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Jugular venous valved conduit (Contegra®) matches allograft performance in infant truncus arteriosus repair☆

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Abstract

Objective: Limited availability and durability of allograft conduits require that alternatives be considered. We compared bovine jugular venous valved (JVV) and allograft conduit performance in 107 infants who survived truncus arteriosus repair. **Methods:** Children were prospectively recruited between 2003 and 2007 from 17 institutions. The median *z*-score for JVV ($n = 27$, all 12 mm) was +2.1 (range +1.2 to +3.2) and allograft ($n = 80$, 9—15 mm) was +1.7 (range −0.4 to +3.6). Propensity-adjusted comparison of conduit survival was undertaken using parametric risk-hazard analysis and competing risks techniques. All available echocardiograms ($n = 745$) were used to model deterioration of conduit function in regression equations adjusted for repeated measures. **Results:** Overall conduit survival was 64 ± 9% at 3 years. Conduit replacement was for conduit stenosis ($n = 16$) and/or pulmonary artery stenosis ($n = 18$) or regurgitation ($n = 1$). The propensity-adjusted 3-year freedom from replacement for in-conduit stenosis was 96 ± 4% for JVV and 69 ± 8% for allograft ($p = 0.05$). The risk of intervention or replacement for branch pulmonary artery stenosis was similar for JVV and allograft. Smaller conduit *z*-score predicted poor conduit performance ($p < 0.01$) with best outcome between +1 and +3. Although JVV conduits were a uniform diameter, their *z*-score more consistently matched this ideal. JVV exhibited a non-significant trend towards slower progression of conduit regurgitation and peak right ventricular outflow tract (RVOT) gradient. In addition, catheter intervention was more successful at slowing subsequent gradient progression in children with JVV versus those with allograft ($p < 0.01$). **Conclusions:** JVV does match allograft performance and may be advantageous. It is an appropriate first choice for repair of truncus arteriosus, and perhaps other small infants requiring RVOT reconstruction.

Keywords: Truncus arteriosus; Allograft; Contegra®; Conduit

1. Introduction

Reduced allograft availability necessitates that alternatives be sought for surgical reconstruction in the infant period. Bovine jugular venous valved conduit (JVV, Contegra®) is a bioprosthesis consisting of a glutaraldehyde-preserved bovine jugular vein with a trileaflet venous valve. It has been established as an appropriate choice for infant right ventricular outflow tract (RVOT) reconstruction in several lesions including tetralogy of Fallot and pulmonary atresia [1—3]. However, its performance in smaller infants has not been formally compared to traditional allograft alternatives.

Truncus arteriosus typically requires complete reconstruction of the RVOT early in infancy. Because a randomized comparison between JVV and allograft seems unlikely, we undertook a propensity-adjusted investigation of JVV and allograft performance in a multi-institutional population of prospectively recruited infants with truncus arteriosus. We chose to investigate a single diagnostic cohort in order to limit the confounding effects of lesion- or procedure-specific factors. Our aim was to determine whether JVV matches allograft performance for RVOT reconstruction in truncus arteriosus.

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2. Methods

2.1. Study cohort and analytic strategy

Between 2003 and 2007, 107 infants with a diagnosis of truncus arteriosus who survived initial corrective surgery were prospectively enrolled with the Congenital Heart Surgeons' Society (CHSS) from 17 member institutions. Participation in this project and submission of patient information were voluntary and confidential. Both parental consent for enrollment and ethics board approval was obtained by individual institutions and the CHSS Data Center.

Patients were eligible if they were diagnosed with any of the Van Praagh subtypes of truncus arteriosus. Surgical RVOT reconstruction with either a JVV (Contegra®, Medtronic Inc, Minneapolis) or cryopreserved allograft conduit and survival to hospital discharge were requirements for entry. The choice and size of conduit used was at the discretion of the child's surgeon. The type of conduit implanted at initial surgical repair was either JVV ($n = 27$), or allograft ($n = 80$; pulmonary = 42, aortic = 38). All JVV conduits used in this study were 12 mm (the smallest available). All allografts were cryopreserved and acquired from the institutions' usual source.[1] Four allograft conduits (two pulmonary, two aortic) were decellularized variants. However, all allograft conduits were analyzed together because the aim of this study was to characterize JVV performance against allograft — regardless of type.

The analytic strategy involved creating a propensity score to represent the probability of any given child belonging to one study group or the other. Baseline features (Table 1) were included in a logistic regression modeling the probability (propensity) of receiving JVV. The logistic model generated a cumulative probability (propensity score) for every child. This propensity score was then included in subsequent multivariable regression models to adjust for baseline differences between the study groups.

2.2. Follow-up and outcomes

Patients and their families were contacted annually by CHSS Data Center staff. All available procedural reports pertaining to cardiac catheterizations, echocardiograms and surgical interventions were obtained. The 538 echocardiogram reports successfully acquired represent 94% of all those known to have taken place during the study period. Endpoints for analyses included: (1) surgical explant or replacement of conduit ('conduit replacement'); or (2) trans-catheter or surgical intervention to the RVOT, conduit or branch pulmonary arteries ('intervention'). In addition, for children undergoing conduit replacement for RVOT stenosis, the medical records were examined to determine whether the principal area of narrowing was either within the conduit ('in-conduit stenosis') or otherwise at or beyond the distal anastamosis ('branch pulmonary artery stenosis').

