Improved outcome with composite graft versus homograft root replacement for children with aortic root aneurysms

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Abstract

Objective: Review of surgical repair of aortic root aneurysms using composite graft or homograft in children. Methods: A consecutive series of 34 children (mean age 10.8 ± 5.4 years) who underwent elective aortic root replacement using composite graft or homograft from 1987 to 2003 (mean follow-up 5.7 ± 3.7 years). Results: Preoperatively, the aortic annulus and aortic root average z-scores were 4.1 ± 2.2 and 9.4 ± 4.7, respectively. Composite graft root replacement was performed in 22 patients, and cryopreserved aortic homograft root replacement in 12 patients. There was one perioperative death in the homograft group due to sudden cardiovascular collapse. There was one late death in the composite graft group due to acute aortic dissection, and two late deaths in the homograft root replacement group, one at 7 months postoperatively due to coronary artery thrombosis and one due to severe chronic myocardial dysfunction 5 years postoperatively. One patient who initially had a homograft died due to mechanical valve thrombosis following reoperative composite graft replacement. Five patients had reoperations at a median of 7.1 years after initial surgery. One patient in the composite graft group underwent arch replacement. There were no graft related reoperations after composite graft root replacement, but 4 patients in the homograft group had reoperative composite graft replacement. Predictors of reoperation included age at surgery, lower weight, and longer ICU time (\(P < 0.05\)). Conclusions: In children with aortic root aneurysms, reoperation is more common after homograft root replacement than composite graft replacement. Composite graft root replacement provides more stable repair of the aortic root.

Keywords: Aortic root aneurysm; Composite graft; Homograft

1. Introduction

In children aortic root dilation is rare, and often secondary to connective tissue disease, most frequently Marfan’s syndrome [1]. Often aortic root dilation begins in infancy. The annual rate of aneurysmal dilation reaches a peak by 6-14 years [2]. The dilation of aortic root can lead to secondary aortic insufficiency or acute aortic dissection or rupture. Progressive dilation of the aortic annulus and the sinuses of Valsalva along with widening of the commissural distance at the sinotubular level results in aortic regurgitation [3,4]. A bicuspid aortic valve has also been associated with ascending aorta and aortic root aneurysms [5].

The isolated forms of aortic root or ascending aorta dilation are rare [6]. Although aortic valve sparing procedures have been employed for adults with aortic root aneurysms including those with connective tissue disorders, our limited experience with aortic valve sparing procedures in children suggests that the aggressive nature of the underlying problem results in aortic valve sparing procedures having an early failure rate. For this reason we no longer consider aortic valve sparing procedures for the pediatric population with aortic root aneurysms.

The safety and efficacy of aortic root operations in adults with Marfan’s syndrome has been demonstrated in numerous studies [7-9], but there are less data concerning the results of such operations in children. Here we report a consecutive series of 34 children and adolescents who underwent aortic root replacement using composite graft or homograft. The purpose of this study was to determine the operative indications and results including survival and need for reoperation.
2. Materials and methods

2.1. Patients

Thirty-four children and adolescents (mean 10.8 ± 5.4 years) underwent an elective aortic root replacement using composite graft or cryopreserved homograft at Children’s Hospital, Boston from 1987 to December 2003. One patient had initial surgery elsewhere, but reoperation and follow up were completed at Children’s Hospital, Boston. There were 25 boys and 9 girls. Twenty-nine patients (85%) had Marfan syndrome with dilation of aortic root. One patient had a dilated aortic root, and one patient had aortic stenosis with an ascending aortic aneurysm but without a specifically diagnosed connective tissue disorder. One child had an insufficient bicuspid aortic valve with dilated aortic root. Two patients had aortic stenosis with left ventricular outflow tract obstruction. Five patients had undergone previous operations (two aortic valvotomy, two ductus ligations, and one mitral valvuloplasty) (Table 1).

2.2. Surgical techniques

Standard hypothermic cardiopulmonary bypass (temperature 24.1 ± 2.2 °C) was used for all cases. Composite graft or cryopreserved aortic homograft techniques were used for replacement of the aortic root. Composite graft technique included aortic valve prosthesis with Dacron tubegraft, and involved coronary reimplantation.

