Short Communication on Novel Concepts in Cardiopulmonary and Structural Heart Disease

Early failure of mitral valve repair with anterior leaflet pericardial patch augmentation in rheumatic and radiation-induced valvulitis

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Introduction

Rheumatic mitral valve disease remains an important cause of mitral regurgitation (MR), accounting for 7% to 15% of organic MR cases in large epidemiologic studies (1,2). Similarly, a history of radiation to the mediastinum, as is common in the treatment of several malignancies, is associated with future valve dysfunction in up to one-third of patients. Mitral valve repair (MVr) is favored over replacement for severe primary MR; this is due to a significant 30-day and mid to long-term mortality benefit, as well as a reduction in peri-operative complications (3,4). However, due to ongoing inflammation and leaflet infiltration, MVr in rheumatic or radiation-induced valvulitis may be associated with decreased durability and an increased risk of reoperation (5).

In order to improve outcomes of MVr in these populations, adjunctive reparative procedures have been introduced. One such technique involves the use of autologous or bovine pericardium to reconstruct or enlarge the anterior mitral leaflet (AML) and normalize its coaptation with the posterior leaflet, with further reinforcement from a supporting annuloplasty ring (*Figure 1*) (6). While small studies suggest excellent mid-term survival with this approach, moderate or greater recurrent MR and reoperation occurs in 11.2% and 4.6% of patients, respectively, with rheumatic MR. Poor outcome data exists in the literature regarding MVr techniques for radiation-induced valvulitis (6,7). Herein, we provide an in-depth clinical and imaging appraisal of two such cases, with a focused review on pathophysiology and management.

Methods and results

The technical and patient selection criteria and operative approach used in our institution's prior surgical era for anterior leaflet augmentation MVr was previously described, and will be briefly reviewed (8). The anterior leaflet was carefully detached from the mitral annulus slightly past the posteromedial and anterolateral commissures, and then displaced towards the P2 scallop of the posterior leaflet. A portion of autologous or bovine pericardium measuring approximately 4 cm wide and 3 cm long, tailored to the size of the intercommisural diameter, was sutured to the mitral annulus and the detached basal portion of the anterior leaflet in an over-and-over fashion. A true-sized annuloplasty ring based on the length of the augmented anterior leaflet was used to stabilize the valvular apparatus (*Video 1,2*). Of note, the pericardial patch was not pretreated with glutaraldehyde to allow for flexible leaflet reconstruction and preservation of dynamic leaflet motion.

Patient one

A 69-year-old female with a history of rheumatic heart disease presented with combined severe rheumatic aortic stenosis and MR, and New York Heart Association (NYHA) functional class IV symptoms. The left ventricular systolic function [ejection fraction (LVEF) =66%] and size [end-diastolic diameter (LVEDD) =46 mm] were normal, and the pulmonary artery systolic pressure (PASP) measured 67 mmHg. On pre-operative echocardiography the mitral valve leaflet mid-body and tips were thickened with

