High incidence of late infective endocarditis in bovine jugular vein valved conduits

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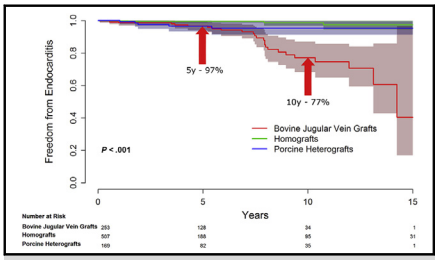
ABSTRACT

Background: Bovine jugular vein (BJV) grafts (Medtronic, Inc, Minneapolis, Minn) are used to restore right ventricle-to-pulmonary artery continuity. Recent studies have associated these grafts with the development of infective endocarditis. The purpose of this study was to report the incidence of endocarditis in BJV grafts.

Methods: All BJV grafts placed in the right ventricle-to-pulmonary artery position between 2001 and 2017 at our institution were included. Freedom from endocarditis was analyzed using the Kaplan–Meier method and parametric survival regression models.

Results: Overall, 228 patients underwent placement of 253 BJV grafts. The median duration of conduit follow-up was 6 years (5 months to 14 years). Twenty-five conduits developed endocarditis, yielding an incidence of 10% at a median of 7.5 years after surgery. Median duration of symptoms before the diagnosis of endocarditis was 21 days (3-180 days). The most common infectious agents were viridans streptococci (n = 13; 52%). Freedom from endocarditis at 5 and 10 years was 97% and 77%, respectively. After controlling for confounders, BJV grafts had a higher incidence of endocarditis compared with homografts ($P < .001$). Twenty-three (92%) of the conduits that developed endocarditis were managed surgically, with no mortality.

Conclusions: The incidence of late endocarditis affecting BJV is high. Increased surveillance and a high index of suspicion for endocarditis are warranted in patients who have undergone implantation of BJV grafts, especially if the graft has been in place for more than 7 years. When infective endocarditis has been diagnosed in these grafts, surgical replacement is recommended, with excellent outcomes. (J Thorac Cardiovasc Surg 2018;156:728-34)



Kaplan–Meier curves depicting freedom from endocarditis according to conduit type.

Central Message

Bovine jugular vein grafts used to restore right ventricle-to-pulmonary artery continuity were shown to have a 10% incidence of endocarditis at a median of 7.5 years after surgery.

Perspective

Bovine jugular vein grafts are routinely used to restore right ventricle-to-pulmonary artery continuity. In this article we report on a long-term follow-up of 253 bovine jugular vein grafts. We encountered a 10% incidence of endocarditis at a median of 7.5 years after surgery. Freedom from endocarditis at 10 years was only 77%. This high incidence of late endocarditis is concerning and warrants intervention.

See Editorial Commentary page 735.

A large spectrum of congenital heart conditions require reconstruction of the right ventricle-to-pulmonary artery (RV-PA) continuity, which is usually achieved with the use of valved conduits. The question of the ideal RV-PA conduit has been extensively investigated, and needless to say a perfect RV-PA conduit does not exist.[1]

In 1999, the Contegra bovine jugular vein (BJV) graft (Medtronic, Inc, Minneapolis, Minn) was proposed for right ventricular outflow tract reconstruction. The Contegra conduit is a glutaraldehyde fixed heterologous BJV graft, containing a naturally integrated trileaflet valve and natural sinus slightly larger in diameter than its lumen. Its preparation includes a final sterilization step, performed using a

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This work was supported by departmental funding.

Received for publication July 5, 2017; revisions received March 6, 2018; accepted for publication March 7, 2018; available ahead of print May 9, 2018.

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0022-5223/$36.00

https://doi.org/10.1016/j.jtcvs.2018.03.156

Scanning this QR code will take you to a supplemental video, figure, and table for the article.

Abbreviations and Acronyms
BJV = bovine jugular vein
RV-PA = right ventricle-to-pulmonary artery

proprietary sterilant that contains 1% glutaraldehyde and 20% isopropyl alcohol, in which the conduit is preserved and packaged until use. The Contegra is available in sizes between 12 and 22 mm. Because of its encouraging initial results in clinical trials, it quickly gained popularity as a possible alternative to the homograft.[2-4] Several studies have reported an unexpected occurrence of graft failure,[5,6] whereas others have reported similar or even better behavior compared with homografts.[7,8]

In 2016 we published our experience with implantation of 792 valved conduits in the RV-PA position, among which 245 were BJV grafts. Despite finding that BJVs were associated with a lower risk for reintervention ($P < .0001$) and replacement ($P = .0002$) than homografts, 14 BJV graft conduits developed endocarditis at a median of 7.5 years (34 days to 10 years) after surgery. After adjusting for other variables, the use of BJVs was found to be the sole significant risk factor associated with endocarditis and it was associated with a 9 times greater risk of endocarditis compared with homografts.[9]

Over the past 3 years we have encountered a concerning increasing incidence of late endocarditis in patients with BJV grafts. This concern has been raised by recent series as well.[10-13] Accordingly, the goal of this study was to evaluate the incidence of late endocarditis in patients who underwent placement of bovine jugular vein grafts in the RV-PA position.

