Use of Pericardium for Cardiac Reconstruction Procedures in Acquired Heart Diseases—A Comprehensive Review

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Abstract

Background Reconstruction of cardiac structures has been the goal of many surgeons even before the advent of open-heart procedures with cardiopulmonary bypass. Unsatisfactory results with synthetic materials has switched the attention to biological tissues, among which pericardium, either autologous or of animal origin, has been widely used as patch material.

Methods We have reviewed the literature to assess the effective role of pericardial tissue in the correction of various acquired cardiac lesions. Particularly, special attention was given not only to established techniques but also to detect any peculiar and unusual application of pericardium.

Results Autologous pericardium is frequently used as patch material particularly when limited valvular lesions must be corrected, while xenograft pericardium appears particularly useful in patients with endocarditis and extensive destruction of the intracardiac structures by infection and abscesses. Pericardium is an extremely versatile material owing to its pliability and strength; however, it tends to calcify in the long term when in contact with blood, although stability of the repair is maintained in most cases.

Conclusions Pericardium plays an important role in various cardiac and aortic pathologies. Tissues resistant to fibrosis and calcification to be used as patch material are the ideal solution for more successful cardiac reconstruction procedures and will hopefully be provided by the ongoing research.

Keywords
- ► autologous pericardium
- ► xenograft pericardium
- ► cardiac reconstruction

Introduction

Reconstruction of the cardiac structures has been the goal of many surgeons even before the advent of open-heart procedures with cardiopulmonary bypass (CPB). In the past years usually foreign synthetic material was used such as Dacron fabric (Koch Industries, Inc., Wichita, Kansas, United States) or expanded polytetrafluoroethylene (e-PTFE) (WL Gore & Ass., Inc., Newark, Delaware, United States); such materials showed evident strength and durability but also limited pliability and biocompatibility, being eventually incorporated by fibrotic reaction, all potential disadvantages when used for intracardiac applications.[1] In recent years, pericardial tissue, either autologous or heterologous, has been used with increasing frequency, both in adult and congenital cardiac surgery to repair various intra- or extracardiac defects[2,3] (►**Table 1**). When compared with prosthetic material, pericardium has shown higher biocompatibility, easier handling, lower bleeding from suture lines, and less incidence of infections.[1,4] Furthermore, xenograft pericardium,

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Table 1 Available GA-fixed pericardium used in open-heart procedures

Product	Manufacturer	Treatment	Suggested uses	Dimensions	Thickness
Bovine pericardial patch Peri-Guard	Lamed GmbH	NA	-Pericardial closure -Heart surgery reconstruction	From 4 × 4 to 12 × 25 cm	NA
Bovine pericardial patch	Edwards Lifesciences	Treated with XenoLogiX anticalcification treatment	-Pericardial closure -Closure of intracardiac or septal defects -Annulus repairs -Great vessels repairs -Suture line buttressing	10 × 15 cm	0.5 ± 0.25 mm
Bovine pericardial patch Surgifoc	FOC Medical	NA	-Flexible annuloplasty -Ventricular aneurysm repair -Leaflets repair -Great vessel repair -Pericardial closure -Suture line strengthening	From 2 × 7 to 10 × 15 cm	From 0.25 to 0.4 mm
Bovine pericardial patch SJM	Abbott	Treated with ENCAP AC technology	-Intracardiac repair -Pericardial closure	From 2 × 5 to 9 × 14 cm	From 0.15 to 0.4 mm
Porcine pericardial patch	Vascutek LTD	NA	-Valve leaflet repair -Pericardial closure	NA	0.32 mm
Porcine pericardial patch No-React	BioIntegral Surgical	Treated with No-React detoxification treatment	-Pericardial closure -Intracardiac repair -Root enlargement	From 1 × 7 to 8 × 14 cm	NA

Abbreviations: GA, glutaraldehyde; NA, not available.

when fixed with glutaraldehyde is sterile and with reduced antigenicity, although toxic effects of such treatment have been recently reported.[5] Many attempts have been made to improve biocompatibility of xenografts: anticalcification treatments to improve durability, substances that might reduce cytotoxic aldehyde release from crosslinked biomaterials, and, more recently, decellularization procedures which should generate scaffolds with intact extracellular matrix through the application of physical, chemical, and/or enzymatic treatments.[5]

This review focuses on the use of pericardial tissue in cardiac surgery presenting the various applications in acquired lesions and discussing the main results obtained.

