Seven decades of valved right ventricular outflow tract reconstruction: The most common heart procedure in children

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Feature Editor Note—We are indeed fortunate to have this very timely review from one of the true experts on the use of valved conduits in children. Dr John Brown has been involved for 5 of the 7 decades of valved right ventricular outflow tract reconstruction described in this invited expert opinion! He was a pioneer who helped introduce the bovine jugular venous conduit more than 20 years ago.

Dr Brown and his colleague Dr Hermann have provided for us a concise review of the advantages and disadvantages of the various valved conduits currently in use. Decision making for these patients is now of course complicated by the competing strategy of various transcatheter options, which are also described in this review.

The surgical options reviewed include homografts, bovine jugular venous conduits, stentless porcine aortic root valves, expanded polytetrafluoroethylene conduits, and transcatheter pulmonary valve replacement. The very current and important issue of endocarditis is also discussed.

Although much progress has been made in the past 7 decades, the authors point out that we continue to need to improve on the currently available options to decrease the number of operations required for our patients.

Carl L. Backer, MD

Pulmonary valve replacement (PVR) is 5 times more common than any other valve replacement in our pediatric cardiac surgical practice, although it remains a weak link in our treatment of congenital heart disease. Pulmonary valve preservation is frequently impossible in complex congenital heart disease with right ventricular outflow tract (RVOT) obstruction, and pulmonary valve reconstruction has been problematic in infants for decades. Many materials for RVOT reconstruction have been used over the past 7 decades, although none has proven lifelong durability.

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CENTRAL MESSAGE

Diverse options exist for right ventricular outflow tract reconstruction in children and adults, each with a unique mix of strengths and weaknesses. We offer a perspective of current data and future advances related to replacement conduit types and materials.

This Invited Expert Opinion provides a perspective on the following paper: *J Thorac Cardiovasc Surg*. 2018;156(4):1629-1636.e3. <https://doi.org/10.1016/j.jtcvs.2018.04.107>.

See Commentary on page 1289.

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Factors affecting choice of prosthesis include patient age and size; graft availability, cost; tissue processing; conduit durability; and ease of insertion that minimizes sternal compression, deformation of the prosthetic valve, and RVOT turbulence. Future suitability for percutaneous pulmonary valve insertion is also given strong consideration. Our institutional preferences are strongly influenced by the senior author's 5 decades of animal research and clinical experience with RVOT reconstruction and include the following:

- valved bovine jugular vein conduit for infants and children <18 years requiring heterotopic conduit reconstruction of RVOT;

- decellularized pulmonary allografts for adolescents and adults when orthotopic placement and size >22 mm is desired (eg, Ross aortic valve replacement); and
- nonstented xenografts or stented porcine valves for adolescents >18 years and adults.

The growing population of adults with repaired congenital heart disease coupled with the increasing recognition of the detrimental effects of chronic pulmonary insufficiency (eg, systolic and diastolic right ventricular dysfunction, atrial arrhythmias) will undoubtedly continue to drive increasing demand for PVR options. Cardiothoracic surgeons need to continue to understand current trends in conduit outcomes as well as avenues for future developments.

HOMOGRAFTS

Cryopreserved pulmonary allografts were the “gold standard” in the United States from the mid-1980s through the late 1990s, given their availability in a wide range of sizes for virtually any patient age. Many centers favor pulmonary homografts over aortic homografts, as pulmonary homografts are less prone to dysfunction and calcification. However, in neonatal patients, results are generally equivocal, given the short durability of both allograft types.¹ Homograft durability in non-Ross children is disappointing at mid-term follow-up, with less than one half of patients free from conduit dysfunction at 5 years.²

Typical risk factors for homograft failure include younger patient age, smaller conduit size, and certain diagnoses such as truncus arteriosus.²⁻⁴ Heterotopic positioning may also adversely affect homograft durability.⁵ Pulmonary allograft performance and longevity are significantly better following the Ross operation because many of the patients are older and an oversized pulmonary allograft is inserted in an orthotopic fashion, which alleviates the turbulent flow seen in extracardiac valved conduits.

Homograft tissue may be used fresh or with cryopreservation techniques through individual institutional protocols or commercial preparation (LifeNet Health, Virginia Beach, Va). However, conventionally processed cryopreserved allografts frequently stimulate host immune responses, which may adversely affect allograft valve function and durability. One approach for extending allograft durability that has gained increasing clinical interest is decellularization of the allograft to minimize immunologic reaction against the allogeneic material. One process we favor at our institution is SynerGraft (SG) processing (CryoLife, Kennesaw, Ga), which removes >99% of the antigenic donor cells while preserving the collagen matrix. Early clinical experience with implantation of SG allografts demonstrated a reduction or prevention of panel-reactive antibodies in recipients of SG allografts compared with patients who received standard allografts, at least in the short term.^{6,7}

Early functional performance of the SG allografts has been encouraging. In the largest multicenter, retrospective study to date, the SG allograft exhibited similar actuarial survival as standard cryopreserved allografts.⁸ However, the SG allograft exhibited superior freedom from conduit dysfunction at 10 years (83% vs 58%, $P < .001$).⁸ The SG allograft is not available in all countries, and its significant cost may be prohibitive for some centers. Long-term studies are needed to evaluate its performance and to determine whether a reduction in reinterventions may offset the initial expense of the allograft.

