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Fresh Homografts Obtained Through a National Organ-sharing Programme for Repair of Congenital Heart Disease

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Homografts have been used in congenital cardiac surgery for over 30 years. We utilized the resources of a national organ-sharing programme to obtain fresh homografts and report their use in correcting cardiac pathologies in 20 children between March 2001 and May 2003. In 16 patients, a valved conduit was used to form a connection between the pulmonary ventricle and the pulmonary artery. In three patients, a non-valved aortic conduit was used to form an extra-cardiac Fontan circulation and in one patient, non-valved pulmonary and aortic conduits were used to repair an infected aortic aneurysm. Three patients died following surgery. Survivors were followed up using echocardiography between 2 and 24 months post-surgery. Results demonstrate that, with the help of a national organ-sharing programme, the use of fresh homograft conduits is feasible in a paediatric patient population with reasonable waiting times.

KEY WORDS: Homograft; Transplantation; Congenital; Cardiac

Introduction

Aortic or pulmonary homografts, either as valved or non-valved conduits, are widely used in congenital cardiac surgery.[1 – 5] They have better haemostatic properties and are easier to implant than bioprosthetic conduits.[6] Fresh homografts stored at 4 °C gradually lose their tissue integrity and must be discarded within 4 – 6 weeks of collection.[1] The logistical problems caused by this time limitation have been greatly alleviated by cryopreservation, which theoretically extends their storage time indefinitely.[1] Cryopreservation, however, requires a certain technology and consequent expense, and thus can only be used in specialized centres, regional organ banks or commercial operations.

Our unit lacks cryopreservation capability, so we used a national organ-sharing programme to obtain homograft aortic and pulmonary artery conduits from hearts that had been refused for transplantation. These grafts were preserved in a simple antibiotic solution at 4 °C for a short time and used to correct various congenital problems requiring a valved or non-valved vascular conduit. This paper describes our initial experience and medium-term results with these conduits in a variety of indications.

Patients and methods

PATIENTS

Paediatric patients admitted to our unit between March 2001 and May 2003 requiring a connection between the pulmonary ventricle and the pulmonary artery or patients requiring a Fontan type circulation were included in the study. Patients who were not suitable for a homograft placement were excluded.

Written consent was obtained from the parents or relatives of all patients. Our unit is one of the leading transplantation centres in Turkey, and cardiac and homograft transplantation is routine in our clinic. We did not need ethical approval, therefore.

All cases were pre-operatively evaluated in the Department of Paediatric Cardiology of Dokuz Eylül University Faculty of Medicine. These data were discussed at weekly meetings attended by paediatric cardiologists and cardiac surgeons. Operative decisions were made at these meetings.

After the decision to use a conduit had been made, patients were registered on the national organ-sharing programme database. If appropriate, patients were then discharged. Patients were recalled for surgery when a homograft became available; surgery was scheduled when negative homograft culture results were obtained.

HOMOGRAFT PREPARATION

Hearts were harvested from multiorgan donors by median sternotomy during liver and/or kidney harvest, wrapped under sterile conditions following saline irrigation and transferred to our institution in an ice cooler. The hearts were initially appraised for transplantation by the national organ-sharing programme but could not be used for various reasons.

Upon arrival at our institute, the hearts were dissected under sterile conditions in an operating suite. Pulmonary arteries were dissected with the bifurcation. Aortas were harvested with the valve, including the anterior mitral leaflet, ascending aorta and the arch. The coronary ostea were ligated. Both pulmonary and aortic valves were checked with saline for competency, and the homografts were sized. Two tissue samples were taken from each homograft after harvesting and were cultured for bacterial and fungal contamination. After irrigation, the homografts were stored in triplicate at 4 °C , in sterile donor bags in saline solution containing vancomycin hydrochloride, clindamycin, ceftazidime, amphotericin B and amikacin.

HOMOGRAFT INSERTION

Operations were performed using standard hypothermic cardiopulmonary bypass, and bicaval venous and central aortic cannulation techniques. In the case of additional intracardiac repairs, the aorta was cross-clamped and cardioplegic solution was infused.

