



PROSTHETIC MATERIAL USED IN RIGHT VENTRICULAR OUTFLOW TRACT RECONSTRUCTION AND ITS LONG TERM OUTCOME: A SYSTEMATIC REVIEW

Cardiology

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ABSTRACT

A best evidence topic in cardiac surgery was written according to a structured protocol. The question addressed is: When using a pericardial patch for reconstruction of the right ventricular outflow tract, is an untreated patch or a patch treated with glutaraldehyde better? 36 papers were found using the pub med search, of which 3 papers (1 human and 2 animal studies) represented the best evidence to answer the clinical question. The authors, journal, date and country of publication, patient group studied, study type, relevant outcomes and results of these papers are tabulated. We included papers that compared fresh untreated autologous pericardial patch with glutaraldehyde treated pericardial patch. We excluded papers that did not compare these two and assessed either one of them alone. In the only available human study comparing outcomes in children undergoing complete transventricular repair for Tetralogy of Fallot (TOF) and RVOT reconstruction with either types of pericardium, it was found that. There was no significant difference in post repair hemodynamics, incidence of transannular patching, or in systolic RVOT pressures. However at 6 months of follow-up, 72% of the patients with untreated patches had a significant increase in the RVOT diameters as indexed to the aortic annulus. In patients with glutaraldehyde treated patches, only one patient had increased RVOT diameters. In the other two experimental studies in animals, there was a lower incidence of pulmonary regurgitation and RVOT aneurysm formation at follow up. This seems to indicate that patients who received glutaraldehyde treated pericardium had a lower incidence of dilation of the right ventricular outflow tract and a lesser incidence of pulmonary regurgitation than non-fixed fresh pericardium. The search for optimal patch material is an ongoing challenge in congenital heart surgery (CHS). In this study, we report our first experience with the use of a novel decellularized bovine pericardial patch material (CardioCel™) for different applications in CHS. Retrospective review of our institutional experience with CardioCel™. Patient diagnoses ranged from valve lesions (e.g., bicuspid aortic valves, Ebstein anomaly, common AV-valve), septal defects (e.g., VSD), conotruncal lesions (e.g., tetralogy of fallot, TGA) and univentricular hearts (e.g., hypoplastic left heart syndrome). Operative details and early postoperative outcome parameters were used to identify graft-related morbidity. Echocardiographic results at discharge were used for the assessment of graft appearance and performance. Data are presented as median values (range). This study demonstrates excellent early results for CardioCel™ patch. Implantation was free of tissue related complications and applicable for manifold indications in complex congenital cardiac repairs.

KEYWORDS

pericardial patch, glutaraldehyde, right ventricular outflow reconstruction, pulmonary regurgitation.

INTRODUCTION:

During intracardiac repair of tetralogy of Fallot (TOF), the insertion of an outflow patch across the infundibulum, pulmonary valve ring and pulmonary artery provides satisfactory relief of the right ventricular outflow tract (RVOT) obstruction. However, it is also leads to significant pulmonary valve incompetence (PI). The long-term significance of PI is still controversial, although it is increasingly being realized that also produces leading to chronic volume load of the right ventricle (RV) that is known to adversely impact the its function and lead to arrhythmias in the long-term. Traditionally, pericardium (either fresh and untreated or fresh but fixed with glutaryldehyde) are used for RVOT reconstruction. However individual practices vary and are often based on personal preference rather than hard clinical data about the efficacy of either of the two types of patch material.

Any discussion on the use of patch material for RVOT reconstruction is expected to elicit multiple, very strongly held opinions, each of them based on individual practices rather than on clinical data. Each choice has advocates who promote Their viewpoint with great fervor. Similarly there is no dearth of individuals who hold the counterpoint with equal intensity. Unfortunately, the body of evidence that supports one strategy or viewpoint over another is often limited and inconclusive.

In order to understand the role of various patch materials fir RVOT reconstruction, me must understand understand that everything we do is associated with potential clinical benefits, limitations, and potential harm, as well as increased cost.