Methods

We have performed a search on PubMed and Medline databases to identify all articles in the English literature potentially useful for the aim of this review. Other data were obtained from archives of the journals present in the CTSNet Web site and from personal files. The keywords entered in the search were: pericardium, autologous pericardium, xenograft pericardium, bovine pericardium, porcine pericardium, equine pericardium, glutaraldehyde-fixed pericardium, pericardial patch, pericardial pledgets, pericardial tube, cardiac reconstruction, pericardial defects, and pericardial closure. Articles detailing the various surgical techniques using pericardial patches were also considered. The literature was searched for the most frequent use of pericardial tissue in adult cardiac surgery, but efforts were made also to detect any unusual application most frequently found in isolated case reports. A flowchart of the selection of articles for the review is shown in ►**Fig. 1**.

Closure of Pericardial Defects

The need for closure of the pericardium after open-heart operations is still controversial. While pericardial closure might reduce the risk of myocardial injury during sternal reentry, the adverse hemodynamic effects of pericardial closure especially in patients with impaired ventricular function are also well recognized.[6–8] Reoperations performed for failure of both acquired and congenital repairs indicate that resternotomy is still associated with significant complications which may be even underreported.[9] Therefore, protecting the heart and limiting the adhesions to both the sternum and the epicardium in view of possible future reoperations appears advisable. To obtain this, several pericardial substitutes have been employed in the past, particularly patches of Dacron, dura mater, fascia lata, silicone rubber, glutaraldehyde-treated bovine or porcine pericardium, e-PTFE, and polyurethane.[10–17] Data available in the literature are quite conflicting on the effectiveness of these materials for pericardial closure. In animals, porcine pericardium has shown a remarkable absence of adhesions as well as bovine pericardium which appeared also free from calcification[14,15]; however, heterologous pericardium implanted in humans and explanted after a maximum of 59 months showed an evident fibrotic reaction.[18] Others, on the contrary, have shown no differences in animals between leaving the pericardium opened, simple pericardial resuture, bovine pericardium, and e-PTFE patches. In most animals, the neo-pericardium became thick and adherent to the epicardium obscuring the

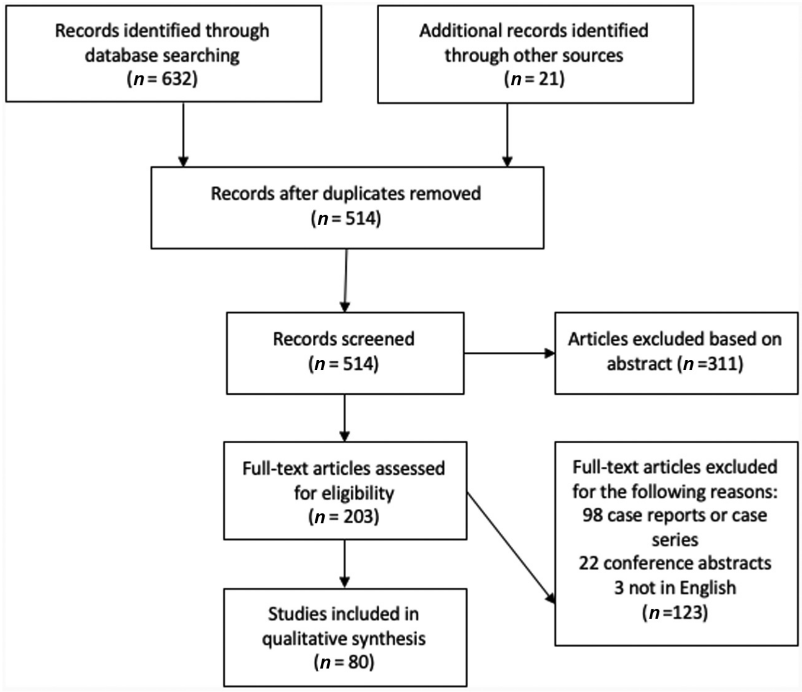

Fig. 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart for article selection.

