Correction of Congenital Cardiac Defects With CorMatrix Extracellular Matrix in Pediatric Patients: Is It Really Safe?

Corrección de defectos cardiacos congénitos con la matriz extracelular CorMatrix en pacientes pediátricos. ¿Es realmente seguro?

To the Editor,

Currently, more than half of patients with congenital heart defects undergo correction procedures in the first year of life and consequently mortality rates are now lower for these patients than in past decades.[1] Some patients, however, still require several interventions at older ages due to the use of certain materials for the repair procedures. New products are under assessment with the aim of reducing the number of interventions. One of the most extensively used materials is extracellular matrix, and CorMatrix (CorMatrix Cardiovascular, Inc.; Alpharetta, Georgia, United States) is one of the matrices with the most extensive clinical and experimental experience.[2,3]

Between October 2010 and June 2014, we used this matrix in our group in 30 patients (Table). These patients were followed-up with serial echocardiography. The mean age of the patients at the time of surgery was 6 months (range, 1 month to 3.8 years) and the mean weight was 7.5 kg (range, 3.5-14.5 kg). No patients were lost to follow-up, which had a mean duration of 268 days (range, 194.5-305.8 days). No patients required repeat interventions during their hospital stay. No patients died in the postoperative period. Two patients, in contrast, required an intervention during follow-up. One of these was patient 7, who had been diagnosed with situs inversus, single ventricle, pulmonary atresia, and infradiaphragmatic total anomalous pulmonary venous return. He underwent an intervention as a newborn with correction of the anomalous venous return and a central fistula. At 9 months, he underwent a bidirectional Glenn procedure and pulmonary artery plasty with a CorMatrix patch. One month after discharge, he was admitted once more because of labored breathing and desaturation caused by right pleural effusion. Echocardiography showed stenosis at the point where the Glenn shunt joined the corrected pulmonary artery. This was treated with angioplasty, with a good outcome. The second case was patient 9, who had complete atrioventricular canal defect, corrected at the age of 5 months by a double-patch technique. Four months after the intervention, the patient attended the cardiologist, who observed substantial hepatomegaly. The echocardiography showed a mass in the right atrium adhered to the atrial septum that caused severe tricuspid stenosis (Figure A and B). In the following intervention, a neoformative tissue was found in the area of the atrial septum. This tissue occupied a large part of the right atrium. The pathology

Table
Demographic and Diagnostic Data and Uses and Complications of CorMatrix

Patient	Age	Weight, kg	Diagnosis	Use	Complications
1	8 mo	6.2	Tetralogy of Fallot	VSD + RVOT patch	No
2	9 mo	7.8	Tetralogy of Fallot	VSD + RVOT patch	No
3	2 mo	3.3	TGA	Neopulmonary + ASD	No
4	5 y	17	SV + PA	Pericardial	No
5	15 d	3.1	VSD	Pericardial	No
6	3 mo	4.1	Pulmonary stenosis	Pulmonary trunk	No
7	9 mo	7	Glenn procedure	Pulmonary artery plasty	Angioplasty after 1 mo
8	7 d	3.6	Type B AAI + VSD	VSD + ASD	No
9	5 mo	6.5	AV canal defect	VSD + ASD	Tricuspid stenosis
10	7 y	22	Fontan procedure	Pulmonary artery plasty	No
11	1.5 y	11	ASD OP	ASD OP	No
12	4 mo	5	AV canal defect	VSD + ASD	No
13	8 y	35.5	ASD	ASD	No
14	1 y	8.5	Truncus arteriosus type II	Pulmonary artery plasty	No
15	9 y	25.5	ASD	ASD	No
16	10 d	2.9	TGA	ASD	No
17	3.5 y	15	ASD OP	ASD OP	No
18	5 y	14.5	VSD	VSD	No
19	1 mo	2.8	TGA + VSD + AoCo	VSD + ASD	No
20	1.5 mo	10	VSD	VSD	No
21	5 y	14.5	Fontan procedure	Pulmonary bifurcation	No
22	1.5 y	10	Pulmonary stenosis	Pulmonary trunk	No
23	3.5 mo	5.5	AV canal defect	VSD + ASD	No
24	1 mo	2.6	Window ductus	Window patch	No
25	1 y	7.5	VSD	VSD	No
27	9 mo	7.8	Pulmonary stenosis	Transannular patch	No
28	4.5 y	16.5	Fontan procedure	Right coronary ostial plasty	No
29	8 d	3.5	AoCo + VSD	VSD	No
30	1 mo	3.2	VSD	VSD	No

AAI, aortic arch interruption; AoCo, aortic coarctation; ASD, atrial septal defect; AV, atrioventricular; OP, ostium primum; PA, pulmonary atresia; RVOT, right ventricular outflow tract; SV, single ventricle; TGA, transposition of the great arteries; VSD, ventricular septal defect.