[1] Allograft manufacturers included: Cryolife Inc. (Georgia, USA) $n = 36$; Lifenet Health (Virginia, USA) $n = 33$; Alabama Tissue Center (Alabama, USA) $n = 5$; American Red Cross (Maryland, USA) $n = 3$; North West Tissue Center (Washington, USA) $n = 2$.

2.3. Analysis of time-related events

Time-related risks of defined events were analyzed using multi-phase hazard domain techniques. Competing risks methodology was then used in order to account for patients who died prior to undergoing intervention or conduit replacement, and were therefore no longer at risk. Separate parametric models of the rate of transition (hazard function) from the point of diagnosis to each competing outcome (intervention, death without intervention or otherwise alive without intervention) were created. These separate time-related hazard functions were then combined to yield the proportion of children reaching the defined endstates at any given point in time.

2.4. Analysis of progression of echocardiographic variables

Time-related progression of peak instantaneous RVOT gradient and echocardiographic grade of conduit regurgitation were explored using linear regression models to produce generalized estimating equations adjusted for repeated measures through autoregressive covariance structure. Univariate exploratory plots were used to indicate possible transformations that might improve correlation between each predictor and outcome. Variable selection was undertaken by backward selection with retention threshold $p < 0.05$.

2.5. Data acquisition

Briefly, functional and morphologic indices were extracted from institutional medical reports. Selected patient-specific variables used in the propensity score and for risk-hazard analysis are shown in Table 1. Dimensional variables were standardized and expressed as z-scores on the basis of published normative data if available, or otherwise indexed to either body surface area or height. Missing heights, weights or body surface areas were imputed from standard percentile growth charts. Missing values in the remaining variables were imputed with the mean for that variable and a general missing value indicator created. This general missing value indicator was subsequently tested as a parameter in the regression analysis to refute the notion that patients with missing data may be different in terms of characteristics or risk from those in whom the data is not missing. Appropriate transformations of covariates were sought to improve model fit and linearity. Variables with excessive (more than 75%) missing values or associated with fewer than five events were excluded during regression analyses to avoid the risk of over-determination. Individual institutions contributing more than five patients were individually tested in multivariable models in order to determine the risk of outcomes being biased by institution-specific factors. No institution tested met the threshold for significance. All data were analyzed using SAS statistical software, version 9 (SAS Institute, Cary, NC). Data are described as frequencies, medians with ranges and means with standard errors as appropriate. Final variable selection was guided by bootstrap bagging ($n = 1000$, threshold for inclusion $p = 0.10$). Variables selected in $>50\%$ resamples or their clusters were considered reliable for inclusion. The

Table 1
Patient characteristics of 107 infants with truncus arteriosus who received either allograft or jugular venous valved conduit to reconstruct the right ventricular outflow tract at the time of corrective surgery

Variable	Model	Allograft, $n = 80$ (pulmonary = 42, aortic = 38)			JVV, $n = 27$			p value
		Missing	Value	% or range	Missing	Value	% or range	
Operative weight (kg)	MV	0	3.1	(1.7–9.7)	0	3.5	(2.4–5.0)	0.09
Operative age (days)	MV	0	19	(1–127)	0	32	(2–88)	0.02
Truncus arteriosus type								
I	PS	2	49	63	0	19	70	0.48
II	PS	2	20	26	0	7	26	0.97
III	PS	2	5	6	0	1	4	0.60
IV	PS	2	4	5	0	0	0	0.23
Truncal valve regurgitation (mod/sev)	PS	0	36	45	0	10	37	0.47
Truncal valve gradient (mmHg)	PS	19	15	(0–90)	5	20	(0–56)	0.30
Truncal valve cusp number	PS							
2	PS	0	10	13	0	1	4	0.11
3	PS	0	51	64	0	17	63	0.45
4	PS	0	19	24	0	9	33	0.72
Coarctation	PS	0	2	2	0	0	0	0.41
LV dysfunction (mild, mod or sev)	PS	0	1	1	0	4	15	<0.01
Mitral valve regurgitation (mod/sev)	PS	25	1	2	13	1	4	0.18
Right aortic arch	PS	0	16	20	0	8	30	0.30
Left superior vena cava	PS	0	2	3	0	1	4	0.74
Atrial septal defect	PS	8	70	97	3	22	92	0.24
Ventricular septal defect	PS	7	69	95	3	22	92	0.62
Left PA stenosis	PS	24	5	9	8	4	21	0.16
Right PA stenosis	PS	25	7	13	7	2	10	0.75
Right ventricular dysfunction	PS	0	5	6	0	3	11	0.34
Left PA z-score	PS	33	−0.65	(−8.3 to +2.1)	7	−0.45	(−3.4 to +2.7)	0.67
Right PA z-score	PS	33	−0.87	(−8.9 to +3.1)	7	0.02	(−3.15 to +2.7)	0.11
Conduit size (mm)	MV	0	11.0	(8–15)	0	12	(All 12)	–
Conduit z-score	MV	0	1.7	(−0.4 to +3.6)	0	2.2	(1.3 to +3.2)	<0.01
PA augmentation	MV	0	4	5	0	4	15	0.09

Left ventricular dysfunction determined from the subjective grading of function in echocardiography reports. Baseline variables were included in the logistic model to generate a propensity score, and procedure-related variables were included in multivariable analysis. JVV, jugular venous valved conduit; PA, pulmonary artery; mod, moderate; sev, severe; LV, left ventricular; PS, propensity score; MV, multivariable.

threshold of significance for final variable retention was considered $p < 0.05$.

