Drug-Eluting Stents Compared With Bare Metal Stents for Stenting the Ductus Arteriosus in Infants With Ductal-Dependent Pulmonary Blood Flow

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There have been no clinical studies evaluating the use of drug-eluting stents (DES) versus bare metal stents (BMS) for infants who underwent ductus arteriosus (DA) stent placement for ductal-dependent pulmonary blood flow (PBF). We aimed to compare the use of second-generation (fluoropolymer-coated everolimus) DES to BMS in infants who underwent DA stenting for ductal-dependent PBF. A retrospective study of infants who underwent DA stenting for ductal-dependent PBF from January 2004 to March 2018 at a single tertiary care pediatric hospital was performed. Of 94 infants identified, 71 (46 BMS and 25 DES) met inclusion criteria. Baseline characteristics of the DES and BMS cohorts were comparable. The patent lumen to stent diameter on subsequent angiographic evaluation was 81% in DES as compared with 50% in BMS group; p = 0.01. There were 2 deaths early in our experience, both in the BMS group. Unplanned reinterventions were less in the DES group (3, 12% patients) compared with the BMS group (13, 28%), p = 0.03. Pulmonary artery size as assessed using Nakata and pulmonary artery symmetry index was comparable in both the groups. There was no difference in infection rates between the groups. On multivariate analysis, prematurity, BMS, and lower oxygen saturations at discharge were associated with subsequent unplanned reintervention (p = 0.01, 0.03 and 0.03, respectively). In conclusion, our clinical experience suggests that in infants who underwent DA stenting for ductal-dependent PBF, (fluoropolymer-coated everolimus eluting) DES results in less luminal loss and lower unplanned reintervention for cyanosis as compared with BMS implantation. **(Am J Cardiol 2019;124:952–959)**

Stenting of the ductus arteriosus (DA) has recently been reported as an acceptable alternative to modified Blalock Taussig Thomas (m-BTT) shunt for infants with ductal-dependent pulmonary blood flow (PBF).[1,2] Superiority and noninferiority in a number of important outcomes with DA stenting compared with m-BTT placement has been reported recently in 2 large multicenter studies.[1,2] However, there are no studies evaluating if the specific properties of the stent influence outcomes. In the current era, a number of coronary platform stents are at the disposal of the pediatric interventional cardiologist. These include bare metal stents (BMS), drug-eluting stents (DES), and second-generation DES,[3] all of which may be considered for DA implantation in neonates with ductal-dependent PBF. Potentially important physiologic benefits of first-generation DES have been recently reported in animal models of neonatal DA[4] and rapamycin-eluting stents implanted in DAs have been shown to develop significantly less intimal proliferation compared with BMS.[5] However, to date, in clinical practice there are no data comparing the use of DES versus BMS in neonates undergoing DA stent implantation for ductal-dependent PBF. The purpose of our study, therefore, was to compare the safety and efficacy of DES (specifically second-generation fluoropolymer-coated everolimus eluting DES) to BMS in neonates undergoing DA stent placement for ductal-dependent PBF.

Methods

The study included all infants who underwent ductal stenting for ductal-dependent PBF at the Department of Pediatric Cardiology at Texas Children's Hospital, Houston, TX from January 2004 to March 2018. Patients with major aorto-pulmonary collateral vessels or with isolation of a pulmonary artery (PA) with PBF supplied by the DA were excluded from the study. Each patient underwent DA stenting in the cardiac catheterization laboratory using a standard protocol, although the choice of the particular stent used was dependent on the treating provider at the time of cardiac catheterization. Stents were advanced through either short- or long sheaths (which facilitated angiograms), depending on the distance from the access point. Procedural data were collected including the morphology of the DA (tortuosity index and origin of the DA[6]).

The primary outcome for this study was rate of luminal loss by angiography. Two blinded observers to the type of stent implanted (VA and GD) reviewed the angiograms to measure the patent lumen (A) to stent diameter ratio (B) and calculated using the formula A/B (Figure 1). In-stent stenosis of 50% or more was considered significant for the purposes

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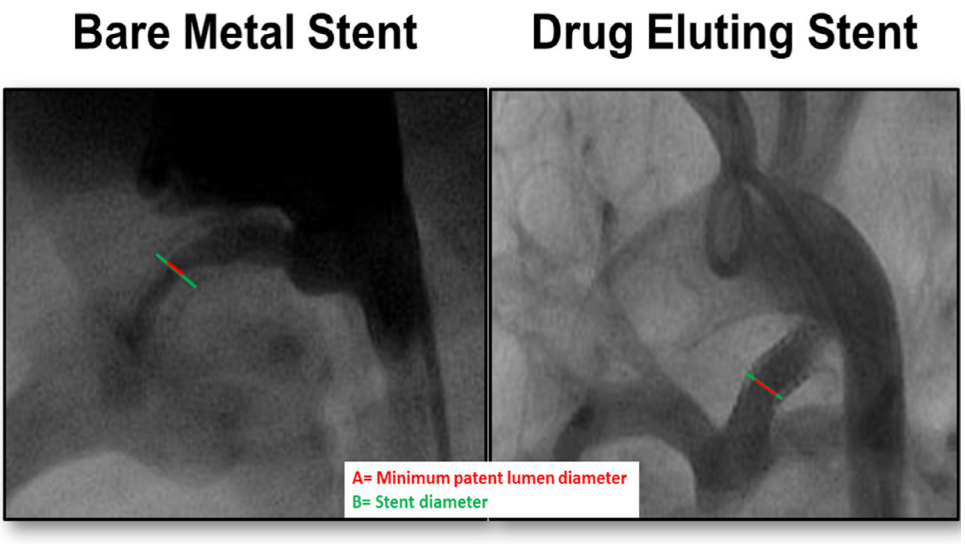

