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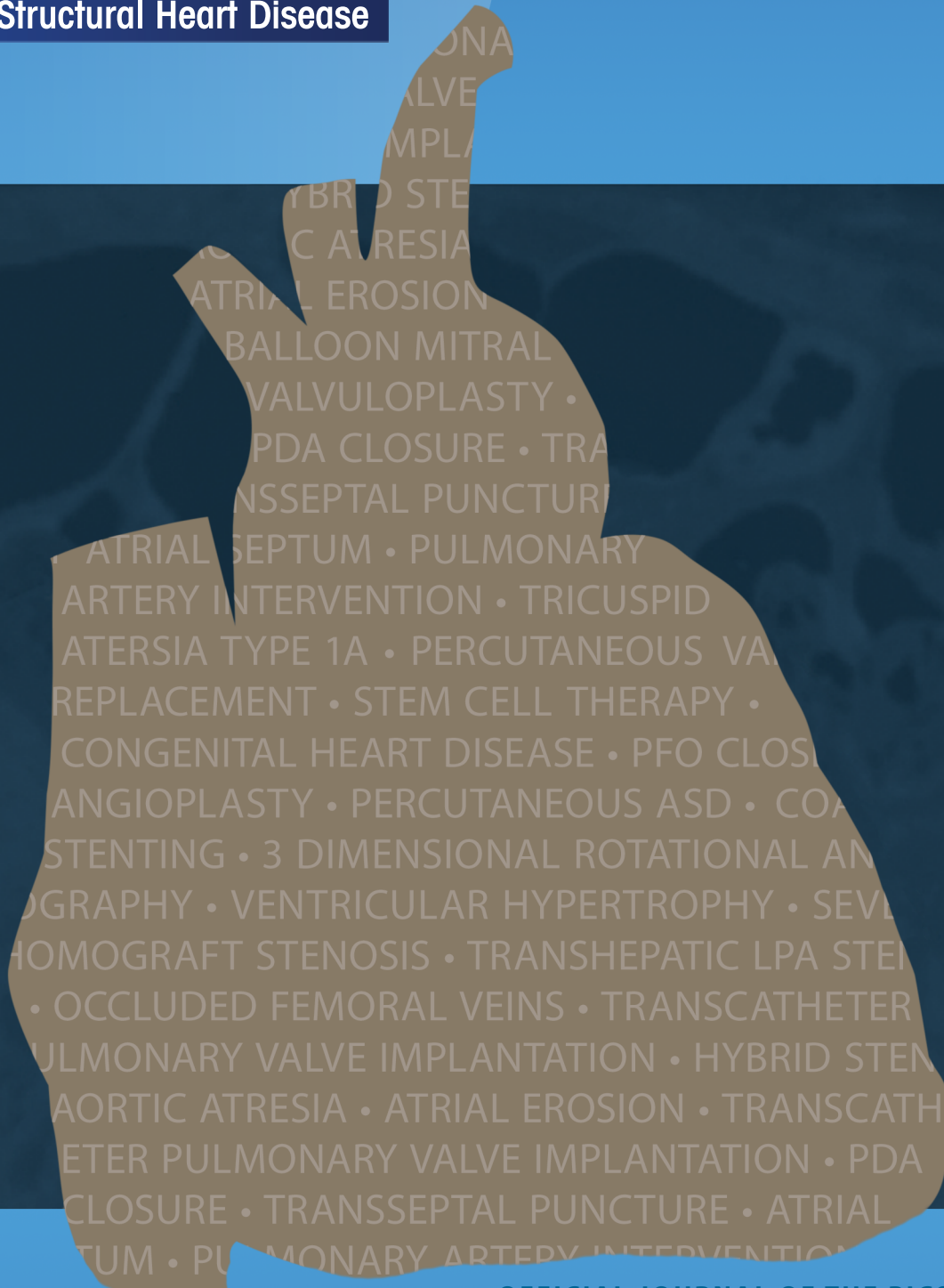
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Percutaneous Atrial Septal Closure in Immunocompromised Patients

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Abstract

Background: Percutaneous closure devices for cardiac defects have been used with a high degree of efficacy and safety. However, patients with autoimmune disease or immunosuppression are excluded in clinical trials due to their presumed higher risk. Percutaneous closure of patent foramen ovale (PFO) or atrial septal defect (ASD) is safe in patients who are immunosuppressed or have autoimmune disease.

