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Long-term Outcomes

Is the Ross procedure as good as we thought it would be?

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For patients requiring intervention because of progressive disease of the aortic valve, the perfect palliation will provide a valve that produces normal dynamics of flow, will not require anticoagulation, will grow with the patient, and have long term durability. Current surgical interventions include aortic valvoplasty, or replacement with either a mechanical or tissue prosthesis. Options for tissue valves include insertion of a pulmonary autograft in the Ross procedure, a cadaveric homograft, or porcine or bovine xenograft valves. The optimal option is still debated.

The Ross procedure, first described in 1967,[1] involves replacement of the diseased aortic valve with a pulmonary autograft, excision of the coronary arteries from the native aortic root, and reimplantation into the neo-aortic root. A pulmonary or aortic homograft conduit is then placed between the right ventricle and pulmonary arteries. Many reports[2–9] have documented the effective use of the Ross procedure for isolated aortic valvar disease, as well as for complex obstruction of the left ventricular outflow tract in neonates, infants, and children. Following the Ross procedure, patients do not require anti-coagulation, and the autograft has been shown to be durable, and to grow in proportion to somatic growth.[10,11] Due to these attributes the pulmonary autograft is an attractive alternative to mechanical, homograft and xenograft valves when treating aortic valvar disease in children and young adults. Despite the encouraging early results relative to other surgical options, however, specific long-term morbidities, including dysfunction of the neo-aortic valve, dilation of the aortic root, and periodic replacement of the homograft, have called into question whether the Ross procedure is the best choice for surgical palliation of significant aortic valvar disease.

Mechanical valves inserted in children frequently require replacement as somatic growth occurs, as well as lifelong anticoagulation. Although the haemodynamic result and long term durability may be acceptable after insertion of mechanical valvar prostheses, the haemodynamics may be better after the Ross procedure.[12] Thromboembolism and haemorrhage in anticoagulated patients remain important complications, especially in children.[13,14] Additionally, placement of a mechanical valve in a female child or adolescent will make child bearing later in life problematic due to possible thromboembolism or haemorrhage, as well as the potential teratogenic effects of warfarin. Porcine bioprostheses, which do not require anticoagulation, deteriorate more rapidly in young patients and have limited durability.[15,16]

Although both aortic valvoplasty and replacement of the aortic valve with a homograft generally result in acceptable post-operative haemodynamics, do not require anti-coagulation, and are associated with a low incidence of thromboembolic phenomenons, both have issues related to durability. Aortic homograft valves have been shown to have limited durability in children, and do not grow with the child.[16,17] Similar to the mechanical valve, the aortic homograft does not perform as well from a haemodynamic standpoint during exercise as the autograft.[18] Techniques for aortic valvoplasty include extension of the leaflets using autologous pericardium, reconstruction of the zones of apposition between the leaflets, reduction of the size of the valvar orifice, reduction of the sinuses of Valsalva, remodelling of the sinutubular junction, thinning and excision of raphes in conjoint leaflets, and complete replacement of leaflets with autologous pericardium. Although the initial results of the newer techniques

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are encouraging, their durability is not yet clear, and likely depends on the specific abnormality of the valve, whether earlier surgical and catheterization based procedures have already been performed, and the strategy used to repair the valve.[19,20] Even if the durability of valvoplasty is ultimately deemed less than that of replacement with a pulmonary autograft, the potential advantage of attempting repair is that, if subsequent replacement is required, all the options, including the Ross procedure, remain available.

In the light of all these considerations, our review will consider the late mortality and specific morbidities after the Ross procedure, including the function of the neo-aortic valve, dilation of the aortic root, reintervention, issues of the coronary arteries, left ventricular size and function, exercise performance, and electrophysiologic abnormalities. We will conclude our discussion with a description of new modifications to the Ross procedure, and the state of other valves for use in future replacements.