BOVINE JUGULAR VENOUS CONDUIT

The Contegra bovine jugular venous conduit (BJVC; Medtronic, Inc, Minneapolis, Minn) has been used in our center since 1999. Its off-the-shelf availability, low immunogenicity, wide range of sizes, easy implantability, favorable cost, and long length for RVOT and pulmonary artery reconstruction make it a versatile option for patients younger than 18 years of age. We recently reviewed our experience involving 315 BJVC implantations in 276 patients with a mean follow-up period of 5.9 years.⁹ Size was a considerable factor in that the smallest conduit group (12-14 mm) demonstrated the lowest 10-year freedom from conduit failure of 13% compared with 69% for the 20- to 22-mm conduit group.⁹ The BJVC has compared favorably with standard (ie, nondecellularized) pulmonary homografts in children younger than 2 years of age in terms of conduit durability and eventual timing of replacement.¹⁰ Similar patterns have been observed in older children who have been followed longer.¹¹ In a study conducted by the Congenital Heart Surgeons' Society involving more than 400 patients from 24 institutions, the choice of BJVC and a larger conduit size z score were important predictors of conduit durability.¹² The risk of endocarditis is one of the most significant concerns about BJVC conduits as will be discussed below.

In terms of BJVC implantation, we typically orient 1 of the 3 commissures directly posteriorly to all for maximum shortening of the conduit. Since the bovine jugular valve leaflets are long, it is critical to shorten the length of conduit as much as possible to avoid conduit buckling or sternal compression. Oversizing the BJVC is helpful for prolonging conduit function.^{11,13,14}

Porcine Aortic Root

Stentless porcine aortic roots (Freestyle; Medtronic, Inc) have been used in off-label fashion for PVR since the mid-1990s, and we have used them in select older patients since 1998. Porcine aortic roots demonstrate less regurgitation than standard pulmonary allografts, are less expensive, provide a good landing zone for transcatheter valve replacement, and do not cause coronary compression as can be seen with stented bioprosthetic valves. They also appear

to carry a very low risk of endocarditis. We typically prefer porcine aortic roots for PVR in patients older than 18 years, particularly if a valve 25 mm or smaller must be implanted.

Porcine aortic roots have demonstrated excellent freedom from reintervention up to 10 years, although results may be inferior in patients younger than 10 years.^{15,16} Similar outcomes between stentless and stented bioprostheses have been observed up to 10 years post-implantation.^{5,17,18} In 116 patients who underwent Freestyle PVR between 1998 and 2018, the 10-year freedom from reintervention was 94%, with only 2 suspected cases of endocarditis, neither of which required reintervention (Kasten MW, Herrmann JL, Brown JW, et al., unpublished data, 1998-2018).

Our technique for stentless porcine aortic root PVR involves resecting a short section of the old conduit or native PA and inserting the Freestyle valve orthotopically to minimize RVOT turbulence. We routinely orient one coronary stump anteriorly and the other leftward such that the rightward sinus faces anteriorly. These stumps often need to be reinforced for hemostasis. We shorten the posterior length of the conduit by making a “V” cut above the posteriorly oriented commissure when necessary.

STENTED BIOPROSTHETIC VALVES

Stented bioprosthetic valves are likely the most common choice for PVR in other institutions for older adolescent and adult patients, given greater surgeon familiarity with their labeled use for aortic valve replacement. These valves are widely available in many sizes. Numerous studies have found no difference in early outcomes between stented bioprosthetic valves and other bioprostheses in older adolescents and adults.¹⁷⁻²¹ We have preferred using stented bioprostheses in the rare situations in which the RVOT is densely scarred and circumferentially mobilizing the main pulmonary artery would be treacherous. However, these valves are limited by their smaller effective orifice area at smaller sizes as well as an inadequate size for subsequent transcatheter PVR below 23 mm.

Our current surgical technique for stented bioprosthetic PVR is to implant the valve within the RVOT as distally as possible and close the infundibulum with a small gusset of bovine pericardium if necessary. When the RVOT is not significantly dilated, an additional gusset with pericardium or other patch material is often necessary to cover the valve and complete the reconstruction. Care must be taken to minimize any outpouching of the gusset material distally or proximally to avoid creating an “energy sink” in the RVOT.

EXPANDED POLYTETRAFLUOROETHYLENE CONDUITS

Miyazaki and colleagues²² introduced expanded polytetrafluoroethylene (ePTFE) conduits in Japan as a solution to the lack of available homografts and BJVC at that time. Their novel construct included bulging sinuses created

with heat and negative pressure application and fan-shaped valves and could be tailored to fit a specific patient's anatomy. Over time, these ePTFE conduits have exhibited favorable mechanical properties, very good durability, and very low rates of endocarditis.²³ Although ePTFE is widely available, only a limited number of centers in the United States and Asia have reported experience using this material or variations of the Yamagishi technique.

