JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
© 2016 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER

VOL. 67, NO. 24, 2016
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2016.04.023

EDITORIAL COMMENT

Aortic Valve Replacement in Children and Young Adults*

Tirone E. David, MD

The perfect heart valve substitute has not yet been developed and matching the patient to existing options to optimize survival and reduce valve-related complications remains challenging. The choices for aortic valve replacement (AVR) are mechanical valves, bioprosthetic valves, and biological valves such as aortic valve homograft and the Ross procedure (pulmonary autograft). The latter is a complex operation because it transfers the patient's own pulmonary valve into the aortic position and uses a biological valve to replace the pulmonary valve, transforming a single-valve disease into a 2-valve disease. These considerations are not important to most North American patients who undergo AVR because they are older and the durability of bioprosthetic valves in this age group is excellent (1,2). The risk of bioprosthetic valve failure 20 years after AVR is <10% in patients 70 years of age and older (1,2). A report based on the Society of Thoracic Surgeons Database from January 1997 to December 2006 showed that 108,687 patients had isolated AVR and the mean age was 69 years (3). The use of bioprosthetic heart valves increased from 43.6% in 1997 to 78.4% in 2006 (3). This shift from mechanical to bioprosthetic valves preceded the introduction of transcatheter aortic valve implantation into clinical practice and there is no rational reason for this because the results of numerous retrospective studies and 3 randomized clinical trials have failed to conclusively show survival benefit of one over the other type of artificial heart valve (4). A simple explanation is that most patients would rather have a reintervention for a failed bioprosthetic aortic valve than be committed to take warfarin for life.

Valve selection in children and young adults is more complicated because of the associated congenital heart defects, somatic growth, and the fact that aortic valve homograft and bioprosthetic heart valves are not as durable in the young as they are in older patients (1,2,5–8). Mechanical valves are durable but require lifelong anticoagulation with coumadin.

SEE PAGE 2858

In this issue of the *Journal*, Sharabiani et al. (9) have an interesting study on AVR in children and young adults based on a dataset extracted from the National Congenital Heart Disease Audit of the United Kingdom. The selected dataset was linked with census of the Office of National Statistics of the United Kingdom to obtain outcomes such as survival and reinterventions. Almost 46% of patients had to be excluded for various valid reasons but 11.3% were excluded for "unclassified" AVR due to "errors in reporting." This relatively high proportion in errors raises concerns about the integrity of the data but the authors believed that they had reliable information in 1,501 patients operated on from April 2000 through March 2012, a 12-year period. The objectives of the study were to examine early and long-term survival and freedom from reoperations in a large cohort of unselected young patients and compare the outcomes of various types of heart valve substitutes for AVR.

The most commonly performed AVR in neonates, infants, and children ≤16 years of age was the Ross procedure at 78.5%, followed by mechanical valves at 17.3%, and only a few bioprosthetic valves and aortic valve homograft. In young adults (17 to 40 years of age) mechanical valves were the most commonly

*Editorials published in the *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of *JACC* or the American College of Cardiology.

From the Division of Cardiac Surgery of the Peter Munk Cardiac Centre at Toronto General Hospital and the University of Toronto, Toronto, Ontario, Canada. Dr. David has reported that he has no relationships relevant to the contents of this paper to disclose.

used for AVR at 53.6%, followed by the Ross at 25.6%, bioprosthetic heart valves at 17.4%, and aortic valve homograft at 3.2%. There were only 61 neonates and infants (<1 year of age) and most of them had the Ross procedure. One-year mortality was 14.3%, and only 1 patient died after the first year. Freedom from reoperation on the pulmonary autograft was 84.7% at 12 years of age, and when combined with reinterventions on the right ventricular outflow tract it dropped to 72.5% (9). These results are very good even considering that the investigators excluded children with complex congenital heart defects such as hypoplastic left heart syndrome and other anomalies commonly associated with aortic stenosis in neonates and infants. The management of these patients is difficult and it remains controversial if the aortic valve should be repaired or replaced, or in cases of aortic stenosis, if it should be treated with surgery or transcatheter balloon valvotomy. Most surgeons believe that open valve repair provides better long-term results than balloon valvotomy or AVR in this age group (10–12).