METHODS

The study cohort included all patients who underwent surgical placement of a BJV graft at Texas Children's Hospital between 2001 and 2017. The study was approved by Baylor College of Medicine's institutional review board (date and number of approval: September 2, 2016, H-15017), and informed consent was waived. All demographic and clinical data were retrospectively collected via review of all medical records, operative reports, procedure notes, discharge notes, and clinic notes. Follow-up was obtained through a combination of clinic notes and telephone interviews of patients, families, and referring physicians. Perioperative mortality was defined as death within 30 days after surgery or before hospital discharge.

For a subanalysis of data, comparing the risk of endocarditis between conduits, homografts (pulmonary and aortic), and porcine heterograft (Hancock bioprosthetic valved conduit; Medtronic, Inc) were also included. All homografts were cryopreserved and provided by LifeNet (Virginia Beach, Va), CryoLife (Kennesaw, Ga), or RTI/Alabama Tissue Bank (Birmingham, Ala).

Valved conduits arising from a morphological left ventricle in the setting of congenitally corrected transposition of the great arteries were included in the study. The cohort was divided into the following diagnostic groups: pulmonary atresia with ventricular septal defect with or without major aortopulmonary collaterals, truncus arteriosus, Ross procedure, and other (ie, history of nonconduit tetralogy of Fallot repair, absent pulmonary valve syndrome, pulmonary atresia with intact ventricular septum, double-outlet right ventricle, and transposition of the great arteries with pulmonary stenosis or atresia). Endocarditis was defined as possible or definitive on the basis of the modified Duke criteria.[14] Pathologic diagnosis was defined as a positive culture from a vegetation or histopathology consistent with infective endocarditis.

Data Analysis

All analyses were performed for each conduit rather than for each patient. Descriptive analyses were performed for the entire cohort. Data are described as percentages and medians with ranges, as appropriate. Univariate analyses for freedom from endocarditis were performed using the Kaplan–Meier method and log rank test. The event endocarditis was registered when the diagnosis of endocarditis was made. For analysis of freedom from endocarditis, noninfected conduits were censored at the time of surgical replacement or placement of a transcatheter pulmonary valve. For patients who died, conduits were censored at the time of death.

To assess risk factors for endocarditis, parametric survival analysis models were created. Variables included were age, conduit size, diagnosis, genetic syndromes, and the conduit type (BJV grafts, homografts, and porcine heterografts). Because the analysis was done according to conduit rather than according to patients, events were modeled as repeated occurrences by including a variable of conduit placement versus replacement in the models. Results are reported as coefficients with standard errors and corresponding hazard ratios with 95% confidence intervals. A P value <.05 was considered statistically significant. All analyses were carried out using SAS for Windows version 9.4 (SAS Institute Inc, Cary, NC).

RESULTS

A total of 228 patients underwent placement of 253 BJV grafts (Table 1); 203 and 25 patients had 1 and 2 BJV grafts,

TABLE 1. Characteristics of patients who underwent conduit implantation

Variable	Bovine jugular graft (n = 253)
Male sex, n (%)	137 (54)
Syndrome, n (%)	66 (26)
Median weight (range), kg	12 (2-77)
Median age (range)	2 y (15 d to 45 y)
Age groups, n (%)	
Neonates and infants	67 (26)
1 to 4 years old	101 (40)
5 to 9 years old	37 (15)
10 to 18 years old	42 (17)
Older than 18 y	6 (2)
Diagnosis, n (%)	
PA/VSD	92 (36)
Truncus	67 (27)
Ross procedure	17 (7)
Other*	77 (30)
Conduit sequence, n (%)	
Primary placement	131 (52)
Replacement	122 (48)
Median conduit size, mm (range)	16 (12-22)

PA/VSD, Pulmonary atresia with ventricular septal defect. *Includes history of nonconduit tetralogy of Fallot repair, transposition of the great arteries with pulmonary stenosis or pulmonary atresia, absent pulmonary valve syndrome, pulmonary atresia with intact ventricular septum, and double-outlet right ventricle.