Figure 1. Angiograms at follow-up in 2 comparable patients. The left panel depicts a patient who had bare metal stent and the right panel depicts a patient with drug eluting stent. Note the degree of intimal proliferation in the 2 patients. Patent lumen to stent diameter ratio was calculated by the formula "patent luminal diameter *(A)*/stent diameter *(B)*."

of this study.[7] Secondary outcomes were death, unplanned reintervention to treat cyanosis, PA size (evaluated by Nakata[8] and PA symmetry indices[1]). An unplanned reintervention was defined as an intervention performed specifically for a decrease in systemic oxygen saturation as clinically indicated by the provider.[1] PA size was assessed by measuring the vessel diameter at the hilum, proximal to the origin of the corresponding upper lobe branches. For patients without follow-up angiographic images, PA size was obtained from CT scan, MRI scan, or echocardiograms in that order of preference. All records were examined to calculate that incidence of infection (defined as culture/viral polymerase chain reaction (PCR) positive infection in the first 90 days after stent placement or before hospital discharge), duration of hospital stay, diuretic usage at hospital discharge, and any other planned reinterventions. The follow-up period for all outcomes included the time to complete anatomic repair (for patients with complete 2-ventricle repair), to palliative superior cavopulmonary connection (for patients with single ventricle repair) or to the last follow-up (for patients who have not undergone surgical repair).

This study was approved by the Institutional Review Board with a waiver of the need for informed consent. All statistical analysis was done using SPSS version 20.0. Normality of continuous variables was assessed using histogram, normal probability plots, and the Shapiro-Wilk test for normality. Continuous data were compared between patients treated with DES to those treated with BMS using Wilcoxon rank-sum tests and comparisons between categorical variables were performed using chi-square tests, or Fisher's exact test when expected cell counts were <5. Similar analysis was done to compare patients who did not undergo reintervention to those who underwent planned and unplanned reinterventions. Binary logistic regression analysis was used to perform multivariate regression for comparison of patients who underwent reintervention as compared with those who underwent planned and unplanned reinterventions using variables with p value ≤ 0.1 on univariate analysis and then backward elimination, keeping only those variables with p value <0.05. A p value <0.05 was considered statistically significant.

Results

A total of 94 infants were identified, of whom 71 met entry criteria. A total of 113 stents (75 BMS and 38 DES) were deployed in the DA of 71 infants (46 BMS and 25 DES) for ductal-dependent PBF during the study period. All BMS implanted were Abbott Vascular Multi-Link stents (Abbott Vascular, Santa Clara, California). All DES implanted were second-generation everolimus eluting stents; Boston Scientific Promus Premier stents (Boston Scientific, Natick, Massachusetts) n = 37, and Abbott XIENCE stent (Abbott Vascular, Santa Clara, California), n = 1.

Demographic, clinical, and anatomic factors of all patients can be seen in Table 1. Only 58% of patients were anticipated to have a 2-ventricle repair in future and antegrade PBF was absent in approximately 50% of patients. The DA originated from the descending aorta in nearly one-half of the patients, followed by the underside of the aortic arch, innominate artery, and subclavian artery (Table 1). The Tortuosity Index was relatively straight in one-half of patients and tortuous in the remainder. Due to concerns for transient arterial access compromise, (13%) of patients received enoxaparin therapy in addition to aspirin. The baseline, clinical, and anatomic characteristics of the patients who underwent DES and BMS were comparable (Table 2). The duration of hospital stay and diuretic usage at discharge after stent placement was comparable in both the groups (Table 3).

