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# **Review**

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# Application of right ventricular to pulmonary valved conduit in the surgical treatment of congenital heart disease

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# Abstract

Pulmonary valve replacement and right ventricular outflow tract reconstruction with valved conduits have been the shortcomings of paediatric cardiac surgeons in the treatment of CHD. In recent decades, encouraging achievements have been made in right ventricular outflow tract technology. Since Klinner reported the first right ventricle-to-pulmonary artery connection using unvalved conduits made of autologous pericardium in 1964, various right ventricle-to-pulmonary artery conduits have gradually been used in the treatment of various complex CHD. Compared with other materials, valved homograft conduit (VHC) is more consistent with physiological characteristics, better haemodynamics, easy suture and good haemostasis, anti-calcification, anti-infection, and without the need for lifelong anticoagulation, which makes VHC the best material for reconstruction of right ventricular outflow tract. However, due to the shortage of donor sources, other alternative conduits such as polytetrafuoroethylene valved conduits have been developed, and the results are not inferior to VHC in clinical application. The emerging tissue engineering technology is expected to utilise recipient-derived endothelial cells for implantation onto the decellularized VHC or degradable synthetic materials in order to construct a recipientspecific tissue-engineered valved conduit. This advancement holds great potential as an ideal biological transplant material and valve replacement for CHD. It will completely solve the problems of immune rejection and the growth of the conduit that cannot adapt to the physical growth of children. This review provides a comprehensive review of the clinical indications for right ventricleto-pulmonary artery conduits application, optimal timing for surgery, current practices in utilising various types of external conduits, and considerations for re-replacement.

Valvular disease in infants and children presents numerous challenges for paediatric cardiac surgeons. The primary objective of surgical interventions is valve reconstruction, which involves utilising the patient's own tissue to restore the anatomy and physiology of the valve, thereby promoting growth and achieving superior long-term outcomes. When repair fails or is not feasible, valve replacement becomes imperative. Valve pathology, patient physiology, and the demands of growth and development are all interconnected factors that contribute to the complexity of valve replacement in neonates, infants, and children. Pulmonary valve is the most commonly replaced valve in patients with CHD. Right ventricular outflow tract reconstruction is necessary when there is no continuous or significant pulmonary stenosis or incomplete closure between the right ventricle and the pulmonary artery in patients with CHD. The first successful implantation of conduits for the treatment of CHD was documented by Klinner et al.<sup>[1](#page-6-0)</sup> in 1964 when they performed the initial right ventricle to PA conduit connection using an autologous pericardium unvalved conduit in a child with pulmonary atresia. The following year, Rastelli<sup>[2](#page-6-0)</sup> published a report by Mayo Clinic that the first commonly used conduit for heart reconstruction surgery was the allograft valved aorta implanted between the right ventricle and the pulmonary artery during tetralogy of Fallot combined with pulmonary atresia. Due to the patient's insufficient pericardium availability and the haemodynamic benefits associated with implanted valvular conduits, Ross and Somerville<sup>[3](#page-6-0)</sup> pioneered right ventricular outflow tract reconstruction utilising the allograft valved aorta in 1966. They treated pulmonary atresia with the allograft valved aorta and pulmonary artery, which gradually expanded to include tetralogy of Fallot, double outlet of the right ventricle, transposition of the great artery, single ventricle, persistent truncus arteriosus, and many other complex CHD. The limitations of treatment and preservation methods for allografts at that time, however, hindered their widespread application due to the potential risks of early calcification, degeneration, and blockage. In the 1970s and 1980s, porcine Dacron conduits were preferred due to their advantage of easier availability of xenogenic conduits in various calibres compared to valved homograft conduit (VHC). However, the occurrence of late obstructive complications, particularly the formation of new neointimal strip in Dacron conduits, resulted in the abandonment of artificial materials.<sup>[4](#page-6-0)</sup> From the mid-20th century to the late 1990s, cryopreserved VHC emerged as the preferred conduit for



