Mitral valve repair in Barlow’s disease with bileaflet prolapse: the effect of annular stabilization on functional mitral valve leaflet prolapse†

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Abstract

OBJECTIVES: Barlow’s disease is the most severe form of degenerative mitral valve disease, commonly characterized by bileaflet prolapse. Abnormal mitral annular dynamics is typically present and results in functional prolapse of the mitral leaflets that may be addressed with annular stabilization alone.

METHODS: Between January 2001 and December 2015, 128 patients with Barlow’s disease and bileaflet prolapse underwent valve repair. This included anterior mitral valve leaflet (AMVL) repair in 70 patients, whereas 58 patients were identified as having functional prolapse and underwent no specific AMVL repair. During the course of the study, the proportion of patients undergoing specific AMVL repair decreased (77% in the first and 33% in the second 64 patients). Semirigid ring annuloplasty was performed in all cases. The median clinical and echocardiographic follow-up duration was 6.5 years (interquartile range (IQR) 2.9–10.5 years; 93.9% complete) and 4.7 years (IQR 2.2–10.2 years; 94.4% complete), respectively.

RESULTS: Early mortality was 1.6%. Postoperative echocardiogram demonstrated no residual mitral regurgitation in all but 1 patient (AMVL repair group). There was no significant difference in the overall survival rate at 6 years after operation between both groups. At 6 years, the freedom from recurrent >Grade 2+ mitral regurgitation rate was 90.7% (IQR 82.9–98.5%) and 89.1% (IQR 75.8–100%) for patients with and patients with no AMVL repair, respectively (P = 0.43). Three patients required late mitral valve reintervention, all from the AMVL repair group.

CONCLUSIONS: Annular stabilization can effectively resolve the functional prolapse of the AMVL. Careful discrimination between functional and true AMVL prolapse allows for a technically less challenging operation that provides excellent repair durability.

Keywords: Cardiac surgery • Mitral valve prolapse • Barlow’s disease • Degenerative mitral valve disease • Mitral valve repair

INTRODUCTION

Degenerative mitral valve disease is the second most common valve disease in Western countries [1]. Surgical repair is the established treatment of choice as it provides optimal results in terms of survival and freedom from valve-related events [2, 3]. However, in the setting of Barlow’s disease, extensive valve degeneration with bileaflet prolapse is typically present. Additionally, leaflet, annular or subvalvular apparatus calcifications are frequently seen. These characteristics make valve repair particularly challenging [4, 5].

The aetiology of Barlow’s disease remains poorly understood. Recently, quantitative 3D echocardiography studies have enabled a better insight into the characteristics of degenerative mitral valve disease [6, 7]. These studies have shown that Barlow’s disease is characterized by diminished annular saddle shape and abnormal annular dynamics with pathological overstretching of the mitral valve annulus towards end systole. Consequently, late-systolic functional prolapse of the mitral valve leaflets will occur [8]. However, functional prolapse is often accompanied by true leaflet prolapse due to ruptured or elongated chordae tendineae, making intraoperative surgical analysis critical. Functional prolapse can be identified by an echocardiographic prolapse of the anterior mitral valve leaflet (AMVL) that cannot be confirmed during surgical valve analysis. Stabilization of the mitral valve


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annulus can resolve functional leaflet prolapse by preventing abnormal annular dynamics.

The aim of this study was to explore the frequency of the need for specific AMVL repair in a subgroup of patients with bileaflet prolapse secondary to Barlow’s disease. Moreover, we compare the durability of mitral valve repair in patients who did with patients who did not undergo AMVL repair.

METHODS

Study population

Between January 2001 and December 2015, 661 consecutive adult (>18 years of age) patients underwent surgical intervention for mitral regurgitation (MR) due to degenerative mitral valve disease at our institution. Patients with accompanying active infective endocarditis were excluded. Barlow’s disease was defined according to preoperative, echocardiographic and intraoperative characteristics that included excessive myxomatous bileaflet degeneration, annular dilatation and posterior displacement of the mitral valve annulus [9, 10] and was present in 181 (27%) patients. On preoperative echocardiography, bileaflet prolapse was defined as the free edge of both leaflets over-riding the plane of the mitral valve orifice at the end of systole and was present in 132 (73%) patients (Fig. 1). Mitral valve repair was performed in 128 (97%) of these patients who present the current study cohort.