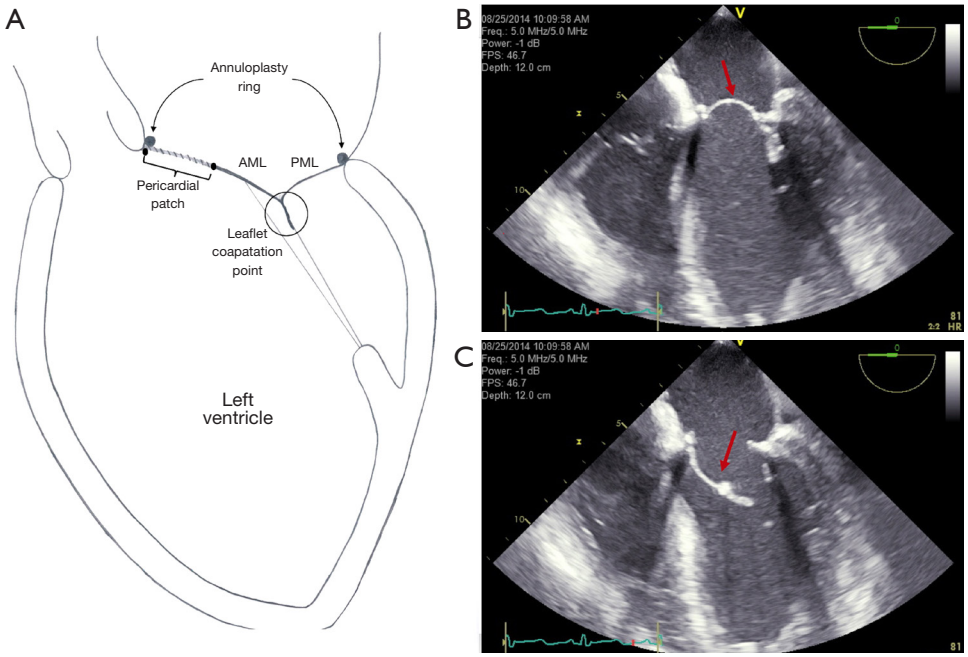

Figure 1 MVr utilizing an annuloplasty ring and AML pericardial patch augmentation. (A) Schematic of AML pericardial patch augmentation MVr. There is a reconstructed and enlarged AML, normalized anterior and posterior leaflet coaptation, and reinforcement from a supporting annuloplasty ring; (B,C) systolic and diastolic transesophageal echocardiography mid-esophageal four-chamber views. Displayed is the augmented anterior mitral leaflet and pericardial patch (red arrow). MVr, mitral valve repair; AML, anterior mitral leaflet; PML, posterior mitral leaflet.

calcified and shortened chordae tendineae. An anterior leaflet augmentation MVr was performed utilizing a Peri-guard bovine pericardial patch (Baxter, Deerfield, IL, USA) and a 35 mm St. Jude Tailor annuloplasty ring (St. Jude Medical, St. Paul, MN, USA), in addition to bioprosthetic aortic valve replacement with a 23 mm Medtronic Mosaic valve (Medtronic Inc., Minneapolis, MN, USA), MAZE procedure, and left atrial appendage ligation. The patient had an uneventful post-operative course and was discharged on day 4.

At 4 years post-MVr she developed progressive dyspnea on exertion, recurrent atrial fibrillation, and NYHA class III symptoms. Echocardiography revealed severe recurrent MR secondary to extensive patch and native anterior leaflet fibrocalcific degeneration with partial patch flail (*Video 3*,*4*). The LVEF, LVEDD, and PASP measured 64%, 49 mm, and 61 mmHg, respectively. A reoperative mitral valve replacement was performed utilizing a 29 mm Carpentier-Edwards Magna Ease bioprosthesis (Edwards Lifesciences, Irving, CA, USA). Gross pathology revealed mitral leaflet and pericardial patch sclerosis, focal calcifications, and granulomatous deposition (*Figure 2*). Post-operatively the patient was treated for right ventricular failure, which required an extended intensive care unit length of stay and inotropic support, with good eventual recovery. She was discharged home on day 15.

Patient two

A 53-year-old female with a history of Hodgkin's lymphoma and mediastinal radiation presented with severe MR, NYHA functional class II heart failure symptoms, normal left ventricular systolic function (LVEF =65%) and size (LVEDD =45 mm), and a PASP of 50 mmHg. On pre-operative echocardiography the mitral valve was diffusely thickened and calcified, with restricted motion of the leaflet tips. An anterior leaflet augmentation MVr was performed utilizing an autologous pericardial patch and a 31 mm St. Jude Tailor annuloplasty ring (St. Jude Medical, St. Paul, MN, USA). The patient had an uneventful post-operative course and was discharged on day 3.

At 4 years post-MVr she developed progressive dyspnea on exertion and NYHA class III symptoms. Echocardiography revealed severe recurrent MR secondary