Mortality

Similar to the techniques of valvoplasty and other strategies for replacement, early and late mortality after placement of the pulmonary autograft is rare, occurring in 2.5% of patients within 30 days of the Ross procedure, and between 1.7 and 2.5% late after placement of the pulmonary autograft.[2–7,21] Late mortality is often linked to progressive pulmonary hypertension secondary to left ventricular or mitral hypoplasia in patients with complex left ventricular disease. Given the low mortality after the Ross procedure, long-term outcomes have focused on specific morbidities related to the procedure.

Morbidity

Function of the neo-aortic valve and dilation of the aortic root

The morphologic development and fibroelastic structure of the pulmonary and aortic valves are different, with the leaflets of the aortic valve being supported more extensively by fibrous structures.[22–24] After placement of the pulmonary valve in the aortic position there is some evidence that there is down regulation of the smooth muscle cells in the pulmonary autograft, along with fracture of the elastin fibres and progressive structural disorganization.[24,25]

Several studies have evaluated the function of the neo-aortic valve after the Ross procedure. Freedom from severe neo-aortic regurgitation at 10 years ranges from 75 to 90%.[9,26–28] This is in contrast to children undergoing replacement of the aortic valve with a mechanical prosthesis, where failure is usually due to thrombosis or ingrowth of pannus,[16,29,30] or "outgrowth" of the valve resulting in obstruction of the left ventricular outflow tract.[16,29,30] In patients who have undergone the Ross procedure, failure due to significant neo-aortic regurgitation may occur early in the post-operative period, or develop over time. Early failure is rare, and has been associated with subtle abnormalities of the native pulmonary valve, such as mild thickening of the leaflets, a quadrifoliate arrangement, or a discrepancy in size of the leaflets, that may be congenital or acquired after repair of a ventricular septal defect, even in the absence of significant pre-operative insufficiency of the native pulmonary valve.[7] The development of neo-aortic regurgitation over time may be related to dilation of the newly constructed aortic root.[9,31,32]

The pulmonary valve also functions as the neo-aortic valve after the arterial switch procedure for repair of transposition, and staged reconstruction for hypoplastic left heart syndrome. Studies in both these groups of patient have shown progressive dilation of the new aortic root over time.[33–35] Unlike patients who have undergone the arterial switch operation and staged reconstruction for hypoplastic left heart syndrome, however, there are two important differences for those undergoing the Ross procedure. Prior to the Ross procedure, the pulmonary valve has been subjected to the low-pressure pulmonary circulation, sometimes for decades, and needs to adapt acutely to an increased afterload. In addition, patients who have undergone the Ross procedure have suture lines above and below the neo-aortic valve. It is not surprising, therefore, that the pulmonary autograft, when placed under systemic pressure and resistance, dilates out of proportion to somatic growth.[21,36–38] Dilation has been found at both the basal level of the neo-aortic valve and the valvar sinuses.[36,37] Tantengco et al.[36] showed a significant increase in the z-score for the diameter of the valvar orifice from 1.4 at the time of hospital discharge to 2.6 after follow-up of 6 months, and an increase for the diameter of the sinuses from 2.0 to 3.3 over the same period of time. Follow-up data on dilation of the root beyond 6 months is conflicting, with some studies demonstrating stabilization of the dimensions, and others suggesting continued dilation over the next 1 to 2 years.[11,36–39] Serial echocardiographic measurements in children are lacking beyond the early post-operative period. Data in adults suggests that dilation progresses over time.[40–42] Simon-Kupilik et al.[42] found that those showing freedom from dilation of the newly constructed aortic root decreased from 80% after follow up of 1 year, to 45% after 7 years. Predictors of such dilation include younger age at surgery, pre-operative dilation of the ascending aorta in presence of a bifoliate aortic valve, and pre-operative dilation associated with aortic insufficiency.[28,41]

