Surgical therapy of organic mitral valve disease: Strategy and outcomes

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Excessive leaflet tissue in mitral valve repair for isolated posterior leaflet prolapse- leaflet resection or shortening neochords?

A propensity score adjusted comparison

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ABSTRACT

Background. Chordal replacement techniques are progressively used to treat posterior mitral valve leaflet (PMVL) prolapse while leaflet resection remains commonly in use to address excessive leaflet tissue. For excessive tissue in height, shortening neochords can be used alternatively. Use of chordal replacement techniques has been suggested to result in lower diastolic transvalvular gradients, higher freedom from reoperation and improved left ventricular function.

Methods. From 1/2005 to 12/2016, 150 patients underwent valve repair for isolated PMVL prolapse with excessive tissue. Excessive tissue in height was treated by leaflet resection (n=99) or shortening neochords (n=51). Excessive tissue in width was always resected. Logistic regression was used to generate propensity scores for risk-adjusted comparison.

Results. Two patients died postoperatively. In the Neochords group, resection of excessive tissue in width was still needed in 28 (55%) cases. Postoperative echocardiography demonstrated residual (≥2+) mitral regurgitation in 2/150 patients (Resect group). No differences in anuloplasty ring size, postoperative diastolic transvalvular gradients or left ventricular function were observed. Median clinical follow-up duration was 4.4 (IQR 2.0-7.0; 98% complete) years. There was no inter-group difference in overall survival or freedom from reintervention. Mean echocardiographic follow-up was 3.0 (IQR 1.2-5.4; 93% complete) years. In the matched population, the 6-year freedom from recurrent mitral regurgitation rates were 91.3% (95% CI 81.9%-100%) and 97.2% (95% CI 91.9%-100%) for the Resect and Neochords group, respectively (P=0.43).

Conclusions. Both leaflet resection and shortening neochords provide a valuable tool to address excessive PMVL height. Repair durability is excellent regardless of the technique utilized.

INTRODUCTION

Mitral valve (MV) repair for isolated posterior MV leaflet (PMVL) prolapse due to degenerative valve disease is highly reproducible and nowadays feasible in almost all cases [1-4]. Cases of isolated PMVL prolapse vary in the extent of excessive leaflet tissue and the status and quality of native chordae tendineae [5]. Mitral valve repair techniques used to treat PMVL prolapse are adapted to these specific characteristics.

The MV repair techniques described by Carpentier focused on PMVL resection to address leaflet prolapse as well as excessive leaflet tissue [6]. Soon thereafter, David was first to demonstrate that extended polytetrafluoroethylene neochords can be used to correct leaflet prolapse occurring due to elongated or ruptured native chordae tendineae [7]. Perier et al. later demonstrated the versatility of chordal replacement techniques in patients with PMVL prolapse by showing that neochords can effectively address not only leaflet prolapse but also excessive PMVL tissue in height [8]. Two recent systematic reviews and meta-analyses speculated that chordal replacement techniques will allow implantation of larger annuloplasty rings and result in improved postoperative left ventricular (LV) function, lower diastolic transvalvular gradients and higher freedom from reoperation when compared to PMVL resection techniques [9, 10]. Such speculations are, however, based on highly heterogeneous patient groups that vary in the extent of excessive tissue. Furthermore, leaflet resection techniques have evolved as annular plication has largely been abandoned while the indication for leaflet resection has shifted primarily to addressing excessive tissue.

The aim of this study was to explore the results of a structured approach to PMVL prolapse and excessive tissue in cases of isolated PMVL prolapse. We further aim to analyze the results of either leaflet resection or implantation of shortening neochords to treat excessive leaflet tissue in height and analyze the early- and mid-term results of both techniques in a propensity score matched analysis.