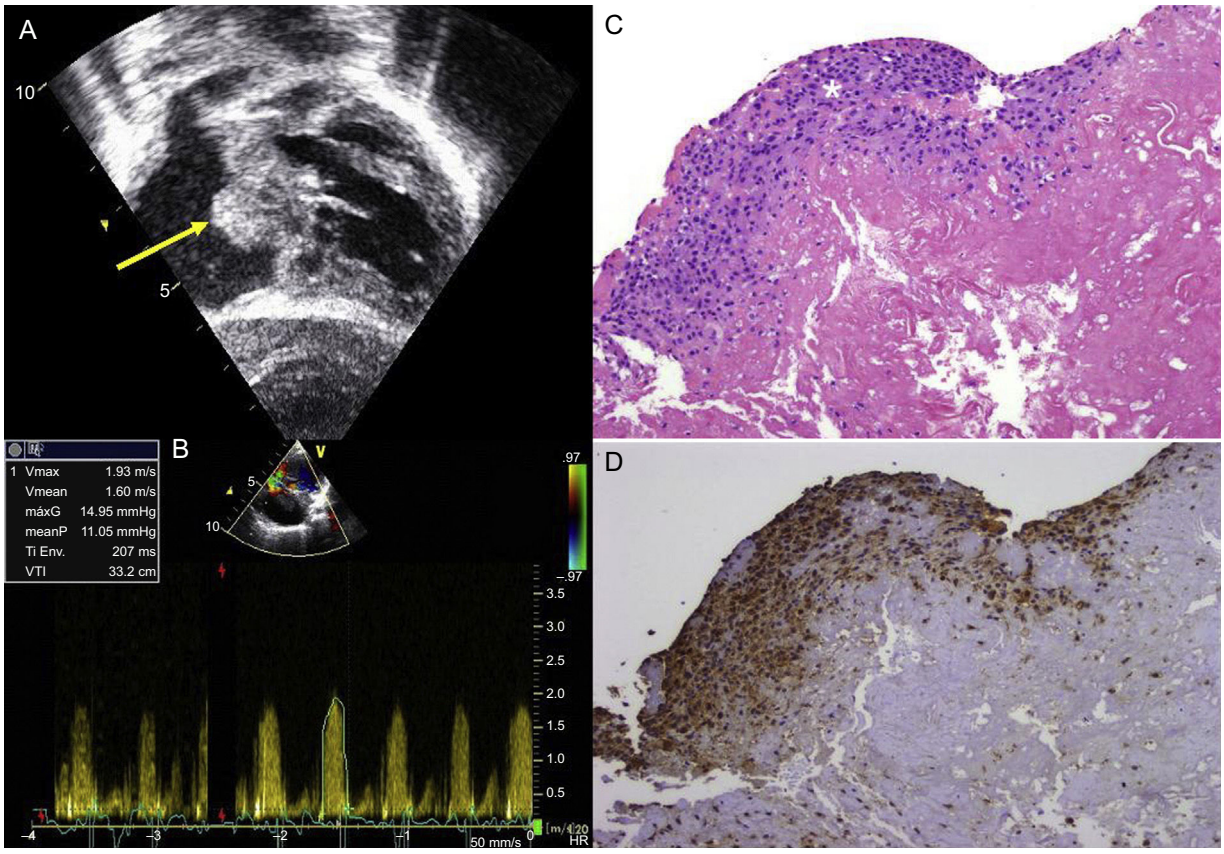

Figure. A: Transthoracic echocardiography showing a mass in the right atrium adhered to the atrial septum (arrow) in a patient who underwent correction of an atrioventricular canal defect. B: Transthoracic echocardiography, transtricuspid gradient. C: Pathology study (hematoxylin-eosin) in which predominantly histiocyte inflammatory infiltrate is observed (asterisk). D: Pathology study (CD68 macrophage marker). maxG, maximum gradient; meanP, mean gradient; Ti Env, envelope time; Vmax, maximum velocity; Vmean, mean velocity; VTI, velocity-time integral.

examination showed vascularized connective tissue with inflammatory foci consistent with foreign-body reaction and an extensive component of fibrin deposits or leukocytes and histiocytes on the surface (Figure C and D), with no evidence of calcification or other cell populations indicative of tissue remodeling.

In our experience, CorMatrix appears to be a manageable material with good hemostatic properties. However, our group has faced 2 important complications associated with its use. The first complication was stenosis after pulmonary artery plasty following bidirectional Glenn surgery. The lack of pulsed flow in a pulmonary artery with laminar flow after a Glenn procedure may contribute to the greater inflammatory response of the matrix, thereby obstructing the vessel lumen. Alternatively, the inflammatory reaction itself may reduce the internal diameter after extension of a pulmonary artery such that reduction in flow impedes optimal growth. In the second patient, the onset of tricuspid stenosis secondary to thickening of the septum was caused by an excessive inflammatory response secondary to the foreign body reaction with no evidence of tissue regeneration associated with CorMatrix.