Patients were divided into two groups according to the surgical techniques employed. Composite graft root replacement was performed in 22 patients (21 with mechanical St. Jude Medical (St. Paul, MN) and one with bovine Carpentier-Edwards (Irvine, CA) aortic prosthesis), and 12 patients underwent homograft root replacement.

2.3. Data acquisition

The protocol was approved by the Institutional Review Board at Children’s Hospital, Boston. Hospital charts and charts of cardiologist following patients were reviewed, as were the computerized databases of Children’s Hospital and the Department of Cardiovascular Surgery and Cardiology. Information on the underlying cardiac diagnosis, echocardiograms, surgical procedures, and follow-up information were collected retrospectively. Follow-up was available for 33 of 34 patients. Follow-up was obtained during outpatient clinic appointments or interviews with the referring cardiologists. The mean duration of follow-up was 5.7 ± 3.7 years (range 0.4–15.9 years).

2.4. Statistical analysis

Continuous data including age, weight, cardiopulmonary bypass time, cross clamp time, length of time in the cardiac ICU, and postoperative hospital stay were tested for normality and were expressed in terms of the mean and standard deviation (SD). Patient survival and freedom from reoperation rates were estimated using the Kaplan-Meier product-limit method to account for censoring [10]. Greenwood’s formula was applied to calculate 95% CI around the survival and freedom from reoperation curves and the log-rank test was used to compare the curves for the composite graft and homograft groups. Univariate and multivariate analysis was performed using Cox’s proportional hazards regression model to identify predictors of mortality and reoperation [11]. The seven covariates tested included: age at surgery, weight, sex, diagnosis, type of graft (composite versus homograft) mitral regurgitation (none, mild, moderate, severe), and aortic insufficiency (none, mild, moderate, severe). A stepwise method (backward selection with the likelihood ratio test) was applied in the multivariate analyses to adjust for possible confounding among variables and to establish the independent predictors of each outcome. The hazard ratio (HR) with a 95% confidence interval (CI) was calculated for significant multivariate predictors. Statistical analysis was performed using the SPSS package (version 12.0, SPSS Inc., Chicago, IL). For all comparisons, a two-sided value of $P<0.05$ was regarded as statistically significant.

3. Results

3.1. Preoperative patient characteristics

There were no statistically significant differences between the groups with respect to age (mean age in
the composite graft group was 11.9 ± 4.9 years, and in the homograft group 8.9 ± 5.9 years), but weight at the time of surgery was lighter in the composite graft group (mean 51.2 ± 26.5 kg) compared to weight in the homograft group (33.8 ± 20.4 kg) (P = 0.05). Twenty-one of 34 patients (62%) were treated with β-blockers before operation (15/22 in the composite graft, and 6/12 in the homograft group).

All patients underwent preoperative echocardiograms. Indications for elective aortic root replacement were aortic root dilation (18 patients), aortic root dilation and mitral regurgitation (13 patients), aortic stenosis with left ventricular outflow tract obstruction (2 patients), and aortic stenosis with dilation of the ascending aorta (1 patient). Sixteen of 34 patients (47%) with aortic root dilation had moderate or greater aortic insufficiency, but only 4 patients had severe aortic insufficiency. Preoperatively, the aortic annulus and aortic root mean z-scores were 4.1 ± 2.2 and 9.4 ± 4.7, respectively. Mean preoperative aortic root z-score was 9.7 ± 5.3 in the composite graft group, and 8.7 ± 3.4 in the homograft group, and mean ascending aorta z-score was 4.7 ± 3.6 in the composite graft group, and 3.7 ± 1.7 in the homograft group. Mild or moderate mitral valve regurgitation was found in 16/22 patients in the composite graft group, and 6/12 in the homograft group. Severe mitral regurgitation was found in four in the homograft group.