3. Results

3.1. Group characteristics

Children who received allograft conduits were younger at operation (19 vs 32 days, $p = 0.02$) but of similar weight (Table 1). In addition, left ventricular dysfunction was more common in those who received JVV. The groups otherwise had similar baseline characteristics. Although the median indexed sizes of conduit implanted were similar (JVV +2.2, allograft +1.7) this difference was significant ($p < 0.01$). These differences highlight the importance of using a propensity- and risk-adjusted comparative approach.

3.2. Time-related hemodynamic performance

3.2.1. Stenosis of the RVOT

Children with either allograft or JVV conduits showed a time-related increase in peak instantaneous gradient across the RVOT (Fig. 1a). The progression of peak RVOT gradient was more rapid in children with allograft conduits, although not to a significant degree ($p = 0.16$). Other baseline patient-specific features that were incremental risk factors for accelerated progression of the peak RVOT gradient included smaller operative weight at the time of initial conduit implantation ($p < 0.001$) and smaller conduit z-score at the time of implantation ($p < 0.001$). The propensity score was significant in this regression model ($p < 0.01$), indicating that differences between the characteristics of the allograft and JVV groups were influential.

3.2.2. Conduit regurgitation

The echocardiographic grade of conduit regurgitation also rapidly progressed with time (Fig. 1b). Within a year of implantation, the regression model estimated the majority of conduits to be at least moderately regurgitant. In propensity-adjusted models, the progression of conduit regurgitation was slightly but not significantly ($p = 0.24$) more rapid in allograft conduits. No patient-specific features — including conduit z-score or operative age — were independent risk factors for accelerated progression of conduit regurgitation.

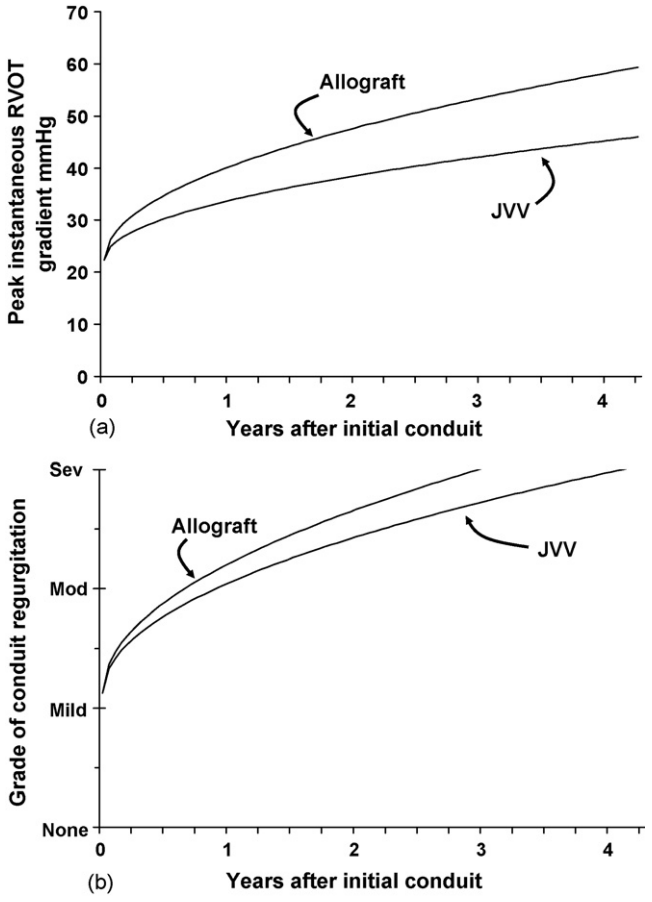

Fig. 1. Propensity-adjusted linear regression estimates in all 107 children of: (a), progression of peak instantaneous right ventricular outflow tract gradient, and (b), echocardiographic grade of conduit regurgitation. Gradients within both allograft and jugular venous valved (JVV) conduits increased with time ($p < 0.01$). Gradient progression was modestly more rapid in the allograft group, but this difference was not significant ($p = 0.16$). Progression of the grade of conduit regurgitation was also modestly more rapid but this difference was not significant ($p = 0.24$). Time has been entered as the square-transformation to improve model fit. In both regression analyses, children were censored at the point of trans-catheter or surgical intervention. Lines are the product of generalized estimating equations adjusted for repeated measures.

3.3. Trans-catheter or surgical intervention to the RVOT

3.3.1. Indications for RVOT intervention

Trans-catheter interventions to the RVOT ($n = 47$) were performed in 40 children (Table 2). Seven of these children had interventions to both the conduit and branch pulmonary arteries. The numbers of trans-catheter interventions (independent of time) were not different between children who received JVV or allograft conduit (Table 2).

In addition, three children underwent open surgical repair of the RVOT without the conduit being explanted or replaced. All three children had a pulmonary allograft as the initial conduit. The indications for repair were branch pulmonary artery stenosis ($n = 2$; patch pulmonary arterioplasty performed) and proximal pseudoaneurysm of the conduit ($n = 1$; conduit repaired with Gore-Tex® patch). No child in this series developed aneurysmal dilatation of a JVV conduit.