reconstruction of right ventricular outflow tract. Since then, cryogenic liquid nitrogen preservation has been developed for the VHC and is widely considered the most effective method for preserving valvular cell activity. In the long history of right ventricular outflow tract reconstruction, there have been many valved conduits, including Dacron conduits with xenograft aortic valves, pericardial conduits with bovine pericardial stent valves or pig xenograft valves, VHC, valved bovine jugular vein conduits, xenograft conduits and polytetrafuoroethylene conduits, tissueengineered valved conduits, etc. Most of the previous reports on the use of external conduit for right ventricular outflow tract are articles, and the reviews are rare. In this article, we will review the main problems in the clinical indications for right ventricle-topulmonary artery conduits application, optimal timing for surgery, current practices in utilising various types of external conduits, and considerations for re-replacement.

## When to perform right ventricular outflow tract reconstructive operation

Right ventricular outflow tract dysfunction is defined as moderate right ventricular outflow tract obstruction and above  $(>$  = 40 mmHg) and/or pulmonary valve regurgitation is moderate or above. In addition to dysfunction, the current indication for intervention meets any of the following conditions<sup>[5](#page-6-0)-[7](#page-6-0)</sup>:

- 1. Fatigue symptoms, New York Heart Association functional class II and above.
- 2. The exercise test revealed reduced exercise capacity.
- 3. Significant right ventricular dilation ( $> 150$ mm/m<sup>2</sup>).
- 4. Right ventricular/left ventricular volume ratio > 1.5 in symptomatic patients;  $>$  = 2 in asymptomatic patients.
- 5. Regurgitation fraction measured by MRI > 35%。
- 6. Significant right ventricular dysfunction.
- 7. Atrial and/or ventricular arrhythmias
- 8. QRS wave duration > 180 ms.

## Types of external conduits

## Reconstruction of the right ventricular outflow tract utilising a single polytetrafuoroethylene valve or core-tex conduit with polytetrafuoroethylene valve

Historically, there have been two treatment options for tetralogy of Fallot with significant pulmonary annulus and/or valve dysplasia: (1) Transannular patch; (2) Implantation of a valved conduit. Transannular patch effectively alleviates right ventricular hypertension and facilitates proportional right ventricular growth in accordance with patient development. Reoperation for right ventricular outflow tract stenosis is infrequent. However, a drawback of this procedure is the potential occurrence of acute pulmonary valve insufficiency, which can abruptly shift the haemodynamics from an obstructed and pressure-loaded right ventricle to a volume-loaded right ventricle, resulting in transient or delayed right ventricular dysfunction. Chronic right ventricular capacity overload can cause advanced biventricular dysfunction and tricuspid valve insufficiency. The primary advantage of a valved conduit is the immediate availability of a well-functioning pulmonary valve. However, it is accompanied by the drawback of structural deterioration caused by calcification, shrinkage, and lack of growth, leading to both early and late valve dysfunction. Another promising approach involves the concept of single-valve