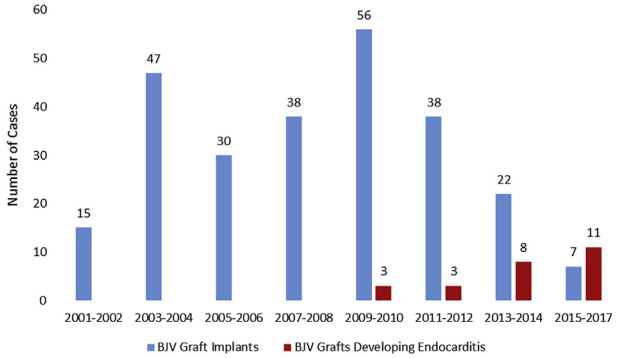


FIGURE 1. Implantation and development of endocarditis of bovine jugular vein (*BJV*) grafts over time.

respectively. The median age at conduit placement was 4 years (range, 3 days to 54 years). The number of conduits implanted increased from 2001 to 2010, after which they gradually began to decrease (Figure 1). Among the 228 patients, 62 (27%) had an identified genetic syndrome or chromosomal abnormality. During a median 6.5 years (range, 3 days to 16 years) of follow-up, 6 (2.6%) of 228 patients died, including 2 (0.9%) perioperative deaths, none of which were related to infective endocarditis. The summary of the deceased patients is shown in Table 2. A total of 131 (52%) primary conduit placements and 122 (48%) conduit replacements were performed. From the 122 conduit replacements, 44 were referred to our center after conduit placement at other institutions and 78 were performed after a previous conduit implantation at our center including: 53 homografts, 24 BJV conduits, and 1 porcine heterograft. The median duration of conduit follow-up was 6 years (range, 3 days to 14 years).

Endocarditis

During the follow-up period, 25 BJV grafts developed endocarditis at a median of 7.5 years (range, 34 days to 14 years) after surgery. Of the 25 patients who developed endocarditis, only 1 (4%) patient had a dental procedure within the month before diagnosis. Median age at endocarditis was 13 (range, 1-21) years and 11 (44%) were female. Patients exhibited clinical symptoms for a median duration of 21 days (range, 3-180 days) before the diagnosis of endocarditis was made. Four patients (16%) were asymptomatic at the time of presentation, whereas 2 (8%) presented in shock, the 19 remaining patients (76%) had nonspecific symptoms such as low-grade fever or malaise. Endocardial involvement was present in 20 patients (80%), 18 (72%) had vegetations on echocardiography, 4 (16%) had emboli, and 4 (16%) had vascular phenomena. No patient presented with immunologic phenomena (Table E1).

Endocarditis was classified as definitive in 22 (88%) and possible in 3 (12%) according to Duke modified criteria for infective endocarditis.[14] Blood cultures were positive in 22 patients (88%) with infected conduits. The most common infectious agents were viridans streptococci (n = 13; 59%). Other pathogens included methicillin-sensitive *Staphylococcus aureus* (n = 3, 14%), *Haemophilus parainfluenzae* (n = 2; 9%), methicillin-resistant *S aureus* (n = 1; 4.5%), *Granulicatella adiacens* (n = 1; 4.5%), *Cardiobacterium hominis* (n = 1; 4.5%), and *Aggregatibacter actinomycetemcomitans* (n = 1; 4.5%). A pathologic diagnosis was made in 13 patients (52%) with infected BJV grafts. In the remaining 10 conduits without pathologic diagnosis, a pathologic report was not available in 7 and signs of chronic inflammation and calcification were found in 3.

The overall incidence of endocarditis among BJV grafts was 10% at a median follow-up of 7.5 years, compared with 0.8% (4 of 507) of the homografts and 2.9% (5 of 169) of the porcine heterografts, and it increased over time after 2010 (Figure 1). Five- and 10-year freedom from endocarditis rates among BJV grafts was 97%, and 77%, respectively, significantly different from that of homografts (Figure 2). After multivariable analysis, BJV grafts remained the only risk factor for developing endocarditis, with a hazard ratio of 15.7 (95% confidence interval, 4.9-50.7; Table 3 and Figure E1).

The management of endocarditis was surgical in 23 (92%) cases, and medical in 2 (8%). Two patients who were managed medically exclusively with antibiotics had complete resolution of symptoms. Of the 23 surgically replaced infected conduits, 19 (83%) were replaced with homografts, 3 (13%) with BJV grafts, and 1 (4%) with a porcine heterograft. Median duration of antibiotic therapy was 6 weeks (range, 4-11 weeks) for the 25 conduits that developed endocarditis. After endocarditis, there were no mortalities or recurrence of endocarditis at a median of 2 years (range, 1 month to 7 years), independent of treatment strategy.