Methods: A retrospective observational multicenter study was performed including 24 patients who were immunocompromised or had autoimmune disease from vasculitis, Human Immunodeficiency Virus, hepatitis, cancer, or renal transplant and underwent percutaneous PFO or ASD closure for cryptogenic stroke (9.38%), desaturation (5.21%), migraine (7.29%), or a combination of these diagnoses (3.13%). Post-procedure follow-up included clinical evaluation at 3–6 months or telephone questionnaire up to 8 years later.

Results: Of the 24 patients who met inclusion criteria (53 ± 14 years of age, follow-up of 21 ± 28 months), 19 had a PFO (79%), 5 had an ASD (21%), and 21 (88%) underwent closure. There was no evidence of endocarditis, device erosion, exacerbation of migraine, or recurrent stroke. Only one patient (4%) experienced a transient neurologic deficit after closure due to complex migraine with visual aura. Mortality status, which was verified by the social security death index, showed five deaths related to non-cardiac conditions.

Conclusion: This observational study of an uncommon condition suggests that percutaneous closure of a PFO or ASD is safe in immunocompromised patients.

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Key Words

Percutaneous closure • Immunocompromised • Atrial septal defect • Patent foramen ovale • Stroke • Migraine

Introduction

Intra-cardiac defects such as patent foramen ovale (PFO) and atrial septal defect (ASD) are often closed off-label for cryptogenic stroke, migraine, or hemodynamically significant ASD. The incidence of device-related infection in patients with normal immune systems who undergo closure is exceedingly rare. In a retrospective survey of PFO closure device explantation, only 38 devices were explanted for various reasons out of 13,736 cases (0.28%), with only one explanted due to endocarditis [1]. Some risk factors may predispose patients to greater risk of infection of a closure device, such as diabetes, renal failure, organ transplant, immunosuppressed state, or autoimmune disease. The safety of PFO or ASD closure in patients who are immunocompromised or have an autoimmune disorder is unknown because patients with these conditions are excluded from randomized

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clinical trials. Therefore, this study was a retrospective observational analysis of percutaneous PFO or ASD closure in immunocompromised patients to determine safety with respect to infective endocarditis or erosion.

Materials and Methods

We conducted a retrospective observational study of patients at two tertiary care centers in the United States that perform a high volume of percutaneous closure procedures. The centers' databases were reviewed to identify any immunocompromised or autoimmune disease patients who had received a PFO or ASD closure device.

Patients were informed of the investigational and non-FDA-approved indication for PFO closure, and they desired closure for prevention of future strokes, complex migraine with transient visual neurologic deficit, or recurrence of migraine headaches. Informed and written consent was obtained from all patients.

Based upon operator preference, all patients received pre- or post-procedural antibiotics (cefazolin, clindamycin, levofloxacin, or vancomycin as the sole agent) up to 48 hours after closure. Patient outcomes were assessed via 3–6-month clinical follow-up or phone questionnaire up to eight years later (mean 21 ± 28 months) consisting of questions pertaining to migraines, palpitations, chest pain, infections, closure complications post-procedure, worsening or improvement in migraines, post-closure stroke, and general health condition post-closure. For patients who were unreachable for phone interview, mortality status was verified by the social security death index.

Results

Our total patient population (n = 1,303) consisted of 908 PFO (69.7%) and 395 ASD (30.3%) patients, of which only 24 patients (1.8%) met our inclusion criteria. These 24 immunocompromised patients were identified from October 2002 to September 2014 and had systemic lupus erythematosus, rheumatoid arthritis, mixed connective tissue disease, non-specific connective tissue disease, scleroderma, end-stage renal disease post-renal transplant, Sjogren's syndrome,

hepatitis A, hepatitis C, or human immunodeficiency virus (HIV). They were treated with various immunosuppressants and had a PFO or ASD. PFO or ASD were documented by transesophageal echocardiography, transthoracic echocardiography, or transcranial doppler evaluation. Patients were referred for PFO or ASD closure due to a history of previous stroke, complex migraine with transient visual neurologic deficit, desaturation, or migraines (with or without aura) in isolation or as a combination of events (n = 21, 87.5%). Other closure indications included chest pain (n = 1, 4.2%), pre-liver transplant work-up (n = 3, 12.5%), and pulmonary embolism with right heart failure (n = 1, 4.2%). Immunosuppressant medications included prednisone, mycophenolate mofetil, methotrexate, leucovorin, cyclophosphamide, azathioprine, hydroxychloroquine sulfate, leflunomide, rituximab, chemotherapeutic agents (folfirinox, gemcitabine, and other unspecified agents), ritonavir, emtricitabine/tenofovir disoproxil (HIV combination medication), elvitegravir/cobicistat/emtricitabine/tenofovir/disoproxil (HIV combination medication), or darunavir as sole agents or in various combination regimens.