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Reintervention

Although the pulmonary autograft has the potential for growth after the Ross procedure, the homograft placed in the pulmonary position does not. Hence, reintervention must be expected when the procedure is performed in young patients. Right ventricular reintervention is nearly always due to stenosis of the pulmonary homograft, with or without pulmonary insufficiency, and may require replacement or augmentation of the conduit, balloon dilation, and/or stenting. Right-sided reintervention is necessary in up to one-fifth of patients at midterm follow-up.[7,9,26,27,43] Predictors of reintervention in the right ventricular outflow tract of children include utilization of an aortic homograft, which tends to calcify more quickly than pulmonary homograft, small size of the initially inserted homograft, and younger age at placement, longer storage time of the homograft, and immune mediated reactions.[43,44]

Reintervention in the left ventricular outflow tract is as frequent as reintervention on the right side, occurring in approximately one-tenth of patients after follow-up of 10 years, and in almost two-fifths after follow-up of 25 years.[9,21,26,27] Rates of reintervention for other types of valvar replacements and aortic valvoplasty are higher. Mechanical valves have a reintervention rate of up to one-fifth at follow-up of 10 years. For those with mechanical valves, the reintervention rate is dependent on the age of the patients in the cohort. The younger the patients, the higher the rate of reintervention.[16,29,30,45] Of patients undergoing aortic valvoplasty, one-fifth have required reintervention at 3 years,[20] while half and two-thirds, respectively, of those having replacements with aortic homografts and xenografts have needed reintervention at 10 years.[16]

The majority of reinterventions on the left side for patients after the Ross procedure are performed due to significant neo-aortic insufficiency, as discussed above, and involve replacement of the valve, usually with a mechanical prosthesis.[9,26,27] Predictors of left sided reintervention include an abnormal native pulmonary valve, and pre-operative aortic insufficiency with dilation of the native aortic root.[7,46] Valve sparing replacements have also been reported in patients who develop severe dilation without significant neo-aortic insufficiency.[26] It is not known whether, in some patients, dilation and insufficiency of the newly constructed aortic root will continue to progress over time, and whether this will lead to higher rates of reintervention in the second to third decades of follow-up. It is also unclear if the same factors that put the patient at risk for dilation or insufficiency of the neo-aortic root also apply to the root subsequent to reintervention, or whether other risk factors will be identified.

Issues relating to the coronary arteries

There are few studies assessing flow in the myocardium and coronary arterial flow reserve after reimplantation of the coronary arteries in the Ross operation. Hauser et al.,[47] in a small series, showed that coronary arterial flow reserve was significantly reduced relative to normal controls in all patients undergoing the arterial switch, while it was normal in those having the Ross procedure, with no exercise induced defects of perfusion. It is not clear, however, whether the differences related to the extent of follow-up between the two groups, the age at surgery, or inherent abnormalities of the coronary arteries in those undergoing the arterial switch that predisposed them to abnormalities of flow.

Left ventricular size and function

At the time of the Ross procedure, myocardial ischaemia secondary to cardioplegic arrest may exacerbate pre-existing left ventricular dysfunction. There is often a mismatch between ventricular mass and volume, with acute reduction of end-diastolic volume in patients with severe aortic insufficiency and/or mitral regurgitation in the presence of a hypertrophied myocardium. As long as significant residual neo-aortic regurgitation is not present, the left ventricle remodels over time, with a reduction in left ventricular end diastolic dimension, left ventricular end systolic dimension, and left ventricular mass.[12,36,48,49] The majority of patients have a normal or increased shortening fraction or ejection fraction before, and have normal function after the Ross procedure.[12,49] Gauthier et al.,[48] for example, showed that two-thirds of patients with severely depressed left ventricular function before the Ross procedure had an increase in ejection fraction of greater than one-fifth after the procedure.

Exercise performance

There is limited data on exercise performance after the Ross procedure is carried out in chidlren. In a study performed by ourselves,[50] we found no significant change in maximal uptake of oxygen indexed to ideal body weight before and after the Ross procedure. In four-fifths of the patients, aerobic capacity improved or was stable after the Ross procedure, and there was no post-operative chronotropic impairment. The patients, however, had significantly increased adiposity after the Ross procedure.