METHODS

Patients

Between January 2005 and December 2016, 520 patients underwent surgical intervention for severe degenerative MR at our institution. Of these, 185 patients presented with isolated PMVL prolapse and excessive tissue in height and underwent MV repair. Excluding patients who underwent annular plication (n=22) or reduction of excessive PMVL height with a combination of techniques (n=13), 150 patients present the final study cohort. Preoperative, intraoperative and postoperative data were retrospectively collected from our computerized database. Follow-up survival, clinical and echocardiographic data were collected through clinical visits at our institution or affiliated clinics and hospitals and through questionnaires to patients. The study was approved by our Institutional Ethics Committee.

Study endpoints

Early mortality was defined as mortality within 30-days after the operation or during the index hospitalization. Postoperative mortality and morbidity endpoints were defined according to the joint Society of Thoracic Surgeons, American Association for Thoracic Surgery and European Association for Cardio-Thoracic Surgery Guidelines [11]. The severity of MR was evaluated using a multi-parametric integrative approach, including qualitative and quantitative assessments, as currently recommended [12]. MR severity was graded on a 4-grade scale: grade 1+ (mild), grade 2+ (moderate), grade 3+ (moderate-to-severe) and grade 4+ (severe). Residual and recurrent MR were defined as MR ≥grade 2+. Diastolic transvalvular gradient was calculated using continuous wave Doppler.

Surgical technique

During the study period, a systematic approach to PMVL abnormalities was applied. The PMVL was assessed for the presence of prolapse and quality of the subvalvular apparatus. Thereafter, the affected segment(s) of the PMVL was assessed for excessive leaflet tissue in height and width.

Valve repair was tailored to the extent of leaflet tissue and 3 scenarios were possible (**Figure 1**). When no excessive leaflet tissue was present only abnormal PMVL motion was to be addressed. This was always corrected with implantation of non-shortening neochords. When excessive leaflet tissue was present, this was addressed accordingly. First, the PMVL was assessed for the presence of excessive issue in height and/or width (**Figure 2**). Excessive leaflet tissue in width was assessed by folding the PMVL into the LV. When wrinkling of the affected segment was seen (that would result in PMVL wrinkling at the level of leaflet coaptation and/or leaflet billowing after valve repair was accomplished), this was treated by leaflet resection in all cases (taking into account that

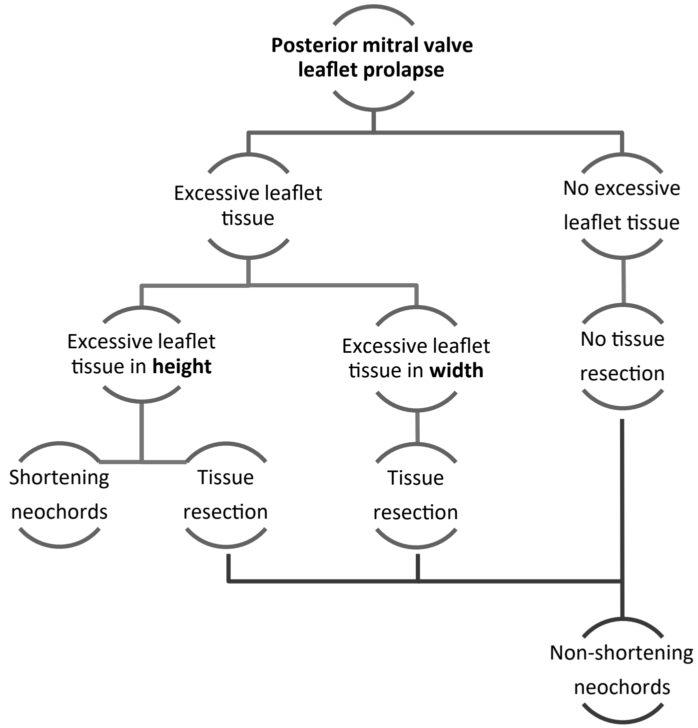

FIGURE 1. A systematic approach to excessive posterior mitral valve leaflet tissue. The leaflet is assessed for the presence of excessive tissue in width and/or height. Excessive tissue in width is always resected. Excessive tissue in height can be treated by either tissue resection or implantation of shortening neochords. Non-shortening neochords are used to resolve any remaining leaflet prolapse.