Study methods

Our Institutional Medical Ethics Committee approved this study, and written informed consent was obtained. Pre-, intra- and postoperative data were collected from our computerized patient registry. Follow-up clinical and echocardiographic data were collected through clinical visits at our institution or affiliated clinics and hospitals and through questionnaires to patients. The median survival follow-up time was 6.6 years [interquartile range (IQR) 3–10.5 years; 98.4% complete], 2 patients were lost to follow-up due to emigration]. The median follow-up time for valve-related events was 6.5 years (IQR 2.9–10.5 years; 93.9% complete). The median echocardiographic follow-up time was 4.7 years (IQR 2.2–10.2 years; 94.4% complete). Patient follow-up was closed in December 2016.

Surgical procedure

During the study period, a repair-all strategy was applied, and eventual mitral valve replacement was only performed in case of an unsatisfactory intraoperative result of valve repair. Median sternotomy (n = 117), partial sternotomy (n = 9) or lateral mini-thoracotomy was performed (n = 6). Standard cannulation techniques with central or peripheral cannulation (according to the surgical approach utilized) and intermittent warm blood cardioplegia for cardioprotection were used in all cases.

Thorough echocardiographic and surgical valve analysis was performed to discriminate between functional prolapse and true AMVL prolapse. On preoperative echocardiography, late-systolic overstretching of the mitral valve annulus in the anterior–posterior diameter with progressive displacement of both mitral valve leaflets towards the left atrium was seen in these patients. Early in our experience, unaware of the phenomenon of functional prolapse, all leaflets that were over-riding the plane of the mitral valve orifice during valve closure on preoperative echocardiography were considered to be prolapsing and treated accordingly. Growing understanding on the contribution of annular abnormalities to valve morphology and functional prolapse has led us to focus more attention on the length and integrity of the chords providing support to the AMVL. When primary chordae tendineae are ruptured, the indication for AMVL repair will be clear—this is, however, not often the case. When prolapse of all segments of the AMVL is seen on preoperative echocardiography/surgical analysis, this suggests that the prolapse will likely be functional in nature. In some patients, the lack of a reference point during surgical valve analysis makes the discrimination between functional prolapse and true AMVL prolapse challenging. In these patients, a ‘posterior mitral valve leaflet (PMVL) repair first’ approach was utilized. Subsequent water test allowed us to determine whether any true AMVL prolapse was present. A single 2-0 TiCron (Medtronic Inc., Minneapolis, MN, USA) suture was placed in the posterior part of the mitral valve annulus (at mid-point) and was kept under traction when the water test was performed. This simulated the presence of an annuloplasty ring and prevented deformation (migration of the posterior part of the mitral annulus towards the apex of the left ventricle) of the floppy mitral valve annulus. In case of a satisfactory water test, no additional repair on the AMVL was performed, despite the echocardiographic findings.

An overview of the surgical techniques utilized is presented in Table 1. Commissural prolapse was treated predominately by papillary muscle head repositioning. For prolapse of the PMVL, quadrangular resection with annular plication (earlier in our series) or leaflet sliding technique (later in our series) was used when excessive tissue in height and width was present. When the
amount of excessive tissue in width was less pronounced, a triangular resection or non-resection techniques with shortening polytetrafluoroethylene neochords were used. True AMVL prolapse was treated predominantly with polytetrafluoroethylene neochords. Full, semirigid ring annuloplasty was performed in all cases. Ring sizing was based on the surface area of the AMVL and did not differ between both groups. Prior to 2010, Physio ring (Carpentier Edwards Lifesciences, Irvine, CA, USA) was our primary choice. Since 2010, Physio II ring (Carpentier Edwards Lifesciences) has been our standard choice in the setting of degenerative mitral valve disease (Table 2).

All patients underwent predischarge echocardiography to confirm the success of valve repair. Oral anticoagulation with a target international normalized ratio of 2.0–3.0 was continued up to 3 months after surgery. In the presence of other indications (e.g. atrial fibrillation), oral anticoagulation was continued indefinitely.