Electrophysiologic abnormalities

The early electrophysiologic abnormalities after the Ross procedure are well documented, and include complete heart block in up to one-twentieth, and

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ventricular tachycardia in one-quarter, both arrhythmias being seen in the first and second days after surgery.[4,7,51,52] After the combined Ross and Konno procedure, however, complete heart block has been reported in up to one-fifth of patients.[5,7,51] Systematic long-term data on the electrophysiologic outcome, however, is sparse. Reports of persistent ventricular tachycardia requiring medication or automatic internal cardiac defibrillator are rare, and the incidence of placement of pacemakers after the early post-operative period is very low.[51]

Modifications of the procedure, and other potential valves

So as to minimize dilation of the newly constructed aortic root, some surgeons have described "wrapping" the autograft with pericardium or the ascending aorta, or with Dacron or Teflon felt at the level of insertion of the pulmonary autograft, albeit with mixed results.[9,53,54] These modifications may have had limited success because dilation of the root is not limited to just the base of the autograft, but instead involves its full length. In an attempt to support fully the entire autograft, Slater et al.[55] suggested that, for adults, the autograft could be encased in a Dacron tube, since subsequent growth is not necessary. They performed their modification in a small cohort of patients, and as yet follow-up data is not available.

Tissue engineered valves, with autologous cell seeding on a polymer leaflet scaffold, may prove to be ideal for replacement of the aortic valve. Efforts thus far to perfect the development of durable valves have been difficult. Loss of cells, and deficient polymers resulting in destruction of the scaffold, have limited the ability for researchers to put these valves into the systemic circulation.[56,57] Instead, some companies and researchers have focused on improving the performance of bioprosthetic valves with technology to reduce calcification. Kanter et al.,[58] for example, inserted the Medtronic Freestyle Porcine Aortic Root in 56 children, with no deaths, mild or no pulmonary insufficiency in nine-tenths of the patients, with a mean peak systolic gradient across the right ventricular outflow tract of 19.7 plus or minus 15.4 millimetres of mercury after two to three years. Gleason et al.[59] achieved comparable results using the porcine St. Jude Toronto Bioprosthesis.

Conclusion

Insertion of the pulmonary autograft provides superior haemodynamics, does not require anti-coagulation, grows with the patient, and has the best long-term durability of the present options available for replacement of the aortic valve using a tissue prosthesis. The Ross procedure, therefore, is the procedure of choice when it is necessary to replace the aortic valve in the neonate, infant, and young child. The procedure is contra-indicated, however, when the native pulmonary valve is structurally abnormal. Whether or not the newer techniques of aortic valvoplasty will have equal or better durability than the pulmonary autograft is not known. Durability of the various techniques for aortic valvoplasty may increase as there is improvement in matching appropriate candidates with specific surgical techniques. To date, tissue engineered valves have not realized the potential that was initially theorized, and it is not clear whether modification of the technique used for implantation of the pulmonary autograft will change the incidence over time of dilation and insufficiency of the neo-aortic root, and left sided reintervention. Given the issues of dilation and insufficiency, and the potential increasing risk of left sided reintervention over time, we suggest that the Ross procedure should be performed only if the patient is not suitable for aortic valvoplasty. Given that all options for valvar replacement are still available after aortic valvoplasty, in appropriate patients an attempt at valvoplasty should be considered prior to undertaking the Ross procedure. Longer term issues of life long neo-pulmonary regurgitation, obesity, exercise performance, coronary arterial perfusion and flow reserve, and risks of atherosclerosis remain to be defined.