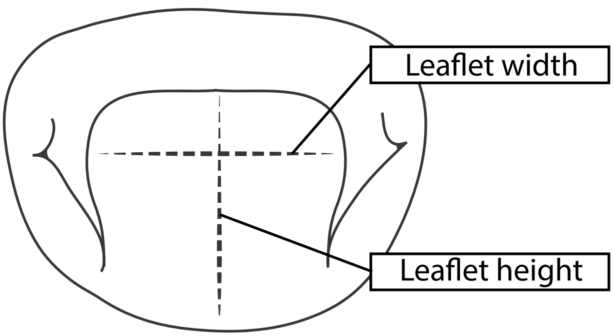

FIGURE 2. Schematic presentation of excessive leaflet tissue of the posterior mitral valve leaflet; excessive tissue in height needs to be distinguished from excessive tissue in width.

neochords cannot address excessive leaflet tissue in width). Redundant leaflet tissue in height was assessed by PMVL inspection- leaflet height ≥20 millimeters was considered excessive. This was address by:

1. Leaflet resection- **Resect group**. Typically, this was combined with resection of excessive tissue in width, resulting in a quadrangular resection of the PMVL. Leaflet integrity was restored by suturing the leaflet remnants together with a 5-0 polypropylene suture and combined with leaflet sliding at the level of leaflet base. This was combined with the implantation of non-shortening neochords –aimed at resolving residual prolapse- in 42 (42%) patients.
2. Shortening neochords- **Neochords group**. In these cases, neochords were used to bring the free edge of the prolapsed area to a lower level, as previously described by Perier et al. [8]. Shortly, neochords were implanted to the free edge of the prolapsing leaflet segment. The length of these was shortened to bring the prolapsed segment under the plane of the annulus and thereby compensate for excess in leaflet height. The final length of these chords was determined on water-test. This was combined with limited triangular leaflet resection (typically shortening the free edge of the affected segments for a few millimeters with care taken to avoid excessive tissue resection that would likely hamper diastolic PMVL motion) to address excessive tissue in width in 28 (55%) patients.

Semi-rigid ring annuloplasty was performed in all cases. Intraoperative echocardiography was performed by an experienced cardiologist to document the result of valve repair.

Statistical analysis

Continuous data are presented as means ± standard deviation for normally distributed data or medians (IQR) when not normally distributed. Categorical data are presented as counts and percentages. In the unmatched patient cohort, comparisons between the two groups were performed using the chi-square test or Fisher's exact test for categorical variables and Student's t-test or Mann-Whitney U test (skewed data) for continuous variables. Propensity score matching was used to balance the covariates due to the non-randomised study design. For each patient, a propensity score was calculated from a multivariable logistic regression model with covariates as independent variables and group allocation as a binary dependent variable. Patients were matched in a 1:1 matching fashion with a calliper width of 0.10. Covariates included in the propensity score model were: age, gender, body surface area, mean preoperative diastolic transvalvular gradient, annular calcification, LV function, hypertension, and EuroSCORE II. The P-value of the Hosmer-Lemeshow test and the c-statistic of the propensity score model were 0.609 and 0.722, respectively. McNemar's test (categorical variables), paired Student's t-test (normally distributed continuous variables), and Wilcoxon signed-ranked test (skewed continuous variables) were performed for the comparison between the matched groups. Survival and freedom from time-related events were estimated using the Kaplan-Meier method and compared using the log-rank test (stratified for the propensity score in the matched population). Statistical analysis was performed using the IBM Statistics for Windows, version 25.0 (SPSS, Inc., IBM Corporation, Armonk, NY, USA).

RESULTS

Baseline characteristics

Baseline characteristics of the unmatched and matched patient populations are presented in **Table I**. Prior to propensity score matching, a higher incidence of annular calcification was seen in the Resect group (14% vs. 2%, P=0.018). Propensity score matching effectively eliminated any significant differences between both groups and yielded 47 well matched patient pairs.