The systematic review is a formal process to identify and evaluate primary studies and other research to make determinations about effectiveness of particular interventions or therapies [1]. Traditional narrative reviews, While providing an overview of an issue, are subjective and suffer from potential selection bias and error. In contradistinction, a systematic review relies on a prospectively defined protocol to identify and appraise the relevant evidence. The aim is to completely identify the relevant publications, minimize selection bias,

and develop an objective summary of the data through pre-established evaluation and grading criteria. We performed a systematic review of the literature describing RVOT reconstruction with different patch materials. The goal of the review was to evaluate the strength of the evidence for the effectiveness of each either type of material and the relationship to its effect on PI, RV function and other factors that impact outcomes after intracardiac repair of TOF. Secondary goals were the following: (1) to determine if the level of evidence for any strategy was sufficient to make recommendations concerning guidelines for clinical practice; and (2) to provide results which could be helpful in planning future clinical trials or Quality improvement initiatives.

A systematic review of the literature was performed to evaluate all clinical studies describing techniques or outcomes of RVOT reconstruction with various patch materials. Types of interventions in the literature included the following: RVOT reconstruction with patch (transannular/ valve sparing), degree o immediate Pi, effects on early and late RV function and dimensions and need for re-intervention.

Eligibility Criteria

Inclusion criteria for the literature search included both human and animal studies in English Medical literature. Editorials, case reports, duplicates, and pure technique papers were excluded. Narrative reviews as well as all of the references were evaluated to avoid publication bias by identifying any potential additional manuscripts that were not initially identified in the search strategy. However, these reviews were not included in the final analysis as they do not represent primary data.

Search Strategy

Pubmed and Google scholar database search was performed using the keywords: [right ventricular outflow tract reconstruction.mp/] AND [fresh.mp OR glutaraldehyde fixed.mp] between 1973 to 2017.

36 papers were found using the reported search. As an initial step, the abstracts of all these 36 papers were reviewed. Once the selected paper

was deemed to fulfill the inclusion criteria, the text was studied in detail and its cross references was also reviewed. Duplicate papers were eliminated. The entire review process finally culminated in...papers being suitable for analysis and recommendations.

Data Review and analysis
THREE – PART QUESTION:

In [patients undergoing right ventricular outflow tract reconstruction using autologous pericardial patch] is [fresh or a glutaraldehyde fixed patch] preferable [for best outcomes?]

Pubmed and Google scholar database search of [right ventricular outflow tract reconstruction.mp/] AND [fresh.mp OR glutaraldehyde fixed.mp] between 1973 to 2013.

36 papers were found using the reported search. From these 3, 6 papers provided the best evidence to answer the question. Out of these, there was only one study in humans [2]; the rest were in animals [] these are presented in table 1. Only those papers where there were comparisons between treated and untreated pericardium were included. Papers that discussed either of these two options without comparisons were excluded.

RESULTS:

In the only available human study, Messina et al [2] analyzed the impact of glutaraldehyde fixed autologous pericardial patch in RVOT among children undergoing complete transventricular repair for Tetralogy of Fallot (TOF). 36 children were studied; of these 18 received fresh pericardial RVOT patch and other 18 received a RVOT patch of pericardium treated with glutaraldehyde. There was no significant difference in post repair hemodynamics, incidence of transannular patching, or in systolic RVOT pressures. However at 6 months of follow-up, 72% of the patients with untreated patches had a significant increase in the RVOT diameters as indexed to the aortic annulus. In patients with glutaraldehyde treated patches, only one patient had increased RVOT diameters. The authors of this study concluded that autologous pericardium treated with 0.625% glutaraldehyde may be a better material for RVOT reconstruction as compared to autologous untreated pericardium.

Chiu IS et al [3] in 1992 investigated the fate of antologous pericardial valved conduits in twenty piglets. Autologous pericardial conduit in the right ventricular outflow tract (RVOT) was connected to pulmonary trunk distally and RVOT proximally. In 10 of them pericardium was fixed with 0.6% glutaraldehyde and rest of the 10, pericardium was not fixed. The observations noticed were increased incidence of aneurysm in the untreated group at a mean interval of 104 days, and an increased incidence of calcification in the treated group at a mean interval of 66 days.