underlying anatomy.[19] It must be observed that most of the pericardial patches have been tested in animals, while the results in humans are very limited. Furthermore, in most animals, pericardial substitutes have been evaluated by replacing the native pericardium after opening the chest, sometimes after creating pericardial abrasions, but almost never at the end of an operation on CPB. This is a drawback of such experimental works since CPB may have a damaging effect on the epicardium and pericardium in humans including reduction of its fibrinolytic activity.[20,21] Accordingly, others have used in dogs heparinized pericardial patches finding that such treatment causes less postoperative inflammatory reaction and adhesions.[22]

Mitral Valve Surgery

Mitral valve (MV) repair is the gold standard treatment in patients with degenerative mitral insufficiency but is performed with satisfactory results also in rheumatic disease and in patients with extensive calcification of the posterior MV annulus.[23,24] Native or xenograft pericardium has been largely used in many mitral reconstructive procedures. Pericardium was used to attempt MV repair in the early 1950s when Bailey et al described the experimental use of pericardial patches to reconstruct the cardiac valves.[25] In 1964, Robert W.M. Frater proposed some anatomical rules to repair the MV replacing in an animal model the posterior MV leaflet with pericardium.[26]

MV repair using neochordae tendineae has been pioneered by the Albert Einstein group in New York, who demonstrated feasibility of mitral chordae replacement with pericardial strips.[27] More than 10 years later, Rittenhouse et al replicated such experiments obtaining excellent results by replacing the MV chordae with autologous pericardium.[28] This stimulated the Albert Einstein group in New York to resume animal experiments and clinical application of pericardial strips as MV chordal substitutes. Feasibility and reproducibility of this procedure was demonstrated also in the clinical setting,[29] while in the experimental model autologous pericardium became uniformly fibrosed while calcification was observed in xenograft pericardium in long-term explants.[15,30]

MV repair is currently performed using well-established techniques. Pericardium has been widely used in patients with rheumatic and functional MV incompetence and in postradiation MV disease. In such instances, the MV leaflets are frequently fibrosed and retracted; leaflet augmentation with pericardial patches, usually made from autologous pericardium fixed in glutaraldehyde, aims to increase the leaflet surface area and to provide a better coaptation area thus restoring valve competence.[31] A recent review on this subject has shown that this technique has provided excellent results in rheumatic disease and that outcomes were similar in patients with augmentation of the anterior or posterior MV leaflet.[31] The same technique has been applied to ischemic mitral regurgitation (type IIIb), demonstrating that it increases coaptation and mobility more than isolated annuloplasty in sheep and it provides good intermediate-term results and improvement in functional status in the clinical setting.[32,33]

Reconstruction of the MV annulus may be performed successfully also in the presence of extensive posterior calcifications. In this case, the posterior mitral leaflet is detached, often from commissure to commissure, and the calcium dissected in a single block; then a crescent-shaped patch of autologous or bovine pericardium is sutured to the left ventricular endocardium anteriorly and posteriorly to the left atrial surface. The patch is then used to pass the stitches for an annuloplasty ring or a prosthesis, should the MV be considered

