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ORIGINAL ARTICLE / ÖZGÜN MAKALE

Bovine jugular vein conduit replacement after homograft degeneration in patients with tetralogy of Fallot: The results of re-redo cases

Fallot tetralojili hastalarda homogreft dejenerasyonu sonrası sığır juguler ven konduit replasmanı: Tekrarlı olgu sonuçları

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ABSTRACT

Background: This study aims to present our experience and results in terms of reconstruction with bovine jugular vein conduit in re-redo patients who developed severe homograft degeneration with pulmonary homograft valve replacement.

Methods: Between May 2018 and May 2021, a total of 10 re-redo patients (4 males, 6 females; mean age: 16.5±3.0 years; range, 12 to 21 years) who underwent bovine jugular vein conduit replacement due to homograft degeneration were retrospectively analyzed. The clinical, pre-, intra-, and postoperative data of the patients were recorded.

Results: The mean age of the second operation (homograft replacement) was 8.5±3.8 (range, 4 to 14) years in the patients who underwent homograft replacement. No postoperative mortality was observed. When the pre- and postoperative findings were compared, the right ventricular outflow tract gradient, the degree of pulmonary and tricuspid regurgitation, and right ventricular dilatation were regressed ($p<0.05$). A significant improvement in the New York Heart Association functional class was observed in all patients after surgery.

Conclusion: After tetralogy of Fallot corrective surgery, repetitive surgical interventions are inevitable due to pulmonary valve deterioration. Therefore, a bovine jugular vein conduit may be a good alternative for conduit preference after pulmonary homograft failure in re-redo cases.

Keywords: Homografts, reoperation, tetralogy of Fallot, xenograft.

ÖZ

Amaç: Bu çalışmada pulmoner homogreft kapak replasmanı ile şiddetli homogreft dejenerasyonu gelişen tekrarlı hastalarda sığır juguler ven kondüit rekonstrüksiyonuna ilişkin deneyimlerimiz ve sonuçlarımız sunuldu.

Çalışma planı: Mayıs 2018 - Mayıs 2021 tarihleri arasında, homogreft dejenerasyonu nedeniyle sığır juguler ven kondüit replasmanı yapılan toplam 10 tekrarlı hasta (4 erkek, 6 kadın; ort. yaş: 16.5±3.0 yıl; dağılım, 12-21 yıl) retrospektif olarak incelendi. Hastaların klinik, ameliyat öncesi, ameliyat sırası ve ameliyat sonrası verileri kaydedildi.

Bulgular: Homogreft replasmanı yapılan hastalarda ikinci ameliyatın (homograft replasmanı) ortalama yaşı 8.5±3.8 yıl (dağılım, 4-14) yıl idi. Ameliyat sonrası mortalite gözlenmedi. Ameliyat öncesi ve sonrası bulgular karşılaştırıldığında, sağ ventrikül çıkım yolu gradyanı, pulmoner ve triküspit yetmezlik derecesi ve sağ ventrikül dilatasyonunun gerilediği gözlendi ($p<0.05$). Ameliyat sonrasında tüm hastalarda New York Kalp Derneği fonksiyonel sınıfında anlamlı bir iyileşme gözlendi.

Sonuç: Fallot tetralojisi düzeltici cerrahi sonrası pulmoner kapak dejenerasyonu nedeniyle tekrarlayan cerrahi müdahaleler kaçınılmazdır. Bu nedenle, tekrarlı hastalarda sığır juguler ven kondüit, pulmoner homogreft yetmezliğinden sonra konduit tercihinde iyi bir alternatif olabilir.

Anahtar sözcükler: Homogreftler, yeniden ameliyat, Fallot tetralojisi, ksenogreft.