**Study end-points**

Postoperative mortality and morbidity end-points were defined according to the joint Society of Thoracic Surgeons, American Association for Thoracic Surgery and European Association for Cardio-Thoracic Surgery Guidelines [11]. Early mortality was defined as mortality within 30 days after the operation or during the index hospitalization.

**Statistical analysis**

Continuous data were presented as means ± standard deviation for normally distributed data or medians and IQRs when not normally distributed. Categorical data were presented as counts and percentages. The $\chi^2$ and the Fisher’s exact tests were used to analyse categorical variables. The independent sample t-test and the Mann–Whitney U-test (skewed data) were used to analyse continuous variables. Survival and event rates were summarized using the Kaplan–Meier method and compared using the log-rank test. Estimates are presented as percentages and 95% confidence intervals (CI). The Cox proportional hazards regression analysis was used to analyse the effect of no AMVL repair on recurrent MR. With no AMVL repair forced into the model, the remaining variables were selected using a backward selection method. Variable retention in the model was set at a $P$-value of 0.10. The following variables were included: gender, left ventricular ejection fraction < 60%, atrial fibrillation, annular plication, annular calcification, height of leaflet coaptation, commissural prolapse and type of ring annuloplasty. A double-sided $P$-value of <0.05 was considered statistically significant. Statistical analysis was performed using the IBM Statistics for Windows, version 23.0 (SPSS, Inc., IBM Corporation, Armonk, NY, USA).

**RESULTS**

### Baseline characteristics and intraoperative details

Baseline characteristics and intraoperative details of the whole patient cohort are listed in Tables 1 and 2, respectively. AMVL repair was performed in 70 (55%) patients, while no AMVL repair was performed in 58 (45%) patients. The frequency of AMVL repair decreased progressively over time (Fig. 2); during the first half of the study period, AMVL repair was performed in 49 of 64 (77%) patients and during the second half in 21 of 64 (33%) patients.
There were a statistically significant higher number of female patients and higher preoperative creatinine values in the AMVL repair group. This partially reflects the improvements in perioperative complications were observed in the AMVL repair group. No other differences between both groups were expected, longer aortic cross-clamp and cardiopulmonary bypass time (min).

### Late mortality and morbidity

There were 16 late deaths. The cause of death was cardiac related in 9 patients (congestive heart failure in 1, acute Type A dissection in 1, sudden unexplained in 4, ventricular tachycardia in 1 and intracranial haemorrhage in 2) and non-cardiac in 7 patients. At 6 years after surgery, the overall survival rate was 93.3% (95% CI 87.4–99.2%) and 86.6% (95% CI 76.0–97.2%) for patients undergoing AMVL repair and for patients in whom no AMVL repair was performed, respectively (P = 0.48; Fig. 4).

No episodes of infective endocarditis occurred. There were 6 thromboembolic events (4 transient ischaemic attacks and 2 cerebrovascular accidents) and 3 severe bleeding episodes (2 resulting in death). At the most recent follow-up, 71% of patients alive at follow-up were in NYHA functional Class I, 23% in NYHA functional Class II and 6% in NYHA functional Class III.

### Echocardiographic follow-up

Recurrent (≥Grade 2+) MR was seen in 14 patients. The overall 1- and 6-year freedom from recurrent MR rates were 98.2% (95% CI 95.7–100%) and 90.6% (95% CI 84.1–97.1%), respectively. At 6 years after surgery, the freedom from recurrent MR rates were 90.7% (95% CI 82.9–98.5%) and 89.1% (95% CI 75.8–100%) for patients undergoing AMVL repair and for patients in whom no AMVL repair was performed, respectively (P = 0.43; Fig. 5). Cox regression analysis failed to demonstrate any significant effect of no AMVL repair on recurrent MR (Supplementary Material, Table S1).
At the most recent follow up, 88% of patients showed mild MR, 10% moderate MR and 2% severe MR.

Late mitral valve reintervention

Three patients underwent late mitral valve reintervention, all due to recurrent MR. All patients underwent AMVL repair during the initial operation. The mechanism of recurrent MR was suture dehiscence at the PMVL (after previous quadrangular resection) in 1; de novo AMVL prolapse and PMVL restriction in 1 and ventricular dilatation secondary to severe aortic valve insufficiency in 1. Upon reoperation, 2 mitral valve re-repairs and 1 valve replacement were performed. All patients survived the reoperation. The 1- and 6-year freedom from operated valve reintervention rate was 99.2% (95% CI 97.6–100%) for both. There was no significant difference in the freedom from late mitral valve intervention rates between both groups (\(P = 0.25\); Fig. 5).