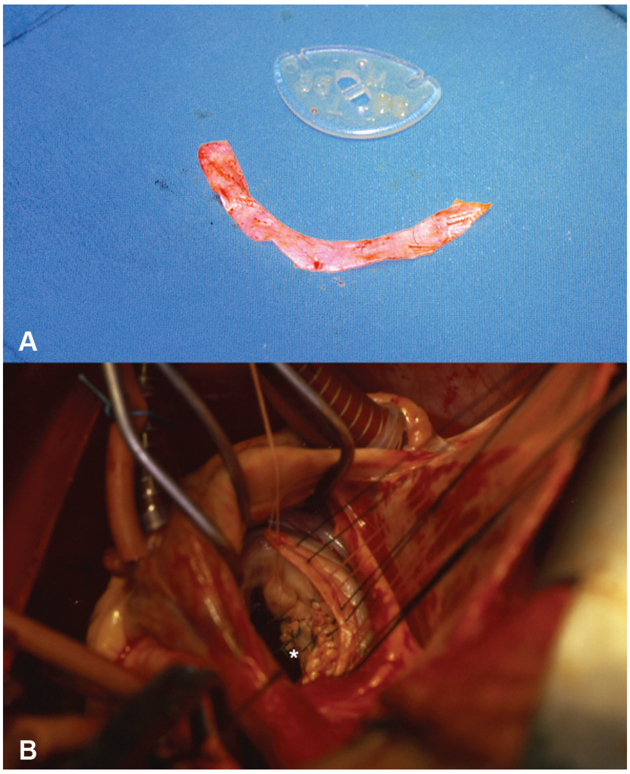

Fig. 2 Posterior mitral annuloplasty with fresh autologous pericardium. (**A**) A pericardial strip is trimmed over a commercially available ring sizer. (**B**) The ring is fixed with interrupted stitches following a quadrangular resection of P_2 (asterisk).

not suitable for repair.[24,34] MV repair almost invariably requires annular stabilization with a prosthetic ring. Alternatively, pericardium, either autologous or bovine, has been used to obtain a partial ring to accommodate and fix the posterior MV annulus (►**Fig. 2**). The pericardium-reinforced annuloplasty has been demonstrated to be feasible, cost-effective, and durable, and free from significant calcification in the long term[35]; others, however, have shown that posterior MV annuloplasty with autologous pericardium can jeopardize durability of repair in patients with degenerative MV disease.[36]

Aortic Valve Surgery

The leading pathology affecting the aortic valve is calcific aortic stenosis which benefits only from surgical or transcatheter prosthetic valve implantation. In patients in whom the aortic valve can be repaired pericardium may play an important role. Aortic cusp reconstruction with autologous pericardium has been reported by Donald Ross in 1963.[37] The widespread diffusion of aortic valve repair techniques has recently renewed the interest in the use of biological tissue for this purpose. Replacement of the aortic cusps with autologous or xenograft pericardium, appears to be somewhat complex but nevertheless has been associated with good results in the mid-term.[38] The largest experience is that by Ozaki et al,[39] who in a large series of patients replaced all aortic cusps using autologous pericardium, fixed in 0.6% glutaraldehyde solution for 10 minutes, and shaped with specific sizers. The rationale is to obtain a truly stentless tissue valve, inexpensive, and nonantigenic avoiding a stent, and therefore with ideal hemodynamics and lower mechanical stresses on the tissue. El Khoury and his group have popularized the use of autologous and bovine pericardium as adjunct in valve-sparing procedures also in patients with complex aortic valve pathology, such as bicuspid or unicuspid morphology[40]; in their experience, this type of repair is feasible, safe, and with acceptable medium-term durability with no differences between autologous or xenograft pericardium.[40] All such techniques appear attractive but very long-term results are still lacking, so a comparison with durability of currently available bioprostheses is not possible. Whether complexity of native valve pathology, type of pericardium, and different surgical techniques might have an impact on late outcomes remains to be defined.