The most common cyanotic congenital cardiac anomaly is tetralogy of Fallot (TOF). It can be repaired with good results in many centers. Advances in interventions have led to the survival of over 95% into adulthood. However, the expected outcome of the transannular patch repair is pulmonary valve regurgitation.[1] It is thought that pulmonary regurgitation (PR) is well tolerated in TOF patients.[2]

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However, these patients must be kept in serial clinical evaluation, as right ventricular (RV) dilation/failure, tricuspid valve regurgitation, and malignant arrhythmias are not far from these patients.[3-6]

Although pulmonary valve replacement (PVR) is the preferred procedure, there is still controversy about which prosthesis to use. Homografts are the standard choice of some clinics; however, long-term outcomes have many drawbacks.[7-10] In the present study, we aimed to present our experience and results in terms of clinical evaluation, surgical procedure, and reconstruction with bovine jugular vein conduit (BJVC) in a specific group of patients who developed severe pulmonary homograft degeneration.

PATIENTS AND METHODS

This single-center, retrospective study was conducted at University of Health Sciences, Tepecik Training and Research Hospital, Department of Pediatric Cardiovascular Surgery between May 2018 and May 2021. Patients with a primary diagnosis of TOF were screened from the clinical database. Patients who developed pulmonary homograft dysfunction after homograft replacement were identified. Patients who underwent TOF correction surgery before and were re-operated in our clinic (n=93) were selected. Among these patients, patients who underwent BJVC replacement (n=44) were reviewed. Among the patients who underwent BJVC replacement, a specific group including 10 patients (4 males, 6 females; mean age: 16.5±3.0 years; range, 12 to 21 years) consisted of patients whose homograft was replaced with BJVC due to homograft degeneration. The first (transannular repair) and second operations (homograft replacement) of the patients in the selected group were performed in an external center. The patient's first and second surgery data in the external center were collected. Homograft information used in the second surgery was obtained. In addition, surgery records of homograft type (aortic or pulmonary) were obtained. Biocompatibility (ABO and Rh group compatibility) data of homografts could not be obtained. Hospital records, including computed tomography angiography (CTA) and echocardiography data, were retrospectively analyzed. Pre- and postoperative New York Heart Association (NYHA) functional class of the patients were determined. Intra- and postoperative data were noted.

Homograft and BJVC status was evaluated by two-dimensional, color flow, and continuous-wave Doppler transthoracic echocardiography (TTE). The degree of PR was mild when the diastolic flow just passed in the pulmonary valve, moderate when the diastolic flow started from the main pulmonary artery, and severe when the diastolic flow arose from the branch pulmonary arteries. Gradation was 0 (none-trivial), 1 (mild), 2 (moderate), and 3 (severe) for PR. Maximum velocities across the pulmonary homograft were recorded with continuous-wave Doppler echocardiography. Stenosis was defined as moderate when a mean gradient of 25 to 40 mmHg or peak gradient of 40 to 70 mmHg, and severe as the mean gradient of more than 40 mmHg or peak gradient of more than 70 mmHg. Gradation was 0 (none-trivial), 1 (mild), 2 (moderate), and 3 (severe) for PS. Pulmonary pressure half-time (PHT) was additionally calculated to confirm PR. The PR jet's echocardiographic continuous-wave Doppler profiles were used to calculate PHT. It is known that PHT of fewer than 100 msec is a good indicator of hemodynamically significant regurgitation. Right ventricular/left ventricular end-diastolic dimension ratio (RVEDD/LVEDD) was used in M-mode echocardiography to evaluate RV dilatation.

Established PVR indications were decreased exercise capacity, worsening of the patient's NYHA functional class, severe pulmonary stenosis, progressive tricuspid regurgitation associated with moderate-to-severe PR, and arrhythmia.[1-4] Therefore, all patients were evaluated for transcatheter PVR. Surgical PVR was decided for these patients due to excessive calcification, distortion, excessive enlargement, lack of a suitable landing site in the homograft RVOT region, and the presence of a lesion in the pulmonary arterial branches that could not be removed by balloon angioplasty.

Early mortality was defined as any death within the perioperative period and up to 30 days of surgery. The overall mortality was defined as all deaths from the time of operation to the most recent follow-up.

The RVOT, homograft calcification (Figure 1, 2), and structural degeneration were evaluated with multi-slice CTA. In addition, pulmonary bifurcation stenosis, right and left pulmonary artery stenosis or dilatation (Figure 2) were evaluated and recorded. Finally, risky adhesions in terms of re-sternotomy and mediastinal anatomy were evaluated in each patient by CT.