References

1. Ross DN. Replacement of aortic and mitral valves with a pulmonary autograft. Lancet 1967; 2: 956–958.
2. Matsuki O, Okita Y, Almeida RS, et al. Two decades' experience with aortic valve replacement with pulmonary autograft. J Thorac Cardiovasc Surg 1988; 95: 705–711.
3. Gerosa G, McKay R, Ross DN. Replacement of the aortic valve root with a pulmonary autograft in children. Ann Thorac Surg 1991; 51: 424–429.
4. Kouchoukos NT, Davila-Roman VG, Spray TL, Murphy SF, Perrillo JB. Replacement of the aortic root with a pulmonary autograft in children and young adults with aortic valve disease. N Engl J Med 1994; 330: 1–6.
5. Reddy VM, Rajasinghe HA, Teitel DF, Hanley FL. Atrioventriculoplasty with the pulmonary autograft: the "Ross-Konno" procedure. J Thorac Cardiovasc Surg 1996; 111: 158–167.
6. Calhoon JH, Bolton JWR. Ross/Konno procedure for critical aortic stenosis in infancy. Ann Thorac Surg 1995; 60: S596–S599.
7. Marino BS, Wernovsky G, Rychik J, Bockoven JR, Godinez RI, Spray TL. Early results of the Ross procedure in simple and complex left heart disease. Circulation 1999; 100 (Suppl II): II162–II166.
8. Ohye RG, Gomez CA, Ohye BJ, Goldberg CS, Bove EL. The Ross/Konno procedure in neonates and infants: intermediate-term survival and autograft function. Ann Thorac Surg 2001; 72: 823–830.
9. Luciani GB, Favaro A, Casali G, Santini F, Mazzucco A. Ross operation in the young: a ten-year experience. Ann Thorac Surg 2005; 80: 2271–2277.