Replacement

A total of 76 (30%) BJV grafts required surgical replacement (n = 63; 83%) or transcatheter pulmonary valve implantation (n = 13; 17%). Of those conduits that required replacement, 12 (19%) were replaced with porcine heterografts, 25 (40%) with homografts, 24 (38%) with BJV grafts, and 2 (3%) with other types of conduit. Five- and 10-year freedom from replacement rates were 84% and 49%, respectively. During the study period, 7 of the conduits had stents placed at a median of 3.3 years (range, 4 months to 9 years) after implantation, 2 of these conduits later developed endocarditis at 3 and 9 years, respectively, after stenting.

DISCUSSION

This study represents one of the largest single-institutional experiences with the use of BJV graft conduits for right ventricular outflow tract reconstruction. The main

TABLE 2. Summary of mortalities

Patient	Age at surgery	Diagnosis	Syndrome	Associated comorbidities	Previous surgery	Surgery	Time to death*	Cause of death
1	10 y	CAVC, ToF	Trisomy 21	Chronic renal failure	Waterston shunt	ToF-CAVC repair with PA reconstruction	1.4 y	Septic shock due to peritonitis
2	17 d	Truncus arteriosus	–	Anomalous LCA with IM course, CHF	–	Rastelli and aortic valvuloplasty and LCA reimplantation	34 d†	Myocardial ischemia
3	11 mo	L-TGA, VSD, PS	–	Extensive intrapulmonary AVMs	BDG	Hemi Mustard and Rastelli	1 d†	Heart failure
4	8 mo	ToF-PA	Trisomy 21	Anomalous LAD artery arising from RCA, pulmonary hypertension	–	Rastelli and PA reconstruction and ECMO	9 d	Heart failure
5	10 mo	ToF-PA	–	–	BT Shunt	Rastelli and PA reconstruction	1.3 y	Pneumonia
6	1 y	ToF-PA	CHARGE	Tracheostomy, G-tube dependency, bilateral cleft lip/palate	BT Shunt	Rastelli and PA reconstruction	6 mo	Septic shock due to NEC

CAVC, Complete atrioventricular canal; *ToF*, tetralogy of Fallot; *PA*, pulmonary artery; *LCA*, left coronary artery; *IM*, intramural; *CHF*, congestive heart failure; *L-TGA*, congenitally corrected transposition of the great arteries; *VSD*, ventricular septal defect; *PS*, pulmonary stenosis; *BDG*, bidirectional Glenn; *AVMs*, arteriovenous malformations; *ToF-PA*, tetralogy of Fallot with pulmonary atresia; *LAD*, left anterior descending; *RCA*, right coronary artery; *ECMO*, extracorporeal membrane oxygenation; *BT*, Blalock-Taussig; *NEC*, necrotizing enterocolitis; *CHARGE*, coloboma, heart defects, atresia choanae, growth retardation, genital abnormalities, and ear abnormalities; *G-tube*, gastrostomy tube. *After surgical intervention. †Perioperative death.

finding of this study was an alarming 10% incidence of late endocarditis affecting BJV grafts (Video 1).

Because of its availability, easy manipulation in the operating room, and wide range of sizes, the BJV graft has gained popularity as an alternative option to homografts for the treatment of congenital heart defects, and valvular heart disease.[4,15] Another potential advantage of this conduit is its longer durability, although this finding still

