (range 1.9–3.8 cm^2; $n = 17$) 1 week after surgery, 2.7 ± 0.5 cm^2 (range 2–3.8 cm^2; $n = 17$) 3 months after surgery, and 2.6 ± 0.5 cm^2 (range 1.8–3.8 cm^2; $n = 21$) in the late postoperative follow-up period (Table 3). The number of patients who had mPG > 5 mmHg was 9 (24%) 1 week after surgery, 9 (28%) 3 months after surgery, and 15 (42%) in the late postoperative follow-up period. None of the patients had mPG > 10 mmHg or MVA < 1.5 cm^2. Figure 3 shows the postoperative values of mPG according to the type of ring and annuloplasty size. Univariate analysis revealed that mPG > 5 mmHg in the late postoperative follow-up period was positively associated with the use of a full ring (odds ratio 9.5; 95% confidence interval 1.6–57; $p = 0.016$), a 26 mm annuloplasty (odds ratio 8.0; 95% confidence interval 1.4–45; $p = 0.016$), atrial fibrillation (odds ratio

Table 3 Echocardiographic measurements before and after mitral valve repair

Resting measures	Pre-op ($n = 38$)	Post-op ($n = 37$)	*p* value
Left atrial dimension (mm)	51 ± 14	50 ± 12	0.36
LV ejection fraction (%)	69 ± 9	67 ± 8	0.15
LV end-diastolic diameter (mm)	59 ± 7	51 ± 5	< 0.01
LV end-systolic diameter (mm)	35 ± 7	31 ± 5	< 0.01
Degree of MR			
None or trivial	0 (0%)	12 (32%)	
Mild	0 (0%)	23 (62%)	
Moderate	1 (3%)	1 (3%)	
Severe	37(97%)	1 (3%)	
Mean PG (mmHg)		4.9 ± 1.7	
Mitral valve area (cm^2)		2.6 ± 0.5	

Values are *n* (%) or mean ± standard deviation

LV Left ventricular, *MR* mitral regurgitation, *Op* operation, *PG* pressure gradient

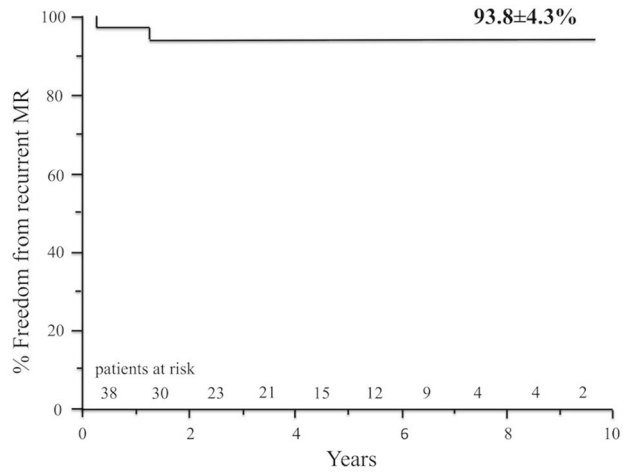

Fig. 2 Kaplan–Meier curve for freedom from recurrent mitral regurgitation after chordal replacement for anterior mitral leaflet prolapse. In the present study, recurrent mitral regurgitation was defined as moderate or severe. *MR* Mitral regurgitation

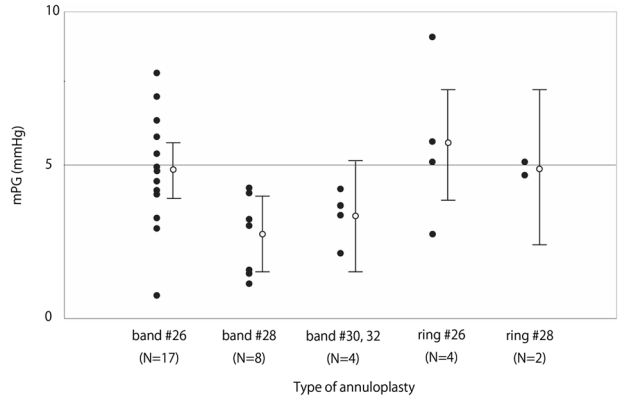

Fig. 3 Postoperative mean pressure gradients through the mitral valve at rest according to the type of ring (partial band or full ring) and annuloplasty size. *mPG* Mean pressure gradient

6.3; 95% confidence interval 1.4–28; $p = 0.018$), and age (odds ratio 1.1; 95% confidence interval 0.99–1.1; $p = 0.071$). Stepwise logistic regression analysis revealed that a full ring (adjusted odds ratio 8.9; 95% confidence interval 1.2–64; $p = 0.031$) and a 26 mm annuloplasty (adjusted odds ratio 7.5; 95% confidence interval 1.1–50; $p = 0.037$) were significant independent risk factors for mPG > 5 mmHg.

We also investigated the effects of this multiple-knot technique on MS by examining the records of patients who underwent an annuloplasty with a 28 mm ring from 2011 to 2013 at our institution. The mPG values in the late postoperative follow-up period were compared between patients who underwent our multiple-knot technique procedure and those who did not, and found to be 3.8 ± 1.2 mmHg for those who underwent the multiple-knot technique ($n = 10$) vs. 4.5 ± 1.4 mmHg for those who did not ($n = 16$). This difference was not significant ($p = 0.4$).

Electrocardiogram

Electrocardiograms were done during follow-up for 32 patients, revealing sinus rhythm in 18 (56%), atrial fibrillation or flutter in 7 (22%), atrioventricular junctional rhythm in 4 (13%), and pacemaker rhythm in 3 (9%).