10. Elkins RC, Knott-Craig CJ, Ward KE, McCue C, Lane MM. Pulmonary autograft in children: realized growth potential. Ann Thorac Surg 1994; 57: 1387–1394.
11. Simon P, Aschauer C, Moidl R, et al. Growth of the pulmonary autograft after the Ross operation in childhood. Eur J Cardiothorac Surg 2001; 19: 118–121.
12. Doss M, Wood JP, Martens S, Wimmer-Greinecker G, Moritz A. Do pulmonary autografts provide better outcomes than mechanical valves? A prospective randomized trial. Ann Thorac Surg 2005; 80: 2194–2198.
13. Edmunds Jr LH. Thrombotic and bleeding complications of prosthetic heart valves. Ann Thorac Surg 1987; 44: 430–445.
14. Streif W, Andrew M, Marzinotto V, et al. Analysis of warfarin therapy in pediatric patients: a prospective cohort study of 319 patients. Blood 1999; 94: 3007–3014.
15. Al-Khaja N, Belboul A, Rashid M, et al. The influence of age on the durability of Carpentier-Edwards biological valves: thirteen year follow-up. Eur J Cardiothorac Surg 1991; 5: 635–640.
16. Turrentine MW, Ruzmetov M, Vijay P, Bills RG, Brown JW. Biological versus mechanical aortic valve replacement in children. Ann Thorac Surg 2001; 71: S356–360.
17. Gerosa G, McKay R, Davies J, Ross DN. Comparison of the aortic homograft and the pulmonary autograft for the aortic valve or root replacement in children. J Thorac Cardiovasc Surg 1991; 102: 51–61.
18. Laforest I, Dumesnil JG, Briand M, Cartier PC, Pibarot P. Hemodynamic performance at rest and during exercise after aortic valve replacement. comparison of pulmonary autograft versus aortic homograft. Circulation 2002; 106(suppl I): I157–162.
19. Duran C, Kumar N, Gometza B, al Halees Z. Treated bovine and autologous pericardium for aortic valve reconstruction. Ann Thorac Surg 1998; 66: S166–S169.
20. Bacha EA, Satou GM, Moran AM, et al. Valve-sparing operation for balloon-inducted aortic regurgitation in congenital aortic stenosis. J Thorac Cardiovasc Surg 2001; 122: 162–168.
21. Oury JH, Hiro SP, Maxwell JM, Lamberti JJ, Duran CM. The Ross procedure: current registry results. Ann Thorac Surg 1998; 66(suppl): S162–165.
22. Maron BJ, Hutchins GM. The development of the semilunar valves in the human heart. Am J Pathol 1974; 74: 331–344.
23. Hokken RB, Bartelings MM, Bogers JJC, Gittenberger-de-Groot AC. Morphology of the pulmonary and aortic roots with regard to the pulmonary autograft procedure. J Thorac Cardiovasc Surg 1997; 113: 453–461.
24. Lalezari S, Hazekamp MG, Bartelings MM, Schoof PH, Gittenberger-De Groot AC. Pulmonary artery remodeling in transposition of the great arteries: relevance for neoaortic root dilatation. J Thorac Cardiovasc Surg 2003; 126: 1053–1060.
25. Rabkin-Aikawa E, Aikawa M, Farber M, et al. Clinical pulmonary autograft valves: pathologic evidence of adaptive remodeling in the aortic site. J Thorac Cardiovasc Surg 2004; 128: 552–561.
26. Hazekamp MG, Grotenhuis HB, Schoof PH, Rijlaarsdam MEB, Ottenkamp J, Dion RAE. Results of the Ross operation in a pediatric population. Eur J Cardiothorac Surg 2005; 27: 975–979.
27. Elkins RC, Lane MM, McCue C. Ross operation in children: late results. J Heart Valve Dis 2001; 10: 736–741.
28. Kouchoukos NT, Masetti P, Nickerson NJ, Castner CF, Shannon WD, Davila-Roman VG. The Ross procedure: long-term clinical and echocardiographic follow-up. Ann Thorac Surg 2004; 78: 773–781.
29. Mazzitelli D, Guenther T, Schreiber C, Wottke M, Michel J, Meisner H. Aortic valve replacement in children: are we on the right track? Eur J Cardiothorac Surg 1998; 13: 565–571.
30. Alexiou C, McDonald A, Langley SM, Dalrymple-Hay MJ, Haw MP, Monro JL. Aortic valve replacement in children: are mechanical prostheses a good option? Eur J Cardiothorac Surg 2000; 17: 125–133.
31. Bellhouse BJ, Bellhouse F, Abbott JA, Talbot L. Mechanism of valvular incompetence in aortic sinus dilatation. Cardiovasc Res 1986; 34: 83–94.
32. Roman MJ, Devereux RB, Niles NW, et al. Aortic root dilatation as a cause of isolated, severe aortic regurgitation. Ann Int Med 1987; 106: 800–807.
33. Marino BS, Wernovsky G, McElhinney DB, et al. Neo-aortic valvar function after the arterial switch. Cardiol Young 2006; 16: 481–489.
34. Cohen MS, Marino BS, McElhinney DB, et al . Neo-aortic root dilation and valve regurgitation up to 21 years after staged reconstruction for hypoplastic left heart syndrome. J Am Coll Cardiol 2003; 42: 533–540.
35. Schwartz ML, Gauvreau K, del Nido P, Mayer JE, Colan SD. Long-term predictors of aortic root dilation and aortic regurgitation after arterial switch operation Circulation 2004; 110 (11 Suppl 1): II128–II132.
36. Tantengco MV, Humes RA, Clapp SK, et al. Aortic root dilatation after the Ross procedure. Am J Cardiol 1999; 83: 915–920.
37. Solowiejczyk DE, Bourlon F, Apfel HD, et al. Serial echocardiographic measurements of the pulmonary autograft in the aortic valve position after the Ross operation in a pediatric population using normal pulmonary artery dimensions as the reference standard. Am J Cardiol 2000; 85: 1119–1123.
38. Puntel RA, Webber SA, Ettedgui JA, Tacy TA. Rapid enlargement of the neo-aortic root after the Ross procedure in children. Am J Cardiol 1999; 84: 747–749.
39. Solymar L, Sudow G, Holmgren D. Increase in size of the pulmonary autograft after the Ross operation in children: growth or dilation? J Thorac Cardiovasc Surg 2000; 119: 4–9.
40. Takkenberg JJ, van Herwerden LA, Galema TW, et al. Serial echocardiographic assessment of neo-aortic regurgitation and root dimensions after the modified Ross procedure. J Heart Valve Dis 2006; 15: 100–106.
41. Luciani GB, Casali G, Favaro A, et al. Fate of the aortic root late after Ross operation. Circulation 2003; 108: II61–II67.
42. Simon-Kupilik N, Bialy J, Moidl R, et al. Dilation of the autograft root after the Ross operation. Eur J Cardiothorac Surg 2002; 21: 470–473.
43. Carr-White GS, Kilner PJ, Hon JK, et al. Incidence, location, pathology, and significance of pulmonary homograft stenosis after the Ross operation. Circulation 2001; 18: 116–120.
44. Tweddell JS, Pelech AN, Frommelt PC, et al. Factors affecting longevity of homograft valves used in right ventricular outflow tract reconstruction for congenital heart disease. Circulation 2000; 102: III130–III135.
45 Lupinetti FM, Duncan BW, Scifres AM, et al. Intermediate term results in pediatric aortic valve replacement. Ann Thorac Surg 1999; 68: 521–525.
46. Laudito A, Brook MM, Suleman S, et al. The Ross procedure in children and young adults: a word of caution. J Thorac Cardiovasc Surg 2001; 122: 147–153.
47. Hauser M, Bengel FM, Kühn A, et al. Myocardial blood flow and flow reserve after coronary reimplantation in patients after the arterial switch and Ross operation. Circulation 2001; 103: 1875–1880.
48. Gauthier SC, Barton JG, Lane MM, Elkins RC. Pulmonary autografts in patients with severe left ventricular dysfunction. Ann Thorac Surg 2003; 76: 689–693.
49. Nimaya K, Elkins RC, Knott-Craig CJ, Santangelo KL, Cannon MB, Lane MM. Normalization of left ventricular dimensions after Ross operation with aortic annular reduction. Ann Thorac Surg 1999; 68: 812–818.
50. Marino BS, Pasquali SK, Wernovsky G, et al. Exercise performance in children and adolescents after the Ross procedure. Cardiol Young 2006; 16: 40–47.
51. Wernovsky G, Marino BS, Spray TL. Immediate outcomes after the Ross operation in children and adults. Prog Pediatr Cardiol 2003; 16: 141–147.