3.3.2. Freedom from intervention

Almost half of the survivors had an intervention within 2 years of implant. After 3 years, $61 \pm 5\%$ had received an intervention, $36 \pm 11\%$ remained alive without an intervention and $3 \pm 2\%$ had died without an intervention. The risk of undergoing any type of invasive intervention, trans-catheter or surgical, to the conduit or branch pulmonary arteries was a single, protracted early hazard phase. In both propensity-adjusted (Fig. 2a) and propensity unadjusted analyses, the time-related freedom from re-intervention was almost identical for children with allograft and JVV conduits. The fact that propensity-adjustment was not influential in this model implies that the overall risk of intervention is independent of both baseline patient features and conduit type. The only factor that determined accelerated risk of intervention was smaller conduit z-score at the time of initial implantation ($p < 0.01$). Smaller conduit z-scores offer a disproportionately worse time-related risk of intervention, and conduit z-scores between +1 and +3 appear to be ideal (Fig. 2b).

3.3.3. Outcomes of trans-catheter intervention

In children who underwent trans-catheter intervention to the RVOT or branch pulmonary arteries ($n = 40$), propensity-adjusted regression models demonstrate that peak instantaneous RVOT gradients increase at comparable ($p = 0.78$) rates in the allograft and JVV groups pre-intervention (Fig. 3). Interestingly, intervention resulted in a significant improvement in time-related progression of peak RVOT gradient in the JVV group ($p < 0.001$ pre- vs post-intervention), but a more modest improvement in the allograft group ($p = 0.15$ pre- vs post-RVOT gradient progression). This implies that trans-catheter intervention is more likely to be successful in an RVOT reconstructed with JVV.

Table 2
Rates of trans-catheter intervention to either the conduit or branch pulmonary arteries in children with truncus arteriosus who received either allograft or JVV for RVOT reconstruction

	Allograft ($n = 80$)		JVV conduit ($n = 27$)		p value
	n	% of total	n	% of total	
Trans-catheter intervention	29	36	11	41	0.68
Intervention to conduit	11	14	3	11	0.73
Balloon dilatation	6	8	0	0	0.14
Stent implantation	5	6	3	11	0.41
Intervention to pulmonary arteries	24	30	9	33	0.76
Balloon dilatation	15	19	4	15	0.64
Stent implantation	9	11	5	19	0.33

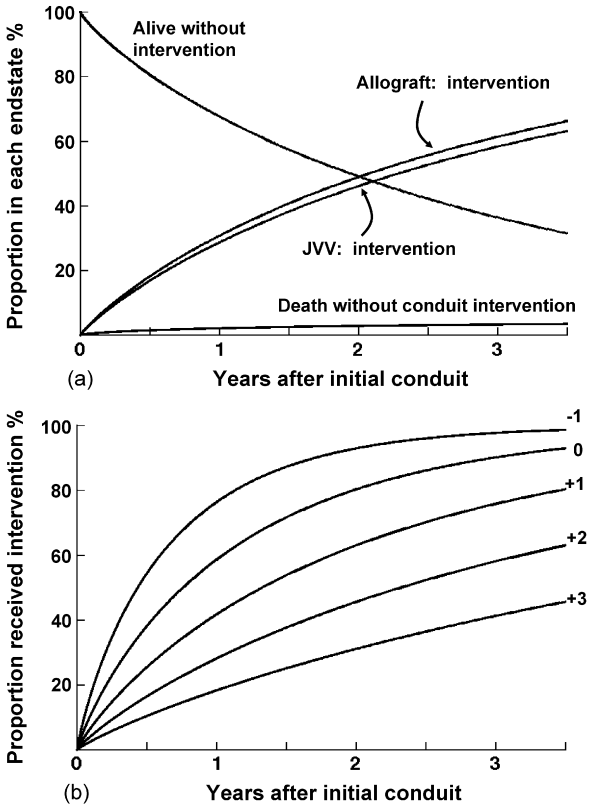

Fig. 2. (a) Propensity-adjusted time-related risk of receiving surgical or transcatheter intervention to the conduit or branch pulmonary arteries stratified according to whether the initial conduit was jugular venous valved (JVV) or allograft. Differences in freedom from intervention were not significant between allograft and JVV in either propensity-adjusted ($p = 0.86$) or propensity-unadjusted ($p = 0.92$) models. Overall, freedom from intervention was $65 \pm 5\%$, $53 \pm 5\%$ and $36 \pm 6\%$ at 1, 2 and 3 years, respectively. Numbers remaining at risk were 56, 41 and 16 at 1, 2 and 3 years, respectively. (b) Propensity-adjusted freedom from intervention stratified by the conduit z-score size at the time of implantation (parameter estimate -0.49, $p < 0.01$). Competing risks models have been used to account for children who died and were, therefore, no longer at risk of receiving an intervention. Lines represent parametric continuous point estimates.