DISCUSSION

Our study demonstrates that mitral valve annuloplasty successfully resolves functional prolapse of the AMVL in patients with
Barlow’s disease and bileaflet prolapse. We also found that functional AMVL prolapse without true prolapse affects the majority of these patients. Annuloplasty will provide annular stabilization and prevent abnormal annular dynamics that otherwise significantly contribute to valve dysfunction. Furthermore, addressing functional prolapse of the AMVL with annular stabilization alone provides excellent valve repair durability.

The mitral valve annulus is a dynamic structure that plays an important role in the normal functioning of the mitral valve. Complementary to annular dilatation, abnormal annular dynamics is additionally present in Barlow’s disease and is characterized by poor early systolic annular contraction and saddle-shaped accentuation [6, 7, 10, 12]. In late systole, an abnormal late-systolic annular enlargement with enlargement of the anterior-posterior and intercommissural diameters further occurs [6, 7]. Annular changes are readily present even in the absence of severe MR [6]. This pathological annular movement directly results in the absence of physiological systolic mitral valve area reduction, impairs mitral valve leaflet apposition and promotes valve regurgitation. Posterior mitral annulus displacement is a prominent structural abnormality in patients with Barlow’s disease [10, 13] that provides a possible explanation for the described abnormalities. Moreover, paradoxical systolic displacement of the papillary muscles towards the left atrium has been described [14–16]. This further contributes to the occurrence of mitral valve leaflet billowing and/or prolapse. Altogether, these observations demonstrate that the mitral valve annulus is the primary substrate of functional leaflet prolapse in Barlow’s disease.

Annuloplasty presents an essential component of surgical mitral valve repair [2, 17]. In Barlow’s disease, the aim of prosthetic annuloplasty is not only annular remodelling but also prevention of abnormal annular dynamics and restoring the physiological systolic annular saddle shape. The effect of surgical annuloplasty on mitral valve morphology was characterized by De Paulis et al. [18] who described their experience in 40 selected patients with Barlow disease’s and a central regurgitant jet in whom valve repair was established by semirigid band annuloplasty alone. Following repair, intraoperative echocardiography revealed marked changes in the morphology of the mitral valve as a reduction of the mitral valve annulus with re-establishment of leaflet coaptation in the left ventricle and increased leaflet coaptation height were observed. Moreover, paradoxical systolic displacement of the papillary muscle was resolved, as a marked increase of the distance between the papillary muscle tip and the mitral annular plane was seen. Similarly, Ben Zekry et al. [19] were able to successfully perform mitral valve repair with ring annuloplasty alone in 24 patients with Barlow’s disease. Following annular stabilization, comparable changes of the mitral valve morphology were observed.

Because of extensive annular abnormalities and functional consequences hereof, bileaflet prolapse is a common observation in patients with Barlow’s disease and has previously been reported in up to 75% of these patients [5, 20–22]. The frequency of bileaflet prolapse in our study cohort is comparable to these reports.

In the context of bileaflet prolapse due to Barlow’s disease, AMVL repair is performed almost uniformly in centres experienced in reconstructive mitral valve surgery [5, 20, 21]. This reflects the approach to AMVL prolapse early in our experience.

Over time, our understanding on the contribution of abnormal mitral annular dynamics to mitral valve dysfunction in Barlow’s disease has grown. The effect of annular stabilization on functional leaflet prolapse has led us to adopt a conservative approach to AMVL prolapse in this setting. This is reflected by a decreasing percentage of patients undergoing specific AMVL repair during the study period. The selection of patients for inclusion in this study was made on careful assessment of the preoperative echocardiogram, and all patients demonstrated bileaflet prolapse. The diagnosis of Barlow’s disease was further confirmed intraoperatively in all cases. The study cohort therefore presents a homogenous population, and the observed decrease presents a direct effect of the newly implemented approach.