A total of 36 patients (10 DES and 26 BMS) underwent a repeat cardiac catheterization in whom the stented DA could be evaluated. The median (IQR) time from placement of stent to angiographic evaluation was 88.5 (64.8, 114.8) days [81.4 (57.5, 129.5) days for DES and 104 (69, 157) days for BMS group; p = 0.062]. Only 10% of the variation in the ratio of patent lumen diameter was explained by time (r squared = 0.103, p = 0.046). The primary outcome of patent lumen to stent

Table 1
Demographic, clinical, and anatomic factors of all patients in the study group

Covariate	Study group n = (71)
Anatomic diagnosis	
Pulmonary atresia/ intact ventricular septum	19 (27%)
Tetralogy of Fallot with Pulmonary stenosis/ Pulmonary atresia	14 (20%)
Tricuspid atresia with Pulmonary stenosis/ Pulmonary atresia	6 (8%)
Critical Pulmonary stenosis	6 (8%)
Double Outlet Right Ventricle with Pulmonary stenosis/Pulmonary atresia	12 (17%)
Pulmonary stenosis or Pulmonary atresia with complex anatomy	14 (20%)
Antegrade pulmonary blood flow	36 (51%)
Expected two ventricle physiology	41 (58%)
Baseline characteristics	
Birth weight, kg	2.95 (2.5, 3.4)
Prematurity (<37 weeks)	12 (17%)
Gestational age, weeks	38.2 (37.4, 39.2)
Genetic syndrome	12 (17%)
Other co-morbid medical conditions	19 (27%)
Demographics at ductus arteriosus stenting	
Age, days	10.5 (5, 18.5)
Body weight, kg	3.3 (2.7, 3.6)
Body length, cm	49 (47, 51)
Ductus arteriosus characteristics	
Origin	
Descending aorta	36 (51%)
Underside of the aortic arch	15 (21%)
Innominate artery	15 (21%)
Subclavian artery	5 (7.0%)
Tortuosity index	
Type I- relatively straight	38 (54%)
Type II- 1 turn	18 (25%)
Type III- multiple turns	15 (21%)
Vascular Access used for stent delivery	
Femoral artery	27 (38%)
Femoral vein	25 (35%)
Umbilical artery	10 (14%)
Carotid artery	8 (11%)
Axillary artery	1 (2%)
Stent characteristics	
Bare metal stents	46 (65%)
Drug eluting stents	25 (35%)
Median stent diameter, mm	3.5 (3.5, 4)
Median stent length, mm	15 (12, 18)
Antiplatelet or anticoagulation postductus arteriosus stenting	
Aspirin	62 (87%)
Enoxaparin ± Aspirin	9 (13%)
Outcome	
Death	2 (3%)
Total reinterventions	36 (51%)
Unplanned reinterventions	16 (23%)
Infection after stent placement	3 (4%)
Vascular access related thrombus	7 (10%)
Limb loss due to vascular access related injury	0 (0%)
Total duration of hospital stay, days	8.5 (6, 22)
Saturation at discharge, %	85 (83, 91)
Diuretic use at discharge	33 (47%)
Age at last follow-up, years	1.98 (0.51, 5.5)

Values reported as N (%) or median (twenty-fifth, seventy-fifth percentile).

diameter ratio at the time of subsequent angiographic evaluation prior to definitive surgical intervention favored the DES group (0.81) as compared with BMS (0.5); p = 0.01 (Table 3, Figure 2). An event-free survival analysis was performed (Figure 3). The odds ratio for a 50% loss in the luminal diameter at the time of subsequent angiographic evaluation before definitive surgical intervention for BMS compared with DES was 1.6 (95% confidence interval 1.2 to 2.3; p = 0.014).

There was no difference in mortality between the 2 groups. Early in our experience, 2 patients who received BMS died in the immediate postprocedure period after stent migration (subsequent aspiration after m-BTT shunt with need for ECMO and multiorgan failure) and respiratory arrest (followed by cardiac arrest with intubation with need for ECMO, m-BTT shunt, subsequent intracranial bleed) respectively. There were 2 late mortalities (1 each in BMS and DES groups) after the subsequent staged surgical repair for the congenital heart disease (unrelated to the DA stenting procedure).

A total of 16 (23%) infants underwent unplanned reinterventions to treat cyanosis and 20 (28%) underwent other reinterventions in the follow-up period. A significantly higher number of infants who had BMS underwent unplanned reintervention to treat cyanosis (13/46, 28%) as compared with DES (3/25, 12%); p = 0.02, Table 3. All patients who had an unplanned intervention had oxygen saturation of <75% at the time of reintervention and all those who had planned reinterventions had saturations of >75%. Receiver operator characteristic analysis demonstrated a luminal loss of 50% had a sensitivity of 80% and a specificity of 62% for predicting a saturation lower than 75% in our cohort (area under curve 0.74; p = 0.01).

Both groups had similar rates of planned reinterventions (p = 0.73). Table 4 depicts the univariate and multivariate analysis for the factors among patients who needed unplanned reintervention and those who do not. On univariate analysis prematurity, average stent diameter, type of stent, and saturations at the time of hospital discharge were significantly different in patients who needed unplanned reintervention than those who did not. However, on multivariate analysis, the only factors which were significantly different among the groups were prematurity, saturations at the time of discharge and type of stent used.

