Clinical experience with CorMatrix extracellular matrix in the surgical treatment of mitral valve disease

Marc W. Gerdisch, MD, FACS, FACC, Richard J. Shea, MD, and Michael D. Barron, MD

Objectives: To determine the clinical utility of an acellular bioscaffold as a structural material for mitral valve repair (MVr).

Methods: This was a retrospective study of patients undergoing partial or subtotal leaflet replacement and/or leaflet extension to treat mitral regurgitation or acute endocarditis and/or reconstruction of atrial–ventricular continuity after annular decalcification. The material used for repair was a bioresorbable extracellular matrix (ECM) material indicated for cardiac tissue repair (CorMatrix Cardiovascular, Inc, Roswell, Ga). After the necessary debridement, the ECM bioscaffold was tailored and sewn to the native mitral valve tissue. Intraoperative photographs and serial, follow-up echocardiograms were used for evaluation.

Results: From September 2008 to February 2013, MVr requiring the addition of patch material was performed in 19 patients. The median echocardiographic follow-up was 10.9 months (range, 4 days to 48 months). One early and 2 late deaths were unrelated to MVr. No perioperative or late strokes occurred. Two patients with a history of cancer, chemotherapy, and radiotherapy experienced failure of the initial MVr, necessitating reintervention. The other MVrs continued to show good valvular function and no calcification on echocardiographic follow-up of 4 days to 48 months.

Conclusions: The ECM bioscaffold is a satisfactory material for MVr in a variety of surgical situations, including endocarditis. It appears to resist calcification and infection. Additional studies are warranted to determine the long-term durability of repairs made with ECM, and its appropriate use in patients who have previously undergone radiotherapy or chemotherapy. (J Thorac Cardiovasc Surg 2014;148:1370-8)

Mitral valve (MV) repair (MVr) offers clinical advantages compared with MV replacement (MVR); therefore, evidence-based guidelines have recommended MVr instead of MVR when possible.[1-4] For many repairs, leaflet augmentation or annular reconstruction with foreign material patching could be required.

A patch material sturdy enough to withstand the mechanical forces within the heart but that does not provoke a foreign body response would be desirable. The biosynthetic materials commonly used for cardiac tissue repair, such as xenografts (eg, glutaraldehyde bovine pericardium), and synthetic materials, such as polytetrafluoroethylene or polyethylene terephthalate, might not be suitable for MVr, because their use results in the permanent implantation of an immunologically reactive foreign body, raising concerns about inflammation, calcification, and degeneration.[1-7] Arguably the best-accepted material for valve repair has been autologous pericardium.[8-11] However, concerns about fresh pericardium's lack of material strength and long-term durability have made glutaraldehyde fixation common, potentially undermining its advantages as a natural biologic material. Finally, because synthetic and fixed biologic materials are inert, they are incapable of adapting to somatic growth in young patients.

During the past 4 years, we have used a material composed of the decellularized extracellular matrix (ECM) of porcine small-intestinal submucosa for MVr.[12] Unlike previously used materials, the ECM bioscaffold is a noncrosslinked, cell-free bioscaffold that serves as a biologically active substrate for constructive remodeling. It has been shown to recruit host stem cells in preclinical models of cardiac and other tissue types and has exhibited growth potential in a preclinical vascular graft model.[12-17] These experimental studies have demonstrated that the ECM provides the unique environment necessary to promote progenitor cell attachment, migration, expansion, and maturation. With time, the ECM bioscaffold will be remodeled by the host progenitor cells to resemble native tissue.

Preliminary findings in both experimental animals and humans have shown that the ECM bioscaffold does not evoke a strong inflammatory response and is resistant to

From the Cardiac Surgery Associates, Franciscan St Francis Heart Center, Indianapolis, Ind.

CorMatrix Cardiovascular provided funds for professional medical editing; the authors maintained control over the study and report.

Disclosures: Marc W. Gerdisch reports consulting and lecture fees from, equity ownership in, and is on the Advisory Board of CorMatrix Cardiovascular, Inc. He also reports consulting and lecture fees from and equity ownership in Atricure, and lecture fees from Medtronic. CorMatrix Cardiovascular provided funds for professional medical editing. The authors maintained control over the study and manuscript. All other authors have nothing to disclose with regard to commercial support.

Received for publication June 12, 2013; revisions received Oct 3, 2013; accepted for publication Oct 29, 2013; available ahead of print Dec 10, 2013.

Address for reprints: Marc W. Gerdisch, MD, FACS, FACC, Cardiac Surgery Associates, Franciscan St Francis Heart Center, 5255 E Stop 11 Rd, Suite 200, Indianapolis, IN 46237 (E-mail: mgerdisch@openheart.net).

0022-5223/$36.00

http://dx.doi.org/10.1016/j.jtcvs.2013.10.055

Abbreviations and Acronyms
ECM = extracellular matrix
MV = mitral valve
MVr = mitral valve repair
MVR = mitral valve replacement

calcification.[12,18,19] It is available for clinical use in the United States and Europe, with indications for pericardial closure, cardiac tissue repair, and carotid artery repair.