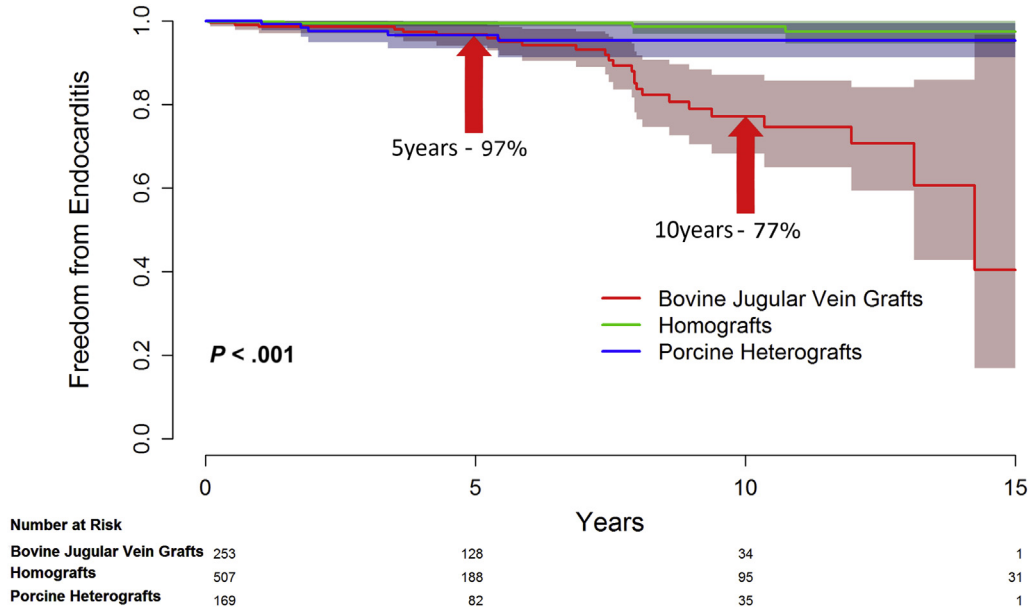


FIGURE 2. Kaplan–Meier curves depicting freedom from endocarditis according to conduit type. Bovine jugular vein grafts had a significantly higher incidence of endocarditis than homografts and porcine heterografts ($P < .001$). The number of infected bovine jugular vein grafts drastically increases after 7 years of conduit implantation.

TABLE 3. Multivariable analysis for development of endocarditis

Covariate	Coefficient ± SE	HR (95% CI)	*P* value
Age, y	−0.02 ± 0.05	0.98 (0.89-1.08)	.6249
Conduit size, mm	0.07 ± 0.09	1.07 (0.9-1.27)	.435
Syndrome			
No		Reference	
Yes	−0.48 ± 0.49	0.62 (0.24-1.61)	.3245
Conduit Type			
Homograft		Reference	
Bovine jugular grafts	2.76 ± 0.6	15.74 (4.89-50.69)	<.0001
Porcine heterografts	1.19 ± 0.72	3.28 (0.79-13.51)	.1007
Diagnosis			
PA/VSD		Reference	
Truncus	0.37 ± 0.51	1.45 (0.53-3.98)	.4658
Ross procedure	0.54 ± 0.72	1.71 (0.41-7.06)	.4598
Others*	0.79 ± 0.46	2.21 (0.89-5.47)	.0861
Initial conduit			
Yes		Reference	
No	0.17 ± 0.44	1.19 (0.5-2.83)	.6998
Z-Score	0.01 ± 0.21	1.01 (0.66-1.52)	.98

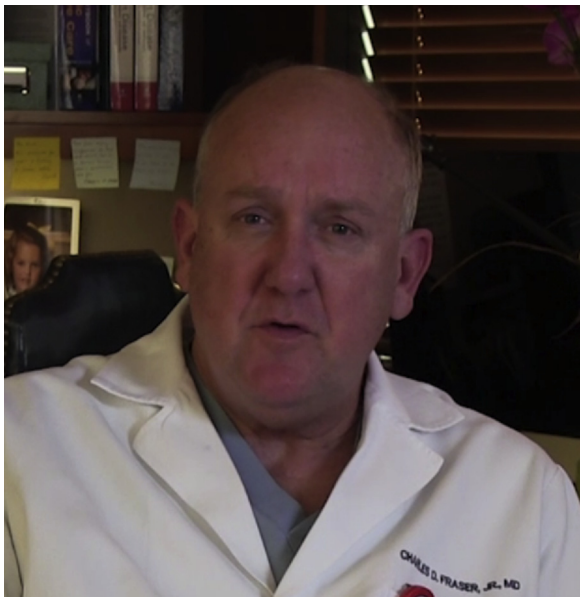
SE, Standard error; *HR*, hazard ratio; *CI*, confidence interval; *PA/VSD*, pulmonary atresia with ventricular septal defect. *Includes history of nonconduit tetralogy of Fallot repair, transposition of the great arteries with pulmonary stenosis or pulmonary atresia, absent pulmonary valve syndrome, pulmonary atresia with intact ventricular septum, and double-outlet right ventricle.

remains controversial, with contradicting evidence in the literature.[16-19] In a multi-institutional propensity-matched study of 107 infants with truncus arteriosus, Hickey and colleagues reported that BJV grafts were associated with a lower risk for replacement than homografts.[20] Similar to that study, we have also reported that BJV grafts are associated with a lower rate of reintervention and replacement after adjusting for significant covariates.[9] Thereby, BJV might still have a role, especially in small patients where a conduit replacement is expected in <7 years, small-sized homografts are not readily available, and other stented bioprostheses might be too rigid to use. Despite these potential advantages of BJV grafts, recent studies, including our own institutional experience, have raised the concern regarding the increasing incidence of endocarditis of up to 11.3% in these grafts.[9,10,12,13,21]