Of the 24 patients (53 ± 14 years of age), 19 had a PFO (79.1%), 5 had an ASD (20.8%), and 21 underwent closure (87.5%). Two patients (8.3%) declined percutaneous closure and were lost to follow-up. Both had obstructive sleep apnea with hypersomnia, which is associated with increased risk of right-to-left shunting in the presence of a PFO [2, 3]. During cardiac catheterization, one patient (4.2%) was deemed an inappropriate candidate for closure secondary to pulmonary hypertension from scleroderma and was referred for lung transplant evaluation. All PFO or ASD closure procedures were successful. Figure 1 shows the proportion of PFO and ASD patient groups. All patients with autoimmune disorders were treated with single or combination immunosuppressive drug regimens, leading to an immunocompromised state.

No periprocedural complications occurred during closure. One patient (4.2%) experienced a transient neurologic deficit during follow-up associated with lightheadedness, scintillating scotoma, and severe headache, which was diagnosed as complex migraine with visual aura. No patient reported endocarditis, device erosion, exacerbation of migraine, or recurrent stroke. Of the seven patients (29.2%) who
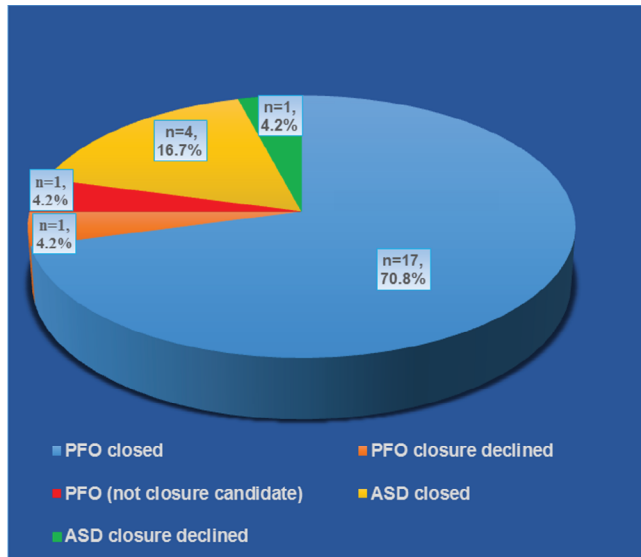
Figure 1. Patent foramen ovale and atrial septal defect patient groups (21 patients underwent closure; two declined closure; one not a closure candidate).

had migraine prior to closure, five (71.4%) reported resolution of migraines. There were five deaths (20.8%); three were due to non-cardiac conditions (one of these patients did not receive a device), one was associated with metastatic pancreatic cancer, and one was due to unknown causes in a 77-year-old woman who did not receive a device. Table 1 shows closure indications and patient outcomes.

Discussion

As patients who are immunocompromised or have an autoimmune disease are at higher risk of developing an infection [4, 5, 6], there is a concern that implanting a permanent foreign body in the vasculature might increase their risk of developing endocarditis. In addition, the healing process in these patients may be compromised, and some devices could be associated with a higher risk of erosion through a thin atrial wall. However, there are no data published regarding the use of cardiac devices in this patient population because these patients are specifically excluded from prospective randomized trials of new devices to diminish the risk of complications that could make the device appear unsafe upon review by the FDA. Nevertheless, clinical indications for closure of ASD

or PFO may arise in immunocompromised patients. Thus, the purpose of this retrospective observational study was to determine whether there is increased risk in immunocompromised patients who have an implanted closure device.

Although this was a small patient population (24 out of 1,303 cases) with a relatively rare combination of disorders, it is encouraging to note that there were no severe complications reported, such as increased risk of endocarditis or erosion of the device.

The occurrence of device infection after percutaneous PFO or ASD closure is extremely uncommon. A few case reports have described the occurrence of endocarditis from a PFO or ASD device, which commonly necessitates surgical explantation [7, 8, 9]. One case describes successful treatment achieved solely with antibiotics [10]. However, no observational or randomized controlled studies have been performed for infections associated with septal closure devices.