Both groups underwent next stage palliation/surgical intervention at similar age, p = 0.14. At the time of surgical repair or the last follow-up (if no subsequent surgical intervention had occurred), the PA size by the Nakata index in the DES group was slightly larger than BMS group, but the difference did not reach statistical difference; p = 0.21 (Figure 4). Both groups had comparable PA symmetry index (Figure 4). A higher rate of bacterial infection (8%) was seen in patients who underwent DES placement as compared with BMS (2%), but the difference did not reach statistical significance. The odds ratio for the risk of bacterial infection for DES was 2.6 (95% confidence interval 0.6 to 10.7); p = 0.22 as compared with BMS group.

Discussion

In this report, we describe single center outcomes of DA stenting in infants for ductal-dependent PBF and present a comparison between BMS and second-generation DES for

Table 2
Differences in patient demographic, clinical, and anatomic factors based on treatment strategy

Covariate	Bare metal stent (n = 46)	Drug eluting stent (n = 25)	p value
Anatomic diagnosis			
Pulmonary atresia/ intact ventricular septum	12 (26%)	7 (28%)	0.99
Tetralogy of Fallot with Pulmonary stenosis/Pulmonary atresia	9 (19%)	5 (20%)	
Tricuspid atresia with Pulmonary stenosis/Pulmonary atresia	4 (9%)	2 (8%)	
Critical Pulmonary stenosis	4 (9%)	2 (8%)	
Double Outlet Right Ventricle with Pulmonary stenosis/Pulmonary atresia	7 (15%)	5 (20%)	
Pulmonary stenosis or Pulmonary atresia with complex anatomy	10 (22%)	4 (16%)	
Expected two ventricle physiology	28 (61%)	13 (52%)	0.54
Intervention prior to PDA stent	16 (35%)	8 (32%)	0.25
Antegrade pulmonary blood flow	23 (50%)	13 (52%)	0.94
Baseline characteristics			
Birth weight, kg	2.83 (2.5, 3.4)	3 (2.4, 3.5)	0.31
Prematurity (<37 weeks)	7 (15%)	5 (20%)	0.55
Gestational age, weeks	38 (37.4, 39)	38.6 (37.3, 39.3)	0.31
Genetic syndrome	8 (17%)	4 (16%)	0.76
Other co-morbid medical conditions	12 (26%)	7 (28%)	0.85
Demographics at ductus arteriosus stenting			
Age, days	11 (5, 20)	8 (5.5, 14.5)	0.69
Weight, kg	3.1 (2.7, 3.6)	3.3 (2.9, 3.7)	0.20
Ductus arteriosus characteristics			
Origin			
Descending aorta	23 (50%)	13 (52%)	
Underside of the aortic arch	11 (24%)	4 (16%)	0.80
Innominate artery	9 (20%)	6 (24%)	
Subclavian artery	3 (6%)	2 (8%)	
Tortuosity index			
Type I- relatively straight	24 (52%)	14 (56%)	
Type II- 1 turn	12 (26%)	6 (24%)	0.29
Type III- multiple turns	10 (22%)	5 (20%)	
Stent characteristics			
Average stent diameter, mm	3.8 (3.5, 4)	4 (3.5, 4)	0.33
Average stent length, mm	16.5 (12, 18)	14 (12, 18)	0.56
Antiplatelet/Anticoagulation therapy			
Aspirin	40 (87%)	22 (88%)	0.68
Enoxaparin ± Aspirin	6 (13%)	3 (12%)	

Values reported as N (%) or median (twenty-fifth, seventy-fifth percentile).

Table 3
Observed differences in outcomes based on treatment strategy

Primary and secondary outcomes	Bare metal stent (n = 46)	Drug eluting stent (n = 25)	p value
Patent lumen/Stent diameter ratio at reintervention (n = 36; Bare metal stent = 26, drug eluting stent = 10)	0.5 (0.38, 0.63)	0.81 (0.69, 0.93)	**0.01**
Death	2 (4%)	0 (0%)	0.83
Total reintervention	26 (56%)	10 (40%)	**0.04**
Unplanned reintervention*	13 (28%)	3 (12%)	**0.02**
Planned reintervention	13 (28%)	7 (28%)	0.73
Nakata Index (mm^2/m^2)	206.2 (145.9,259.4)	265.3 (219.5, 283.0)	0.21
PA symmetry index	0.82 (0.75, 0.97)	0.82 (0.69, 0.94)	0.93
Other outcomes			
Oxygen saturation (at discharge), %	85 (83, 91)	86 (83, 88)	0.51
Total duration of hospital stay, days	9 (7, 24)	7.8 (4, 18)	0.78
Diuretic use at discharge	23 (50%)	10 (40%)	0.74
Infection (culture positive) after stent placement	1 (2%)	2 (8%)	0.16
Age at definitive surgical repair, years	0.65 (0.44, 0.98)	0.52 (0.13, 0.72)	0.14

p- values < 0.05 are in bold.
Values reported as N (%) or median (twenty-fifth, seventy-fifth percentile).
* Unplanned reintervention was defined as reinterventions for cyanosis to treat in-stent restenosis.

this indication. Our study is unique not only from the standpoint of reporting clinical and anatomic outcomes in this patient population, but also due to the fact that the stents used in each treatment arm were strikingly similar (e.g., consistent BMS types and second-generation DES types in each group, with stents in both groups having the similar