The study of Sharabiani et al. (9) also had 568 children (1 to 16 years of age) and the 2 most common operations were the Ross procedure in 77.2% and mechanical valves in 17.3%. Survival at 10 years was slightly higher in AVR with the Ross procedure than with mechanical valves but the difference did not reach statistical significance, and the cumulative incidence of reintervention at 10 years was 9.9% higher among patients with mechanical valves ($p = 0.07$). A possible explanation for this higher rate of reintervention in patients with mechanical valves is progressive prosthesis-patient mismatch due to somatic growth. A recently published meta-analysis on AVR in children included the Ross procedure in 2,409 children with a mean age of 9.4 years, mechanical valves in 696 with a mean age of 12.8 years, and aortic valve homograft in 224 with a mean age of 8.9 years (8). The pooled data showed an operative mortality of 4.2% for the Ross, 7.3% for mechanical valves, and 12.8% for homograft AVR, and an annual mortality rate of 0.64% for the Ross, 2.6% for mechanical, and 1.99% homograft (8). The annualized rates of reoperation on the aortic valve were 1.6% for the Ross, 1.3% for mechanical valves, and 5.4% for aortic valve homograft (8). That meta-analysis study showed that the Ross procedure offered survival advantages over mechanical valves and aortic valve homograft but the overall results of AVR in children were deemed suboptimal (8).

The third subgroup in the Sharabiani et al. (9) study dealt with 872 young adults (17 to 40 years of age) and the Ross procedure was performed in 25.6%, mechanical valves in 53.6%, bioprosthetic valves in 17.4%, and aortic valve homograft in 3.2%. Reintervention-free survival at 10 years was 89.6% for the Ross, 86.3% for mechanical valves, and 78.8% for bioprosthetic heart valves. By matching patients from the 3 main groups, the Ross procedure was found to be superior to mechanical valves and mechanical valves to be superior to bioprosthetic valves. Other investigators also found a survival advantage of the Ross procedure over mechanical valves in young adults (13). We have shown that patients' survival after the Ross procedure at 20 years is similar to that of the general population matched for age and sex (14). The Ross procedure was the only type of AVR that resulted in survival similar to that of matched general population in the study of Sharabiani et al. (9).

The quest for a better heart valve substitute goes on, particularly in children. None is perfect but the Ross procedure offers the best chance of long-term survival and the lowest risk of valve-related complications (5,8,9). This evidence imposes problems when recommending AVR in the young because the Ross procedure is a difficult operation and the published results are highly variable (8,13–17). There was a great deal of enthusiasm for this operation in the early 1990s but it soon faded as patients began to come back for complex reoperations (18–20). Valuable information has been accumulated on the Ross procedure during the past 2 decades. Technical errors aside, pre-operative aortic insufficiency and dilated aortic annulus are the main reasons for late failure of the pulmonary autograft (14–16). Surgical reduction of the dilated aortic annulus to match the size of the pulmonary autograft does not prevent late development of aortic insufficiency (14). The pulmonary autograft is more durable in women than in men (14). Thus, ideal patients for the Ross procedure have aortic stenosis with normal aortic annulus, and in particular women. These patients will likely have a neoaortic valve for life but they will still be troubled by the valve used to replace the native pulmonary valve. Pulmonary valve homograft failure is highly dependent on patients' age, and it often precedes the development of symptoms and can damage the right ventricle if left unattended. Thus, there is need for periodical surveillance of both the pulmonary autograft and pulmonary homograft after the Ross procedure.

The aortic valve should be repaired whenever possible in children, and if not feasible, the Ross procedure should be performed because it offers the best event-free survival. Young adults with aortic insufficiency should have aortic valve repair

whenever possible and mechanical valves are the second-best option. Young adults with aortic stenosis and normal aortic annulus are best served by the Ross procedure. This summarizes the best evidence available today on the choices of aortic valve substitute in the young.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Tirone E. David, Division of Cardiac Surgery of the Peter Munk Cardiac Centre at Toronto General Hospital, 200 Elizabeth Street, 4N453, Toronto, Ontario M5G 2C4, Canada. E-mail: tirone.david@uhn.ca.