Scavo et al [5] experimented with transannular patch reconstruction of the right ventricular outflow tract using either polytetrafluoroethylene (PTFE, n=9), untreated pericardium (n=6) or glutaraldehyde fixed pericardium (n=6) to construct monocusp valves in a dog model. Hemodynamics, angiography, echocardiography, gross and microscopic pathology were evaluated. They did not find any significant differences among the three groups with regard to stenosis across the valve, but demonstrated less regurgitation in PTFE (1/9) and glutaraldehyde treated groups (0/6) when compared to fresh pericardium group (5/6).

While interpreting the results of these studies, caution must be exercised. In none of these studies, the actual size comparisons of the patches at the time of implantation were made. In the personal experience of the author, there has been a tendency to oversize the fresh patch as accurate sizing is not often easy. The treated patch has the advantage that accurate sizing can be performed. Over sizing the patch that may commonly occur with the use of untreated pericardium may at the time of implantation itself, lay the substrate for future RVOT dilatation and aneurysm formation.

CLINICAL BOTTOMLINE:

Immediately after intracardiac repair of TOF, early results with the use of treated or untreated pericardium are no different. At increasing follow up, patients who receive glutaraldehyde treated pericardium have a lower incidence of dilation of right ventricular outflow tract and lesser incidence of pulmonary regurgitation than untreated fresh pericardium.

Table 1 : Best Evidence Papers

Author, date and country, Study type (level of Evidence)	Patient group	Outcomes	Key results	Comments
Messina et al, 1994 J Card Surg [4] Well designed non randomized controlled trial (level IIa)	36 children undergoing repair of TOF were analyzed. The impact of glutaraldehyde fixed autologous pericardium Group I (non fixed pericardium) and Group II (0.625% glutaraldehyde fixed pericardium) Scoring system was devised to describe the degree of RVOT dilation None (+0), Mild (+1), Moderate (+2), Severe (+3)	Parameters 1.Number 2.Age (mean) – months 3.Transannular patch incidence 4. pRV/LV pressure ratios 5.Systolic RVOT pressure (mmHg) 6. follow up (months) 7. RVOT dilation	Group I Group II 18 18 29 34 44% 41% 42% 41% 24 29 6.2 5.7 6 (+2) 1(+1)	Children receiving Glutaraldehyde fixed pericardium have lesser incidence of RVOT dilation than non-fixed pericardium. The experience described in this study demonstrates the safety and efficacy of the use of glutaraldehyde treated pericardium.
Chiu IS et al, 1992 Proc Natl Sci Councc Repub China [3] Well designed experimental trial (level IIb)	Studied the fate of autologous pericardial valved conduits in RVOT among 20 piglets. 10 of them received fresh pericardium immersed in normal saline (PN) whereas other 10 received Glutaraldehyde fixed pericardium (PG)	Groups 1.Number 2.Survival (days) 3.Increase in body wt (Kg) 4. Aneurysm 5. Calcification	PN PG 10 10 82±50 114±92 30±9 42±29 01 07 5/10 9/10	Increase in survival is observed in piglets receiving glutaraldehyde fixed pericardium, whereas decrease in incidence of aneurysm and calcification is observed in non-fixed pericardium.
Scavo VA Jr et al, 1998 ASAIO Journal, Indiana Well designed experimental study (level IIa) S.Nordmeyer et al. Thorac cardiovasc Surg 2015; well designed experimental trial (level IIb)	Evaluated three valve types in repair of right ventricular outflow tract obstruction (RVOTO) with a transannular patch (TAP) in a chronic dog model. Polytetrafluoro –ethylene (PTFE), glutaraldehyde treated pericardium (GLU) and non fixed pericardium (PERI) were evaluated. Between February 2014 and August 2014, CardioCel™ patch material was used during CHS in 37 patients with a median age of 6,1 years (6 days–49,7 years) and	Parameters 1.Number 2.Follow-up (days) 3.RV/Ao % 4.Gradient(mmHg) 5.PA pulse pressure 6. RVOT Stenosis 7. RVOT Regurgitation 8. Calcification	PERI GLUPTFE 06 06 09 135 134 164 34 29 29 06 05 04 14 15 10 00 00 00 5/6 0/6 1/9 0/6 1/6 3/9 (aortic, n = 13; pulmonary, n = 1; mitral, n = 2; tricuspid, n = 5),	By 2D-Echo, Less regurgitation was seen in GLU and PTFE group when compared to PERI group (p < 0.05), which is statistically significant. This data is confirmed by angiography too. There were no intraoperative difficulties implanting the patch material. Our experience