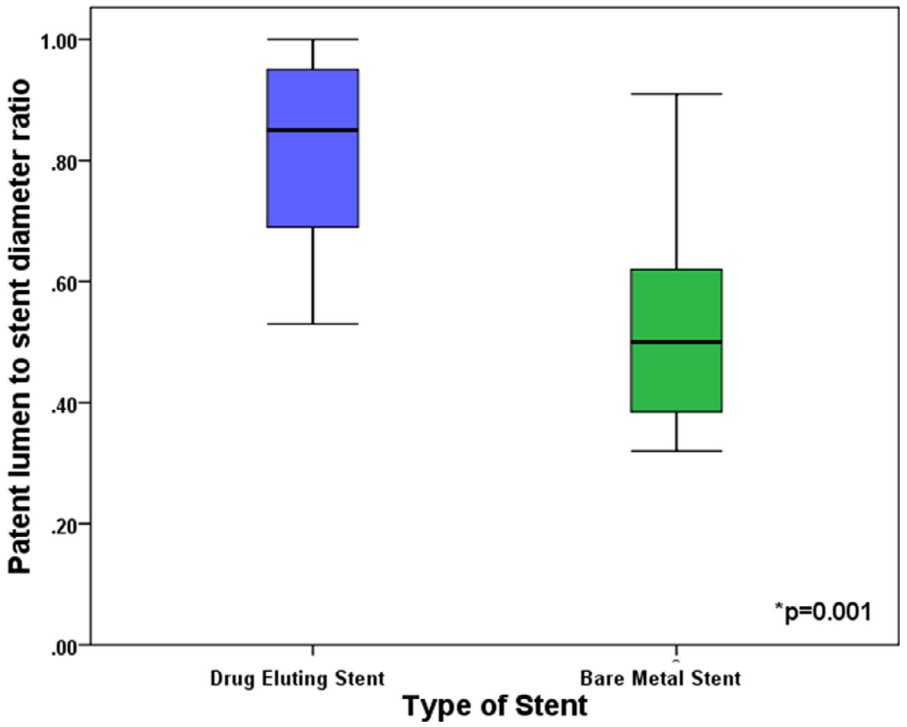

Figure 2. Box-and-whiskers plot showing the difference in patent lumen to stent diameter ratio at the time of subsequent angiographic evaluation prior to surgical repair/palliation among drug-eluting and bare metal stents. The center lines of the boxes delineate the medians, the edges of the boxes the twenty-fifth and seventy-fifth percentile values, and the diamonds the outliers.

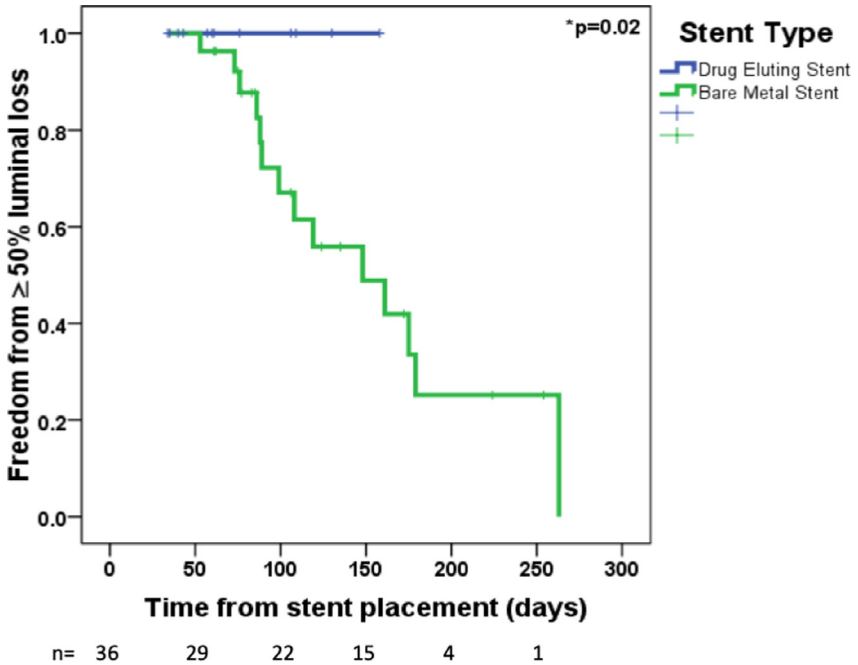

Figure 3. Kaplan-Meier curve depicting the freedom from luminal loss ≥50% at subsequent reintervention before definitive surgical intervention among the patients who received bare metal stents and drug-eluting stents.

strut thickness). We found that unplanned reinterventions were significantly less common in patients in whom a DES was implanted (12%) versus those in whom a BMS was implanted. Luminal loss was significantly less in the DES group. PA size at follow-up was comparable in both groups. DA stenting was able to be performed despite the varied site of origin of the ductus and ductal tortuosity, and overall in our experience, mortality was low.