Functional class

At the most recent follow-up, 31 (97%) patients were in functional class I, 1 (3%) was in class II, and none were in class III or IV.

B-type natriuretic peptide

The BNP level was 149 ± 146 pg/ml (range 5–523 pg/ml; $n = 34$) preoperatively, 86 ± 72 pg/ml (range 3–315 pg/ml; $n = 32$) 3 months after surgery, and 103 ± 79 pg/ml (range 18–320 pg/ml; $n = 35$) in the late postoperative follow-up period, respectively (p = NS). The BNP level was not associated with mPG > 5 mmHg in the late follow-up period ($p = 0.72$).

Discussion

The findings of the present study confirmed favorable outcomes of our original chordal replacement technique for anterior mitral leaflet prolapse, including low mortality and a high rate of freedom from recurrent MR in the intermediate term. A great merit of our multiple-knot technique is that it is easy to understand and perform in a reproducible manner, even by surgeons with limited experience. Notably, the rate of freedom from residual MR at 5 years in the present cohort was nearly 95%; noted in the guidelines as being indicative of a successful and durable repair [10]. On the other hand, half of the patients who received a 26 mm annuloplasty or a complete ring had a resting mPG > 5 mmHg in the late operative follow-up period, which is associated with a risk of functional MS.

According to the current guidelines [10], the indications for MR are dependent on the outcomes of mitral valve repair at each institution. Among previous reports from high-volume centers, the rate of freedom from reoperation at around 10 years ranged from 82 to 94% [1, 4, 11–15]. In the present study, we found that the 5-year rate of freedom from reoperation was 97.3% at our institution, which is comparable to centers with higher volume. These results may demonstrate

that our chordal replacement technique with ePTFE sutures is simple to perform in a reproducible manner.

Investigating the cause of recurrent MR among the various techniques is important to confirm the validity of each technique and make necessary improvements. In our series, two patients suffered recurrent MR, one of whom required a reoperation during the late follow-up period. Prolapse of a previously normal segment was the cause of the MR in both patients. Artificial chordae were found to be intact in the operative and echocardiogram findings. David et al. [1] reported that most cases of late recurrent MR in patients undergoing reoperation were caused by prolapse of a previously normal or repaired segment. In our series, no technical problems causing recurrent MR were identified, as the cause was degenerative change of the native leaflet, in accordance with other reports.

Functional MS following mitral valve repair for degenerative MR is a concern. A mitral annuloplasty procedure is usually necessary during mitral valve repair and Cohn et al. [16] reported that omitting that procedure is a risk factor for reoperation. On the other hand, Mesana et al. [2] compared the echocardiographic and functional characteristics of patients who underwent mitral repair with either a full ring or partial band and found that annuloplasty using a full ring was associated with a higher mitral valve gradient at rest and peak exercise in certain patients. Importantly, patients who received a full ring annuloplasty had poorer quality of life. In their report, the resting mPG was 3.7 ± 1.9 mmHg in patients with a partial band and 5.8 ± 2.6 mmHg in those with a full ring, respectively. Thus, in the present study, we defined an mPG > 5 mmHg as a risk of functional mitral stenosis and more than half of patients who received a 26 mm or full ring annuloplasty had mPG > 5 mmHg in the late follow-up period, although their symptoms and BNP levels were satisfactory. During the study period, we chose a 26-mm ring for some patients with anterior mitral valve prolapse and/or reduced LV function. However, we now consider that the decision to use a 26-mm or full ring annuloplasty should be made carefully, even for patients with a relatively small body surface area (Table 1). Unfortunately, our findings do not clarify which patients do not suit a 26-mm annuloplasty. Further study of functional MS following mitral valve repair for degenerative MR is needed, according to the various techniques of mitral repair.

Several studies have reported techniques for artificial chordal replacement, the majority of which state that the most important points are simplicity and reproducibility. The characteristics of our strategy are that it enables us to achieve the correct length of artificial chordae using an easy and reproducible technique. We also perform resection suturing or commissuroplasty for posterior or commissure prolapse to reduce the number of artificial chordae. We believe that this strategy contributed to the favorable outcomes in the present study. However, the technical concerns related to our method include a possibility of cell proliferation or thrombus formation around the knotted PTFE, which can lead to recurrent MR or affect leaflet motion in the late period. In this study, the number of patients with mild MR increased in the late period, although restricted movement of the mitral leaflet was not found when a normal postoperative anticoagulation management method was used. Long-term follow-up is necessary to investigate these technical concerns.

Limitations of the study

The main limitations of our study are the small number of patients and the fact that the various concomitant surgical procedures used may have influenced the outcome. We did not utilize echocardiographic quantitation of MR, such as regurgitant volume, effective regurgitant orifice, or vena contracta in all patients. Moreover, we did not perform stress echocardiography. There were also some limitations regarding the comparison of mPG between patients who underwent our multiple-knot technique vs. those who did not, especially considering the small number of cases, the various plasty techniques used, and the different patient characteristics. Thus, the possibility that our technique may be related to higher mPG due to tissue proliferation coating the knotted artificial chordae cannot be excluded.

Conclusions

The intermediate-term outcomes of our simple and reproducible chordal replacement technique were not inferior to those presented in previous reports. The findings of this study suggest that our mitral chordal replacement technique for anterior leaflet prolapse can be performed successfully with durability. However, more than half of the patients who underwent repair with a 26 mm annuloplasty had mPG > 5 mmHg in the late follow-up period, which may be associated with postoperative functional MS.

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Compliance with ethical standards

Conflict of interest We have no conflicts of interest to report.

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