In pulmonary ventricle to pulmonary artery connections, optimal valve function was achieved by performing a proximal patch roof over the pulmonary ventricle incision for gap closure. This patch was tailored from autologous pericardium. The anterior mitral leaflet formed all or part of the roof when using an aortic homograft.

Operations on the thoracic aorta were performed with right atrial to (ascending and thoracic) biaortic bypass. Extra-cardiac Fontan procedures were performed with the heart beating on cardiopulmonary bypass (Fig. 1).

FOLLOW-UP

Patient data were recorded prospectively. All survivors were studied with echocardiography

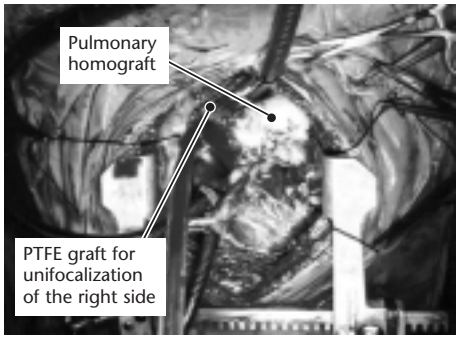


FIGURE 1: This image shows a Rastelli reconstruction of the right ventricular outflow tract. PTFE, polytetrafluoroethylene

before discharge, and all underwent one or more control echocardiograms during follow-up at the end of the first postoperative month and within the following 6 months. Patients showing flow disturbances on echocardiographic examinations underwent repeat cardiac catheterization. Patient charts were reviewed when follow-up echocardiography was performed and patient contact maintained by telephone.

Results

PATIENTS

We carried out surgery on 20 paediatric patients (11 female, nine male) using a fresh, antibiotic-sterilized, homograft aortic or pulmonary arterial conduit. The diagnosis, age at the time of the operation and operations carried out are shown in Table 1. The youngest child in the study was 40 days old and the oldest was 11 years old (mean 4.8 ± 3.4 years). The mean weight of the patients was 13 ± 4 kg (range 3.4 – 20 kg).

Thirteen patients had previously had surgery: 10 had received shunts, three of which were bilateral shunt procedures, with two of these being part of a unifocalization procedure; two patients underwent pulmonary artery banding (truncus arteriosus and double outlet right ventricle); and one had had a xenograft conduit placement.

Two patients, an infant with truncus arteriosus and a child with an infected aortic aneurysm complicating aortic coarctation, were operated on urgently while hospitalized. The mean waiting time for a homograft was 8 ± 4 (range 1 – 16) weeks, and no patients died while on the waiting list.

TYPE OF REPAIR

Valved homografts were used in 16 patients (nine aortic, five pulmonary, two both) as part of a complete repair for anomalies requiring pulmonary ventricle to pulmonary artery connection. In three patients we used non-valved aortic homografts to create an extracardiac Fontan circulation. We used a non-valved aortic and pulmonary artery homograft in one child to repair an infected thoracic aorta aneurysm.

GRAFTS

Between March 2001 and May 2003 we received hearts from a total of 23 heart-beating donors and one cardiac recipient who received transplantation due to end-stage heart failure. Seventeen of the hearts were transferred to our institution by commercial flights and seven were removed from local donors, including the heart transplant recipient. The hearts we received were not suitable for transplantation for a variety of reasons, including distance from potential recipients, deteriorating donor cardiac function, history of cardiac trauma, or advanced donor age. We were able to obtain aortic and pulmonary arterial homografts from the hearts, however.

The mean age of the heart donors was 30.2 ± 16.4 years (range 5 months to 60 years). Mean size of the homografts was 22 ± 5 mm (range 11 – 28 mm). Thirteen of the donors were male, nine were female and in

TABLE 1:
Diagnosis, age at the time of operation and operations carried out on 20 paediatric patients in this study requiring cardiac homografts