Other implantable therapeutic foreign bodies in patients with normal immune function, such as pacemakers or implantable cardioverter defibrillators, are more prone to infections (1–6%), which increases the risk of mortality even after successful treatment of the infection [11, 12, 13]. Pacemaker infection rates from the 1970s to 1980s were even higher (1–19.9%) [14].

Our study patients received medications that are known to suppress the immune system and had various medical conditions that predisposed them to an immunocompromised state (Table 1). Autoimmune disease also may induce a prothrombotic state promoting stroke, such as an HIV patient with protein C and protein S deficiency who developed a stroke in the presence of a PFO [15]. The prevalence rates of anti-cardiolipin antibodies in patients with ischemic strokes were 17–21% [16]. A retrospective case series of 40 patients showed that anti-phospholipid antibodies and hypercoagulability is common in patients with PFO [17]. A case-controlled study also showed that anti-phospholipid antibodies are strongly associated with PFO and atrial septal aneurysms [18]. Hence, autoimmune diseases with various hypercoagulable factors may increase the risk of stroke, which may be reduced with PFO closure. Of the patients in our study, one had anti-phospholipid antibodies with Sjogren's syndrome and another had anti-cardiolipin antibodies with systemic lupus erythematosus. Both patients developed a

Table 1. PFO and ASD closure indications and outcomes (n = 24)

Patient	Closure Indication	Device	Size (mm)	Complications	Residual Shunt (TEE/ TCD/ICE)	Post-Procedure Symptoms	Post-Procedure Follow-Up (months)
1	Stroke	Cardioseal	28	None	Trace (TEE)	None	2
2	Desaturation	Amplatzer	35	None	No (TEE)	None (died, non-cardiac etiology)	89
3	Desaturation	Amplatzer	Unspecified	None	Small (TEE)	None (died, non-cardiac etiology)	47
4	Stroke, Desaturation	No closure (PHTN, referred for lung transplant evaluation)	N/A	N/A	N/A	N/A (died, non-cardiac etiology)	7
5	Stroke	Amplatzer	35	None	Moderate (TEE)	None	3
6	Migraine without area, orthodex-ia-platypnea	Cribiform	35	None	No (TEE)	Migraine and orthodexia-platypnea resolved	3
7	Migraine without aura	Helex	25	None	No (ICE)	Migraine resolved	62
8	Migraine (ocular)	Helex	25	None	No (TEE)	Migraine resolved, transient neurologic deficit	57
9	Stroke	Helex	25	None	No (TEE)	None	3
10	Stroke, migraine with aura, TIA	Helex	25	None	No (TEE)	None	None
11	Migraine without aura	No closure (patient declines)	N/A	N/A	N/A	N/A	2
12	Migraine with aura	Helex	25	None	No (TEE)	Migraine resolved	50
13	Desaturation	Amplatzer	15	None	No (ICE)	None	None
14	Stroke	Amplatzer	6	None	No (TEE)	None (died, pancreatic cancer with metastasis on chemother-apy)	None
15	Stroke	Helex	25	None	Yes (ICE)	None	1
16	Chest pain	Cribiform	35	None	No (ICE)	Unknown	None
17	Pre-liver transplant evaluation	Helex	25	None	No (TEE)	None	3
18	Stroke	Helex	25	None	No (ICE)	None	None
19	Stroke	Amplatzer	14	None	No (TEE)	Musculoskeletal chest pain	3
20	Pre-liver transplant evaluation	Cribiform	25	None	No (TEE)	None	3
21	Pre-liver transplant evaluation	Helex	25	None	No (TEE)	None	6

(*Continued*)

Table 1 (*Continued*). PFO and ASD closure indications and outcomes (n = 24)

Patient	Closure Indication	Device	Size (mm)	Complications	Residual Shunt (TEE/TCD/ICE)	Post-Procedure Symptoms	Post-Procedure Follow-Up (months)
22	Pulmonary embolism with right heart failure	Helex	30	None	No (TEE)	None	1
23	Right atrial and right ventricular enlargement	No closure (patient declined)	N/A	N/A	N/A	N/A (died, unknown etiology)	None
24	Migraine with aura	Amplatzer	10	None	No (TEE)	Migraine resolved	3

PFO = patent foramen ovale; ASD = atrial septal defect; TEE = transesophageal echocardiography; TCD = trans-cranial Doppler; ICE = intracardiac echocardiography; PHTN = pulmonary hypertension; N/A = non-applicable; TIA = transient ischemic attack

stroke in the presence of a PFO. Conversely, the PFO in Cryptogenic Stroke Study and the Anti-Phospholipid Antibodies and Stroke study (PICSS-APASS) post-hoc retrospective analysis did not show an increased risk of stroke in patients with anti-phospholipid antibodies and PFO [19].