As shown in Figure 1, our institution began to adopt the use of BJV grafts during the first 10 years after it became available. The first 3 cases of endocarditis occurred in 2010, after which the number of infected grafts began to increase. Accordingly, the number of conduits implanted began to decrease, and after our own institutional results were explored in 2015 (published in 2016), which elucidated concise data about the growing incidence of infection of these conduits, our practice shifted toward the use of other available conduits whenever possible.

In our previous report, the incidence of endocarditis among BJV grafts was 6% (14 conduits), at a median follow-up of 7 years over a 13-year period.[9] In that report, the use of BJV grafts was associated with a 9 times greater risk of endocarditis compared with that of homografts ($P = .006$). Calculated estimates suggested that as many as 17% of patients with a BJV graft would develop endocarditis at 10 years after conduit placement, and that risk seems to increase with time. Since then, after an additional 2.5-year follow-up period, 11 more patients have developed endocarditis, raising the overall incidence of BJV graft endocarditis to 10%, and an estimate of 23% endocarditis incidence at 10 years of follow-up. During this additional follow-up time, there were no homograft or porcine heterograft conduits that developed infective endocarditis. These findings stand alongside that of other series. Ugaki and colleagues analyzed 244 BJV grafts and 135 homografts with a median follow-up of 3.4 years, and reported that 9.4% of BJV grafts became infected during the follow-up period, compared with 0.7% of the homografts.[10] The highest incidence of BJV graft endocarditis reported in the literature is that of Albanesi et al in Switzerland, with an incidence of 11.3% over an 11-year period and a median follow-up of 7.6 years.[13]

Various possible hypotheses have been raised for the increased incidence of endocarditis among BJV grafts. Jalal et al reported bacterial adhesion to be higher on the BJV wall for *S aureus*[22] and Delmo-Walter et al reported that histologic examination of an explanted BJV graft revealed an acellular homogenous material with fragile, diffuse, and complex collagenization throughout the BJV grafts, and inflammatory tissues.[23] This might be a result of the



VIDEO 1. Dr Charles D. Fraser, Jr, provides a brief introduction and discusses the most important findings of this study. Video available at: https://www.jtcvs.org/article/S0022-5223(18)30979-6/fulltext.

anticalcification treatment that the conduit undergoes, which might minimize endothelial surface growth.[4] These factors might contribute to flow turbulence and thrombus formation, increasing the risk of infection.[16] Somewhat contradictory is the recent report from Veloso et al, who showed similar adherence of 3 bacterial strains to small pieces of bovine pericardial patches, BJV, and cryopreserved homografts,[24] however, these are in vitro studies using commercially available strains analyzing short-term adhesions, and thereby might not reflect long-term adhesion.[25] The longevity of the conduit has also been proposed as a substrate for graft endocarditis, with the hypothesis that this complication is more likely to occur the longer the graft remains in place[9,10]; this likely explains why previous studies focused on mid-term outcomes and shorter follow-up of BJV grafts might have not been able to detect higher rates of endocarditis in these conduits.

Transcatheter pulmonary valve replacement, which is essentially a BJV graft within a stent has raised similar concerns. A large multicenter study showed a 92% freedom from endocarditis at 4 years.[26] Van Dijck et al reported a similar 5-year survival free from endocarditis for transcatheter pulmonary valves and BJV grafts (84.9% vs 87.8%), significantly lower than that of homografts (98.7%).[27] With increasing use of transcatheter pulmonary valves, the risks associated with these should be further elucidated.

An important finding of the present study is the dramatic increase in incidence of endocarditis after 7.5 years of conduit implantation. This is evidenced in Figure 2, which shows that at 5-year follow-up, there is no significant difference in the number of endocarditis events between conduit types, a freedom from endocarditis estimate of 97%. However, at 7.5 years after conduit implantation, the number of events in the BJV graft group drastically increases, decreasing the 10-year estimated freedom from endocarditis to 77%, which is significantly different than that of other conduit types.