Diagnosis	Number of patients	Age of patients	Operation
Pulmonary atresia + VSD	3	3, 9, 7 years	PV-PA conduit + VSD closure
Pulmonary atresia + VSD s/p unifocalization	3	3, 4, 6 years	PV-PA conduit + VSD closure
Truncus arteriosus	3	40/365 days, 10/12 months, 17/12 months	PV-PA conduit + VSD closure
DORV + TGA + pulmonary stenosis/atresia + subpulmonic VSD + ASD	2	4 years	PV-PA conduit + intraventricular tunnel
TGA + pulmonary stenosis, small VSD	1	2 years	PV-PA conduit + VSD enlargement + intraventricular tunnel
Left TGA + pulmonary stenosis + VSD + ASD + atrial situs inversus	1	8 years	PV-PA conduit + VSD closure
TOF + absent pulmonary valve	1	11 years	PV-PA conduit + VSD closure
Conduit stenosis s/p TOF absent pulmonary valve repair	1	10 years	PV-PA conduit
TOF + coronary artery anomaly	1	2 years	PV-PA conduit + VSD closure
Tricuspid atresia + TGA + pulmonary stenosis	2	4, 9 years	Extracardiac Fontan procedure
DORV + single ventricle s/p banding	1	4 years	Extracardiac Fontan procedure
Aortic coarctation + infected aortic aneurysm	1	2 years	Thoracic aortic aneurysm repair

VSD, ventricular septal defect; PV-PA, pulmonary ventricle to pulmonary artery; DORV, double outlet right ventricle; TGA, transposition of the great arteries; ASD, atrial septal defect; TOF, tetralogy of Fallot; s/p status post – describes a previous operation.

two cases, gender was unknown. The grafts were refrigerated at 4 °C for a mean of 6 ± 2 days (range 1 – 13 days) before use.

The harvested pulmonary artery and aorta from one donor were used in two separate recipients as valved pulmonary ventricle to pulmonary artery conduits in two hearts. The pulmonary artery and the aorta were used together (anastomosed in an end-to-end fashion) in four patients to create pulmonary ventricle to pulmonary artery conduits and in one patient with an aortic aneurysm (Fig. 2). Grafts from five hearts (20%) were wasted due to delays or cancellations in the planned operation, lack of appropriate patients or positive cultures (one donor).

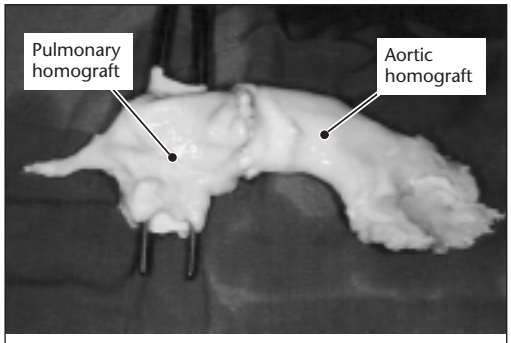


FIGURE 2: In this study of homograft aortic and pulmonary homograft outcomes, the pulmonary artery and the aorta were used together, anastomosed in an end-to-end fashion, to create pulmonary ventricle to pulmonary artery conduits in five paediatric patients

SURGICAL OUTCOME

Mortality

Hospital mortality was 15% (3/20 patients) and all patients who died after surgery underwent a procedure involving a pulmonary ventricle to the pulmonary artery valved conduit.

A 22-month-old patient with double outlet right ventricle with pulmonary atresia, confluent pulmonary arteries and subpulmonic ventricular septal defect and a previous left-sided modified Blalock-Taussig shunt died on post-operative day 3, from low cardiac output following correction with a 22 mm aortic homograft.

A 7-year-old patient with pulmonary atresia, confluent pulmonary arteries, ventricular septal defect and previous left-sided Blalock-Taussig shunt received a 24 mm aortic homograft. His post-operative course was complicated by bleeding and low cardiac output. He was examined using cardiac catheterization 2 days after surgery and this revealed a left ventricle ejection fraction of 81%, right ventricle to left ventricle pressure ratio of 0.4 and a peak gradient of 17 mmHg in the homograft. He died on post-operative day 28 from complications following a tracheostomy.