Our study has some limitations. This was a retrospective observational study of a complex but small patient population, which limits the generalizability of the results and prohibits adequate power for statistical analysis. Also, 10 out of the 21 patients (47.6%) underwent closure with the Helex device, which has not been associated with erosions. This fact may have diminished the risk of erosions even in an autoimmune population. Nevertheless, this study provides a small database on the use of device closure in these vulnerable patients, as no prior studies describe their treatment. This study was set at tertiary care centers with highly experienced operators who routinely perform PFO or ASD closures.

In conclusion, this small observational study shows the safety of PFO or ASD closure in patients who are immunocompromised or have autoimmune disorders. Patients reported an improvement or resolution of debilitating migraine, and there was no recurrence of stroke after closure. In this high-risk patient population, there were no procedural complications, local or systemic infection, endocarditis on the implanted device, or complications such as erosion across a follow-up period of up to 8 years (mean of 21 months).

Conflict of Interest

The authors have no conflict of interest relevant to this publication.

Comment on this Article or Ask a Question

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Moderate Altitude Is Not Associated with Pulmonary Arterial Hypertension in Adult Patients Referred for Transcatheter Device Closure of Atrial Septal Defects

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Abstract

Background: Pulmonary arterial hypertension (PAH) occurs in 6–10% of adults with atrial septal defects (ASDs). Although larger defect size and older age are two risk factors for the development of PAH in these patients, little is known about the impact of elevation. Thus, we aimed to determine whether the incidence of PAH is higher among patients living at moderate altitude who are referred for transcatheter device closure of an ASD. **Methods:** Our multicenter, retrospective cohort study included patients at least 18 years of age who were referred for device closure of an ASD (> 4 mm) during a 10-year period (2003–2013). Catheterization records from three centers were reviewed. **Results:** Thirty-seven moderate altitude (4983–5633 ft) and 126 low altitude (74–839 ft) patients were identified (p < 0.0001). After controlling for age, living at moderate altitude was associated with a greater likelihood of pulmonary hypertension (odds ratio 2.29, 95% confidence interval 1.01–5.19, p = 0.046), but there was no such association with PAH (p = 0.9). **Conclusion:** Patients with ASD living at moderate altitude are more likely to exhibit pulmonary hypertension but not PAH compared with patients living at sea level. Therefore, while moderate altitude can increase pulmonary pressures, it did not contribute to the development of PAH in our cohort of patients with ASDs.

Key Words:

Atrial septal defect • Pulmonary hypertension • Pulmonary arterial hypertension • Altitude

Introduction

Atrial septal defects (ASDs) represent 6–10% of all congenital heart defects [1]. Left unrepaired or if diagnosed later in life, ASDs are associated with pulmonary hypertension (PH, elevated pulmonary artery pressures) or pulmonary arterial hypertension (PAH, elevated pressures and pulmonary vascular disease with normal left heart pressures). The latter condition results from years of left-to-right shunting and excessive pulmonary blood flow, which in turn can lead to irreversible pulmonary vascular remodeling characterized by medial hypertrophy, intimal thickening, and arteriolar muscularization [2]. Although ASDs cause a minority of cases of PAH associated with congenital heart disease [3, 4], progressive pulmonary vascular disease and elevated resistance can result in right heart failure, reversal of the intracardiac shunt, or Eisenmenger syndrome. Other morbidities can also arise in the setting of an unrepaired ASD, such as paradoxical embolism and stroke due to transient right-

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to-left shunt across the defect. For these reasons, patients with unrepaired ASDs are often referred for cardiac catheterization to assess pulmonary vascular resistance (PVR) and shunt fraction (Qp:Qs) followed by transcatheter device closure of the defect should there be favorable anatomy and hemodynamics.