<p>with Bovine Pericardial Monocusp Patch Texas Heart Institute journal L.iszlo Lukacs Vol. 11, No. 3, September, 1984,</p> <p>Complete Repair of Tetralogy of Fallot in the Neonate Results in the Modern Era Jennifer C. Hirsch, ANNALS OF SURGERY Vol. 232, No. 4, 508–514 © 2000</p> <p>Photo-oxidized bovine pericardium in congenital cardiac surgery: single-centre experience ChristopherW. Baird Interactive CardioVascular and Thoracic Surgery 24 (2017) 240–244</p> <p>The Use of Extracellular Matrix Patches in Cardiac Surgery Tomas Holubec, J Card Surg2015;30: 145–148)</p>	<p>a median weight of 18 kg (3.2 - 111.6). From November 1980 to May 1982,19 patients underwent surgery in this institution for right ventricular outflow tract obstruction. Surgery was performed by placing a bovine pericardial monocusp patch across the pulmonary annulus.</p> <p>retrospective review from August 1988 to November 1999 TOF who underwent complete repair. TOF with pulmonary stenosis, TOF with pulmonary atresia, TOF with nonconfluent pulmonary arteries.</p> <p>Dye-mediated photo-oxidation of pericardium is an alternative method to chemical treatment with glutaraldehyde for cross-linking collagen, providing biostability of the patch material while avoiding late calcification and cytotoxicity.</p> <p>A noncellular xenogenic extracellular matrix derived from the porcine small intestinal submucosa can be used as a new patch material with potential advantages. The first use of CorMatrix ECM 1 in the cardiac tissue repair and reconstruction was published by Scholl et al</p>	<p>for patch enlargement of great arteries in 18 patients and for creation of venous anastomosis in 2 patients</p> <p>one hospital death (5.3%), and one late Death. The follow-up ranged from 24 to 42 months (mean 32.5 ± 5.3 months; total, 552 patient months)</p> <p>61 consecutive symptomatic neonates. 31 24 6</p> <p>total of 490 patches in 383 consecutive operations (364 patients) were used in the surgical repair of congenital heart defects At our institution from October 2008 to October 2011.</p> <p>experience in 43 congenital cardiac operations.11 The SIS-ECM was used for pericardial closure, cardiac or great vessel repair (atrial septal defect repair, pulmonary rterioplasty, right ventricular outflow tract patch, pulmonary monocusp valve creation, superior vena cava patch, aortoplasty, valve leaflet augmentation, and repair of unroofed coronary sinus).</p>	<p>(atrial, n = 2; ventricular, n = 3 aorta, n = 4; pulmonary, n = 14) (Glenn-anastomosis, n = 1; atrial switch with Senning-technique, n = 1)</p> <p>The condition of the remaining 17 Patients are good. Repeat cardiac catheterization was performed in 11 patients and revealed that the right ventricular/ pulmonary artery systolic Gradient was reduced to 13.7 ± 9.7 mm Hg postoperatively. Angiography Showed a freely mobile, thin valve cusp. No calcification, aneurismal Dilatation or shrinkage of the monocusp patch was observed.</p> <p>The mean age at repair was 16 days, and the mean weight Was 3.2 kg. Before surgery, 36 patients were receiving an infusion of prostaglandin, 26 were mechanically ventilated, And 11 required inotropic support. Right ventricular outflow tract obstruction was managed with a transannular patch in 49 patients and a right ventricle-to-pulmonary artery conduit In 12. Cardiopulmonary bypass time averaged 71 minutes. Hypothermic circulatory arrest was used in 52 patients (mean 38 minutes) Median age at operation was 5.3 years, ranging from <1 month to 56 years. The overall survival rate at late follow-up was 92%, And no deaths were related to failure of the tissue substitute.</p>	<p>suggests that right ventricular outflow tract reconstruction with bovine pericardial monocusp patches can be safely performed with good hemodynamic results.</p> <p>The 1-month, 1-year, and 5-year freedom from reoperation rates were 100%, 89%, and 58%, respectively. Conclusions Complete repair of TOF in the neonate is associated with excellent intermediate-term survival.</p> <p>Photo-oxidized bovine pericardium demonstrated excellent performance when used as a patch material in cardiovascular repair in children. Its handling characteristics and biocompatibility are consistent with a wide range of applications.</p> <p>This report demonstrates the acellular xenogenic SIS-ECM membrane as an excellent alternative material to synthetic or biological substitute materials to treat various cardiac defects. At this moment, there are no known contraindications for the use of this patch material.</p>
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			<p>Two patients (0.5%) underwent reintervention late due to patch material failure</p> <p>This report demonstrates the acellular xenogeneic SIS-ECM membrane (CorMatrix ECM1, CorMatrix Cardiovascular, Inc.) as an excellent alternative material to synthetic or biological (pericardial) substitute materials to treat various cardiac defects. Compared to conventional pericardial patches, the advantage of this material is excellent pliability and easy handling, therefore less risk of tearing of myocardium/tissue as well as very easy stitching by thin composition of the material. Hemostasis seems to be superior with this. Despite the thin layer (around 0.25 mm), the patch is highly tear Proof.</p>
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RVOT=right ventricular outflow tract, PN= untreated group, PG= glutaraldehyde treated group, PERI= untreated pericardium, PTFE= polytetrafluoroethylene, GLU= glutaraldehyde treated group, Pa= pulmonary artery, Ao= aorta, RV=right ventricle.