Tricuspid Valve Surgery

Tricuspid valve (TV) surgery consists mainly in treating valve incompetence by suture annuloplasty or implantation of prosthetic rings. As early as 1949, Templeton and Gibbon replaced a TV leaflet with a patch of pericardium shaped to reproduce also chordal attachments.[41] Pericardium can be employed for TV annuloplasty with excellent medium-term results. De La Zerda et al, in fact, reported stability of this procedure at a maximum of 7 years after TV repair in 59 patients without any incidence of failure.[42] Autologous pericardium was used by Dreyfus et al to correct TV functional regurgitation due to severe tethering of the anterior TV leaflet; in a series of patients leaflet augmentation was effective in obtaining TV competence.[43] Furthermore, pericardial pledgets have been used in TV regurgitation to reinforce sutures used for an edge-to-edge procedure to join all leaflets giving a clover appearance to the valve.[44]

Valvular and Prosthetic Endocarditis

Endocarditis on one or more cardiac valves may still represent a surgical challenge, particularly when infections cause large abscesses of destruction of intracardiac structures.

When infection is limited to the MV, very often vegetations and part of the leaflets must be removed making repair by direct suture impossible. In such instances, patches of pericardium, alone or associated to other maneuvers, are extremely effective in obtaining MV competence.[45,46] When a single leaflet is involved by infection, repair is generally recommended and feasible.[46] A recent review of this subject concluded that MV repair is always preferable to replacement in infective endocarditis.[47] Repair has been associated to a 72% of freedom from reoperations and 98% freedom from reinfection at 10 years.[46] Also, when the posterior MV annulus is involved by infection with abscess formation, pericardium may be used to close the cavity left over after debridement. Occasionally, a circumferential strip of pericardium may be used to reconstruct the entire MV annulus.[34] At the end of the repair, pericardial annuloplasty may be still a good option in MV endocarditis, when the use of a prosthetic ring may not be advisable in an infected area.[46] Should the MV be nonreparable, the pericardial patch is used as a supporting structure for the stiches used to fix the prosthesis at the posterior annulus.[48]

When infection damages the intervalvular fibrous body between the aortic valve and MV, debridement of infected tissues leave a large lack of tissue which may be complex to repair. David et al have successfully managed this situation by using a properly tailored patch of bovine pericardium sutured to the right and left fibrous trigones and the aortic root reconstructing the aortic and mitral annuli followed by prosthetic insertion and closure of the left atriotomy with a separate patch.[2,34]

Native aortic valve or prosthetic endocarditis is generally treated by cusp excision, prosthesis removal, and valve replacement; the presence of annular abscesses or aortic root destruction renders repair technically difficult. In such instances, extensive use of pericardial tissue is frequently indicated. Valve repair may be performed by simple patch closure of cusp perforations when infection is extremely limited.[49] In most cases, however, abscesses must be cleaned off together with excision of all necrotic tissue and, after thorough irrigation, closed with patches of pericardium which at the same time are used to reconstruct the left ventricular outflow.[50] Prosthetic implantation may be performed by reinforcing the annulus with pericardial strips in a sandwich fashion to provide a better hold for the sutures; generally, in aortic valve replacement (AVR) for endocarditis we favor the use of interrupted sutures reinforced by hand-made pledgets of bovine pericardium to avoid the use of felts in an infected area.

When the infection involves the aortic root, root replacement may be mandatory. Xenopericardial tube grafts (Shelhigh, Inc., Millburn, New Jersey, United States), made of a porcine stentless bioprosthesis incorporated into a pericardial tube, have been used in this setting but the results have been disappointing.[51] Nevertheless, pericardial tissue has extended applications in aortic root infection. Self-made tubes of bovine pericardium have been used to replace the ascending aorta and root with promising results.[51,52] When implanting a composite conduit in a fragile aortic annulus, the proximal anastomosis may be reinforced with pericardium.[53] Others have proposed variations of this technique still using pericardium to obtain a doughnut-shaped skirt of bovine pericardium to reinforce the aortic annulus.[54]