right ventricular outflow tract patch reconstruction. This technique allows for the implantation of a single valve in patients regardless of their size, with the valve tailored to fit the extended pattern of the right ventricular outflow tract transannular patch. Generally speaking, this method tends to have better longevity in infants compared to using a valved conduit. Single-valve right ventricular outflow tract patches can be constructed using autopericardium or bovine pericardium, allogeneic pulmonary valves, or polytetrafuoroethylene film. The construction process for either pericardial or PTEE single valves is straightforward, costeffective, and reproducible. The primary advantage of the 0.1 mm thick polytetrafuoroethylene single valve lies in its ability to maintain long-term mobility without any internal tissue growth. Recently, some two- or three-valved Core-Tex conduits have been utilised with satisfactory initial outcomes. Ravil Sharifulin et al.<sup>[8](#page-6-0)</sup> presented the results of right ventricular outflow tract reconstruction using polytetrafuoroethylene conduits in Ross operation. Between 2007 and 2015, 28 patients underwent right ventricular outflow tract reconstruction using polytetrafuoroethylene conduits. The mean age of the patients was  $35.9 \pm 18.1$ (range 4–58) years. The mean polytetrafuoroethylene conduit size was  $25.3 \pm 2.3$  mm. The early mortality rate was 3.6%. The mean follow-up duration was  $48.5 \pm 31.2$  months; there were no late deaths. The transprosthetic gradients increased significantly over time. The conduit size was the only independent predictor of peak right ventricular outflow tract gradient progression. None of the patients demonstrated significant right ventricular outflow tract regurgitation. One patient required an right ventricular outflow tract reoperation. The polytetrafuoroethylene conduit demonstrates acceptable haemodynamic results at the mid-term followup. The team at the Heart Center of the Pediatric Hospital of Fudan University also achieved encouraging clinical practice results. Their study included 46 patients aged 3–146 months who received implanted simplified hand-sewn trileaflet valved conduits: 31 patients (Group A) received 0.1 mm expanded polytetrafuoroethylene valved conduits and 15 patients (Group B) received autologous pericardium valved conduits. Follow-up outcomes up to 3 years after the surgeries were evaluated. After 6, 12, and 36 months, 95.2%, 88.9%, and 88.9% of Group A patients and 92.3%, 68.4%, and 42.7% of Group B patients were free from valved conduit dysfunction. All Group A patients had no conduit failure and 92.3%, 80.8%, and 80.8% of Group B patients were free from valved conduit failure. 0.1 mm expanded polytetrafuoroethylene novel simplified hand-sewn trileaflet valved conduits appear to be associated with a lower incidence of graft failure than autologous pericardium valved conduits.<sup>[9](#page-6-0)</sup> The polytetrafuoroethylene conduits are widely regarded as the optimal choice in many cardiac centres, second only to allograft valved conduits, owing to their straightforward construction, cost-effectiveness, easy accessibility, and favourable long-term haemodynamic outcomes. The expanded polytetrafuoroethylene conduit is shown in Figure [1.](#page-2-0)

## Valved homograft conduit

The use of VHC for right ventricular outflow tract reconstruction has a history of over 50 years. However, there are several challenges associated with its initial clinical application, including preservation and storage issues as well as the high risk of calcification, degeneration, and blockage.<sup>[10](#page-6-0)</sup> In 1987, O'Brien introduced the use of ultra-low temperature liquid nitrogen for VHC preservation. This technique effectively maintains the activity of valve cells and preserves the biomechanical parameters of VHC.<sup>[11](#page-6-0)</sup> Consequently,

<span id="page-2-0"></span>

Figure 1. A hand-sewn trilobed valved ePTFE conduit from our institution is shown.

it not only broadens the availability of VHC but also significantly enhances its durability in clinical applications.<sup>[12](#page-6-0)</sup> Currently, VHC remains the optimal material for right ventricular outflow tract reconstruction. Preserved at low temperatures, VHC offers advantages such as biological activity and tissue structure integrity, convenient application, favourable blood flow dynamics, easy suturing, effective haemostasis, anti-calcification, and anti-infection properties. Additionally, it ensures complete valve function with a prolonged lifespan while eliminating the need for anticoagulation.<sup>[13](#page-6-0)</sup> Post-transplantation, conduit patency is guaranteed to align closely with the anatomy of the right ventricular outflow tract. This anatomical and haemodynamic correction of cardiac malformations promotes cardiac function recovery without an increased risk of right-sided heart failure. Although complications like bacterial endocarditis-induced haemolysis are rare following implantation, there are limitations in terms of available materials. Claudia Oeser et al. $^{14}$  $^{14}$  $^{14}$  published their 25 years of experience in the long-term durability and function of pulmonary allografts for right ventricular outflow tract reconstruction in Ross surgery. Pulmonary homografts provide very satisfying long-term results after the Ross procedure. Freedom from homograft reintervention was 95.6%, 90.4%, and 87.5% at 10, 15, and 20 years, respectively. Differences in long-term performance are related to undersizing and young age. Similarly, Azahara Fernandez-Carbonell et al.<sup>[15](#page-6-0)</sup> also reported promising long-term follow-up results. At 1, 5, and 20 years, 89.4%, 74.6%, and 69% of these patients, respectively, were free from moderate-severe stenosis, and 99.3%, 95.7%, and 90.9%, respectively, had freedom from homograft reintervention. Pulmonary homografts implanted in the Ross procedure offer satisfactory long-term results, but the level of homograft dysfunction is not negligible. Young recipient and donor age were associated with a higher rate of homograft stenosis during follow-up. Moreover, homograft dysfunction usually occurred during the first few years of follow-up, which may have been related to immune responses.