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TABLE 1
Characteristics (Advantages and Disadvantages) of Different Materials Used as Patches in Cardiac Surgery

Patch Material/ Characteristics	Pliability and Easy Handling	Strength	Durability	Scar Formation and Calcification	Biocompatibility and Low Infectivity	Potential Remodeling and Tissue Regeneration
Autologous pericardium	+	-	-	+	+	-
Cross-linked xenopericardium	+/-	-	-	+	+/-	-
Woven nylon (Dacron)	-	+	+	+/-	-	-
ePTFE	-	+	+	-	-	-
Porcine SIS-ECM	+	+	+	-	+	+/-

ePTFE, expanded polytetrafluoroethylene; SIS-ECM, small intestinal submucosa extracellular matrix.

TABLE 2
List of Currently Available Porcine Small Intestinal Submucosa Extracellular Matrix-Derived Products

Product	Company	Material	Processing	Form	Clinical Use
CorMatrix ECM*	CorMatrix Cardiovascular, Inc., Roswell, GA, USA	Porcine SIS	Natural	Dry sheet	Pericardial repair and reconstruction; cardiac tissue repair; carotid repair
Durasis*	Cook Biotech, Inc., West Lafayette, IN, USA	Porcine SIS	Natural	Dry sheet	Repair dura matter
Oasis*	Cook Biotech, Inc., West Lafayette, IN, USA	Porcine SIS	Natural	Dry sheet	Partial and full thickness wounds; superficial and second degree burns
Restore* orthobiologic soft tissue implant	DePuy Synthes Joint Reconstruction, Warsaw, IN, USA	Porcine SIS	Natural	Dry sheet	Reinforcement of soft tissues
Stratasis*	Cook Biotech, Inc., West Lafayette, IN, USA	Porcine SIS	Natural	Dry sheet	Treatment of urinary incontinence
Surgisis*	Cook Biotech, Inc., West Lafayette, IN, USA	Porcine SIS	Natural	Dry sheet	Soft tissue repair and reinforcement

ECM, extracellular matrix; SIS, small intestinal submucosa. Adopted and modified from Badyaluk⁷ and Scholl et al.¹¹

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