All patients were operated via re-sternotomy. Injuries and adverse events during dissection were recorded. Cardiopulmonary bypass was started with bi-caval venous cannulation and ascending aortic arterial cannulation. All procedures were done under cross-clamping, and the heart was arrested

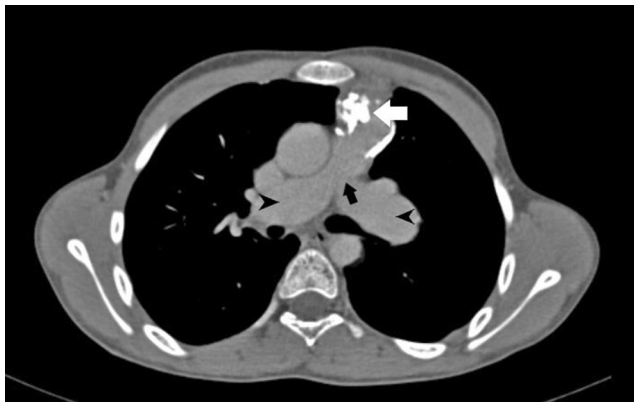

Figure 1. Pulmonary artery bifurcation stenosis (black arrow), post-stenotic dilatation (arrowhead) are seen in the right and left pulmonary arteries. In addition, extensive calcification (white arrow) is seen in the homograft.

with antegrade cold blood cardioplegia. Next, the left heart was vented via the right upper pulmonary vein. After meticulous dissection, the calcified homograft was completely excised (Figure 3).

Additionally, all previous Dacron®, pericardial, or other RVOT patches were excised. If there was any stenosis at pulmonary artery branches, this area was repaired with augmentation patch plasty (bovine pericardial patch, Edwards®, Irvine, CA, USA). The average pulmonary valve size was determined the BJVC for the patient's body surface area (Z-score). Oversizing was defined as a Z-score of 2.0 or higher, and oversizing was avoided. The BJVC was first anastomosed to pulmonary bifurcation and, then, to the RV outflow tract (RVOT) in an end-to-end fashion. In case of a need for an RVOT hood, BJVG self-tissue was used.

For anticoagulation, only antiaggregant dose acetylsalicylic acid was used. Patients with BJVC implantation had a mean follow-up of 24.7±9.5 (range, 15 to 49) months with a total of 247 patient months. In addition, all patients were examined with TTE in the pre- and postoperative periods.

Statistical analysis

Statistical analysis was performed using the SPSS version 18.0 software (SPSS Inc., Chicago, IL, USA).

