Growth of composite conduits utilizing longitudinal arterial autograft in growing lambs

We examined the growth potential of a longitudinal strip of autologous aortic wall incorporated in an autologous pericardial conduit in 10 lambs (mean age 26 days, mean weight 10.1 kg). A 15 mm length of descending thoracic aorta (diameter 11.5 ± 7 mm) was excised and replaced with a composite autograft conduit of autologous pericardium with a longitudinally inserted aortic strip 5 mm in width taken from the excised aortic tissue. Radiopaque markers along all suture lines allowed determination of growth of the aortic strip relative to growth of the composite conduit and descending aorta, in addition to growth assessment by pathologic analysis. Plain x-ray films and aortograms were performed at 7 days (baseline) and at 3, 6, 9, and 12 months. No graft became stenotic or aneurysmal. The diameter of the descending aorta distal to the conduit increased from 11.7 ± 1.3 mm to 18.7 ± 2.1 mm. Appropriate growth of the autograft conduit was demonstrated by a minimal change in the diameter ratio of conduit to distal aorta from 1.00 to 1.02 during a period of 12 months. The aortic strip increased to 172% ± 19%, 148% ± 15%, and 256% ± 31% of baseline width, length, and area, respectively ($p < 0.05$). Histologic study confirmed the maintenance of normal architecture in the aortic strip and colonization of the pericardial tissue by aortic intimal and medial elements. A clinical implant with an autologous aortic strip in an aortic homograft in a 4-year-old child with tetralogy and pulmonary atresia has also grown, according to angiography, from 15 to 21 mm in diameter at 1 year's follow-up. This study confirms that the incorporation of a free autologous arterial patch graft as part of cardiovascular reconstructive procedures permits growth. (J THORAC CARDIOVASC SURG 1992;103:47-51)

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Many reconstructive procedures for congenital heart disease, such as those requiring conduit insertion, would be more corrective than palliative if they were to incorporate growth potential. The growth potential of tubular segments of arterial autograft in children has been confirmed by the experience with renovascular reconstruction.¹ ² Furthermore, the potential for a relatively narrow strip of autologous tissue to provide appropriate growth when incorporated as a small part of the circumference of an otherwise nongrowing tube has been observed in a number of situations, including the Mustard procedure, the Norwood procedure, and coarctation repair.³ We hypothesized that incorporation of a free arterial autograft as a longitudinal strip within a pericardial or homograft conduit would allow appropriate growth of the conduit. The following study conducted in neonatal lambs was designed to test this hypothesis.

Materials and methods

Surgical technique. Ten lambs 21 to 31 days old (mean 26 days), with a weight range of 7 to 13 kg (mean 10.1 kg), were preanesthetized for endotracheal intubation with intramuscular ketamine hydrochloride (20 mg/kg) and intravenous barbiturate (1 mg/kg). Anesthesia was subsequently maintained with halothane (0.5% to 1.0%) and a 50:50 mixture of oxygen and nitrous oxide. Under sterile conditions, a left thoracotomy in the fifth intercostal space was made. The descending thoracic aorta was dissected and mobilized. An appropriate rectangular seg-
principle of Laboratory Animals Care" formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" prepared by the National Academy of Sciences and published by the National Institute of Health (NIH Publication No. 85-23, revised 1985). Measurements. Plain x-ray films and aortograms were performed at 7 days (baseline measurement) and at 3, 6, 9, and 12 months. The radiopaque markers allowed determination of growth of the aortic strip. Intravascular pressure was measured with a pigtail catheter inserted retrogradely from the femoral artery, and an aortogram was made by injection of contrast material (Renovist, 1 to 2 ml/kg). The internal diameter of the composite conduit was measured at its midportion, and the diameter of the descending aorta was measured 1 cm distal to the conduit. The lambs were also weighed at each assessment. All sheep were killed after 12 months of graft implantation by intravenous injection of barbiturate and potassium, the composite autograft conduits were retrieved, and final measurements of each were made before fixation for histologic study. For statistical analysis, Student’s t tests for paired and unpaired data were used. A p value <0.05 was considered significant.

Histology. All tissue for histologic examination was fixed in 10% neutral buffered formalin. Blocks were cut from the midpoint of each autograft conduit (a complete ring including both pericardium and aortic strip) and from either end of the graft, passing through the suture lines and recipient aorta. After being embedded in paraffin wax, control and conduit blocks were sectioned at 5 μm, and the sections were stained with hematoxylin and eosin, elastic-van Gieson, and Masson’s trichrome stain.

Results
Postoperative course. All 10 sheep survived and continued to do well up to the completion of the study. Body weight increased consistently during the 12-month study period from 10.1 ± 2.2 kg to 48.4 ± 4.4 kg.

Composite conduit and aortic strip. No conduit became stenotic or aneurysmal, and there was no thrombus formation (Fig. 1). A transconduit pressure gradient greater than 10 mm did not develop in any of the sheep. The diameter of the distal aorta increased in 12 months from 11.7 ± 1.3 mm to 18.7 ± 2.1 mm (p < 0.05), while the diameter of the conduit significantly increased from 11.7 ± 1.3 to 19.1 ± 2.0 mm (p < 0.05) (Figs. 2 and 3). The diameter ratio of conduit to distal aorta changed minimally from 1.00 to 1.02. Aortic strips significantly increased to 172% ± 19%, 148% ± 15%, and 256% ± 31% of baseline in width, length, and area, respectively (p < 0.05) (Fig. 4). Under unpressurized conditions at harvest, autograft strips showed 101% ± 23%, 59% ± 15%, and 216% ± 31% increases in width, length, and area, respectively.