TV endocarditis can be treated by valve repair in most cases; those with isolated involvement of the TV have an operative mortality between 0 and 15%, but an excellent survival rate.[55] Surgical techniques are usually based on vegetectomy, debridement of the infected tissues, and reconstruction by patch closure of tissue defects or leaflet augmentation with pericardium, at times associated to annuloplasty and/or chordal replacement.[56]

Surgery of the Ascending Aorta

When performing AVR care must be taken to implant a prosthesis of adequate size so to avoid prosthesis–patient mismatch.[57] In the presence of a diminutive or hypoplastic aortic annulus, various solutions are available among which enlargement of the annulus still plays an important role.[58] Since the first one proposed in 1970 by Nicks e al,[59] several techniques have been described differing mostly in the type and extension of the aortotomy incision.[58] A simplified technique is performed by extending the aortotomy into the commissure between the left and noncoronary sinus into the underlying interleaflet triangle, without entering the left atrium; the aortic annulus is then enlarged closing the aortotomy with a teardrop-shaped patch of pericardium.[60] Long-term follow-up in a series of 53 consecutive patients has demonstrated that this technique is safe, effective, and reproducible; moreover, computed tomographic controls revealed absence of aneurysmal dilatation in the pericardial patch, which at times becomes calcified without interfering with the repair.[61] For such procedure, patches of fabric or autologous pericardium has been used[60,62]; currently, we favor glutaraldehyde-fixed bovine pericardium since it is readily available, comes in different sizes, it is extremely pliable, and strong enough to hold sutures being highly hemostatic.[61]

In patients requiring combined aortic valve and ascending aorta replacement, the Bentall operation is still the procedure of choice. Since the early 1990s, a totally biological valved conduit has been available as an alternative to conduits incorporating a mechanical or a biological prosthesis. Although this device may have definite indications, such as endocarditis or old patient age, nevertheless a word of caution has been raised due to high rate of reoperations warning against its use.[51,52] The use of valved conduits implies many suture lines with the potential for bleeding complications; the weakest points are at the coronary buttons anastomosis and pseudoaneurysm formation has been observed at this level in patients with fragile tissues such as those with dissection of Marfan's syndrome.[63] For such reason, some suggest the routine use of pericardial strips to reinforce these sutures.[64]

Pericardium finds other applications in surgery of the thoracic aorta. Bovine pericardium has been used for wrapping the ascending aorta to reinforce the aortic wall, to prevent further dilatation, or to control excessive bleeding (►**Fig. 3**)[65]; strips of pericardium may be used to reinforce aortic suture lines in elective or acute repairs[66] and bovine pericardium has been used for hemostatic purposes in graft-to-graft anastomosis during replacement of the ascending aorta.[67] Bleeding is an important issue especially in aortic surgery and we routinely favor pledgets made from autologous pericardium, particularly to eliminate bleeding from the aortotomy line in the fragile

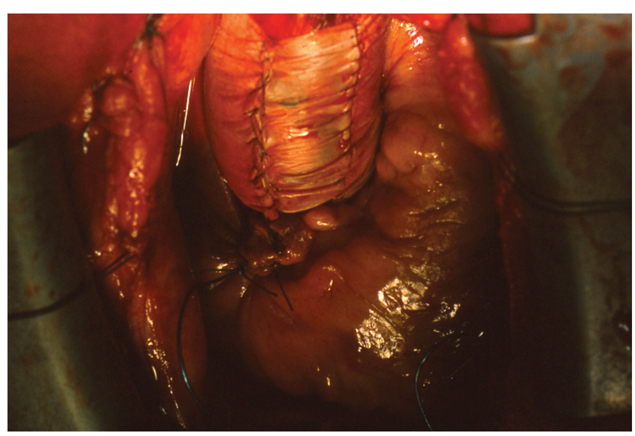

Fig. 3 External wrapping of a dilated ascending aorta with bovine pericardium.

aorta, avoiding sutures reinforced by felts to render less cumbersome dissection of adhesions in future reoperations.