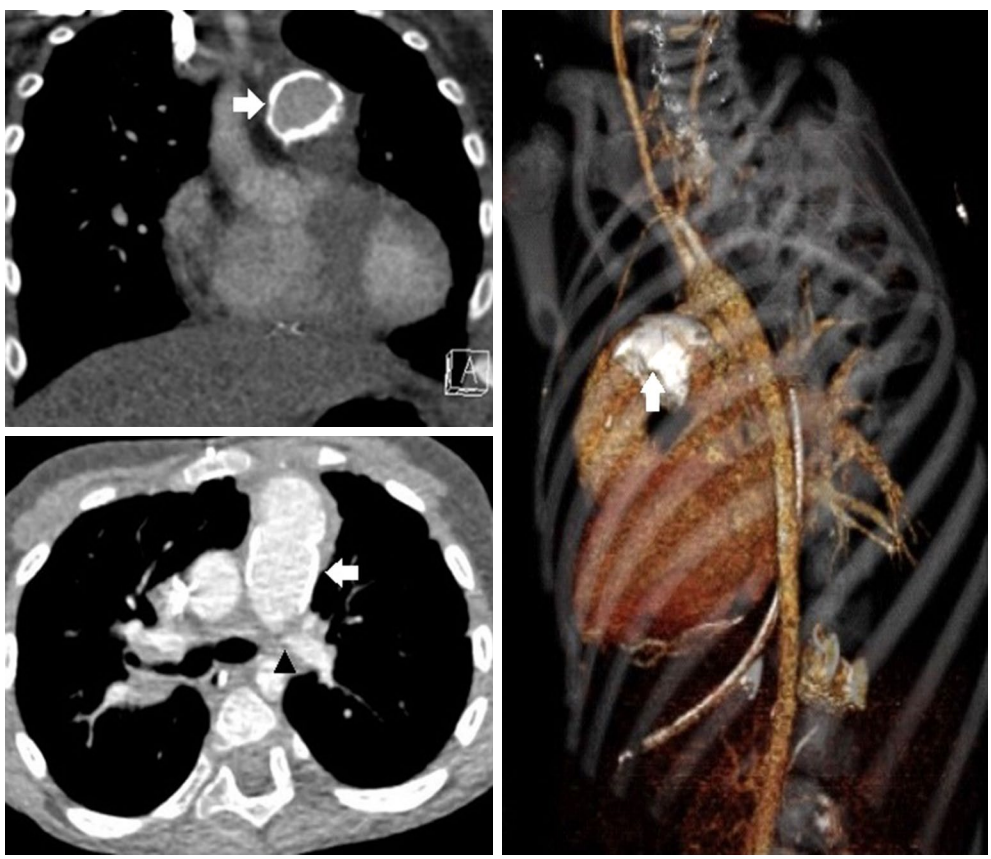

Figure 2. Calcified areas in the homograft (white arrow) are seen in the coronal and axial sections and in the three-dimensional reconstruction image on computed tomography.

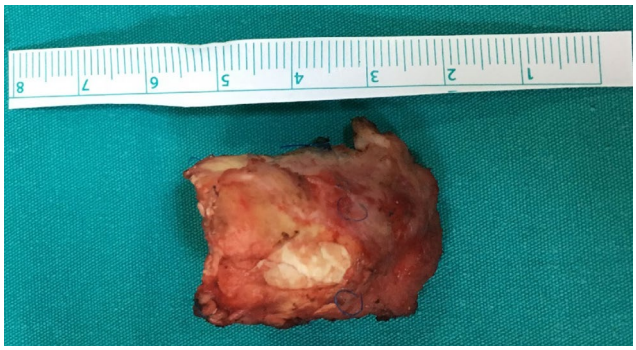

Figure 3. The appearance of the calcified aortic homograft removed from the patient.

Descriptive data were expressed in mean ± standard deviation (SD) or median (min-max) for continuous data and in number and frequency for categorical data. When evaluating the differences between patients' transthoracic echocardiography findings and NYHA class at the preoperative and final follow-up period, Wilcoxon signed ranks test was used. A two-sided *p* value of <0.05 was considered statistically significant.

RESULTS

Bovine jugular vein conduit implantation was performed after homograft excision due to homograft degeneration. The primary diagnosis of all of these patients was TOF, and their first operation was ventricular septal defect (VSD) closure and transannular patch repair. The second operation for all patients was homograft repair for PR. The Contegra® (Medtronic Inc., MN, USA) was used as an alternative graft after excision in all patients presenting with homograft degeneration in the third operation. The demographic data of the patients, previous operations, homograft characteristics, and RVOT pathologies at the time of admission to our clinic are presented in Table 1. The mean weight of the patients was 51.7±9.8 (range, 31 to 63) kg.

The mean age of the second operation (homograft replacement) was 8.5±3.8 (range, 4 to 14) years in patients who underwent homograft replacement. The replaced homografts were 25 mm in diameter in four patients, 27 mm in three patients, and 23 mm in three patients. In homograft replacement operation,

Table 1 Demographic data and patient characteristics

No	Sex	Age (year)	Weight (kg)	Age of first repair (year)	Age of homograft replacement (year)	Homograft type and size	Associated anomalies	Valvular pathologies		
								PR	PS	TR
1	F	21	60	3*	12	Pulmonary 19 mm	LPA stenosis	3	2	2
2	F	19	58	2*	14	Aortic 23 mm	Bifurcation stenosis	1	3	1
3	M	12	31	2*	5	Aortic 17 mm	LPA stenosis	1	3	2
4	F	18	63	6†	12	Aortic 21 mm	Homograft aneurysm	2	3	2
5	M	19	53	3*	12	Aortic 19 mm	Severe TR, RPA stenosis	2	3	3
6	M	17	55	5†	4	Pulmonary 21 mm	PA bifurcation stenosis	3	2	1
7	F	14	48	9†	5	Pulmonary 21 mm	Homograft aneurysm	3	2	2
8	F	13	41	1.5*	6	Aortic 17 mm	Homograft aneurysm	1	3	2
9	F	18	59	1*	10	Pulmonary 21 mm	PA bifurcation stenosis	3	2	2
10	M	14	49	6†	5	Pulmonary 17 mm	Homograft aneurysm	2	2	2