52. Bockoven JR, Wernovsky G, Vetter VL, Wieand TS, Spray TL, Rhodes LA. Perioperative conduction and rhythm disturbances following the Ross procedure in children and young adults. Ann Thorac Surg 1998; 66: 1383–1388.
53. Skillington PD, Fuller JA, Grigg LE, Yapanis AG, Porter GF. Ross procedure: inserting the autograft using a fully supported root replacement method; techniques and results. J Heart Valve Dis 1999; 8: 593–600.
54. Sievers H, Dahmen G, Graf B, Stierle U, Ziegler A, Schmidtke C. Midterm results of the Ross procedure preserving the patient's aortic root. Circulation 2003; 108 (Suppl 2): 1155–1160.
55. Slater M, Shen I, Welke K, Komanapalli C, Ungerleider R. Modification of the Ross procedure to prevent autograft dilatation. Semin Thorac Cardiovasc Surg Pediatr Card Surg Ann 2005; 8: 181–184.
56. Schoen FJ, Levy RJ. Tissue heart valves: current challenges and future research perspectives. J. Biomed Mater Res 1999; 47: 439–465.
57. Rabkin E, Schoen FJ. Cardiovascular tissue engineering. Cardiovasc Pathol 2002; 11: 305–317.
58. Kanter KR, Fyfe DA, Mahle WT, Forbess JM, Kirshbom PM. Results with the freestyle porcine aortic root for right ventricular outflow tract reconstruction in children Ann Thorac Surg 2003; 76: 1889–1895.
59. Gleason TG, David TE, Coselli J, Hammon JW, Bavaria JE. St. Jude Medical Toronto biologic aortic root prosthesis: early FDA phase II IDE study results. Ann Thorac Surg 2004; 78: 786–793.