The third patient who died was 6 years old with pulmonary atresia, non-confluent pulmonary arteries and a ventricular septal defect. He was previously palliated with both left- and right-sided modified Blalock-Taussig shunts. He underwent a simultaneous unifocalization and total correction procedure through a bilateral thoracotomy. A non-valved pulmonary artery homograft conduit was used to create a pulmonary bifurcation, and the aortic valved homograft from the same donor was used to form the main pulmonary artery. He could not be weaned from ventilatory support following surgery. Control studies showed a right ventricle to left ventricle pressure ratio of 0.3 with no gradient on the homograft conduits. Diaphragmatic dysfunction was suspected, and he died on post-operative day 37 from massive pulmonary haemorrhage.

Complications

In seven patients (35%), the sternum was left open or reopened immediately after surgery due to low cardiac output or bleeding. Sternal closure was performed on post-operative days 1 – 4 (mean 2.7 ± 1.1). All of these patients had a homograft right ventricle to pulmonary artery connection, and their mean age was 2.7 ± 2.0 years.

Four other patients also experienced complications. One patient with pulmonary atresia and ventricular septal defect needed additional surgery because of a residual ventricular septal defect. A 10-month-old infant with truncus arteriosus required intra-operative opening of the ventricular septal defect patch when he could not be weaned from cardiopulmonary bypass. A patient with transposition of the great arteries, left

ventricular outflow tract obstruction and small ventricular septal defect, who had ventricular septal defect enlargement during the repair, developed complete atrioventricular block. This required permanent pacemaker placement. The fourth patient had tricuspid atresia and underwent an extracardiac Fontan procedure. This patient had pericardial effusion 1 month after the operation, which was drained surgically.

Follow-up findings

Fifteen of the survivors underwent one or more echocardiographic examinations between 2 and 24 months after surgery (the latest being at a mean of 12 ± 5 months). Three patients who had had extra-cardiac Fontan circulation showed normal flow patterns and all were well when last contacted. The patient with the infected thoracic aortic aneurysm recovered completely from the infection and showed no signs of dilatation or pseudoaneurysm formation 2 years after surgery.

Follow-up has been completed on all 13 patients who survived pulmonary ventricle to pulmonary artery conduit placement; mean follow-up time was 16 ± 9 months (range 3 – 27 months). One patient, who had pulmonary atresia and a ventricular septal defect and underwent a unifocalization procedure, has limited exercise capacity. Echocardiography and cardiac catheterization studies have revealed a diffusely stenosed right pulmonary artery system and a severely narrowed left pulmonary artery in this patient. Right ventricular pressures are severely elevated and the pulmonary artery homograft has dilated to a diameter of 42 mm from an initial size of 28 mm. Currently this patient is being evaluated for left pulmonary artery reconstruction. Freedom from re-operation at 24 months for the whole group is 89%, including the patient awaiting further surgery. Twelve patients were clinically asymptomatic at the end of follow-up, but two have moderate gradients (peak gradients of 40 – 50 mmHg on echocardiography) in the homograft conduits. One of these patients had a previous xenograft conduit replaced at 3 years, but neither patient shows any signs of right ventricular dysfunction, and homograft conduit replacement is not indicated. The other patients have no or insignificant gradients (less than 25 mmHg) across the homografts. Two patients have grade 1 valvular insufficiency and one patient has small supravalvular calcifications.

Discussion

Homografts currently fall into three main groups. Homovital grafts are harvested under sterile conditions, not treated, kept in a nutrient medium and considered viable if implanted within a few days. Cryopreserved grafts are sterilized in antibiotic solution and considered viable if cryopreserved within 4 days of procurement. Antibiotic-sterilized grafts are stored at 4 °C for up to 6 weeks and are considered non-viable.[2,7,8] In our patient group, all grafts can be considered as non-viable. Despite the fact that they were harvested under sterile conditions and used within a relatively short time, the use of antibiotics, particularly amphotericin B, renders them practically non-viable.[9,10] The importance of viability in homograft durability is not well defined. Experience with homovital aortic valves and aortic root replacement in adults has demonstrated a freedom from structural degeneration of 98% and 89% at 10 years, which is higher when compared with valves that were either cryopreserved or stored at 4 °C.[2,11] Cryopreserved homografts are generally more viable than antibiotic-sterilized homografts,

but long-term experience in children with subpulmonary homograft conduits has failed to show any advantage with cryopreservation compared with storage at 4 °C.[3,4,12]

Cryopreserved homograft implantation provokes a vigorous antibody reaction to HLA antigens in children.[13] Experiments in animals have demonstrated that viable homografts induce immunological activation, and cryopreservation might result in increased structural failure.[14,15] Studies in humans have so far failed to show a relationship between HLA antibodies and homograft survival, but decellularized homografts with diminished antigenicity are currently being studied.[16,17] It is possible that non-viable antibiotic-preserved homografts might also have reduced antigenicity and antibody reaction.