Early mortality and morbidity

There was 1 death in the Resect and 1 death in the Neochords group. The first patient died due to cardiogenic shock with multi-organ failure. The latter patient (who underwent minimal invasive surgery) failed to wean form cardio-pulmonary bypass due to acute biventricular failure, presumably due to inadequate intraoperative cardioprotection. In general, no statistically significant differences in the early clinical outcomes were observed between both groups in the unmatched and matched patient population (**Table II**).

TABLE I. Baseline characteristics.

	Unmatched population			Matched population		
	Resect group (n=99)	**Neochords group (n=51)**	**P-value**	**Resect group (n=47)**	**Neochords group (n=47)**	**P-value**
Age	64.1±11.0	62.4±12.1	0.70	62.9±12.3	62.4±12.1	0.85
Gender (female)	38 (38)	11 (22)	0.038	12 (26)	10 (21)	0.77
Body surface area	1.95±0.23	1.94±0.24	0.79	1.94±0.19	1.96±0.23	0.57
NYHA class			0.13			0.49
I	27 (27)	19 (37)		13 (28)	17 (36)	
II	50 (50)	27 (53)		28 (59)	25 (53)	
III-IV	22 (22)	5 (10)		6 (13)	5 (11)	
Hypertension	40 (40)	13 (26)	0.070	16 (34)	13 (28)	0.51
Atrial fibrillation	27 (27)	13 (26)	0.82	10 (21)	13 (28)	0.68
Previous cardiac surgery	2 (2)	2 (4)	0.49	0 (0)	2 (4)	0.16
Renal impairment			0.87			0.75
Moderate (CC 85-50 ml/min)	44 (44)	21 (41)		19 (40)	19 (40)	
Severe (CC <50 ml/min)	7 (7)	3 (6)		4 (9)	3 (6)	
History of TIA/CVA	6 (6)	3 (6)	0.97	4 (9)	2 (4)	0.69
Chronic lung disease	11 (11)	6 (12)	0.91	4 (9)	4 (9)	1.00
Diabetes mellitus	2 (2)	0 (0)	0.55	1 (2)	0 (0)	1.00
Pulmonary hypertension (≥50 mmHg)	15 (15)	9 (18)	0.69	5 (11)	9 (20)	0.39
EuroSCORE II	1.73 (IQR 0.93-3.05)	1.36 (IQR 0.89-2.12)	0.33	1.54 (IQR 0.81-2.79)	1.36 (IQR 0.89-2.27)	0.74
Annular calcification	14 (14)	1 (2)	0.018	3 (6)	1 (2)	0.50
Concomitant procedures						
Tricuspid valve repair	51 (51)	19 (37)	0.097	27 (57)	31 (34)	0.027
RF-ablation	22 (22)	9 (18)	0.51	8 (17)	9 (19)	1.00
CABG	20 (20)	7 (14)	0.33	9 (19)	7 (15)	0.77
AVR	3 (3)	1 (2)	0.70	2 (4)	1 (2)	1.00
Thoracic aorta replacement	1 (1)	1 (2)	0.63	1 (2)	1 (2)	1.00

Data are presented as n (%), means ± standard deviation or medians (interquartile range). Abbreviations: AVR: aortic valve replacement; CABG: coronary artery bypass grafting; CC: creatinine clearance; CVA: cerebrovascular accident; NYHA: New York Heart Association; TIA: transient ischemic attack.

TABLE II. Postoperative complications.

	Unmatched population			Matched population		
	Resect group (n=99)	Neochords group (n=51)	P-value	Resect group (n=47)	Neochords group (n=47)	P-value
Mortality	1 (1)	1 (2)	1.0	0 (0)	1 (2)	1.00
Prolonged intubation (>24 hours)	11 (11)	1 (2)	0.050	4 (9)	1 (2)	0.38
Early reoperation	7 (7)	2 (4)	0.44	3 (6)	1 (2)	0.63
Surgical re-exploration	5 (5)	2 (4)	0.76	2 (4)	1 (2)	1.00
Early valve reoperation	2 (2)	0 (0)	0.55	1 (2)	0 (0)	1.00
Renal failure	0 (0)	1 (1)	0.34	0 (0)	1 (2)	1.00
Permanent stroke	1 (1)	2 (4)	0.27	1 (2)	2 (4)	1.00

Data are presented as n (%).