Such unraveling findings have important implications for patients who have undergone implantation of this grafts. These results warrant increased surveillance in these patients. We suggest that any patient who has undergone implantation of a BJV graft in the past, especially those who have had these grafts in place for more than 6 or 7 years, be followed-up closer and undergo a thorough evaluation by their cardiologists, to detect early signs and symptoms of infection or graft failure, which might be a surrogate for turbulent flow, further increasing the risk of endocarditis.[16] Furthermore, if a patient presents with malaise or low-grade fever, there should be a higher index of suspicion for endocarditis in the differential diagnosis, and a more thorough evaluation, including echocardiography and blood culture drawing, should be performed.[10,28]

Another interesting finding in our study is the relative indolent clinical course of the patients who were diagnosed with BJV graft endocarditis. More than 50% of these patients had low-grade fevers, malaise, and other nonspecific symptoms for several months, with 1 patient having symptoms for up to 6 months. This might have, in some instances, delayed their presentation for evaluation and diagnosis. Looking back at some of these patients, they had even been seen several times by their primary care physicians, before presenting to our institution, and the diagnosis had been missed. This might help explain the median time of symptoms duration of 21 days, which is higher than that reported with other type of infected conduits.[9]

The current American College of Cardiology/American Heart Association guidelines for intervention in patients with infective endocarditis of prosthetic valves recommend early surgical intervention in cases in which valve dysfunction results in symptoms of heart failure, when infection is complicated by heart block, or persistent infection after appropriate antibacterial therapy.[29] Albanesi et al concluded that surgery was the therapy of choice for infected BJV grafts, with 83% of their patients undergoing surgical replacement of the infected conduits.[13] Similar to those findings, in our own series, 92% of the patients underwent surgical intervention to replace the infected conduit, with no surgical morbidity or mortality. These findings suggest that surgical therapy is a safe and the recommended treatment strategy for these patients. The decision as to which treatment strategy to pursue, as well as the timing of surgical intervention, whenever surgery is the treatment of choice, should be made by a multidisciplinary team including cardiologists, infectious disease specialists, and cardiothoracic surgeons.

Limitations

This study has multiple limitations, mainly related to its retrospective nature. The number of BJV grafts implanted at our institution decreased in the past 2.5 years, after the findings of our previous study. The present investigation is the result of a single institutional experience and as such, results might vary in different institutions. However, this might also be one of its strengths because the conduit selection, management strategy, and follow-up is more uniform than in retrospective multi-institutional studies.

CONCLUSIONS

In conclusion, in this large single-institutional cohort, we found a concerning 10% incidence of late endocarditis affecting BJV grafts, which appears to increase after 7 years of conduit implantation. Because of the increased risk for endocarditis and the relative indolent course of the initial disease, a more adherent and frequent clinical follow-up is warranted in patients who have undergone placement of a BJV graft in the past, especially those who have had a graft in place for more than 7 years. When endocarditis is diagnosed, surgical intervention is a safe strategy, and might alleviate the morbidity and mortality related to endocarditis with excellent outcomes.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

The authors thank Wei Zhang, PhD, for her support with the statistical analysis and review of the manuscript.

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Key Words: Contegra, bovine jugular vein, conduit, endocarditis, right ventricular outflow tract

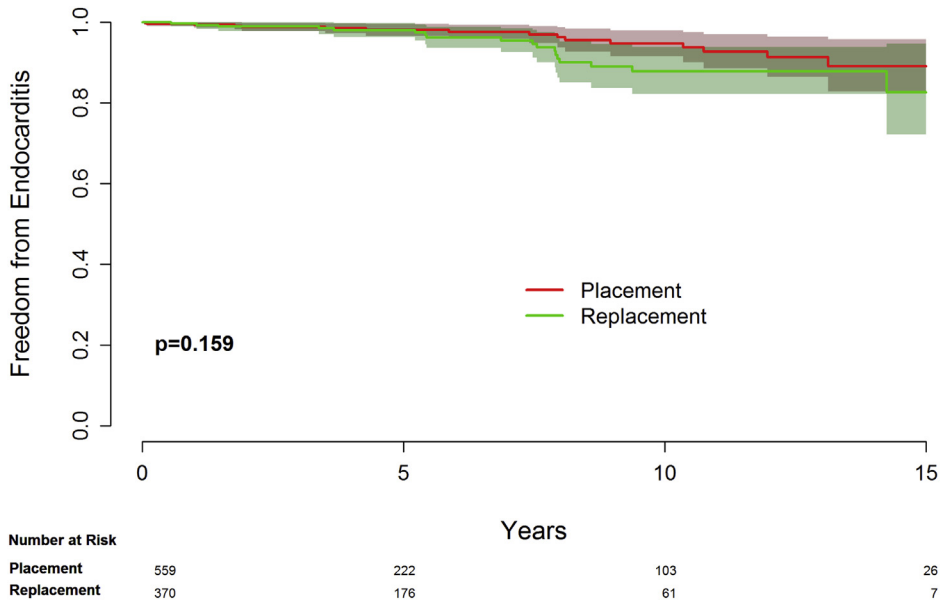

FIGURE E1. Kaplan–Meier curve depicting freedom from endocarditis according to placement and replacement. Those in the placement group are first-time conduit placement of any type, the replacement includes the second (n = 295), third (n = 65), fourth (n = 6), and fifth (n = 4) conduit placed.