In a large multicenter report from the Society of Thoracic Surgeons Congenital Heart Surgery Database, a cohort of neonates who underwent m-BTT shunt placement without concomitant procedures experienced in-hospital mortality

Table 4
Predictors of unplanned reintervention among the study group

Covariate	Planned or no reintervention (n = 55)	Unplanned reintervention† (n = 16)	Univariate p value	Multivariate* p value
Number of stents placed	2 (1, 2)	1 (1, 2)	0.12	–
Intervention prior to Ductus Arteriosus stent	19 (35%)	5 (31%)	0.34	–
Antegrade pulmonary blood flow	27 (49%)	9 (56%)	0.61	–
Expected two ventricle physiology	33 (60%)	8 (32%)	0.07#	–
Baseline characteristics				
Gestational age, weeks	38.3 (38, 39.3)	37.8 (35.9, 39)	0.11	–
Prematurity (<37 weeks)	5 (9%)	7 (44%)	**0.01**#	**0.01**
Birth weight, kg	3.0 (2.9, 3.5)	2.7 (1.99, 3.36)	0.23	–
Demographics at ductus arteriosus stenting				
Age, days	11 (5, 20)	8 (4.8, 16)	0.47	–
Weight, kg	3.3 (2.9, 3.6)	2.8 (2, 3.6)	0.06#	–
Stent characteristics				
Average stent diameter, mm	4 (3.5, 4)	3.5 (3, 3.6)	**0.02**#	–
Average stent length, mm	15.5 (12, 18)	15.5 (12, 18.5)	0.77	–
Drug Eluting Stent	22 (40%)	3 (19%)	**0.04**#	**0.03**
Saturations at discharge	88 (85, 94.5)	83 (81.2, 87.5)	**0.05**#	**0.03**
Enoxaparin ± *Aspirin at discharge*	8 (15%)	1 (6%)	0.06#	–

p- values less < 0.05 are in bold.

Values reported as N (%) or median (twenty-fifth, seventy-fifth centile).

* Multivariate analysis was performed including all variables with p value ≤0.1 (marked by # in the table) by univariate analysis and then backward elimination, keeping only those variables with p value <0.05.

† Unplanned reintervention was defined as reinterventions for cyanosis to treat in-stent restenosis.

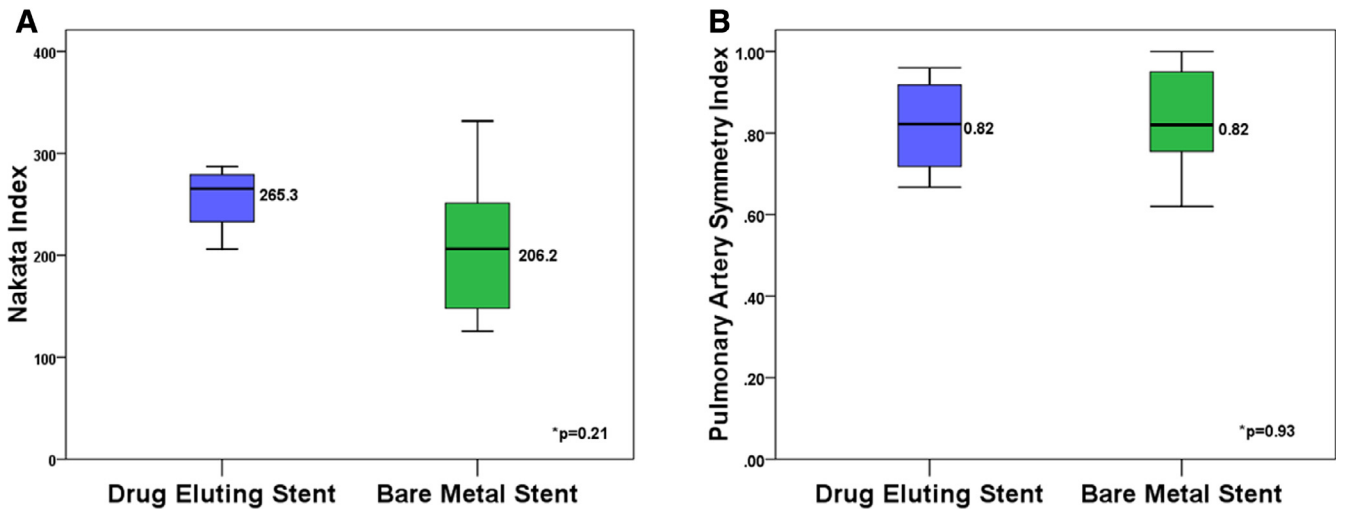

Figure 4. *(A)* Box-and-whiskers plot showing the difference in pulmonary artery size measured by the Nakata index (mm^2/m^2) prior to surgical repair/palliation or latest follow-up among drug eluting and bare metal stents. *(B)* Box-and-whiskers plot showing the difference in pulmonary artery symmetry measured by the pulmonary artery symmetry index (ratio of the smaller pulmonary artery to the larger pulmonary artery) before surgical repair/palliation or latest follow-up among drug-eluting and bare metal stents. The center lines of the boxes delineate the medians, the edges of the boxes the twenty-fifth and seventy-fifth percentile values, and the diamonds the outliers.