Early valve-related results

Residual MR was seen in 2/150 (1.3%) patients (Resect group). Both underwent early reoperation. The cause of residual MR was residual PMVL prolapse and residual excessive tissue with PMVL billowing and residual leakage through an open indentation. A MV re-repair was performed in both cases. All other patients demonstrated ≤mild residual MR and no systolic anterior motion on pre-discharge echocardiography.

Interestingly, no significant difference in the size of annuloplasty ring implanted was observed between both groups (**Table III**). Sufficient height of leaflet coaptation was achieved in both groups. There were no significant differences in the postoperative LV end-diastolic diameter and LV ejection fraction between both groups in both the matched and unmatched population.

Late results

Median survival follow-up duration was 4.2 (IQR 1.9-6.8) years and was 99% complete (2 patients were lost to follow-up due to emigration). During the follow-up period, 12 late deaths occurred. The cause of death was cardiac related in 5 (intra-cerebral hemorrhage in 2, heart failure in 1 and sudden unexplained in 2) and non-cardiac related in 7 patients. At 6 years after surgery, the overall survival rate for the unmatched population was 92.5% (95% CI 86.6%-98.4%) and 80.1% (95% CI 61.5%-98.7%) for the Resect and Neochords group, respectively (P=0.24; **Figure 3**). In the propensity score matched patient population, the 6-year overall survival rate was 93.2% (95% CI 85.8%-100%) and 79.7% (95% CI 61.1%-98.3%) for the Resect and Neochords group, respectively (P=0.20; **Figure 3**).

TABLE III. Valve-related results of mitral valve repair.

	Unmatched population			**Matched population**		
	Resect group (n=99)	**Neochords group (n=51)**	**P-value**	**Resect group (n=47)**	**Neochords group (n=47)**	**P-value**
Preoperative						
Diastolic transvalvular gradient (mmHg)	2.10 (IQR 1.54-2.98)	1.64 (IQR 1.15-2.78)	0.045	2.03 (IQR 1.53-2.86)	1.64 (IQR 1.15-2.78)	0.62
LVEDD (mm)	55±7	55±6	0.99	55±6	55±7	0.71
LVEF (%)	66.2±7.7	63.6±8.3	0.081	64.5±7.7	63.5±8.4	0.56
Annuloplasty ring size	34 (IQR 32-36)	34 (IQR 32-36)	0.15	34 (IQR 31-36)	32 (IQR 32-36)	0.29
Leaflet coaptation height (mm)	7.7±1.6	8.6±1.7	0.002	8.0 (IQR 7.0-8.0)	8.0 (IQR 8.0-9.0)	0.15
Postoperative						
Diastolic transvalvular gradient (mmHg)	3.31±1.41	3.19±1.11	0.64	3.33 (IQR 2.46-4.23)	3.22 (IQR 2.61-3.86)	0.35
LVEDD (mm)	51 (IQR 45-55)	52 (IQR 46-57)	0.12	49 (IQR 45-54)	52 (IQR 46-58)	0.070
LVEF (%)	55.4±7.4	53.7±7.6	0.19	55.4±7.7	54.2±7.7	0.35

Data are presented as means ± standard deviation or medians (interquartile range). Abbreviations: IQR: interquartile range; LVEDD: left ventricular end diastolic diameter; LVEF: left ventricular ejection fraction; LVESD: left ventricular end systolic diameter.