Complications of Myocardial Infarction

Correction of mechanical complications of myocardial infarction is still challenging and associated with high mortality and morbidity. LV free wall rupture is the most frequent complication and can be generally treated conservatively either by securing a pericardial patch with glue or by suturing a large patch of xenograft pericardium over the infarcted area which is then filled with glue before completing the suture.[68]

LV aneurysms or pseudoaneurysms may be corrected with excision of the scarred tissue and closure of the neck of the aneurysm by a pericardial patch.[69,70] Interestingly enough, this technique has been also recently proposed by the Texas Heart Institute group in Houston who has pioneered the endoaneurysmorrhaphy technique with a Dacron patch.[71] We generally prefer to use a double patch made internally by bovine pericardium and externally by Dacron (►**Fig. 4**); as a result, a biological surface will face the LV

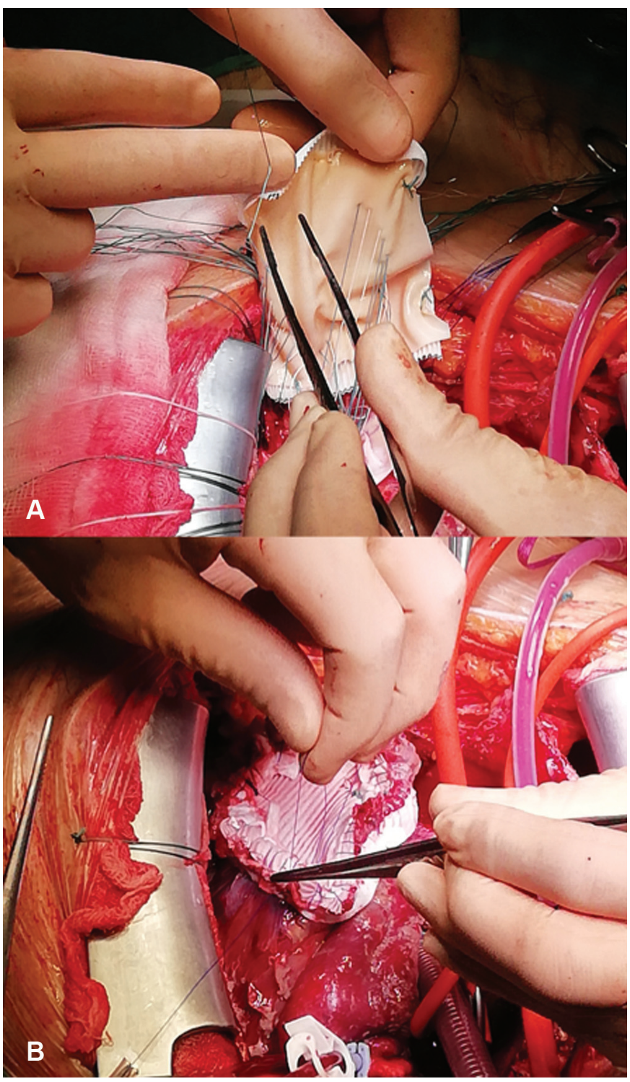

Fig. 4 (A) Repair of a left ventricular aneurysm using a double patch with an inner layer of bovine pericardium and Dacron externally. (B) Both patches are fixed in place with single stitches buttressed with felts.

cavity minimizing the risk of clot formation over a noncontracting area.[72]

The outlook of patients with postinfarction LV septal rupture has dramatically changed after the technique of infarct exclusion by an endocardial patch was introduced by Tirone David.[2] A large patch of bovine pericardium is sutured with full-thickness bites to the healthy endocardium of the noninfarcted septum and anterolateral wall to close the defect excluding the infarcted area. This procedure is modified based on the location of the interventricular defect, being those located in the posterior septum more complex to repair also because of the proximity of the MV annulus. This technique has subsequently been widely applied and recently some modifications have been proposed.[73]