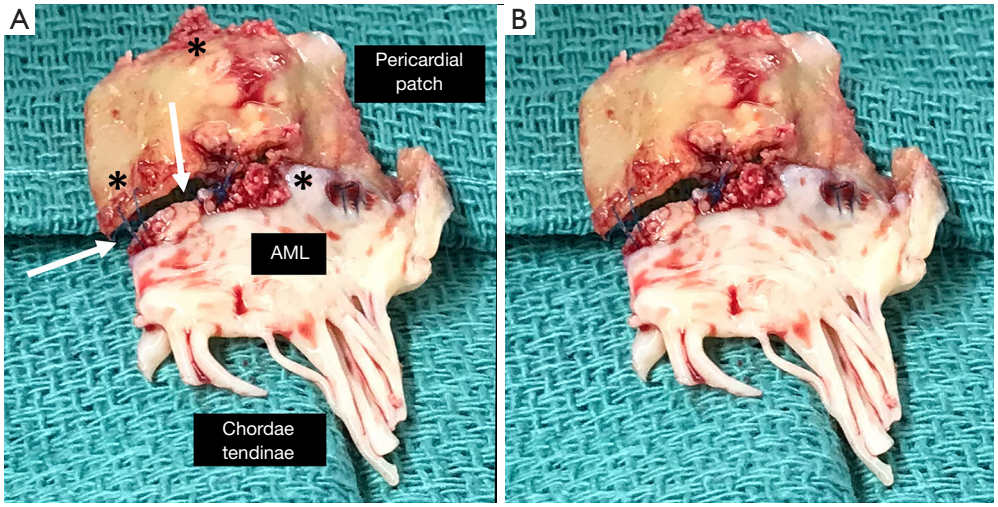

Figure 2 Failure of pericardial patch augmentation MVr in rheumatic mitral valve disease. (A) Gross pathology of a transected failed AML pericardial patch augmentation MVr. There is extensive post-inflammatory fibrocalcific degeneration along the AML-pericardial patch continuity (asterisks), with partial patch dehiscence (white arrows); the glistening appearance of the patch and leaflet indicates fibrosis; findings are consistent with rheumatic heart disease (B) unmarked gross pathology. MVr, mitral valve repair; AML, anterior mitral leaflet.

to patch calcification, retraction, and central dehiscence, as well as moderate-to-severe secondary/functional tricuspid regurgitation. The LVEF, LVEDD, and PASP measured 63%, 47 mm, and 66 mmHg, respectively. A combined reoperative mitral valve replacement and tricuspid valve repair was performed, utilizing a 31 mm St. Jude Masters mechanical mitral valve prosthesis (St. Jude Medical, St. Paul, MN, USA) and a 26 mm Carpentier-Edwards tricuspid valve annuloplasty ring (Edwards Lifesciences, Irving, CA, USA). Gross pathology revealed diffuse dystrophic calcification with focal areas of hemorrhage (*Figure 3*). The patient had an uneventful post-operative course and was discharged on day 7.

Conclusions

The feasibility of MVr for rheumatic or radiation-induced mitral valve disease and MR is highly dependent upon several factors including: (I) anterior leaflet pliability; (II) severity and extent of subvalvular apparatus calcification; and, (III) the ability to address pseudoprolapse of the AML, which often occurs in the setting of a severely diseased posterior leaflet with chordal retraction and leaflet tethering (9,10). In addition to leaflet and subvalvular debridement and mobilization, annuloplasty rings are pivotal to remodel and stabilize the mitral annulus. A minimum ring size of 30 mm in females and 32 mm in males is recommended to avoid iatrogenic mitral stenosis in the setting of instric leaflet abnormality, which may require leaflet pericardial patch enlargement to increase the surface area and height, as in the present cases (11).

Pericardial tissue is mainly composed of cross-linked collagen fibers and is used in reconstructive cardiac operations, including complex MVr, due to its elastic and conformative properties (12,13). Autologous and bovine pericardium are nonthrombogenic with a very high threshold for infection; autologous patches are also nonantigenic (13,14). Pretreatment with glutaraldehyde may be performed to stiffen and improve handling of the pericardium, however, there is a risk of patch calcification and retraction post-implantation (15). An alternative to bovine or autologous pericardium in valvular reconstruction is decellularized porcine small intestine submucosa (CorMatrix, CorMatrix Cardiovascular Inc., Roswell, GA, USA). Despite its ability to stimulate cell differentiation and host cell ingrowth, there is a concern regarding immune-mediated patch degeneration and a rate of recurrent severe MR as high as 32% after CorMatrix leaflet augmentation (16,17).