Clinical follow-up was 90% complete with a median follow up of 3.4 (IQR 1.7-6.2) years. There was 1 late MV reintervention (Resect group) due to severe MR, performed 7.8 years after the initial operation as a consequence of infective endocarditis. A successful MV re-repair was performed. The 6-year freedom from MV reintervention was 100% for both the Resect and Neochords group in both the unmatched and matched patient population. A second episode of infective endocarditis occurred during the follow-up period (Neochords group) that was treated conservatively.

Median echocardiographic follow-up was 3.0 (IQR 1.2-5.4) years and was available in 93% of patients. In the unmatched patient population, the 6-year freedom from recurrent MR rates were 86.9% (95% CI 77.3%-96.5%) and 97.4% (95% CI 92.5%-100%) for the Resect and Neochords group, respectively (P=0.42; **Figure 4**). For the propensity score matched population, the 6-year freedom from recurrent MR rates were 91.3% (95% CI 81.9%-100%) and 97.2% (95% CI 91.9%-100%) for the Resect and Neochords group, respectively (P=0.43, **Figure 4**).

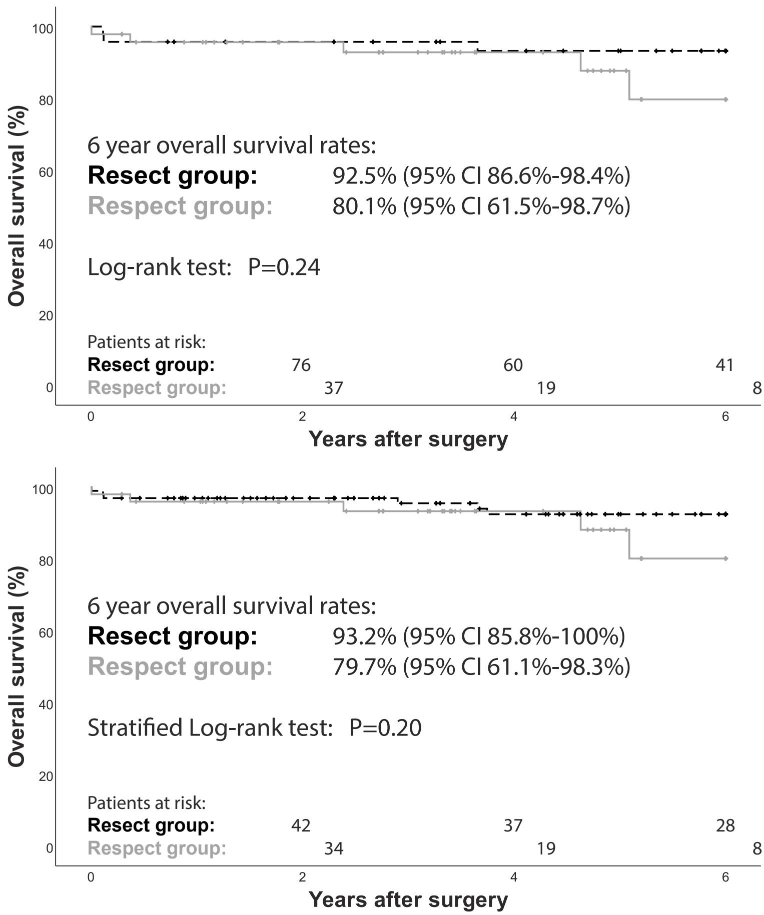

FIGURE 3. Overall survival for the Resect and Neochords groups (above: unmatched patient population, below: propensity score matched patient population).