According to previous literature reports,[16](#page-6-0)–[18](#page-6-0) the occurrence of VHC dysfunction may be associated with patient age, surgical technique, VHC implantation site, VHC diameter, and VHC

source (aorta or pulmonary artery). Younger patients have a higher risk of experiencing VHC dysfunction due to their ability to only accommodate smaller-diameter implants. This susceptibility increases with age and weight gain. Additionally, in young or low-body-weight patients, the implanted VHCs are often sourced from younger donors. The immunogenicity of these younger donor-derived VHCs may also impact long-term functionality.<sup>[19](#page-6-0)</sup> Most studies<sup>[19](#page-6-0)-[21](#page-7-0)</sup> have found that the long-term durability of VHC implanted in Ross surgery is superior to non-Ross surgery. Ross patients generally have normal right ventricular outflow tract and pulmonary artery anatomy and pulmonary vascular resistance, while non-Ross patients may have right ventricular outflow tract dysplasia, pulmonary artery branch stenosis, or increased pulmonary vascular resistance. This may result in the long-term durability of VHC in Ross group being better than that in non-Ross group[.22](#page-7-0) In addition, the long-term durability of VHC with in-situ implantation is generally better than that of VHC with ectopic implantation, because VHC with ectopic implantation is prone to sternal compression and blood turbulence in VHC, thus increasing the incidence of VHC dysfunction.<sup>23</sup> In most cardiac centres, allogeneic pulmonary arteries are preferred over allogeneic aortic arteries because they are less prone to dysfunction or calcifica-tion.<sup>10,19[,21](#page-7-0),[24](#page-7-0)</sup> The higher elastin content of the allograft aorta makes it more prone to early dense calcification and adhesion to adjacent structures, which poses a challenge for conduit removal during secondary surgery. The majority of studies<sup>[15,16](#page-6-0),[23](#page-7-0)</sup> suggest that a smaller conduit is associated with poorer long-term durability of VHC. The application of VHC in Ross procedure is shown in Figure [2.](#page-3-0)

## Allogeneic femoral vein duct

In many countries, due to cultural traditions and low organ donation, it is difficult to collect sufficient numbers of VHC with a diameter of 12–18 mm from young age donors. A workaround that can be easily implemented in any country is to take allogeneic femoral veins from an adult donor to avoid removing the heart and leave an incision that does not affect aesthetics. Commercially available cryopreserved adult femoral veins are 20–30 cm in length and 10–15 mm in diameter and usually have several valves with closing functions. As a right ventricle-to-pulmonary artery conduit in newborns and young infants, it is thin, strong, and non-bleeding, performing well.[25,26](#page-7-0)

# Valved bovine jugular vein conduit

The limitations of VHCs, particularly smaller ones, in terms of source and durability, support the utilisation of alternative materials for reconstructing the right ventricular outflow tract in patients with CHD. In 1999, Contegra valved bovine jugular vein conduit was developed as a substitute for VHC in right ventricular outflow tract reconstruction. Valved bovine jugular vein conduit is a buffered glutaraldehyde-fixed bovine neck vein segment (12–15 cm in length, 12–22 mm in diameter) that operates under low pressure. Early studies have shown that valved bovine jugular vein conduit exhibits favourable haemodynamics comparable to allogeneic conduits. Its advantages include its ability to be stocked in large quantities, natural continuity between the valve and conduit without requiring near-end extension, and implementation of anticalcification treatment. However, conflicting reports on the longterm performance of these conduits exist, with some describing early occurrences of severe distal anastomotic fibre formation and stenosis.<sup>27,28</sup>. Kenta Hirai et al.<sup>29</sup> compared right ventricular outflow tract reconstructions using valved bovine jugular vein conduit and

<span id="page-3-0"></span>

Figure 2. The VHC was used to reconstruct the right ventricular outflow tract during the Ross procedure.