TABLE E1. Characteristics of 25 patients diagnosed with endocarditis of a bovine jugular vein graft conduit

	Age in years, sex	Surgery	Fever	Associated symptoms (d)	Time to endocarditis	Cultures	Endocardial involvement	Vegetation	Emboli	Vascular phenomena	Immunologic phenomena
1	19, F	Yes	Yes	Chills, SOB (21)	7.9 y	Viridans streptococci	Yes	Yes	Yes	No	No
2	15, M	Yes	Yes	Cough, congestion (7)	8.5 y	Negative	Yes	Yes	No	No	No
3	18, M	Yes	Yes	Fatigue, jaundice, shock (21)	6.8 y	*Haemophilus parainfluenzae*	Yes	Yes	No	No	No
4	16, M	Yes	Yes	Night sweats, syncope (30)	14.2 y	Viridans streptococci	Yes	Yes	No	No	No
5	13, M	Yes	Yes	Lethargy (28)	7.8 y	*Granulicatella adiacens*	Yes	Yes	Yes	Yes	No
6	13, F	Yes	Yes	Lethargy, decreased appetite, chills (7)	9.3 y	Viridans streptococci	Yes	Yes	No	No	No
7	10, M	Yes	Yes	None (7)	7.9 y	Viridans streptococci	Yes	No	No	No	No
8	15, M	Yes	Yes	Headache (5)	7.4 y	Viridans streptococci	Yes	Yes	No	Yes	No
9	11, M	Yes	Yes	Vomiting, decreased appetite (3)	10.3 y	Viridans streptococci	No	No	No	No	No
10	14, F	Yes	Yes	Malaise, headache (11)	13.1 y	Viridans streptococci	No	No	No	No	No
11	12, M	Yes	Yes	Cough, chest pain (7)	5.8 y	Negative	Yes	No	No	No	No
12	15, M	Yes	Yes	Cough, syncope (2)	11.9 y	Negative	No	No	No	No	No
13	13, M	Yes	Yes	Vomiting, shock (3)	7.9 y	*Haemophilus parainfluenzae*	Yes	Yes	Yes	No	No
14	9, M	Yes	Yes	Fatigue, SOB, congestion, decreased appetite (28)	8.9 y	Viridans streptococci	Yes	Yes	No	No	No
15	6, M	Yes	Yes	Abdominal pain, vomiting (14)	3.5 y	MSSA	Yes	Yes	No	No	No
16	9, M	Yes	Yes	Vomiting, dizziness (28)	8 y	MSSA	Yes	Yes	No	No	No
17	20, F	Yes	Yes	Cough, rigors (180)	4.3 y	*Cardiobacterium hominis*	Yes	Yes	No	No	No
18	17, M	Yes	Yes	None (7)	6 mo	MSSA	Yes	Yes	Yes	Yes	No
19	21, F	No	Yes	Weakness weight loss, palpitations, dizziness (42)	3.6 y	Viridans streptococci	Yes	Yes	No	Yes	No
20	9, F	Yes	Yes	Fatigue, weakness (45)	7.5 y	Viridans streptococci	Yes	Yes	No	No	No
21	14, F	Yes	Yes	Cough, abdominal pain (14)	5.4 y	Viridans streptococci	Yes	Yes	No	No	No
22	8, F	Yes	Yes	None (30)	7.4 y	*Aggregatibacter actinomycetemcomitans*	No	No	No	No	No
23	1, F	No	Yes	None (14)	34 d	Viridans streptococci	Yes	Yes	No	No	No
24	6, F	Yes	No	Chills (14)	5 y	Viridans streptococci	No	No	No	No	No
25	2, F	Yes	Yes	SOB, anemia (5)	1 y	MRSA	Yes	Yes	No	No	No

Viridans streptococci include *Streptococcus mitis*, *S sanguis*, *S mutans*, and *S parasanguinis*. *F*, Female; *SOB*, shortness of breath; *M*, male; *MSSA*, methicillin-sensitive *Staphylococcus aureus*; *MRSA*, methicillin-resistant *Staphylococcus aureus*.