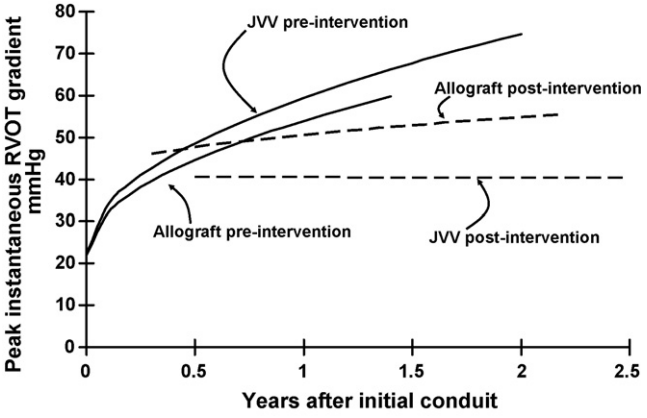

Fig. 3. Propensity-adjusted linear regression estimates of the progression of peak instantaneous right ventricular outflow tract gradient at any point to the distal branch pulmonary arteries in all children ($n = 40$) who underwent a transcatheter intervention to the conduit or branch pulmonary arteries. The regression equations have been stratified according to: (a) the type of conduit, and (b) whether the values were pre- or post-transcatheter intervention. Gradients within both allograft and jugular venous valved (JVV) conduits increase with time ($p < 0.01$), but at comparable rates ($p = 0.78$). The group of children with JVV conduits demonstrated significant improvements in the progression of RVOT gradients ($p < 0.001$ pre- vs post-gradient progression), whereas children with allograft conduits did not ($p = 0.15$ pre- vs post-RVOT gradient progression). Time has been entered as the square-transformation to improve model fit. Lines are the product of generalized estimating equations adjusted for repeated measures.

3.4. Longevity of RVOT conduit

3.4.1. Indications for conduit replacement

Conduit replacement was undertaken in 26 children (JVV = 8; allograft = 18). The primary indication for conduit replacement was in-conduit stenosis in 16 and branch pulmonary artery stenosis in 18 patients. Eight children were judged clinically to have both in-conduit stenosis and branch pulmonary artery stenosis equally contributing to the clinical decision to undergo surgical replacement of the conduit. One child with branch pulmonary artery stenosis also had severe conduit regurgitation with a dilating right ventricle as a reason for conduit replacement.

3.4.2. Freedom from conduit replacement

The risk of having the conduit replaced was a single late hazard phase that became prominent approximately a year after initial conduit replacement. After 3 years, $5 \pm 3\%$ had died without conduit replacement, $31 \pm 5\%$ had undergone conduit replacement and $64 \pm 9\%$ remained alive without conduit replacement. The propensity-adjusted longevity of allograft and JVV conduits is almost identical ($p = 0.93$, Fig. 4a). Smaller conduit z-score at the time of initial implantation was the only independent risk factor for accelerated risk of replacement ($p < 0.01$). Smaller conduit z-scores offer a disproportionately worse time-related risk of replacement, and conduit z-scores between +1 and +3 appear to be ideal (Fig. 4b). The time-related risk of conduit replacement was independent of age or weight at the time of initial conduit implantation.

3.4.3. Conduit replacement for in-conduit stenosis

The propensity-adjusted freedom from conduit replacement for in-conduit stenosis was significantly better for JVV versus allograft conduits ($p = 0.05$, Fig. 5). The risk of conduit replacement for in-conduit stenosis was a gradually increasing late hazard that became prominent after 1–2 years. Smaller conduit z-score at the time of implantation was again an independent risk factor for accelerated in-conduit stenosis as the indication for conduit replacement ($p = 0.03$).

3.4.4. Conduit replacement for branch pulmonary artery stenosis

The risk of conduit replacement for branch pulmonary artery stenosis is a constant hazard. The propensity-adjusted freedom from conduit replacement for branch pulmonary artery stenosis was not different for children with allograft or JVV conduits ($p = 0.50$, Fig. 6). Smaller conduit z-score at the time of implantation was again an independent risk factor for branch pulmonary artery stenosis as the indication for conduit replacement ($p < 0.01$). The need for pulmonary artery augmentation at the time of initial conduit implantation approached the threshold for significance ($p = 0.06$) as an independent risk factor for earlier conduit replacement