TRANSCATHETER PVR

Transcatheter PVR bears mention, given its rapidly expanding use, although technical specifics are beyond the scope of this topic. The Melody transcatheter valve (Medtronic, Inc) was the first device approved for transcatheter PVR and uses the same bovine jugular venous valve as the Contegra valve up to 22 mm in diameter. The Sapien valves (Edwards Lifesciences Inc, Irvine, Calif) have been used off-label for transcatheter PVR in diameters up to 29 mm. The safety and feasibility for both platforms have been established with a greater emphasis on pre-stenting the RVOT to improve device stability.

The most common complications of transcatheter PVR include device malposition, stent fracture, RVOT rupture, and coronary artery compression. Transcatheter PVR is associated with the greatest reported rates of endocarditis (as discussed to follow) as well as the lowest freedom from reintervention in patients 12 years and younger.²⁴ In addition, transcatheter PVR carries greater procedural and hospital costs than surgical PVR.²⁵ The cost equation could be even more substantial if the management of late complications such as endocarditis are included. Currently, the Harmony trial (Medtronic) is underway to evaluate a self-expanding device for larger RVOT diameters with heterogeneous shapes and sizes.²⁶ Only preliminary data are available, however.

The rapid adoption of transcatheter PVR will eventually lead to questions of when and how the technology should be employed as longer-term data become available. Anecdotally, RVOTs become more fibrotic when stents are deployed, often as a result of the stents protruding through some or all the native RVOT. This may make subsequent surgical PVR much more difficult, especially compared with surgical PVR without an existing RVOT prosthesis. Unlike the clinical team model for transcatheter aortic valve replacement, the decision to proceed with transcatheter PVR can be made without surgical consultation. At our institution, we continue to advocate for surgical PVR in younger patients with suitable surgical risk with the hope that at least 10 to 15 years may be attained before reintervention, at which time transcatheter PVR may be a suitable option to postpone a future surgical intervention. The optimal conduit sizes for future transcatheter PVR are 22 mm for the bovine jugular venous conduit and at least 25 mm for the porcine aortic root. The thicker tissue of

the porcine aortic root, less calcification, and proximal cloth skirt may make it an ideal landing zone for a transcatheter PVR, although comparative studies are needed. What is not known currently is the difficulty that surgeons will encounter in removing the embedded prosthesis after it has been there several years.

ENDOCARDITIS

The contemporary cumulative incidence of endocarditis following PVR ranges from 2% to 11%.^{9,27-30} A recent registry report from Denmark found an annualized incidence of infective endocarditis at 5 years of 0.27% for homografts, 1.12% for BJVC, and 2.89% for Melody valves.³¹ The BJVC and Melody valves, which have the same tissue composition, typically have greater reported rates of endocarditis than other conduit types. In the Melody trials, the rate of endocarditis was as high as 21% at 5 years for Melody valve in children 12 years or younger, a rate much greater than for BJVC in other reports.³² However, up to 50% to 70% of BJVC and Melody valve–related endocarditis may be medically managed without the need for immediate intervention.^{9,27,29} In our and others' experiences, the stentless porcine aortic root carries a very low risk of endocarditis for reasons that are not entirely clear but could relate to better laminar flow dynamics. Endocarditis risk may also increase as patients live longer and undergo repeated procedures.^{9,28}

CHALLENGES AND FUTURE DIRECTIONS

Although the collective experience with PVR continues to grow rapidly, many of the reported data derive from retrospective studies from a limited number of institutions with a limited number of conduits. Clearly, more prospective, direct comparisons of valves and conduits from multiple centers is needed. Tracking of conduit types in existing databases is needed to understand not only major trends in conduit performance, but also the possible myriad of conduit-, patient-, and institution-related factors that affect outcomes.

A number of new bioabsorbable materials are in development for RVOT reconstruction in a variety of 3-dimensional—printed and scaffold constructs.³³ A replaced valve that can grow with a patient could be a market game changer, although these technologies are currently remote from clinical application.

The effects of laminar conduit flow on long-term function and susceptibility to endocarditis remain poorly understood but may be helpful in understanding how certain conduits and valves fare better in certain age groups and anatomic positions. Opportunities for improving outcomes of patients requiring RVOT reconstruction include standardizing decision-making algorithms for timing of PVR as well as understanding how PVR positively affects cardiac remodeling. We also need to better understand how transcatheter valves compare with standard surgical conduits in the

long term, especially given the excellent track record of repeat PVR procedures in most centers.

CONCLUSIONS

The past 70 years of surgically managing the RVOT has generated important advances in replacement technique and conduit materials. Progress will continue to be made in this field because the pulmonary valve remains the most common valve requiring replacement in children. However, many of the original challenges remain. Prospective, and ideally multicenter, studies are needed to comprehensively compare these diverse options for RVOT reconstruction throughout a patient's lifetime.

Conflict of Interest Statement

Teaching honoraria from CryoLife, Inc (Kennesaw, Ga) and Medtronic, Inc (Minneapolis, Minn).

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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