REFERENCES

1. David TE, Armstrong S, Maganti M. Hancock II bioprosthesis for aortic valve replacement: the gold standard of bioprosthetic valves durability? Ann Thorac Surg 2010;90:775–81.

2. Bourguignon T, Bouquiaux-Stablo AL, Candolfi P, et al. Very long-term outcomes of the Carpentier-Edwards Perimount valve in aortic position. Ann Thorac Surg 2015;99:831–7.

3. Brown JM, O'Brien SM, Wu C, Sikora JA, Griffith BP, Gammie JS. Isolated aortic valve replacement in North America comprising 108,687 patients in 10 years: changes in risks, valve types, and outcomes in the Society of Thoracic Surgeons National Database. J Thorac Cardiovasc Surg 2009;137:82–90.

4. David TE. Surgical treatment of aortic valve disease. Nat Rev Cardiol 2013;10:375–86.

5. Karamlou T, Jang J, Williams WG, et al. Outcomes and associated risk factors for aortic valve replacement in 160 children: a competing-risks analysis. Circulation 2005;112:3462–9.

6. Une D, Ruel M, David TE. Twenty-year durability of the aortic Hancock II bioprosthesis in young patients: is it durable enough? Eur J Cardiothorac Surg 2014;46:825–30.

7. Forcillo J, El Hamamsy I, Stevens LM, et al. The Perimount valve in the aortic position: twenty-year experience with patients under 60 years old. Ann Thorac Surg 2014;97:1526–32.

8. Etnel JR, Elmont LC, Ertekin E, et al. Outcome after aortic valve replacement in children: A systematic review and meta-analysis. J Thorac Cardiovasc Surg 2016;151:143–52.

9. Sharabiani MTA, Dorobantu DM, Mahani AS, et al. Aortic valve replacement and the Ross operation in children and young adults. J Am Coll Cardiol 2016;67:2858–70.

10. Siddiqui J, Brizard CP, Galati JC, et al. Surgical valvotomy and repair for neonatal and infant congenital aortic stenosis achieves better results than interventional catheterization. J Am Coll Cardiol 2013;62:2134–40.

11. Soulatges C, Momeni M, Zarrouk N, et al. Long-term results of balloon valvuloplasty as primary treatment for congenital aortic valve atenosis: a 20-year review. Pediatr Cardiol 2015;36:1145–52.

12. Konstantinov IE, d'Udekem Y, Brizard CP. Ross operation or aortic valve repair in neonates and infants? J Thorac Cardiovasc Surg 2014;148:362–4.

13. Andreas M, Wiedemann D, Seebacher G, et al. The Ross procedure offers excellent survival compared with mechanical aortic valve replacement in a real-world setting. Eur J Cardiothorac Surg 2014;46:409–13.

14. David TE, David C, Woo A, Manlhiot C. The Ross procedure: outcomes at 20 years. J Thorac Cardiovasc Surg 2014;147:85–93.

15. Skillington PD, Mokhles MM, Takkenberg JJ, et al. The Ross procedure using autologous support of the pulmonary autograft: techniques and late results. J Thorac Cardiovasc Surg 2015;149:S46–52.

16. Charitos EI, Stierle U, Hanke T, et al. Long-term results of 203 young and middle-aged patients with more than 10 years of follow-up after the original subcoronary Ross operation. Ann Thorac Surg 2012;93:495–502.

17. Mokhles MM, Rizopoulos D, Andrinopoulou ER, et al. Autograft and pulmonary allograft performance in the second post-operative decade after the Ross procedure: insights from the Rotterdam Prospective Cohort Study. Eur Heart J 2012;33:2213–24.

18. Takkenberg JJM, Klieverik LMA, Schoof PH, et al. The Ross procedure: a systematic review and meta-analysis. Circulation 2009;119:222–8.

19. Stulak JM, Burkhart HM, Sundt TM, et al. Spectrum and outcome of reoperations after the Ross procedure. Circulation 2010;122:1153–8.

20. David TE. The Ross procedure at the crossroads. Circulation 2009;119:207–9.

KEY WORDS aortic valve disease, aortic valve replacement, congenital heart disease, Ross procedure