Cardiac Neoplasms

Excision of tumors infiltrating the cardiac structures is extremely challenging. Cooley et al, in 1985, described a patient with a large pheochromocytoma requiring cardiac explantation and subsequent retransplantation for complete tumor removal. A flap of autologous pericardium was needed for reconstruction of the left atrium.[74] A similar operation was performed later also in a large series of patients with cardiac sarcomas with patches of autologous or bovine pericardium.[75] According to this experience, patients with cardiac sarcomas treated with excision and multimodal therapy can have reasonable survival provided that an aggressive treatment is instituted. Others have also reported a large use of patches (almost 60% of cases), including pericardium, for cardiac reconstruction after removal of cardiac tumors.[76] Excision of benign cardiac tumors may also require the use of pericardium; in one patient with papillary fibroelastoma of the aortic valve, excision of the mass caused perforation of one cusp which was repaired with a patch of glutaraldehyde-fixed autologous pericardium.[77]

Discussion

This review aimed to recall the techniques in which the use of pericardial tissue has played or still plays an important role in the repairing of acquired cardiac lesions. We have found that many simple and even curious but still ingenious applications emerged from the literature search. Through the years, pericardium has been employed in a wide range of lesions with established techniques and even with minor variations. Some of these have been probably inadvertently overlooked or not included because of space limitations or to avoid repetitions. Nevertheless, we believe that this overview is sufficiently exhaustive to underline the role of pericardium in the modern cardiac surgery armamentarium. Finally, we have not considered commercially manufactured bioprosthetic valves made of xenograft pericardium, one of the major fields of pericardium utilization, since this was not among the aims of this review. It may be considered that pericardium has been extensively used also in the repair of simple or complex congenital heart defects, an issue not addressed in this review.

There is a large amount of research performed to find the ideal biomaterial for cardiovascular repair, corrective and

Table 2 Available decellularized pericardium used in open-heart procedures

Product	Manufacturer	Treatment	Suggested uses	Dimensions	Thickness
Bovine pericardial patch PhotoFix	CryoLife	Dye-mediated photo-oxidation	-Intracardiac repair -Great vessel repair -Suture line buttressing -Pericardial closure	From 1×6 to 6×8 cm	NA
Equine pericardial patch Matrix Patch[M]	Autotissue	Shipped in an antibiotic solution	-Defect repair in pediatric cardiac surgery	From 3×3 to 10×10 cm	From 0.17 to 0.37 mm
Porcine pericardial patch CardioCel	Admedus	Treated with ADAPT anticalcification treatment	-Aortic valve leaflet repair/reconstruction -Valve annular reconstruction -Aortic root expansion/repair -Mitral valve leaflet augmentation -Aortic valve leaflet replacement -Great vessel reconstruction -Bicuspidization of unicuspid aortic valve	NA	NA

Abbreviation: NA, not available.

reconstructive surgery.[1,4,5,78] Most of the studies on new materials, such as extracellular matrix patches, decellularized tissues (►**Table 2**), and different fixation treatments, are mainly conducted in vitro to evaluate their structural and biomechanical properties.[78,79] Some of these new materials have been already used clinically but the results are limited and, in some cases, unexpectedly unfavorable so further research has been recommended.[1,80]

Conclusion

This review has shown the wide variety of applications of pericardial tissue in the repair of most of the acquired cardiac lesions. Furthermore, it confirms the extreme versatility of this material which can be used for extremely complex repairs or even as simple methods which could at times appear too naive, nevertheless being almost always creative and original. When choosing among various types of pericardium, autologous fresh or fixed and xenograft tissue fixed in glutaraldehyde, the characteristics of each one should be considered based on the type of repair to be performed, such as available quantity, pliability, stiffness, strength, and immunological properties. Implanted pericardium tends to calcify once implanted, particularly if it is in contact with blood, but in many cases, calcification does not adversely influence the result of repair. However, tissues resistant to fibrosis and calcification to be used as patch material are the ideal solution for more successful cardiac reconstruction procedures and will hopefully be provided by the ongoing research.

Conflict of Interest
None declared.

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