Valve repair in Barlow’s disease remains technically challenging. This is also reflected by our experience as various techniques were utilized to secure valve competency. In Barlow’s disease, excessive leaflet tissue and thickened chordae tendineae are typically seen [9]. Valve degeneration will affect all valve segments, often making the valve appear prolapsing on all levels. In such cases, the differentiation between surgical and functional prolapse needs to be made with respect to the morphological changes that follow annular stabilization [8, 18]. Although this will resolve the functional prolapse, it will not resolve true leaflet prolapse, normally occurring due to chordae elongation and/or rupture. Although ruptured chords can be easily identified intraoperatively, the identification of elongated chords can be difficult, especially when the reference point in the PMVL is difficult to establish. In these cases, PMVL repair and annular stabilization (with annuloplasty sutures) are performed first, and only in that phase, the AMVL can be properly assessed. As mentioned earlier, a water test is helpful to understand the motion of the AMVL. This test has to be properly performed with adequate filling of the ventricle.

In our more recent experience, AMVL repair was still needed in about one-third of patients. When possible, addressing AMVL prolapse with annuloplasty alone will result in a technically less challenging procedure and helps reduce the length of cardiopulmonary bypass. Moreover, it prevents the inadvertent implantation of neo chords that are too short and might cause leaflet restriction. During the follow-up period, we failed to observe any difference in the incidence of recurrent MR between both groups. Moreover, no patient from the no AMVL repair group needed mitral valve reintervention during the follow-up period. These observations demonstrate that annular stabilization provides an effective resolution of the functional prolapse at mid-term and that future chordal elongation will not occur if excessive leaflet strain will be resolved by a sound repair. Studies with longer follow-up duration are needed to confirm our findings. Interestingly, papillary muscle head repositioning for commissural prolapse was performed more commonly in the no AMVL repair group. In these cases, the papillary muscle head repositioning provides support to the commissural region was identified and repositioned, thereby preventing the free edge of this segment to prolapse in systole. This has some effect on the motion of the paracommissural segments of the AMVL. However, this could not resolve the prolapse of the whole AMVL that is typically observed in cases of functional mitral valve leaflet prolapse.

We regularly perform excessive PMVL tissue resection to reduce excessive leaflet tissue height and width. In our opinion, resection and sliding of the PMVL can effectively simultaneously address both issues. When only limited excessive tissue is present, though rarely seen in Barlow’s disease, non-resection techniques present an alternative. A central regurgitant jet seen on preoperative echocardiography might suggest that MR could occur solely as a consequence of abnormal annular dynamics with functional prolapse of both mitral valve leaflets. This can potentially be addressed by annular stabilization only [18, 19]. A proportion of
patients undergoing PMVL repair in our cohort might therefore have undergone valve repair with ring annuloplasly alone. On the basis of the studies by De Paulis et al. [18] and Ben Zekry et al. [19], this does, however, result in a noticeable risk of systolic anterior motion. Large annuloplasty rings combined with leaflet height reduction are effective at preventing this complication [23]. The performance of PMVL height reduction seems therefore important and is, in our opinion, essential as has previously been advocated to prevent systolic anterior motion [24].

Limitations

This is a single-centre study in a selected group of patients with Barlow’s disease. Our surgical approach has evolved during the study period. This resulted in some differences in the surgical techniques performed between both groups. However, both groups demonstrated satisfactory long-term repair durability that compare favourably with the results previously described in the literature. The difference in the surgical techniques performed does, therefore, not obscure our results. The duration of clinical and echocardiographic follow-up was limited to mid-term results. The long-term durability of mitral valve repair in this setting will need to be confirmed in the future.

CONCLUSION

Mitral valve repair in Barlow’s disease with bileaflet prolapse is technically challenging. The strategy for surgical mitral valve repair should take into account the contribution of the mitral valve annulus to the expressed valve dysfunction and the changes in mitral valve morphology that follow annular stabilization. Functional prolapse of the AMVL can effectively be treated by annular stabilization alone. Discrimination between the functional prolapse and the true prolapse allows for a simplified valve repair that provides excellent long-term valve durability.

SUPPLEMENTARY MATERIAL

Supplementary material is available at ICVTS online.

Conflict of interest: none declared.

REFERENCES