expanded polytetrafuoroethylene conduits performed in a single institution. No significant difference in peak right ventricular outflow tract velocity  $(1.8 \pm 0.9 \text{ m/s}$  versus  $2.1 \pm 0.9 \text{ m/s}$ ,  $p = 0.27$ ), branch pulmonary stenosis ( $p = 0.50$ ), pulmonary regurgitation ( $p = 0.44$ ), and conduit infection or conduit replacement (20.0% versus 8.3%,  $p = 0.43$ ) were found between the valved bovine jugular vein conduit and expanded polytetrafuoroethylene conduit groups, respectively. Aneurysmal dilatation of the conduit was observed in 25.0% of the patients in the valved bovine jugular vein conduit conduit group but not in the expanded polytetrafuoroethylene conduit group ( $p = 0.011$ ). They suggest that expanded polytetrafuoroethylene conduits are appropriate for patients with risk factors of branch PS to prevent aneurysmal conduit dilatation. Hui-Feng Zhang et al.<sup>30</sup> reported the medium and long-term efficacy of valved bovine jugular vein conduit implantation in Chinese children. Fifty-three hospital patients implanted with valved bovine jugular vein conduit conduits from January 2002 to December 2013

were recruited. The proportion of patients who were free of valved bovine jugular vein conduit conduit failure at 1, 3, 5, and 7 years was 98.0, 85.8, 76.8, and 62.1%, respectively. There were nine cases of endocarditis (17.0%). Multivariate logistic regression analysis showed that endocarditis was a significant risk factor associated with valved bovine jugular vein conduit conduit failure. They found that the durability of valved bovine jugular vein conduit was suboptimal after a mid-term follow-up period. Endocarditis was found to be a significant risk factor that accelerates valved bovine jugular vein conduit deterioration. The valved bovine jugular vein conduit is shown in Figure 3.

## Dacron conduit

In the early 1970s, valved Dacron textile conduits were fabricated through glutaraldehyde treatment of pig valves.<sup>31,[32](#page-7-0)</sup> Unlike VHC, this approach offers significant logistical advantages and enables complete dimensional storage. However, reports of dissatisfaction with these conduits soon emerged. $33$  These conduits rapidly become dysfunctional in paediatric patients due to the formation of a false membrane on the low-porosity Dacron material and calcification of the glutaraldehyde-treated xenograft valve. Nevertheless, in older adolescents and young adults, the performance of these conduits is comparable to that of allogeneic ones.

## Xenovalves with and without scaffolds

The implantation of valved bovine jugular vein conduit is limited to patients under the age of 18 due to patent restrictions. The



Figure 4. A 5 mm unvalved conduit was used as the main pulmonary artery in a patient with pulmonary atresia in our institution.

optimal replacement valve for older children and adults remains a topic of debate. Relevant studies have demonstrated that there are no significant differences in postoperative data between groups receiving stencilled or unstenciled porcine aortic valves at right ventricle-to-pulmonary artery sites, including survival rate, resting pulmonary artery pressure difference during follow-up, re-treatment intervention, and valve removal rates, as well as incidence of valve dysfunction.

# Unvalved conduit

The unvalved right ventricle-to-pulmonary artery conduit is worth mentioning and is still in use in a few centres. Early results are satisfactory, but many patients develop late right ventriclular dilation within 10 years. However, Dearani and colleagues reported 126 cases of unvalved conduit and concluded that there was no difference in the loss of function between unvalved and valved conduit.<sup>[35](#page-7-0)</sup> At present, valvular duct is often used in the surgical treatment of CHD in the palliative care of pulmonary atresia with ventricular septal defect in Sano shunt, aiming at promoting the development of pulmonary vessels. As shown in Figure 4.

# Mechanical valves at the position of the pulmonary artery

A few centres have used mechanical valves for pulmonary valve replacement. As few cases have been reported, we do not discuss them too much. It is generally recommended to consider mechanical pulmonary valve replacement only in adult patients who have had mechanical valves implanted in other locations that also require warfarin.