METHODS

Study Design and Patients

The Western institutional review board approved the present retrospective chart review. Patient consent requirements were waived. Preoperative, intraoperative, and follow-up data were collected from the charts of all patients who had undergone MVr after August 2007, when the ECM biomaterial was adopted into our practice.

Operative Techniques

All procedures were performed at the same institution by the same surgeon (M.W.G.). Transesophageal echocardiography was used to confirm the valve pathologic features immediately before surgery and to evaluate the repair afterward. The surgical approaches and procedures varied according to the specific pathologic features; however, generally, a midline sternotomy was performed. Cardiopulmonary bypass was initiated and the heart arrested with cold antegrade and retrograde cardioplegia. Cardioplegia was subsequently administered intermittently. The left atrium was entered through the interatrial groove and the diseased MV tissue debrided or resected as necessary. The resulting leaflet defects, or other pre-existing deficiencies, were patched with the ECM bioscaffold (CorMatrix Cardiovascular, Inc, Roswell, Ga) tailored to the appropriate size and shape. The material was sutured into place with running 5-0 polypropylene suture (Prolene; Ethicon Inc, Somerville, NJ). Horizontal sutures of 2-0 polyester (Ethibond, Ethicon Inc) were placed around the circumference of the annulus using an appropriately sized annuloplasty ring (Physio, Edwards Lifesciences, Irvine, Calif; ATS, LeviBio Medica, Rome, Italy; CG Future, Medtronic, Minneapolis, Minn; or 3D, Medtronic). The potential for the development of systolic anterior motion and resulting obstruction of the left ventricular outflow tract was minimized using best-practice techniques, such as "sliding leaflet" valvuloplasty.[20-22]

For decalcification and reconstruction of the mitral annulus, the valve leaflets were dissected away from the annulus when possible to allow removal of calcified tissue and then reattached using 4-0 polypropylene suture. The resulting defects in annular tissue were repaired by sewing into place an appropriately tailored piece of the ECM bioscaffold using 4-0 polypropylene sutures. The patch was made redundant and then imbricated into the defect to fill it with ECM. An annuloplasty ring was sewn into place, as described.

The chordae tendineae were either preserved or replaced with polytetrafluoroethylene neochordae (Gore-Tex, W L Gore & Assoc, Inc, Flagstaff, Ariz). Concurrent procedures (eg, valve replacement, Cox-maze IV) were performed as needed (Table 1). Two cases required MVR, one with a Mosaic tissue valve (Medtronic, Inc) and one with an On-X mechanical valve (On-X Life Technologies, Austin, Tex). The reconstructed valves were tested for leaflet coaptation and competence, the left atrium was closed and the heart de-aired, and the patients were rewarmed and weaned from cardiopulmonary bypass. Valve function was confirmed using transesophageal echocardiography before chest closure.

Echocardiographic Assessments

All patients underwent preoperative and intraoperative transesophageal echocardiography. The patients were evaluated by transthoracic echocardiography approximately 1 week postoperatively, within 1 to 3 months postoperatively, and at least annually thereafter.

RESULTS

From September 2008 to February 2013, 19 patients underwent MVr or reconstruction requiring the addition of patch material. Detailed case information is listed in Table 1, and representative intraoperative photographs are shown in Figures 1 to 3. The etiology of MV dysfunction included calcific-degenerative disease in 6, endocarditis in 5, congenital disease in 3, myxomatous disease in 2, degeneration of previous repairs in 2, and intraoperative correction of valve distortion secondary to aortic root replacement in 1. The specific procedures included 12 leaflet reconstructions, 5 annular reconstructions after decalcification, and 2 combined leaflet reconstructions and annular reconstructions after decalcification. All were performed using the CorMatrix ECM product as the repair material.

The median duration of follow-up (calculated from the date of the procedure to the date of the latest echocardiographic evaluation) was 10.9 months (range, 4 days to 48 months). This included 8 patients for whom follow-up echocardiographic data >12 months were available.

Four of the MV procedures were second (redo) repairs and one was a third-time repair. Annuloplasty rings were used in 16 patients. Neochordae were implanted as a part of 7 repairs. Two annular decalcification cases required MVR. Concurrent procedures included tricuspid valve repair in 2, aortic valve replacement in 7, repair of the ascending aorta and proximal arch in 1, Cox-maze IV in 6, left atrial appendage occlusion in 1, coronary artery bypass grafting in 3, and removal of an infected implantable cardioverter-defibrillator in 1.

With 2 exceptions (detailed below), all patients demonstrated sustained repair integrity and valve competence throughout the follow-up period, with evidence of only mild leaflet thickening, zero to mild regurgitation, and no development of stenosis. No echocardiographic evidence of calcification of the ECM patch was identified in any patient. All patients experienced an improvement in New York Heart Association functional classification (Table 1).

Adverse Events

No early or late strokes occurred. The intraoperative and early postoperative complications were typical of complex valve operations in patients with severe comorbidities. They included new permanent pacemaker implantation in 4, blood transfusions in 7, methicillin-resistant *Staphylococcus aureus* bacteremia in 1, and right ventricular failure requiring extracorporeal membrane