at a rate of just over 7%.[9] A recent multicenter comparison of m-BTT shunt to ductal stents for infants with ductal-dependent PBF showed no difference in primary outcome of mortality or unplanned reintervention to treat cyanosis.[1] However, the DA stent group had lower intensive care unit length of stay, lower risk of diuretic use at discharge, lower procedural complications, and better PA size in follow-up.[1] Therefore, DA stenting was proposed as a reasonable alternative to m-BTT shunt placement.[1] A large UK multicenter study[2] showed a reduced risk of death before repair in the DA stent group but a slightly increased risk of reintervention as compared with BT shunt group. Our data showed lower mortality (2%) than that reported from the Society of Thoracic Surgeons Congenital Heart Surgery database[9] for m-BTT shunt patients, and a lower mortality than after either m-BTT shunt or DA stenting from the 2 large multicenter studies recently published.[1,2] A detailed examination of the causes for unplanned reinterventions and whether stent properties may play a role in their occurrence was not evaluated in the previous large studies.[1,2]

Most procedures in the current era for DA stenting in infants with ductal-dependent PBF involve off-label

implantation of stents approved for adults for placement in patients with coronary artery disease. Lower rates of target lesion revascularization in patients with DES as compared with BMS were found in the NORSTENT trial.[10,11] A large meta-analysis by Palmerini et al[12] found significantly lower odds of stent thrombosis in DES than BMS as early as 30 days. Interestingly, everolimus eluting stents (similar to the DES we used in our current study) performed better than zotarolimus and paclitaxel eluting stents.[12]

Lee et al[5] found that the median luminal diameters of BMS were significantly less as compared with DES (rapamycin-eluting stents) placed in arterial ducts in pigs at 4 weeks poststent implantation. At 6 weeks, the BMS group continued to have less luminal diameter compared with DES, though the difference was not significant at that time interval. We used second-generation everolimus eluting stents in all of our patients − Promus Premier (Boston Scientific, Massachusetts) stents in all except 1 patient who received a second-generation everolimus eluting Xience (Abott Laboratories, Illinois) stent. However, both of these stents are fluoropolymer-coated everolimus eluting stents.[13] Moreover, importantly, the strut thickness (which can play a role in differences with regards to luminal loss[14]) were near identical in all of the stents (81 μm − BMS, 86 μm in DES group). From a technical standpoint, newer generation BMS and DES are flexible and relatively easy to advance across even highly tortuous DAs.

Preliminary pharmacokinetics data of a single first-generation, sirolimus DES to stent the DA suggests significantly lower clearance of sirolimus in neonates and peak sirolimus levels being >20 times higher than older children and adults, with no observable adverse clinical outcomes due to the prolonged sirolimus levels.[4] Based on our experience of not noting toxic drug levels and any clinically relevant adverse events from using DES in neonates in other locations, we did not measure drug levels in this cohort of patients. There was a nonsignificant trend of higher rate of infections in patients who received DES than BMS, but this needs to be studied prospectively in a larger cohort of patients.

Whether dual antiplatelet therapy further reduces luminal loss in infants with ductal-dependent PBF underdoing DA stenting is unknown and cannot be answered from our study, as none of our patients received clopidogrel. Dual antiplatelet therapy is recommended for appropriate time periods in adults undergoing implantation of coronary artery stents with and without acute coronary syndrome.[15,16] As the use of DES for neonatal DA stenting increases, it will be important to evaluate the benefits and safety of dual antiplatelet therapy for these patients.

The study is limited by small numbers from a single center which reduces the generalizability of the results. Serum everolimus levels were not measured and a surrogate for immunosuppressive side effects of the drug (in the form of infection) was used. Our data were unable to discern whether the beneficial effect is due to the fluoropolymer coating or the everolimus on the DES or a combination of both. The study was not prospectively randomized (the choice of the stent used was at the discretion of the treating physician) and factors other than what we controlled for may have played a role in luminal loss in these patients. Despite that, the choice of stent type and stent properties was very consistent in both treatment arms.

In conclusion, in infants who underwent DA stent placement for ductal-dependent PBF, fluoropolymer-coated everolimus eluting stents offer promise over BMS with less intimal proliferation, less need for unplanned reinterventions and similar PA growth to BMS.

Disclosures

The authors have no conflicts of interest to disclose.