Not all patients with unrepaired ASDs develop PAH. Although older age and defect size are independent predictors of PAH in patients with ASDs [5, 6, 7], other risk factors are unknown. One possible risk factor may be living at higher altitude. Living at higher elevations may increase a person's risk of developing PH/PAH due to lower oxygen tension, contributing to more substantial oxygen saturation variability, pulmonary vasoconstriction, and pulmonary vascular remodeling irrespective of the presence of structural heart defects [8, 9]. In patients with unrepaired ASDs, little is known about these effects of elevation. Specifically, how much does living at a moderately high altitude raise pulmonary artery pressures, and is this associated with pulmonary vascular remodeling? Thus, we aimed to determine whether living at moderate altitude (4500–6000 ft or 1372–1829 m) is associated with a greater likelihood of developing PAH among patients referred for transcatheter device closure of ASDs.

Materials and Methods

This was a multicenter, retrospective cohort study of adult patients who were referred for transcatheter device closure of an ASD during a 10-year period (2003–2013). Catheterization databases and records from three academic centers were reviewed after individual institutional review boards approved the study. Variables extracted from records were demographic information including the patient's zip code of residence, presence of other risk factors for PH such as lung disease or sleep apnea, use of PH/PAH medications, and catheterization measurements including mean pulmonary artery pressure (mPAp), pulmonary capillary wedge pressure (PCWp), PVR, Qp:Qs, and defect size (balloon-sized or pre-procedure size measured by echocardiography). Elevation was defined as 'moderate altitude' if the zip code elevation was ≥ 4500 ft. Otherwise, elevation was considered 'low altitude'. The primary outcome was the presence of PAH, defined as mPAp ≥ 25 mmHg, PVR > 3 Wood units × m², and

PCWp ≤ 15 mmHg. The secondary outcome was the presence of PH, defined as mPAp ≥ 25 mmHg without elevated PVR and/or with PCWp > 15 mmHg.

Patients aged 18 to 99 years with an ASD or ASD physiology (i.e., partial anomalous pulmonary venous return) were included. Patients with a patent foramen ovale, ASD < 4 mm (in any one imaging plane), residual ASD after prior surgical or transcatheter device closure, or other types of congenital heart disease were excluded. Raw catheterization data were collected, and Qp:Qs and PVR were independently calculated for each patient (reported values were not used). In cases in which catheterization data were incomplete, such as in reports lacking pulmonary vein and/or systemic arterial saturations, a value of 95% was used. Oxygen consumption (VO2) was derived from the LaFarge equation and table, which provides an estimated VO2 based on the patient's age and heart rate.

Study data were collected and managed using REDCap electronic data capture tools hosted by the University of Colorado [10]. Data were tested for normality using Shapiro-Wilk tests. Non-normally distributed continuous data are presented as median (interquartile range), and categorical data are presented as frequency (percentage). Comparative statistics were calculated using Wilcoxon rank-sum or Chi-square tests, as appropriate. As pulmonary pressures are known to increase with age, catheterization data were further analyzed for differences between elevation categories using logistic regression controlling for age. All analyses were performed with Statistical Analysis Software (SAS Institute, version 9.4, Cary, NC).

Results

Thirty-seven moderate altitude and 126 low altitude patients were identified. Baseline patient characteristics are outlined in Table 1. Elevations of patients' zip codes of residence ranged from 74 to 7110 ft above sea level, with a median elevation of 246 ft in the low-altitude group (74–839 ft) and 5334 ft in the moderate altitude group (4983–5633 ft, p < 0.0001).

Defect size and PCWp were similar between groups as shown in Table 2. Despite the lack of difference in Qp:Qs between groups (median Qp:Qs 1.5 vs. 1.6, p = 0.07), there was a trend toward higher pulmonary artery pressures in the moderate altitude group

Table 1. Demographic data.

	Moderate Altitude, n = 37	Low Altitude, n = 126	P
Male gender	11 (30%)	29 (23%)	0.40
Age (years)	45 (35–61)	36 (23–55)	0.01
Body surface area (m^2)	1.8 (1.7–2.1)	1.8 (1.6–2.0)	0.13
Presence of lung disease	3 (8%)	2 (2%)	0.29
Presence of obstructive sleep apnea	1 (3%)	2 (2%)	0.39
Taking PH medication	3/22 (25%)*	13/22 (59%)*	0.05
Elevation (ft)	5334 (4983–5633)	246 (74–839)	< 0.0001

PH = pulmonary hypertension

Table 2. Catheterization data.