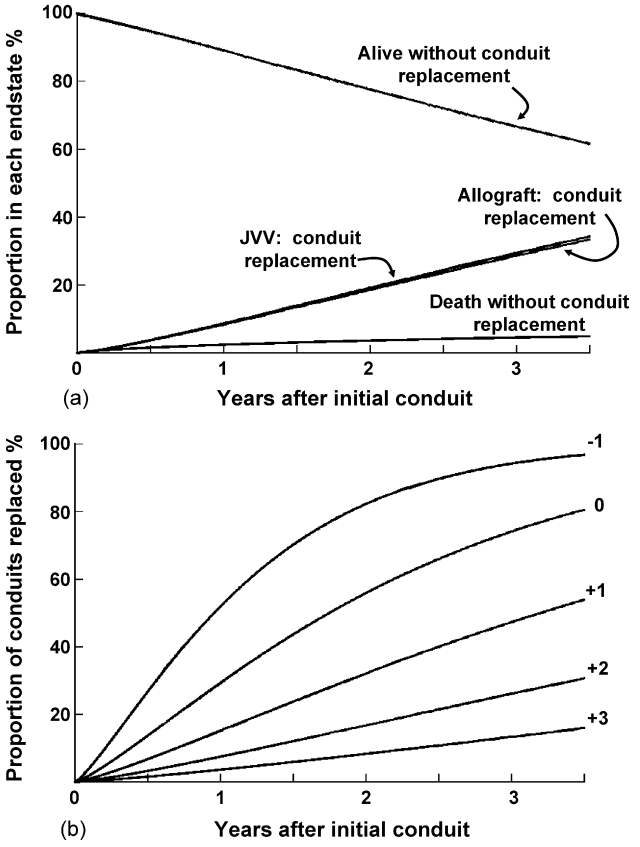

Fig. 4. (a) Propensity-adjusted time-related risk of conduit replacement stratified according to whether the initial conduit was jugular venous valved (JVV) or allograft. Differences in time-related freedom from conduit replacement were not different in either propensity-adjusted ($p = 0.93$) or propensity-unadjusted ($p = 0.36$) models. Overall, freedom from conduit replacement was $88 \pm 3\%$, $82 \pm 4\%$ and $66 \pm 6\%$ at 1, 2 and 3 years, respectively. Numbers remaining at risk were 77, 64 and 26 at 1, 2 and 3 years, respectively. (b) Propensity-adjusted freedom from conduit intervention stratified by conduit z-score at the time of implantation (parameter estimate -0.75, $p < 0.01$). Competing risks models have been used to account for children who died and were therefore no longer at risk of conduit replacement. Lines represent parametric continuous point estimates.

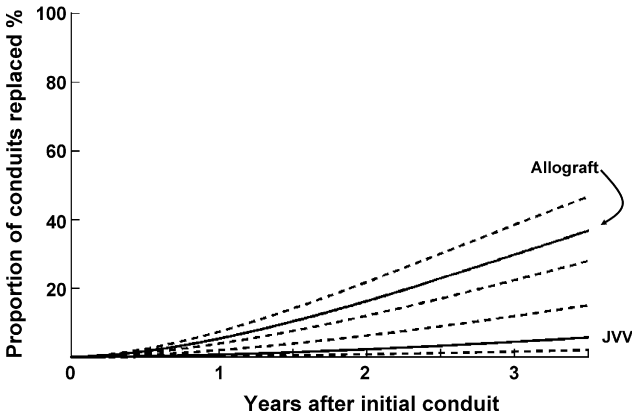

Fig. 5. Propensity-adjusted freedom from conduit replacement for stenosis within the conduit stratified by whether the conduit was allograft or jugular venous valved conduit (JVV). Freedom from replacement was $69 \pm 8\%$ and $96 \pm 5\%$ at 3 years for allograft and JVV, respectively ($p = 0.05$). Propensity-unadjusted freedom from conduit replacement for stenosis within the conduit was not significant ($p = 0.19$). Overall, freedom from conduit replacement for conduit stenosis was $94 \pm 2\%$, $91 \pm 3\%$ and $77 \pm 6\%$ at 1, 2 and 3 years, respectively. Solid lines represent parametric continuous point estimates. Dashed lines enclose 70% confidence intervals.

secondary to branch pulmonary artery stenosis. The inference is, therefore, that the presence of small native branch pulmonary arteries is a more important determinant of whether branch pulmonary artery stenosis subsequently triggers the need for conduit replacement than the type of conduit used for repair.

4. Discussion

This study suggests that bovine jugular venous valved conduit is an appropriate first choice for RVOT reconstruction in small infants with truncus arteriosus. Allograft performance was at least matched by JVV in all outcomes explored. In addition, although the risk of conduit replacement for branch pulmonary artery stenosis was not different to allograft, JVV offers significantly better freedom from replacement due to stenosis within the conduit. This report therefore adds to the increasing number of non-comparative observational studies describing acceptable JVV function, even in small infants [1,3–8]. Our multi-institutional propensity-adjusted approach corroborates the findings of the few (unadjusted) comparative studies examining the use of JVV as an alternative to allograft [8,9].

The need to find alternatives to allograft is driven by a progressive decline in allograft availability. Aside from additional medico-legal requirements for donor recruitment, high profile organ procurement scandals have thwarted efforts in some countries to increase donors via introducing 'presumed consent' [10,11]. Therefore, despite the recognition in the late 1990s that additional cardiovascular tissue banks were necessary, aside from a few exceptions [12–14], they have not been introduced. The number of allograft valve banks presently operating has now fallen to just one in the

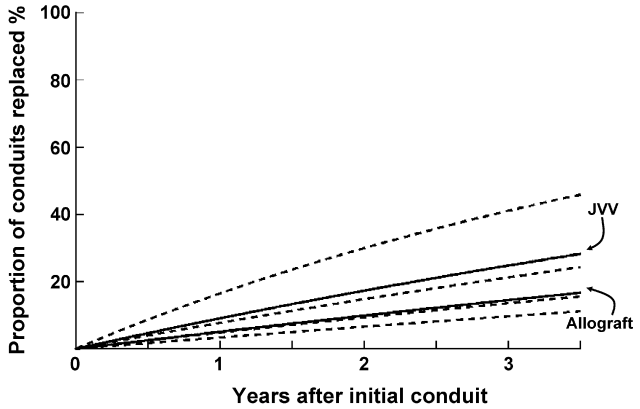

Fig. 6. Propensity-adjusted freedom from conduit replacement for stenosis at or distal to the distal anastamosis stratified by whether the conduit was allograft or jugular venous valved conduit (JVV). Differences were not significant in either this propensity-adjusted model ($p = 0.50$), or a propensity-unadjusted model ($p = 0.08$). Overall, freedom from conduit replacement for stenosis at or distal to the distal anastamosis was $90 \pm 3\%$, $87 \pm 4\%$ and $76 \pm 5\%$ at 1, 2 and 3 years, respectively. Solid lines represent parametric continuous point estimates. Dashed lines enclose 70% confidence intervals.