1. Glatz AC, Petit CJ, Goldstein BH, Kelleman MS, McCracken CE, McDonnell A, Buckey T, Mascio CE, Shashidharan S, Ligon RA, Ao J, Whiteside W, Wallen WJ, Metcalf CM, Aggarwal V, Agrawal H, Qureshi AM. Comparison between patent ductus arteriosus stent and modified Blalock-Taussig shunt as palliation for infants with ductal-dependent pulmonary blood flow: insights from the congenital catheterization research collaborative. *Circulation* 2018;137:589–601.
2. Bentham JR, Zava NK, Harrison WJ, Shauq A, Kalantre A, Derrick G, Chen RH, Dhillon R, Taliotis D, Kang SL, Crossland D, Adesokan A, Hermuzi A, Kudumula V, Yong S, Noonan P, Hayes N, Stumper O, Thomson JDR. Duct stenting versus modified Blalock-Taussig shunt in neonates with duct-dependent pulmonary blood flow: associations with clinical outcomes in a multicenter national study. *Circulation* 2018;137:581–588.
3. Kalra A, Rehman H, Khera S, Thyagarajan B, Bhatt DL, Kleiman NS, Yeh RW. New-generation coronary stents: current data and future directions. *Curr Atheroscler Rep* 2017;19:14.
4. Lee KJ, Seto W, Benson L, Chaturvedi RR. Pharmacokinetics of sirolimus-eluting stents implanted in the neonatal arterial duct. *Circ Cardiovasc Interv* 2015;8. pii: e002233.
5. Lee KJ, Hinek A, Chaturvedi RR, Almeida CL, Honjo O, Koren G, Benson LN. Rapamycin-eluting stents in the arterial duct: experimental observations in the pig model. *Circulation* 2009;119:2078–2085.
6. Qureshi AM, Goldstein BH, Glatz AC, Agrawal H, Aggarwal V, Ligon AR, McCracken C, McDonnell A, Buckey TM, Whiteside W, Metcalf CM, Petit CJ. Classification scheme for ductal morphology in cyanotic patients with ductal dependent pulmonary blood flow and association with outcomes of patent ductus arteriosus stenting. *Catheter Cardiovasc Interv* 2019;93:933–943.
7. Lee MS, Banka G. In-stent restenosis. *Interv Cardiol Clin* 2016;5:211–220.
8. Nakata S, Imai Y, Takanashi Y, Kurosawa H, Tezuka K, Nakazawa M, Ando M, Takao A. A new method for the quantitative standardization of cross-sectional areas of the pulmonary arteries in congenital heart diseases with decreased pulmonary blood flow. *J Thorac Cardiovasc Surg* 1984;88:610–619.
9. Petrucci O, O'Brien SM, Jacobs ML, Jacobs JP, Manning PB, Eghtesady P. Risk factors for mortality and morbidity after the neonatal Blalock-Taussig shunt procedure. *Ann Thorac Surg* 2011;92:642–651.
10. Wiseth R, Bønaa KH. Potential implications of NORSTENT (Norwegian Coronary Stent Trial) in contemporary practice. *Circulation* 2017;136:701–703.
11. Bønaa KH, Mannsverk J, Wiseth R, Aaberge L, Myreng Y, Nygård O, Nilsen DW, Klow NE, Uchto M, Trovik T, Bendz B, Stavnes S, Bjornerheim R, Larsen AI, Slette M, Steigen T, Jakobsen OJ, Bleie O, Fossum E, Hanssen TA, Dahl-Eriksen O, Njolstad I, Rasmussen K, Wilsgaard T, Nordrehaug JE, Investigators N. Drug-eluting or bare-metal stents for coronary artery disease. *N Engl J Med* 2016;375:1242–1252.
12. Palmerini T, Biondi-Zoccai G, Della Riva D, Stettler C, Sangiorgi D, D'Ascenzo F, Kimura T, Briguori C, Sabate M, Kim HS, De Waha A, Kedhi E, Smits PC, Kaiser C, Sardella G, Marullo A, Kirtane AJ, Leon MB, Stone GW. Stent thrombosis with drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. *Lancet* 2012;379:1393–1402.
13. Byrne RA, Stone GW, Ormiston J, Kastrati A. Coronary balloon angioplasty, stents, and scaffolds. *Lancet* 2017;390:781–792.
14. Ormiston JA, Webster MW, Ruygrok PN. Stent strut thickness and restenosis. *Circulation* 2002;105:E12.

15. Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, Falk V, Filippatos G, Hamm C, Head SJ, Juni P, Kappetein AP, Kastrati A, Knuuti J, Landmesser U, Laufer G, Neumann FJ, Richter DJ, Schauerte P, Sousa Uva M, Stefanini GG, Taggart DP, Torracca L, Valgimigli M, Wijns W, Witkowski A. 2014 ESC/EACTS guidelines on myocardial revascularization: the task force on myocardial revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *Eur Heart J* 2014;35:2541–2619.
16. Levine GN, Bates ER, Bittl JA, Brindis RG, Fihn SD, Fleisher LA, Granger CB, Lange RA, Mack MJ, Mauri L, Mehran R, Mukherjee D, Newby LK, O'Gara PT, Sabatine MS, Smith PK, Smith SC Jr. 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: An Update of the 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention, 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease, 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction, 2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes, and 2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery. *Circulation* 2016;134:e123–e155.