# Tissue-engineered valved conduit

Vascular tissue engineering uses tissue engineering technology to implant living cells on vascular scaffolds to construct a biological blood vessel with strong biocompatibility with receptor block, nonimmunogenicity, certain growth vitality, good durability and plasticity, and other physical properties. This ideal blood vessel not only has the ability to self-repair, can maintain the long-term patency of the organ after transplantation but also has the ability to grow. Tissue-engineered valved conduits are promising for right ventricle-to-pulmonary artery reconstruction. Biodegradable biological skeletons have been built, and host cells are said to customise the skeleton, and in some cases, the skeleton will disappear in the future. The design of the skeleton is critical to current methods of constructing tissue-engineered blood vessels, and the skeleton must simultaneously provide the desired function and transfer stress to the new extracellular matrix. From the point of view of bioengineering, it is necessary to create a continuous tissue engineering relationship between cell underpinning and cell underpinning steps by cascading method. Gottlieb et al.<sup>[36](#page-7-0)</sup> confirmed that autologous tissue-engineered valved conduits functioned well when implanted, and then their morphology and function were examined by magnetic resonance imaging. The valve underwent structural and functional remodelling in vivo without stenosis, but regurgitation worsened after 6 weeks. Delving into the mechanisms of in vivo remodelling of connections is valuable for future reconstruction of heart valves.

It is worth noting that in 2020, Fujita et al. $37$  reported for the first time the application of in vivo tissue-engineered vascular graft instead of autologous pericardium in pulmonary artery reconstruction surgery. The researchers first transformed silicone drainage into tissue-engineered vascular mould and implanted it under the abdomen during the initial surgery. One case was a 1-year-old boy who underwent palliative right ventricular outflow tract dredge and implanted a mould. After 13 months, the tissue was removed and cut to repair pulmonary artery stenosis. Another 4-year-old boy had tissue-engineered grafts for repair of residual pulmonary artery stenosis 26 months after primary pulmonary artery replacement. Among them, the 1-year-old child was in good condition five years after surgery, and CT showed no stenosis or aneurysm formation at 40 months. The feasibility of in vivo tissue engineering for repairing pulmonary artery stenosis was preliminarily confirmed. The following year, the team added examples of in vivo tissue-engineered vascular grafts in patients with  $CHD<sub>38</sub>$  $CHD<sub>38</sub>$  $CHD<sub>38</sub>$ and performed in vivo grafts on a total of four children with pulmonary atresia with main collateral arteries or ventricular septal defects. After a follow-up of up to 4 years, the pulmonary arteriovenous pressure was relieved to varying degrees in all patients, and there was no pulmonary restenosis or dilatation. Therefore, the authors believe that in vivo tissue-engineered vascular graft is a promising alternative to autologous pericardium for children with CHD requiring staged surgery.

# **Discussion**

# Reasonable selection and reconstruction of VHC

Currently, the benefits of utilising ultra-cryopreserved VHC for reconstruction of the right ventricular outflow tract have been widely acknowledged by scholars. The compatibility between the donor's pulmonary artery and the recipient's pulmonary artery is advantageous for transplantation. The long-term efficacy of pulmonary allografts is better than that of aortic allografts, which is characterised by a lower incidence of long-term calcification, stenosis, or dysfunction. The main reason is that the contents of collagen fibres, elastin, and extracellular matrix in the pulmonary artery wall are much less than those in the aorta, and elastin is the deposition of calcium ions. The pressure gradient across the pulmonary homograft of the same radius was lower than the aortic