United Kingdom and only a handful in the United States. Availability of pediatric allografts is especially unpredictable. Surgeons have, through necessity, devised methods of downsizing adult allografts for use in small children [15]. However, identifying readily available alternatives would be the more ideal solution.

Bovine jugular venous valved conduit (JVV) is a bioprosthesis consisting of a bovine jugular vein with its native trileaflet venous valve. The conduit is preserved in buffered glutaraldehyde at a concentration low enough to preserve tissue flexibility which is typically lost at higher concentrations. It is available in a range of adult and pediatric sizes. The smallest available is currently 12 mm.

Small infants are especially vulnerable to early failure of surgical RVOT reconstructions. Young patient age, small patient size and small conduit diameter have all been identified as independent risk factors for early deterioration of conduit function [2,16]. Patient-prosthesis mismatch has been cited as a reason for early failure and therefore there has been a demand for small pediatric allografts ($<$12 mm). Nevertheless, both here in infants with truncus arteriosus and previously in a heterogenous cohort of infants receiving valved RVOT conduits within 3 years of age, we have demonstrated that optimal conduit longevity is offered by conduit *z*-scores in the range +1 to +3 [2]. Despite the smallest available JVV size of 12 mm, its range of *z*-score was narrower than that of allograft, and it more consistently matched the ideal of between +1 and +3. Intentionally oversizing conduits beyond a *z*-score of +3 is probably not advantageous [17] and may be detrimental [2]; somatic outgrowth is not believed to be the primary cause for conduit replacement [18]. Instead, localized stenosis at some point within the conduit or branch pulmonary arteries is the more common indication for replacement.

The precise site of stenosis has been of considerable interest because of several descriptions of severe neointimal inflammatory fibrosis occurring at the distal anastamosis in children who receive JVV [7,19–21]. Distal stenosis may also contribute to the development of severe JVV regurgitation and aneurysmal conduit dilatation [22]. However, the few reports describing high rates of distal stenosis [7,19–21] with JVV are in stark contrast to others [1,3–6,8] including our series, in which this complication was not common. Other explanations for distal anastamotic stenosis have been offered, including excessive conduit length, glutaraldehyde reactions, thrombosis and technical issues [1]. Interestingly, anastamotic stenosis has been described following Ross operations using allografts [23]. The risks of all-cause intervention and conduit replacement for branch pulmonary artery stenosis were not different between allograft and JVV in this present study. This finding supports the idea that factors other than conduit type may be more important, for example whether pulmonary artery augmentation was necessary at the time of initial conduit implantation.

It is difficult to draw conclusions regarding JVV performance against historical practices. For example, repair of truncus arteriosus without use of an extra-cardiac conduit has been previously advocated [24], especially for small neonates. Despite concerns regarding high pulmonary vascular resistance in the neonatal period, a series of 45 selected infants underwent reconstruction of the RVOT using a pericardial patch incorporating a monocusp valve. Early mortality was acceptable ($\approx$30%) and re-operation to the RVOT was deferred up to 11 years age [25,26]. Nevertheless, larger series have not been reported and primary repair of truncus arteriosus without an extra-cardiac conduit has not been widely adopted in modern practice.

Similarly, excellent longevity has been described with antibiotic-sterilized allografts in the late 1970s and 1980s with 10-year freedom from replacement approaching 80% [27] although the analysis was not adjusted for early operative deaths. Importantly, despite the comparable patient size (mean 3.4 kg) to our cohort (mean 3.2 kg for all 107 infants), the sizes of antibiotic-sterilized allografts were considerably larger (11–17 mm, mean 14.9, vs mean allograft size 10.7 mm in our cohort). This latter point indicates that a certain reticence exists in contemporary practice towards implanting large allografts in small children. Because antibiotic-sterilized allograft conduits are no longer available and because modern practice avoids excessive over-sizing, we do not feel the isolated experience with antibiotic-sterilized allografts should serve as a contemporary benchmark.

We have analyzed the various allograft subtypes as a single study group. Pulmonary allografts may offer greater durability than aortic allografts [2,16]. Similarly, some have suggested that methods of allograft preparation and preservation are important [15]. Therefore, we may not have compared JVV to the 'best possible' allograft subtype. However, this study was prompted by limited allograft availability. Therefore, further defining optimal allograft characteristics would not lessen the clinical dilemma of conduit choice. Lastly, the indexed size of JVV conduits was slightly, but significantly, larger than allograft conduits. Because the JVV conduits more consistently matched the ideal, their favorable durability may be attributable to these significant differences in indexed conduit size. Nevertheless, this limitation does not detract from our aim in assessing JVV performance against current surgical practices using allograft.

Several other limitations to this study should be considered. First, despite our multi-institutional approach, the sample sizes are small. Nevertheless, this represents the largest single comparative study of allograft and JVV in a homogenous series of infants with a uniform diagnosis. Second, there is the potential for institution-specific factors to affect outcomes. On the other hand, a major advantage of a multi-institutional strategy is that local technical expertise in any given center should not bias the results.