We believe that using valves stored at 4 °C in this study has not affected early and medium-term results. Our early mortality of 15% is similar to other reports of conduit placement in children[5,6] and we could not identify a homograft-related factor in the three patients who died. Mortality was more likely to be related to complexity of the procedures (unifocalization compared with the presence of a confluent pulmonary artery) or existing pulmonary hypertension. Additional surgery is planned for one patient who has a pulmonary artery branch stenosis following the unifocalization procedure. Freedom from surgery at 2 years is 89%.

Currently there is no evidence to support the use of homovital grafts in paediatric populations. Future studies may show longer graft survival with homovital grafts, however, similar to experiences in adults with aortic valves. Procurement of homograft conduits through a national organ-sharing programme opens up the possibility of homovital graft usage in paediatric populations. Warm ischaemic time in these grafts is very short and our current valve storage times could easily be reduced to homovital limits. Antibiotic sterilization, which significantly reduces viability, could also be omitted due to low contamination rates.

The question remains whether homografts or xenografts are superior in terms of durability. Actual conduit durability cannot be ascertained directly and conduit replacement is usually substituted as an indicator of durability. It appears that conduits below 15 mm in size require replacement at a mean of 3 – 6 years after implantation, regardless of the type of conduit.[4] The most frequent causes of conduit failure leading to replacement are calcification, patient-to-conduit mismatch resulting from patient growth, and sternal compression.[12] Evidence from the Mayo Clinic and Toronto experiences suggest longer durability with xenografts in patient groups with a mean age of 9 years.[5,18] European studies in younger children with mean ages similar to our patient group tend to show better graft survival with homografts.[4,19,20] Xenografts have the inherent advantage of being easy to obtain, but our experience has shown that most patients can tolerate the waiting times associated with fresh homograft procurement and that even very small homografts can be obtained within a relatively short time if a national organ-sharing database can be used.

Our experience with valved homograft conduits has encouraged us to use non-valved homografts for repair of congenital cardiac problems. We used homograft ascending aortas for fashioning an extracardiac cavapulmonary anastomosis in three children. The extracardiac conduit Fontan procedure has the benefits of less surgical injury and higher intra-operative flexibility, which might reduce post-operative rhythm problems.[21] The number of

patients in our series is too small to compare with lateral tunnel patients, but non-valved homograft conduits provide surgical ease and better haemostasis compared with synthetic materials in creating an extracardiac Fontan circulation. They have performed satisfactorily, and have not had any adverse effects during follow-up.

In an unusual case with an infected aortic aneurysm, we used a composite pulmonary artery and aortic homograft to replace the thoracic aorta. Cryopreserved aortic root homografts are currently recommended for treating prosthetic valve endocarditis with annular abscess, and infected aorto-femoral grafts can be replaced with homografts even in the presence of an aorta-enteric fistula.[22,23] Wide experience in replacing various infected vessels with homografts encouraged us to treat this patient with a composite homograft, and even in this patient we were able to quickly procure a fresh homograft.

This study demonstrates that antibiotic-sterilized homograft conduits stored at 4 °C can be useful in paediatric heart surgery. With the help of a national organ-sharing programme, homografts were obtained quickly; both aortic and pulmonary homografts were implanted and have had satisfactory early and mid-term performance. We believe the use of homografts, both as valved or non-valved conduits, in centres lacking cryopreservation capability, makes use of otherwise unused resources. This method has helped us to treat 20 children in only 3 years without the additional expense of cryopreservation or a commercially purchased xenograft.

Conflicts of interest

No conflicts of interest were declared in relation to this article.

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