3.2. Operative results

All operations were performed electively. The mean diameter of the composite graft prosthesis was 24.2 ± 3.0 mm (range 19-29 mm), and homografts 21.0 ± 2.9 mm (range 17-25 mm) (P = 0.02). Associated procedures included mitral valve repair (3 patients), mitral valve replacement (1 patient), repair of an atrial septal defect (1 patients), repair of pectus excavatum (1 patients), and a Cabrol (1 patient), repair of an atrial septal defect (1 patients), mitral valve repair (3 patients), mitral valve replacement (1 patients), and one for aortic arch replacement. Four patients in the homograft group had reoperative composite graft replacement, two of whom underwent a second reoperation (one for mitral valve replacement, and one for aortic arch replacement). Univariable predictors of reoperation were age at surgery, lower weight, and longer ICU time (P = 0.02, P = 0.01, and P = 0.04, respectively). Freedom from reoperation was 100% at 1 year and 93% at 5 years for patients in the composite graft group and 100% at 1 year and 88% at 5 years in the homograft group (Fig. 1). No significant difference was observed between the composite graft and homograft groups with respect to reoperations rates (P = 0.14, log-rank test = 1.93).

There were 5 of 12 patients in the homograft group alive at last follow up who had not required reoperative composite graft replacement. Latest follow up echocardiography showed that the homograft functioned normally without regurgitation in three patients (follow up times: 0.5, 1.1, and 6.9 years), but in one case there was mild regurgitation (9.0 years postoperatively), and in one case moderate regurgitation was found (4.3 years postoperatively).

Twenty-eight patients have complete follow up and were alive at last follow-up (mean 5.8 ± 3.8 years, range 0.4-15.9 years). One patient was lost to follow up, and current data is not available. All survivors were in New York Heart

3.3. Late results

Follow-up has been completed to a mean of 5.7 ± 3.7 years (range 0.4-15.9 years). There has been one late death in the composite graft group due to acute aortic dissection 3.9 years postoperatively. There have been two late deaths in the homograft group, one at 7 months postoperatively due to coronary artery thrombosis and one due to severe myocardial dysfunction associated with a calcified homograft with severe obstruction and regurgitation 5 years postoperatively. One patient who initially had a homograft died due to mechanical valve thrombosis following reoperative composite graft replacement. Five patients have undergone a second operation at a median time of 7.1 years after the initial surgery. There was no graft related reoperation after composite graft root replacement, but one patient underwent arch replacement. Four patients in the homograft group had reoperative composite graft replacement, two of whom underwent a second reoperation (one for mitral valve replacement, and one for aortic arch replacement).

Fig. 1. Ten-year estimated Kaplan–Meier freedom from reoperation in children after aortic root replacement for patients undergoing composite graft or homograft. At 5 years, patient survival was 93 and 88% for these groups, respectively. The errors bars denote 95% confidence intervals as determined using Greenwood’s formula. The numbers in parentheses indicate the patients remaining at risk at selected points during the follow-up in the composite graft (top) and homograft (bottom) groups.
Association class I or II. Twenty-five of 28 survivors have been maintained on β-blocker therapy. All patients who received composite graft were treated with coumadin after operation. In the homograft group only one patient with poor ventricular function had anticoagulation therapy. This patient died 5 years following operation due myocardial dysfunction associated with a calcified homograft. There was one thromboembolic event resulting in sudden cardiac death 8 months after aortic root replacement using a homograft with a Gore-Tex tube graft to the left coronary artery (Cabrol modification). Thrombus was found near the ostium of the left coronary artery. No anticoagulation therapy had been maintained. There have been no episodes of prosthetic or native valve endocarditis.

3.4. Limitations of the study

Replacement of the aortic root using composite graft or homograft is a complex procedure with numerous variables that may play a role in overall outcome. The small sample sizes in this study prevent more comprehensive analysis.

4. Discussion

Numerous studies in adolescent and young adult patients have shown that aortic root replacement can be performed with low operative mortality and favorable long-term survival [12-16]. The majority of children with aortic root dilation have a connective tissue disorder. The most frequent reason for aortic root dilation in children is Marfan’s syndrome [1]. In our series 29 of 34 patients had Marfan’s syndrome. Better screening, particularly echocardiography, for Marfan’s syndrome has refocused attention on children [17]. In selected cases prenatal diagnosis of Marfan’s syndrome has become possible using fetal echocardiography [18].