PR: Pulmonary regurgitation; PS: Pulmonary stenosis; TR: Tricuspid regurgitation; LPA: Left pulmonary artery; RPA: Right pulmonary artery; PA: Pulmonary artery; * Year; † Month.

five homografts used in the pulmonary position were aortic, and five were pulmonary homografts. The mean freedom from re-intervention time of patients using aortic homograft was 6.3±0.9 (range, 5 to 7) years, while it was 9.5±1.9 (range, 9 to 13) years in patients using pulmonary homografts. All homografts selected were oversized.

There was no type of adhesion barrier used in the previous surgery. No mortality was observed in the group of patients who underwent BJVC replacement. Therefore, no additional intervention was required during the follow-up period of the operated patients.

Accompanying cardiac anomalies in the patients are also shown in Table 1. Two patients had left pulmonary artery stenosis in the operated group, and one had right pulmonary artery stenosis. Simultaneous patch plasty with a xenograft pericardial patch was applied to these patients. Three patients had stenosis at the level of the pulmonary artery bifurcation. In these three patients, post-stenotic dilatation (Z-score >+3) occurred in the right or left pulmonary artery branches. In patients with pulmonary artery bifurcation stenosis, the BJVC distal tissue was anastomosed with a diamond shape, and the stenosis was relieved. Homograft aneurysm (homograft diameter >40 mm) was detected in four patients. Seven patients operated on homograft dysfunction had mild-to-moderate tricuspid regurgitation, while one had severe tricuspid regurgitation. This patient also underwent simultaneous De Vega annuloplasty.

Intra- and postoperative data are presented in Table 2. The mean total duration of surgery was 174.4±54 min, while the mean duration of dissection was 44.5±10 min.

Adverse events and injuries during dissection were observed in seven patients; the patient who injured innominate vein during mediastinal dissection was performed by femoral cannulation. The innominate vein was repaired uneventfully. In addition, junctional ectopic tachycardia (JET) and pleural effusion developed in two patients during the postoperative intensive care unit. Junctional ectopic tachycardia was treated with a combination of moderate hypothermia and intravenous amiodarone. The patient with pleural effusion was treated by inserting a chest tube.

Pre- and postoperative TTE findings and NYHA class are shown in Table 3. The latest TTE was performed at a mean of 24.7±9.5 (range, 15 to 49) months. In all patients, the RVOT gradient was <20 mmHg postoperatively, and no PR was observed. During the follow-up period, a significant decrease in the RVEDD/LVEDD was observed in all patients. In addition, the degree of tricuspid regurgitation decreased. The NYHA class improved in all patients.

Table 2. Intra- and postoperative data

	n	Mean±SD
Intraoperative data		
Dissection duration (min)		44.5±1
Aortic clamping duration (min)		49.7±1
CPB duration (min)		80.7±4
Total surgery duration (min)		174.4±5
Injuries during dissection		
Right ventricle	2	
Right atrium	3	
Innominate vein	1	
Adverse events during dissection		
Bradycardia	1	
Ventricular extrasystole	3	
Desaturation	2	
Emergency femoral cannulation	1	
Postoperative data		
Amount of drainage (mL/kg)		5.9±1.0
Amount of blood used (mL/kg)		9.1±0.5
Inotropic score after surgery (VIS)		8.2±3.1
Extubation time (h)		4.3±3.4
ICU stay (day)		3.3±2.2
Duration of discharge (day)		9.9±5.4
Postoperative adverse events		
Junctional ectopic tachycardia	1	
Pleural effusion	1	

SD: Standard deviation; CPB: Cardiopulmonary bypass; ICU; Intensive care unit; VIS: Vasoactive inotropic score.