Failure of anterior leaflet pericardial patch augmentation MVr in patient one was the consequence of the progressive exudative inflammatory processes of her rheumatic disease (9). A complex immunologic reaction triggers the deposition of granulomatous Aschoff bodies and fibrin on the pericardial patch and mitral valve leaflets, in particular

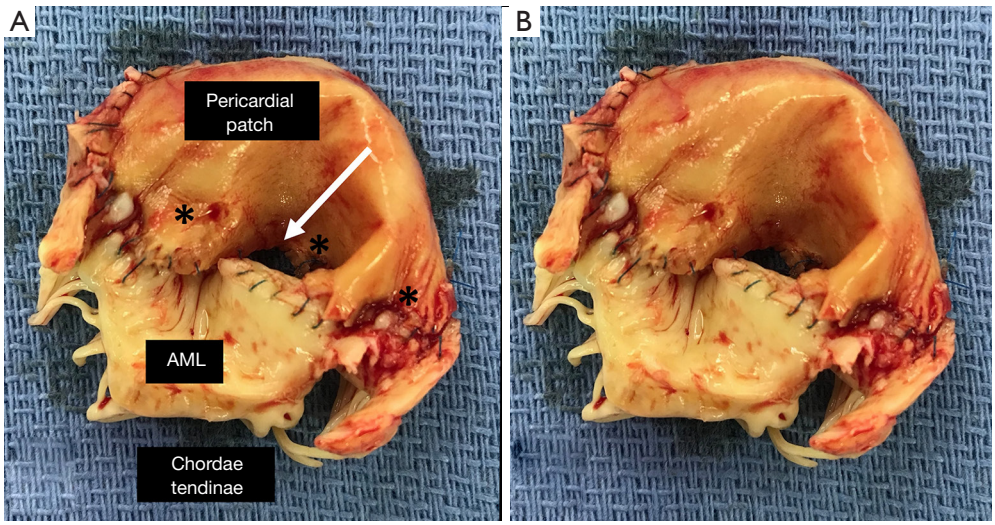

Figure 3 Failure of pericardial patch augmentation MVr in radiation-induced valvulitis. (A) Gross pathology of a transected failed AML pericardial patch augmentation MVr. There is diffuse fibrosis (glistening appearance) and calcification (asterisks) of the pericardial patch and native AML. The patch is retracted and centrally dehisced (white arrow); (B) unmarked gross pathology. MVr, mitral valve repair; AML, anterior mitral leaflet.

at the leaflet tips and chordal apparatus, as well as osteoblast upregulation and neoangiogenesis (18-20). In patient two with radiation-induced valvulitis, osteogenic and fibrogenic growth factors induce mitral leaflet fibrosis and calcification, similar to bone formation; converse to rheumatic mitral valves, there are no inflammatory or vascular changes (21-23). Both pathologies resulted in destruction of the pericardial patch-AML continuity (suture line), with patch dehiscence and partial flail.

While pericardial leaflet augmentation MVr for rheumatic disease appears to have a lower rate of reoperation for recurrent MR when compared with conventional MVr at early 3- to 5-year follow-up (4.6% *vs.* 8% to 13%), it is similar to what patients with organic/degenerative MR experience at a much longer surveillance of 20 years (7,24). This is important as data from the Society of Thoracic Surgeons National Database shows that reoperative mitral valve surgery has an operative mortality of 6.6%, with new onset renal failure and stroke occurring in 5.6% and 2.4%, respectively (25). Post-operative right ventricular failure, as seen in the case of patient one, occurs in up to a quarter of cardiac operations and is associated with an in-hospital mortality of 35% to 50% (26,27). Thus, stratification of patients with rheumatic or radiation-induced valvular heart disease at risk for progressive sequelae and early reoperation post-MVr, both with pericardial leaflet augmentation or conventional techniques, is warranted. Carpentier and colleagues reported age, calcium metabolism, and chronic kidney disease as the most important patient-related factors, and inflammatory response (i.e., extent of valvular apparatus involvement) and tissue components and preservation as the valve-related factors associated with patch MVr failure for rheumatic MR (6,28,29). While no such data exists for radiation valvulitis, a cutoff of 33 Gy for whole heart radiation dose or 30 Gy to either the left atrium or left ventricle identifies patients at higher risk of valvular disease (30,31). In the above scenarios, the risk versus benefit discussion of MVr and chordal-sparing mitral valve replacement should be at the center of a multi-disciplinary Heart Valve Team approach.

In conclusion, MVr utilizing an annuloplasty ring in conjunction with AML pericardial patch augmentation is feasible in rheumatic and radiation-induced mitral valve disease and MR. However, careful patient selection for MVr versus mitral valve replacement is paramount as rheumatic and radiation valvulitis are ongoing, smoldering processes with incremental risk for MVr failure and reoperation in this higher risk population.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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