Manifestations of Marfan’s syndrome in childhood are variable. Aortic root dilation is the most common surgical indication in children with Marfan’s syndrome [19]. Some degree of mitral valve regurgitation can be found in almost all cases, and aortic root dilation is present in greater than 80% of affected children [17,20]. Aortic root dilation and mitral valve dysfunction tend to progress with time [20]. In the infantile form of Marfan’s syndrome, mitral regurgitation is often the predominant reason for increased morbidity and mortality [21].

In this study we report the results of operations in 34 children with aortic root dilation. The mean age of patients is younger than in other published larger series of aortic root replacement [12-15]. Four patients underwent surgery before the age of 2 years, and 29 of 34 were 15 years or younger at the time of surgery. Predictors of reoperation were age, and lower weight at surgery. Two severely affected patients with infantile Marfan’s syndrome who were less than 1-year-old at the time of operation had concomitant mitral regurgitation. One of these very young patients died shortly postoperatively due to cardiovascular collapse. This confirms previous reports documenting the unfavorable prognosis in severely affected infants with mitral valve disease [20].

Aortic root replacement using cryopreserved aortic homografts was once considered an attractive surgical option since it avoids anticoagulation, and provides better resistance to endocarditis. In our series there were no graft related reoperations following composite graft root replacement, but 4 of 12 homografts have been replaced with a composite graft due to worsening aortic regurgitation. Although homograft aortic root replacement remains an option, several reports have documented limited long-term durability especially in young patients [22,23]. Also the risks at reoperation may be greater than at the initial operation due to the calcified nature of the homograft. The Ross operation probably should not be employed in the setting of a connective tissue disorder since the neoaorta is presumably also at risk of aneurysmal dilation. We also avoid aortic valve preserving procedures in children who appear to have an accelerated form of connective tissue disorder which is likely to affect the valve as well as the aortic root.

Aortic root replacement should be recommended to prevent aortic rupture or dissection. The timing of surgery should take into account the aortic diameter or z-score of the aortic root and ascending aorta, the rate of progression of the dilation, the function of the aortic valve, and the potential deterioration of valve function according to the known natural history of a given connective tissue disorder. Currently it is our empirically derived practice to recommend aortic root replacement when the z score is greater than +10 in the child who is asymptomatic and who has normal aortic valve function.

The results of cardiac operations in children with Marfan’s syndrome compare favorably with those in adults. In our series the Kaplan-Meier estimated 5-year survival was 86%. In the series from Johns Hopkins 10-year survival for children was 93% [24], and most series report 70-81% 10-year survival rates in adults undergoing cardiac operations for complications of Marfan’s syndrome [12,13,19]. The 4 late deaths in this series occurred all in patients with Marfan’s syndrome and were all cardiac related, demonstrating that cardiac operations cannot eliminate all cardiovascular morbidity and mortality associated with this connective tissue defect. The primary morbidity has been the need for reoperation. The incidence of reoperation in children is higher than in adults undergoing cardiac operations for complications of Marfan’s syndrome [25]. In adults, aortic dissection is the commonest reason for late reoperation [8].

Aortic dissection is uncommon in children with Marfan’s syndrome, but in our series one late death occurred due to aortic dissection 3.9 years after initial surgery at age of 14 years. The most common indications for a second cardiac procedure in our series were increasing aortic regurgitation following homograft placement and distal aortic pathology. Risk factors for a second operation were younger age and weight at surgery.

In conclusion, operations of aortic root in children can be performed with reasonably low mortality and morbidity. Ascending aortic dissection and rupture are rare during the first 10 years of life, but children with Marfan’s syndrome who have undergone aortic root surgery require careful follow-up. Reoperation is more common after homograft
root replacement. Composite graft root replacement may provide a more stable repair with better long-term results.

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References