DISCUSSION

In the follow-up after TOF surgery, pulmonary valve dysfunction, pulmonary insufficiency, pulmonary stenosis, or both, particularly during the adulthood, are still severe problems in the post-RVOT reconstruction period. Pulmonary regurgitation during follow-up is well tolerated, particularly in patients with transannular repair of TOF.[2-5] However, RV dilatation may develop over the years due to RV volume overload. After RV dilatation, RV failure and tricuspid regurgitation may occur. This process carries the risk of QRS prolongation, arrhythmias, and sudden cardiac death.[3-5] Re-intervention is required to correct this pathology, and PVR is the gold-standard treatment modality.

A wide variety of materials have been utilized for PVR. Homografts are the most commonly used

Table 3. Preoperative and final follow-up transthoracic echocardiography findings and NYHA class

No	RVOT max gradient (mmHg) Before > After	PR grade (0-3) Before > After	TR grade (0-3) Before > After	Pressure half time (ms) Before > After	RVEDD/LVEDD (M mode) Before > After	NYHA Class Before/After	Postop follow-up (months)
1	60>12	3>0	2>0	96>290	1.13>0.75	3 /1	49
2	89>17	1>0	1>0	220>300	0.96>0.76	2/1	29
3	95>11	1>0	2>1	255>290	0.93>0.68	3/1	24
4	91>9	2>0	2>1	185>295	1.21>0.88	3/1	22
5	106>10	3>0	3>1	79>280	1.16>0.72	3/1	26
6	57>8	3>0	1>0	85>280	1.23>0.84	2/1	15
7	50>7	3>0	2>0	82>276	1.21>0.74	3/1	21
8	98>9	1>0	2>1	243>295	1.04>0.69	2/1	19
9	65>12	2>0	2>1	190>300	1.11>0.81	3/1	24
10	60>11	3>0	2>0	89>280	1.02>0.73	3/1	18
P value	0.01	0.02	0.04	0.03	0.01	0.02	-

NYHA: New York Heart Association; RVOT: Right ventricular outflow tract; PR: Pulmonary valve regurgitation grade; TR: Tricuspid regurgitation; RVEDD: Right ventricle end-diastolic diameter; LVEDD: Left ventricle end-diastolic diameter.

conduits. Other materials include bioprosthetic or mechanical valves, Dacron® conduits, and BJVC (Contegra®). Several factors affect the choice of any of these valved conduits, such as the patient's age, the original pathology, previous procedure/conduit used, and availability.[10-13]

Traditionally, cryopreserved homografts, particularly pulmonary homografts, have been considered the first-choice valved conduit for RVOT reconstruction.[11,13-16] Freedom from reintervention rates in the literature ranges widely, from 30 to over 80% at 10 years.[10,12-14,16] However, despite the excellent hemodynamic conditions provided by homografts, the number of patients requiring surgery is increasing due to the rate of structural degeneration.[10,12] In addition, there is no clear standardization among the centers where homografts are obtained. While homografts obtained from some centers may give excellent results, homograft results prepared in a different center may be disappointing. It is not always possible to obtain an appropriately sized pulmonary homograft. The availability of pulmonary homografts, tiny sizes (10 to 18 mm), is insufficient.[7] The other downsides include the limited shelf life of each homograft (approximately two years), calcifications, and high cost.[13-15] The use of aortic homografts in the pulmonary position, residual branch pulmonary artery stenosis, ABO and Rho-mismatch, and elevated pulmonary artery pressures increase the risk of conduit failure.[12,16] In addition, aortic homografts have poor durability in the pulmonary position and are more prone to calcification. In particular, the calcification rate in aortic homografts is higher due to the high elastin tissue content in the aortic conduit wall.[16,17]

The most commonly used xenograft conduits include bovine jugular vein grafts. The BJVC has a natural trileaflet valve stored in diluted and buffered glutaraldehyde solution. Buffering the conduit retains leaflets and compliance and provides a non-antigenic structure.[7,9] Previous studies have demonstrated that xenografts can be an alternative to homografts in left ventricular outflow tract (LVOT) repair in terms of both early hemodynamic performance and ease of implantation.[7,9,11-16] Promising early results have been reported with the use of BJVC in LVOT reconstruction. No dilatation or severe calcification has been described after the utilization of the Contegra® conduit.[12,16,18]