homograft. The branches can also be utilised for distal pulmonary artery reconstruction. However, due to the thin wall of the pulmonary homograft, its tensile resistance is inferior to that of the aortic homograft. Therefore, it is not suitable for implantation in high-pressure pulmonary circulation and severe pulmonary hypertension to prevent aneurysm formation. The minimum diameter of HVC, which is predominantly observed in adults, ranges from 18 to 20 mm, rendering it suitable solely for children aged three years and above. A retrospective analysis of 93 conduits  $\langle$  = 20 mm, implanted over 23 years, was performed by Katrien Francois et al.<sup>[39](#page-7-0)</sup> The conduits comprised 40 pulmonary homografts, 12 aortic homografts, 17 bicuspidalized homografts and 24 xenografts. Freedom from structural valve degeneration was  $79 \pm 5\%$  at 5 years and  $47 \pm 6\%$  at 10 years  $[68 \pm 8\%]$  for pulmonary homograft,  $42 \pm 16\%$  for bicuspidalized homograft,  $31 \pm 15$ % for aortic homograft, and  $20 \pm 9$ % for xenografts (p < 0.001)]. They demonstrated that a cryopreserved pulmonary homograft remains the most durable option for a right ventricleto-pulmonary artery conduit in neonates and young children who are inevitably at risk for valve failure. When a small-sized standard pulmonary homograft is unavailable, bicuspidalization appears preferable to the use of xenograft conduits. It offers freedom from structural valve degeneration and conduit explant that is noninferior to the standard pulmonary or aortic homograft at midterm follow-up, whereas xenografts are prone to early replacement for reasons other than pure tissue degeneration. In comparison with the currently available small xenograft conduits, bicuspidalized conduits have the additional advantage of excellent handling characteristics, minimal valve regurgitation under high pulmonary pressure, and resistance to endocarditis.

# Immune response after VHC transplantation

Although acute and hyperacute rejection rarely occurs, degeneration and calcification are present in the VHC. Most scholars believe that degeneration and calcification of the homograft have a direct and important relationship with immunity. It was also found that the degeneration after transplantation was related to the age of the recipients. The younger the age, the greater the risk of degeneration, which is related to the immune status of infants and young children, which is more likely to mediate inflammatory and immune responses. The activity of endothelial cells plays an important barrier role in the durability of human VHC and is also the most important immune tissue component. Cryopreservation in liquid nitrogen can significantly improve the viability of endothelial cells and the integrity of tissue structure, but the immunogenicity is also significantly enhanced. Therefore, it is better to make ABO blood group and human leukocyte antigen match first for transplantation of VHC, and a small dose of immunosuppressant can be tried. However, it is difficult to do this in practice because of the limited availability of materials. Decellularized pulmonary homografts has been applied in clinical practice to reduce the immune rejection of VHC. Five-year data from a prospective European multi-centre trial and 15-year registry data indicate decellularized pulmonary homografts as the potentially best current option for PVR. The combined decellularized pulmonary homografts cohort,  $n = 319$ , comprising both Trial and Registry data, showed significantly better freedom from explantation for decellularized pulmonary homografts 95.5% than cryopreserved homografts  $83.0\%$  (p < 0.001) and less structural valve degeneration at 10 years when matched to 319 cryopreserved homografts (CH) patients [decellularized pulmonary homografts

65.5% and cryopreserved homografts 47.3%,  $p = 0.11$ ].<sup>[40](#page-7-0)</sup> Samir Sarikouch et al.<sup>[41](#page-7-0)</sup> found mid-term outcomes of decellularized pulmonary homografts used for PVR confirm earlier results of reduced reoperation rates compared with the current gold standard cryopreserved homografts and valved bovine jugular vein conduit. At 10 years, the rate of freedom of explantation was 100% for decellularized pulmonary homografts, 84.2% for cryopreserved homografts ( $p = 0.01$ ), and 84.3% for valved bovine jugular vein conduit BJVC ( $p = 0.01$ ); the rate of freedom from explantation and peak trans-conduit gradient  $>$  = 50 mmHg was 86% for decellularized pulmonary homografts, 64% for CH, and 49% for valved bovine jugular vein conduit ( $p < 0.001$ ); the rate of freedom from infective endocarditis was 100% for decellularized pulmonary homografts,  $97.3 \pm 1.9\%$  within the matched cryopreserved homografts patients ( $p = 0.2$ ), and  $94.3 \pm 2.8\%$  for valved bovine jugular vein conduit patients ( $p = 0.06$ ). Decellularized pulmonary homografts valve annulus diameters converged towards normal Z-values throughout the observation period, in contrast to other valve prostheses. For future investigations, more data, especially on smaller grafts and recellularization conditions, are required, together with long-term performance monitoring, to conduct a more detailed evaluation.