All reports of this product to date in pediatric patients mention complications associated with its use. We note the study by Zaidi et al,[4] who published a nonrandomized comparative study of histological assessment after explantation of CorMatrix used in valve repair. In the patients in that study, the use of CorMatrix was associated with an intense inflammatory response that included eosinophils and giant cells, with no evidence of remodeling. The authors postulated that the differences found compared with experimental studies could be the result of implanting the material in congenitally abnormal tissue, which might have lacked certain molecules that would have favored tissue growth. These authors also noted that another mechanism may have been a different inflammatory response which caused the matrix in humans triggered by anti-GAD (decarboxylase glutamate) antibodies.

Our group was unable to demonstrate benefit in terms of the regenerative capacity compared with other patches. However, an inflammatory response has been identified that is consistent with foreign body reaction.

Although our series included a small number of cases and follow-up was less than 1 year, the presence of substantial comorbidity along with other evidence suggests that this material should not be used in children.

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Minimally Invasive Approach for Valvular Surgery and Atrial Septal Defect

Abordaje mínimamente invasivo en cirugía valvular y del septo interauricular

To the Editor,

Over the last 20 years, cardiac surgery has evolved toward less invasive procedures, with the aim of reducing the surgical insult to the body and achieving early patient recovery. Currently, the standard surgical approach for the treatment of mitral disease remains full median sternotomy; however, minimally invasive techniques have become established as a safe and effective alternative used routinely in specialized centers, associated with excellent short-term and long-term outcomes and lower morbidity.[1,2] The right anterior minithoracotomy is the most common minimally invasive approach for mitral valve surgery. This technique allows treatment of the tricuspid valve, atrial defects, and atrial fibrillation at the same time.[3]

We present our initial experience and results with this minimally invasive approach. Between January 2012 and December 2015, 40 patients underwent intervention in our hospital. There was a predominance of men (62.5%), and the mean age was 58.5 years (range, 22-81 years). All patients had a right anterior minithoracotomy (incisions of 6 cm to 8 cm) plus 3 accessory ports < 5 mm, according to the surgical requirements (for Chitwood clamp, atrial retractor, and vent). All patients were connected to extracorporeal circulation by peripheral cannulation of the femoral vessels (artery and vein): a single 2-stage venous catheter was positioned in the superior vena cava in the first 12 patients, with subsequent cannulation of the right jugular vein in the remaining patients. A CO_2 laser was used in all operations. Beating heart surgery was performed, without ischemia in 4 patients, and with moderate hypothermia in 8 patients who were in ventricular fibrillation. The remaining patients proceeded to transthoracic aortic cross-clamping with a Chitwood clamp, with antegrade cardioplegia through the aortic root via the ministernotomy. The mean time on extracorporeal circulation was 140 ± 38 minutes and the mean ischemia time was 98 ± 27 minutes. The Table shows the types of operation performed in these patients; notably, around half the operations were mitral valve repairs.

In our series, there have been no recorded deaths, either in-hospital or in the longer-term. At follow-up, all the repaired mitral valves were competent and free from regurgitation and reoperation. The most significant postoperative complications were as follows: 1 case of air embolism with mild transient neurological deficit (delirium and psychomotor agitation) with complete recovery at the time of hospital discharge; 1 case of failed mitral valve repair, with reintervention via minithoracotomy during the same admission to perform a new valvular repair; 1 patient with prolonged mechanical ventilation due to adult respiratory distress syndrome with complete recovery at the time

Table
Type of Surgery Performed Via Right Anterior Minithoracotomy

Type of surgery	Patients, n
Mitral valve surgery	32
Mitral valve replacement	13
Mitral valve repair	19
Annuloplasty	19
Neochordae implantation	6
Central Alfieri	1
Commissural closure	4
Posterior leaflet resection	11
Tricuspid valve replacement	4
Ostium secundum ASD closure	5

ASD, atrial septal defect.

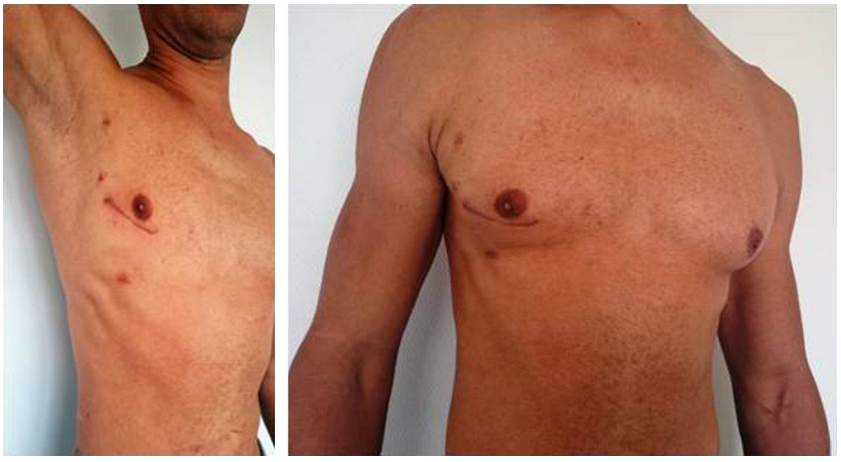

Figure. Appearance of surgical wounds in a patient who underwent right anterior minithoracotomy for mitral valve repair, 2 weeks after surgery.