Advantages of xenograft conduits include abundant supply, availability of small conduits for neonatal implantation, excellent handling characteristics, and low cost. Freedom from reintervention rates reported in the literature range from 66% at three years to 90% at seven years.[13-16,18] Several studies have demonstrated similar freedom from reintervention between BJVC and homografts.[7-10,12] In addition, the BJVC is very surgeon-friendly and needs no additional material to facilitate connection to the RV. Also, there is a significant difference between BJVC and homograft cost. The price of the Contegra® BJVC to our hospital is $4,000, and the average price of a pulmonary homograft (CryoLife/LifeNet) is $6,900.[7]

The patients we included in the study needed pulmonary homograft replacement as the second intervention after the first corrective surgery for TOF and the third intervention after pulmonary homograft degeneration. During mediastinal dissection, we observed extensive calcification in all patients. In addition, patients had tissue fragility due to redo surgical intervention. We believe that BJVC is the prosthesis that provides an excellent hemostatic solution in this group of patients undergoing surgery for the third time with a high bleeding incidence. As the graft structure is flexible and has excellent suturability, it provides good sealing in suture transition areas, particularly in the anastomosis lines.

Complete excision of the pulmonary homograft as a block must be necessary for patients undergoing pulmonary homograft excision. If residual homograft tissue remains in RVOT, it is predicted that the immunological process that causes calcification would continue. Therefore, Contegra® is a good option for reconstruction after complete excision. As this graft naturally has a three-valve central valve, a wide channel length proximal and distal to the valve allows for unique adaptation options. In particular, during the reconstruction of the proximal anastomosis region, using different grafts (xenograft pericardial graft, hemashield patch, or other materials) may cause the formation of additional suture lines. As a result, it may disrupt the laminar flow.[7,10] However, the channel length of the Contegra® enables graft implantation without any additional patch material.[7]

The most optimal conduit for PVR has yet to be discovered, and these patients would experience one or more pulmonary valve interventions during their lifetime. Nevertheless, conduits with biological pulmonary valves are future substrates for transcatheter valve placement, and the minimum landing zone for percutaneous PVR is 16 mm.[19] Therefore, we preferred BJVC with diameters of 16 mm and above in all patients we operated. In addition, in case of possible pulmonary valve degeneration that may develop in the long-term in patients, there may be a chance for percutaneous intervention.

According to our early and mid-term results, RV dilatation regressed, and tricuspid regurgitation was significantly decreased in all patients. Furthermore, we observed a significant decrease in pulmonary gradient after Contegra® implantation and no PR in any patient. In addition, there was a significant increase in the functional capacity of all patients. Our results show a significant increase in the quality of life of patients after PVR, and RV dilatation is reversible. These results have been also demonstrated in many previous studies.[8,12,20-22]

Nonetheless, there are some limitations to our study. This study was designed retrospectively in a single-center, and our sample size is relatively small. The reason why our study group is small is that it is a quite specific patient group. Therefore, further large-scale, prospective, randomized-controlled studies are needed.

In conclusion, after tetralogy of Fallot corrective surgery, repetitive surgical interventions are inevitable due to pulmonary valve deterioration. Bovine jugular vein conduit is a good alternative for selecting conduits after pulmonary homograft failure with extensive calcification. Considering its structure to ensure complete canal integrity and good hemodynamic results, we believe that it can be used safely, particularly after total homograft excision, in proximal and distal anastomosis regions. In addition, bovine jugular vein conduit offers a natural alternative in conduit failure for re-redo cases due to its easier accessibility, a more comprehensive range of sizes, and low cost.

Ethics Committee Approval: The study protocol was approved by the University of Health Sciences Tepecik Training and Research Hospital Clinical Research Ethics Committee (date: 16.08.2021, no: 2021/08-06). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from the parents and/or legal guardians of the patients.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Conceived and designed the analysis, wrote the paper: O.I.; Contributed data or analysis tools: M.A.; performed the analysis; Collected the data, wrote the paper: İ.M.; All authors read and approved the final version of the manuscript.

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