In summary, late survival in children after successful repair of truncus arteriosus are currently excellent. However, the rate of re-operations is high (50% within 2 years) and predominantly attributable to stenosis of the reconstructed RVOT and pulmonary arteries. Allografts have traditionally been favored as the 'gold standard' [28] conduit material for RVOT reconstruction. Bovine JVV conduits have emerged as potential alternatives in an era of reducing allograft availability, but have not been formally compared to allograft conduits in small infants with truncus arteriosus. In this study, using a multi-institutional propensity-adjusted strategy JVV matched allograft performance and freedom from conduit replacement for branch pulmonary artery

stenosis was comparable. Jugular venous valved conduit offered significantly improved freedom from replacement for stenosis within the conduit. This report suggests that JVV is an appropriate first choice for valved RVOT reconstruction in truncus arteriosus.

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Appendix A. Conference discussion

Dr M. Hazekamp (*Leiden, The Netherlands*): It's good to hear that the Contegra bovine jugular vein graft and allografts are comparable in this specific subgroup.

I have several questions. You said that for in-conduit stenosis the allograft performed worse than Contegra, but in my opinion, sometimes it's very difficult to distinguish in-conduit stenosis in Contegra from pulmonary artery branch stenosis, because if there is a problem in the Contegra, at least in our experience, it's mainly located at the distal anastomosis, which is a fibrous pannus problem, an overgrowth, and that extends from the end of the bovine jugular vein graft into the proximal pulmonary artery branches. So how did you exactly distinguish between proximal PA branch stenosis and distal in-conduit stenosis in the Contegra?

Dr Hickey: You've raised a couple of important points. We differentiated based on reviewing repeated echocardiograms and intraoperative reports and clinical notes prior to the operation. It is subjective, but nevertheless, the advantage of having all the case notes in our data center is that we can review them individually, and we categorized each patient with either having a primary indication of stenosis proximal to the distal anastomosis or otherwise at and distal to the anastomosis. We were aware of the concerns regarding neointimal proliferation at the distal anastomosis site that certain centers have reported, and that's why we specifically wanted to categorize them as such, and a small minority of patients had stenosis in both the conduit and the distal PAs. So that's how we differentiated them, and unlike previous reports, we have not seen an increased risk of stenosis at the distal anastomosis with the use of Contegra.

The second point is that, yes, we did see in this dataset an improved longevity of conduits because of in-conduit stenosis. Our primary aim was actually to determine whether Contegra was at least comparable to allograft, and so in that respect we have achieved our aims. Our data is suggestive that actually Contegra may be better and we may well need to continue follow-up

and enrollment to confirm that that is the case in larger cohorts over longer periods of time.

Dr Hazekamp: There's another comment I wanted to make. You say that the ideal conduit size in this population of neonates would be around a *z*-score of plus 2. Well, the Contegra obviously doesn't go lower than a diameter of 12 mm, and I think that 12 mm to connect to tiny pulmonary arteries may be too big. So the point of having this plus 2 *z*-score in a Contegra when it means that 12 mm is okay may be open for discussion. So what do you think about that? Don't you think that sometimes it's better to have a graft that is a bit smaller, has a diameter that's less than 12 mm?

Dr Hickey: Both in this and previous CHSS studies, the conduit *z*-score is revealed as a strong determinant of conduit longevity, and this study and our previous one from the data center suggests that perhaps we should be placing more emphasis on conduit *z*-score rather than necessarily the conduit type. It is certainly the case that putting a 12 mm conduit in an extremely small child may be technically difficult, especially because Contegra is a slightly longer prosthesis with a longer valve than a homograft. We saw a slight age difference in the two groups, allograft and Contegra, and I suspect that may be because some surgeons are reluctant to put a 12 mm Contegra in very small infants and are therefore opting to try and seek a 9 or 10 mm allograft. Our data that compares the 12 mm conduit as a *z*-score of plus 1 to plus 3 suggests that actually that bias for smaller allografts may not be justified and it may be appropriate to select a 12 mm for the smaller children.

Dr Hazekamp: In your study you showed that after 2 years, 50% of the patients are free from reintervention, meaning that the other 50% have been reintervened at 2 years, which is rather high. One of the implications may be that it would be better, as we now do and many other surgeons do, to repair the truncus without the use of any conduit at all because then the freedom of reintervention is a lot higher. What is your point on that?

Dr Hickey: That is a perfectly valid point. We haven't included in either this study or other CHSS studies truncus repairs that don't employ conduit. Nevertheless, the rate of reintervention described here is comparable to other series, for example, Dr Brown's in Indianapolis, which have a comparable rate at around 24 months of intervention.

Dr B. Maruszewski (*Warsaw, Poland*): Did you differentiate between the pulmonary and aortic homograft? I think this is one of the major issues for the postop, especially if you find stenosis as a postop problem.

Dr Hickey: That's an important point. The primary aim here was to compare Contegra with what we have currently available regardless of whether it's pulmonary or aortic. We have done separate propensity-adjusted comparisons looking at pulmonary versus aortic and then Contegra versus the better of the two allografts, and in terms of longevity, pulmonary allografts did outperform aortic allografts, but when we compared Contegra and pulmonary allografts, again, Contegra matched or exceeded the function of pulmonary allografts.