#### Conduit dysfunction and re-replacement

The most frequent cause of HVC failure in paediatric patients is attributed to the child's physical growth exceeding the appropriate diameter of the conduit, resulting in longitudinal elongation and constriction. Extensive calcification may protrude into the lumen, causing stiffness and narrowing of the valves or even calcification itself. Additionally, compression by the sternum can occur at the proximal anastomosis. Conduit dysfunction mainly includes the following aspects.

## Conduit obstruction

Some signs, such as an increased right ventricular pulse, an increased or altered systolic ejection murmur in the territory of the conduit, and an increased right ventricular voltage on electrocardiography, are suggestive of obstruction. Increased venous pressure and hepatomegaly suggest obstruction, which is severe and has led to heart failure. Ultrasound, MRI, and CT can provide information about the conduit. Catheter angiography is the most important, it can determine the location and extent of obstruction, and the severity of each stenosis. When right ventricular hypertension occurs, if there is no serious obstruction of the conduit, it is necessary to measure and calculate the pulmonary artery resistance through cardiac catheterisation to determine whether the operation can be performed. In conclusion, when the right ventricular pressure rises to the level of systemic pressure due to severe obstruction, reoperation for catheter replacement is required.

## Valvular regurgitation

It is generally tolerated, but valve regurgitation greater than grade 3 and marked impairment of right ventricular function often indicate the need for valve replacement or valved conduit replacement.<sup>42</sup>

# Aneurysm or pseudoaneurysm

The aneurysm has the potential to rupture at any given moment, therefore prompt surgical intervention is imperative upon diagnosis.

## <span id="page-6-0"></span>Infective endocarditis

If there were vegetations on the valve or in the conduit, the patients were treated as infective endocarditis. If the patients still had bacteraemia or increased vegetation after reasonable antiinflammatory treatment, the vegetation or the whole conduit should be removed surgically.<sup>43</sup>

## Several key points to be noted during surgery

The external conduit occupies a large space in the thoracic cavity. If the length is not designed properly, the external conduit is often compressed when the chest is closed, especially in infants and young children. The location of the great vessels plays an important role in the placement of the extracardiac conduit. C-shaped extracardiac conduit is selected for L-type transposition of the great arteries, reverse C-shaped extracardiac conduit is selected for R-type transposition of the great arteries, and C or reverse C-shaped extracardiac conduit can be selected according to the relationship between the aorta and the right ventricle. In this way, distortion and sternal compression are not easy to occur, and satisfactory haemodynamic results can be obtained. The diameter of the external conduit should not increase with the increase of age, so the diameter of the conduit passage anastomosis in children should be as large as possible. The distal anastomosis should be sutured oblique, and the conduit should be stretched as straight as possible to increase the height of the semilunar valve. If the proximal conduit needs to be prolonged, the ventricular incision should be closed with pericardial patch to avoid valve deformation. The prevention of infection is the key to the success of surgery. The aseptic technique of material collection and preservation and the prevention of postoperative infection should be strengthened.

## Conclusion

With the development of cardiac surgery and other disciplines, many scholars have carried out a lot of research to explore the best way to improve the efficacy of VHC transplantation. Through strengthening the protection of VHC, improving the preservation method, using decellularization technology, using low dose immunosuppressant, and using ABO blood group and human leukocyte antigen matching to reduce the immune response after transplantation, the service life of VHC can be prolonged and better clinical efficacy can be achieved. With the development of genetic engineering technology, it is expected to induce immune tolerance and reduce immune response through molecular biology technology. The emerging tissue engineering technology is expected to utilise recipient-derived endothelial cells for implantation onto the decellularized VHC or degradable synthetic materials in order to construct a recipient-specific tissueengineered valved conduit. This advancement holds great potential as an ideal biological transplant material and valve replacement for CHD.

Data availability statement. All data are incorporated into the article, and the data underlying this article are available in the article.

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Author contribution. Zhangwei Wang: Conceptualisation; Data curation; Formal analysis; Investigation; Methodology; Software; Validation; Visualisation; Writing – original draft. Kai Ma: Writing – review & editing. Shoujun Li: Writing – review & editing.

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