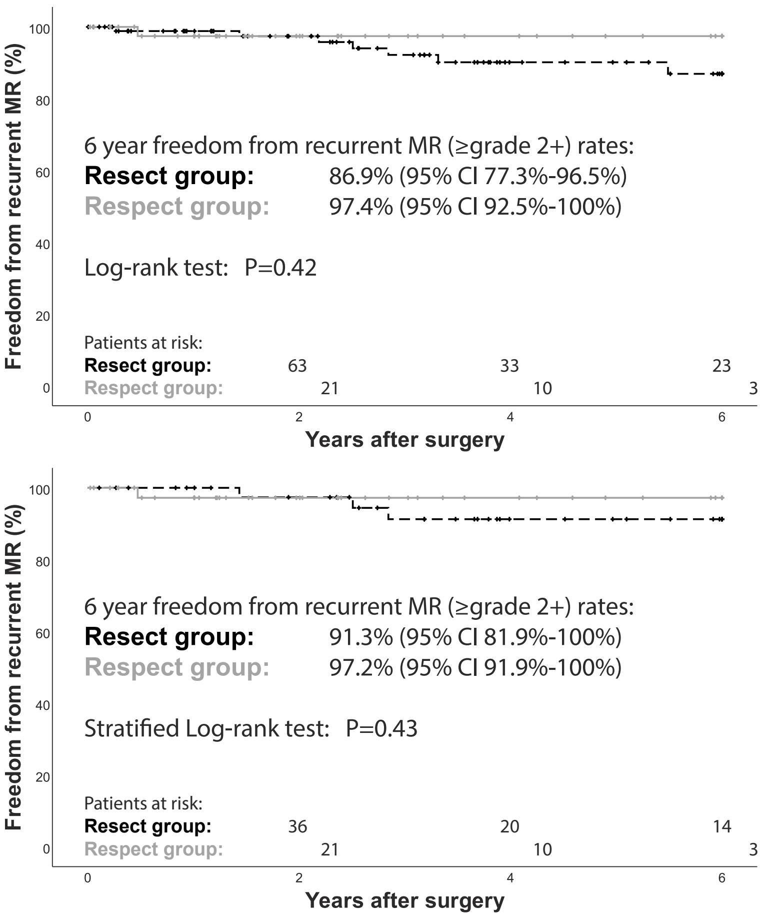

FIGURE 4. Freedom from recurrent mitral regurgitation (≥grade 2+) for the Resect and Neochords groups (above: unmatched patient population, below: propensity score matched patient population).

DISCUSSION

Our results demonstrate that in case of a structured approach to PMVL abnormalities, tailored to valve specific characteristics, leaflet resection and chordal replacement techniques are often used concomitantly. Excessive PMVL tissue in height can effectively be treated by either leaflet resection or implantation of shortening neochords. The choice of repair technique will not affect early or late repair performance, postoperative LV function or diastolic transvalvular gradients.

With the widespread utilization of chordal replacement techniques, leaflet resection techniques are nowadays used less commonly than before [13]. When leaflet prolapse/flail is not accompanied by excessive leaflet tissue, leaflet resection is best avoided and chordal replacement has readily become the preferred repair strategy. This helps avoid the disadvantages of annular plication that is believed to alter LV morphology and function [14]. Such cases should, however, be distinguished from cases when PMVL prolapse/flail is accompanied by excessive leaflet tissue. In such cases, the aim of valve repair is to (I) resolve any leaflet prolapse, (II) address excessive leaflet tissue in height and (III) address excessive tissue in width.

To address excessive PMVL tissue in width, leaflet resection or plication remain the only surgical options. Care should be made to avoid *excessive* leaflet resection with excessive shortening of the free margin of the PMVL. This has been shown to result in elevated transvalvular gradients (data are often derived from an *ex vivo* model of acute MR without excessive leaflet tissue where any resection will be excessive) and leaflet resection should always be made with respect to preservation of leaflet mobility [15-17]. As demonstrated by our results, when PMVL resection is performed purely to treat excessive leaflet tissue, additional neochords to correct leaflet prolapse are often needed and help prevent excessive resection.