Histologic observations. The general architecture of the aortic strip of the autografts remained essentially normal relative to the control specimens. Focal calcification was seen in a number of grafts, chiefly in relation to sutures, and in one instance calcification was widespread.
as a result of medial smooth muscle cell necrosis occurring before implantation.

Events at both sites of the grafts examined were similar. Aortic intima proliferated and extended over the surface of the adjacent pericardium (Fig. 5), where it usually became up to 10 times as deep as normal aortic intima and had the effect of giving the pericardium a thickness comparable to that of the aortic strip. A discontinuous endothelium was present on the luminal surface of the intimal ongrowth. Medial smooth muscle cells from the aortic strip invaded and proliferated within the collagen of the pericardium and the deeper layers of the intimal ongrowth (see Fig. 5). Where smooth muscle cell replication was most advanced, the formation of new elastic fibers could be seen. These processes were usually somewhat better developed at the junction of recipient aorta and autograft than at the junction of aortic strip and pericardium within the autograft.

Discussion

This study has demonstrated the growth potential of a composite autograft conduit composed of autologous pericardium and a strip of autologous aortic wall in a rapidly growing sheep model. Appropriate growth was
Histologic section passing through junction of aortic strip (A) and pericardium (P) and showing radiopaque marker (M). Proliferating aortic intima (I) extends over surface of pericardium, and medial smooth muscle (arrows) is migrating into pericardial collagen. (Elastic-van Gieson stain; ×95.)

There have been several reports on arterial autografts used in renovascular reconstruction. There have been reports of the successful use of autologous pericardium at systemic pressure in adults. 

There are many potential applications of the principle illustrated in this study. The most obvious is the development of a conduit with growth potential for establishing ventricular-pulmonary artery continuity. We have created a composite aortic homograft and ascending aortic autograft that was placed between the right ventricle and the pulmonary artery bifurcation in a 4-year-old girl with tetralogy of Fallot with pulmonary atresia. The ascending aorta was transected at the level of a previously placed central shunt. A strip of ascending aortic autograft 1 cm wide was harvested at the level of the ascending aortic division. The ascending aorta was reconstituted by direct anastomosis with absorbable suture. The autograft strip was incorporated longitudinally in a 15 mm cryopreserved aortic homograft. The strip separates two valve leaflets at a commissure so that there is some obligatory homograft valve regurgitation. The strip was placed posteriorly so that it was sutured directly to the right ventricular myocardium as well as distally to the pulmonary arteries. Thus there is the patient's own tissue-to-tissue continuity throughout the repair. Follow-up catheterization at 1 year revealed growth of the homograft from a diameter of 15 mm to 21 mm. There was a 25 mm gradient across the distal anastomosis with no proximal gradient. Homograft regurgitation was not prominent.

There are many potential sources of arterial autograft. The subclavian arteries as well as the ascending aorta are accessible through a median sternotomy. The neonatal arterial switch experience has demonstrated that circumferential anastomoses, even when performed under a modest degree of tension, rarely develop late anastomotic stenoses.

References


Discussion

Dr. Yasunaru Kawashima (Osaka, Japan). I agree with your results and conclusions that tissue from young animals can grow after implantation if it is alive, even though it is implanted in other than its normal site.

We reported the results of a similar experiment several years ago. We removed the pulmonary valve together with the pulmonary arterial wall from puppies and implanted it back in the same place. The dogs were killed after they grew up, and the growth of the pulmonary valve was confirmed.

Many investigators who are using fresh homografts insist that the valve is alive, but I do not believe it. We did the same experiment with homograft pulmonary valves of puppies, and when they were killed the homograft had not grown. I believe if it grows it is alive; if it does not grow, I do not think it is alive.

Dr. Jonas. Certainly this is a controversial area. In 1989 Dr. Molina reported a study of pulmonary homografts in lambs. He described an increase in size of the pulmonary homografts, which we have also found in a study of pulmonary homografts implanted at systemic pressure in lambs. Whether viability of cells is essential for the dilation observed in homografts is not clear.

Dr. Francis Robicsek (Charlotte, N.C.). I fail to see the presence of a control group, namely, a homograft composed entirely of pericardium and put in the same type of a group of sheep. Maybe that homograft would have grown also. I do not believe that clinical application was justified on the basis of this experiment.

Dr. Jonas. I agree with you that it would have been of interest to include a separate group of animals in which a conduit composed entirely of pericardium was inserted. Our initial intention had been to construct a conduit composed of homograft aorta plus autograft aorta since we had our own historical control group defining the behavior of aortic homografts in the neonatal lamb. Dr. Sawatari, who was responsible for the design of the experiment, preferred to use pericardium and aortic autograft with an ingenious system of radiopaque markers to define growth of the two separate components of the conduit. Growth was indeed observed in the pericardial component, as you have suggested, as well as in the aortic autograft.

We are encouraged by the result in our initial clinical implant, in which the arterial autograft strip was inserted in a homograft aorta. Clearly, in the clinical situation there is frequently insufficient autologous pericardium available to construct a complete conduit, which, in addition, would be nonvalved.