	Moderate Altitude, n = 37	Low Altitude, n = 126	P
Defect size (mm)	20 (18–27)	22 (17–26)	0.61
Qp:Qs	1.5 (1.1–2.0)	1.6 (1.2–2.4)	0.07
mPAp (mmHg)	25 (16–33)	19 (15–26)	0.05
PCWp (mmHg)	11 (7–14)	10 (7–13)	0.82
PVR (Wood units)	1.8 (1.1–2.7)	1.1 (0.7–1.8)	0.008
mPAp ≥ 25 mmHg	20 (54%)	37 (29%)	0.006
PCWp ≤ 15 mmHg	32 (86%)	110 (87%)	0.90
PVR > 3 Wood units × m^2	6 (16%)	17 (13%)	0.68
PH present†	18 (50%)	34 (27%)	0.010
PAH present‡	5 (28%)	10 (29%)	0.90

Qp:Qs = shunt fraction; mPAp = mean pulmonary artery pressure; PCWp = pulmonary capillary wedge pressure; PVR = pulmonary vascular resistance; PCWp = pulmonary capillary wedge pressure; PH = pulmonary hypertension; PAH = pulmonary arterial hypertension
†Criteria for PH: mPAp ≥ 25 mmHg only
‡Criteria for PAH: mPAp ≥ 25 mmHg, PCWp ≤ 15 mmHg, and PVR > 3 Wood units × m^2
* Incomplete information was available for the entire cohort

(median mPAp 25 mmHg vs. 19 mmHg, p = 0.05), and PVR was significantly higher in the moderate altitude group than in the low altitude group (median PVR 1.8 vs. 1.1 Wood units × m^2, p = 0.008).

When evaluating components of the clinical definition of PAH (i.e., mPAp ≥ 25 mmHg, PCWp ≤ 15 mmHg, and PVR > 3 Wood units × m^2), we found a significant difference in the prevalence of PH (mPAp ≥ 25 mmHg) between groups, even when controlling for age (odds ratio 2.29, 95% confidence interval 1.01–5.19, p = 0.046). However, there was no difference in the prevalence of PAH between groups (5/37 (28%) at moderate altitude vs. 10/126 (29%) at low altitude, p = 0.9).

Discussion

Although ASDs are a relatively small contributor to the overall prevalence of PAH in congenital heart disease, significant morbidity can occur when these defects are unrepaired. Referral for transcatheter device closure remains an important part of the management of ASDs but requires an accurate assessment of Qp:Qs and PVR with right heart catheterization (RHC) before deciding on the need and safety of device closure. If PVR is significantly elevated (i.e., > 8 Wood units × m^2 [11]) closure of the defect may result in pressure-overload of the right ventricle with subsequent chamber enlargement and failure. By evaluating RHC data from a large cohort of patients who were referred for tran-

scatheter device closure of ASDs at different elevations, we sought to determine whether elevation is an independent risk factor for the development of PAH in these patients.

We evaluated individual RHC hemodynamic data as well as data contributing to the clinical classifications of PH and PAH (with PAH referring to pulmonary vascular disease with elevated pulmonary artery pressures and normal left heart pressures). We found that patients living at moderate altitude showed a trend toward higher pulmonary artery pressures and that more patients living at moderate altitude met the clinical definition of PH than those living at low altitude. We suspect this is secondary to lower oxygen tension and more hypoxic vasoconstriction, as defect size, shunt fraction, and the presence of other causes of PH or use of PH medications were similar between groups.

In looking at PVR and PAH, the presence of which is the main contributor to morbidity in these patients and thus was our choice for primary outcome, we found that although PVR was significantly higher in the moderate altitude group, it was not elevated to the clinically important threshold that defines PAH. We believe that the higher pulmonary arterial pressures seen in the moderate altitude group contribute to higher calculated PVR (as mPAp makes up one half of the numerator in the PVR calculation, (mPAp-PCWp)/Qp), but there is likely no significant difference between groups in actual pulmonary vascular disease.