Our study was the first to select only patients with PMVL prolapse and excessive tissue in height and aimed to address the unanswered question on whether leaflet resection of shortening neochords provide comparable results in this setting. Perier et al., who introduced the "*Respect rather than Resect*" paradigm, did report in the initial experience that leaflet resection –aimed at reducing excessive tissue in width- was still performed in one third of patients in whom leaflet prolapse and/or excessive tissue in height were otherwise addressed with chordal replacement techniques [8]. Too often, the results of their study are misinterpreted and used as an argument to support a chordal replacement PMVL repair only. As we selected only patients with excessive leaflet tissue, the high proportion of patients in the Neochords group who additionally underwent leaflet resection in width comes to no surprise. Addressing excessive leaflet tissue is important to secure long-term repair stability and durability. While clinical data to support such statements are currently lacking, Choi et al. have previously shown –in a virtual MV model- that excessive PMVL tissue will result in excessive leaflet stress [18].

This promotes activation of valve interstitial cells with ensuing myxomatous degeneration (often referred to as disease progression) and should therefore be reduced to minimum [19].

It has been suggested that chordal replacement techniques will allow annuloplasty ring oversizing and result in lower diastolic transvalvular gradients when compared to leaflet resection techniques [9, 10, 20]. In our opinion, such observations need to be interpreted with care. When no excessive PMVL tissue in height is present, oversizing the annuloplasty ring will inevitably lead to insufficient height of leaflet coaptation. In these patients, small annuloplasty ring size might indeed present a true clinical problem as functional MV stenosis might ensue [21]. Moreover, when leaflet prolapse with excessive leaflet height is present at a single segment, the same problem (insufficient height of leaflet coaptation) will occur at the level of non-affected segments. In our opinion, oversizing of the annuloplasty ring is feasible only in cases where excessive tissue in height is present at all segments of the PMVL. In these patients, large rings are usually needed to complement valve repair, making clinically significant elevated transvalvular gradients unlikely the occur. This is partially reflected by the somehow larger annuloplasty ring sizes used in our experience in the Resect group. We reason that this is probably related to our preference to perform tissue resection when a large amount of excessive PMVL tissue is present.

Several studies have suggested that chordal replacement might lead to improved postoperative LV function when compared to leaflet resection because of better preservation of the mitral-ventricular continuity [1, 4, 9, 22]. However, the demonstrated (statistically significant) difference of about 3% makes us question the clinical significance of such observations [1]. In all of the studies that seem to support this idea, a proportion of patients in whom leaflet resection was performed also underwent mitral annular plication. This likely presents the cause of LV functional decline and, when avoided, the reason here for is likely eliminated. To the best of our knowledge, there is no available data that support the theory that a properly sized leaflet resection without annular plication will disturb the mitral-ventricular continuity. The questionable and, indeed present, limited benefit of performing PMVL repair exclusively with chordal replacement techniques should be weighed against the concerns that arise by systematically not addressing excessive PMVL leaflet tissue.

Our results are in line with previous studies that have demonstrated excellent MV repair durability for patients with isolated PMVL prolapse [3, 8]. We believe that such outcomes are a result of a structured approach to PMVL prolapse that aims to resolve any leaflet prolapse, addresses excessive leaflet tissue and secures annular remodeling and stabilization [3, 8, 23].

LIMITATIONS

This is an observational single center study with limitations inherent to the study design. We have performed propensity score matching to compensate for the lack of patient randomization. Furthermore, the number of patients included in the study was limited, somehow limiting the value of the results presented. Moreover, the resect techniques were more commonly in use early and chordal replacement techniques later in the predefined study period. This might have had an effect on the perioperative outcomes related to the improvements in perioperative care. Our results (in particular freedom from recurrent MR and MV reintervention) will have to be validated in properly powered, larger scale studies with longer follow-up in the future. However, this was the first study to truly compare the resect and shortening neochords techniques in a contemporary setting, hereby eliminating study bias attributable to addition of patients with annular plication or no excessive leaflet tissue.

CONCLUSIONS

A structured approach to PMVL prolapse and excessive leaflet tissue provides excellent repair performance. Excessive PMVL tissue in height can effectively be addressed by both leaflet resection or shortening neochords techniques with comparable results. The decision on which technique to use is best adapted to other valve characteristics, including presence of annular calcification and the presence/amount of excessive tissue in width.

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