Patients with unrepaired ASDs or ASD physiology and defect size ≥ 4 mm were chosen because these patients are most likely to have a hemodynamically significant shunt that may predispose to the development of pulmonary vascular changes and PAH. By excluding patients with a patent foramen ovale or small defects, we intended to avoid a false underestimation of PAH prevalence in patients with interatrial communications. By excluding other types of congenital heart disease, such as ventricular septal defects, aortopulmonary connections, or other causes of left-to-right shunt and excessive pulmonary blood flow, we intended to prevent a false overestimation of the burden of PAH. We did not exclude patients with multiple PH risk factors or multifactorial PH/PAH because it is quite common for a patient to have more than one cause of PH/PAH, such as having an ASD and obstructive sleep apnea. By looking primarily at PAH (and not PH), we focused on patients with true pulmonary vascular disease rather than those with excessive pulmonary blood flow and/or increased pulmonary pressures from lung or left heart disease.

There are several limitations of this study. First, inaccurate hemodynamic analysis using false data can often be a challenge when studying cardiac catheterizations. Specifically, a catheterization lab's computer software generates results of complex calculations of multiple variables, of which the software attempts to select variables from the data it 'sees' and/or a human operator chooses. This can result in reported calculations or results that are not physiologically correct. To avoid the problem of comparing software-generated results, we reviewed the catheterization reports closely for the values that should be used in the calculations and performed the calculations independently. In some cases, assumptions were still necessary. For instance, we used pulse oximeter saturation as a surrogate for pulmonary vein and systemic arterial saturations when these data were not available or used a value of 95% as the pulmonary vein and systemic saturation when no pulse oximeter saturation was available. Furthermore, the assumed value of 95% may vary at moderate elevation compared to sea level.

Second, we made several assumptions about our patients. We assumed that the zip code of a patient's residence at the time of chart review was the same zip code and elevation at which he or she was living at the time of the catheterization. For catheterizations 7–10 years ago, however, this may not be the case. We also assumed that a patient was living at a particular elevation long enough for it to impact his or her risk of developing PAH. Unfortunately, data regarding duration of residence at that elevation prior to catheterization was not available.

Third, residence in Denver or at elevations similar to Denver's may not be high enough to reveal a difference in the development of PAH compared with residence at sea level. Previously, 8200 ft (2500 m) or higher has been described as a threshold at which significant pulmonary vascular disease can develop [12], and Denver's population is well below that mark at 5280 ft (1600 m). Although elevation-related increases in pulmonary pressures are certainly present

at elevations below 8200 ft, the effect of Denver's elevation (i.e., the elevation at which the majority of our moderate altitude patients were living) may be less significant than expected. Still, we feel that reporting these results is important for centers at moderate elevation.

In conclusion, patients with ASDs living at moderate altitude (4500–6000 ft or 1372–1829 m) were more likely to have PH or a mPAp $\geq$ 25 mmHg than those living at low altitude, but there was no difference between groups in Qp:Qs or clinically relevant PVR (> 3 Wood-units $\times$ m^2). That is, while living at moderate altitude can raise pulmonary pressures, even when controlling for age, this did not appear to contribute to the development of PAH in our cohort of patients with ASDs.

Acknowledgements

Conflict of Interest

The authors have no conflict of interest relevant to this publication.

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Direct Left Atrial Pressure Measurement with Pressure Sensing Wires in Complex Univentricular Heart Disease

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Abstract

In congenital heart disease, pressure-sensing wires provide an alternative method of obtaining important hemodynamic information when it cannot be obtained with traditional fluid-filled catheters. Here, we illustrate how pressure-sensing wires are vital for patients with univentricular heart physiology and an atrial stent *in situ* to prove candidacy for bidirectional cavopulmonary anastomosis.

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Key Words

Pressure wire • Congenital heart disease • Pediatric cardiology

Introduction

Pressure-sensing wires are guidewires, typically 0.014 inches in diameter, with high fidelity tip sensor technology for pressure measurement. In adult cardiology, their use has become routine for functional assessment of atherosclerotic coronary artery lesions by calculating fractional flow reserve [1]. This technique has also been described in pediatric patients with Kawasaki disease [2], but few reports have been published on the use of pressure wires for pediatric patients with congenital heart disease.

In children with single ventricle physiology, the accurate measurement of pulmonary vascular resistance (PVR) is critical for assessing the suitability of bidirec-

tional cavopulmonary anastomosis. Occasionally, the sequelae of previous interventions may preclude the use of traditional fluid-filled catheters to obtain this critical hemodynamic data. Pressure wires provide an alternative method of obtaining this information. Here, we present two cases in which the use of pressure wires allowed an accurate pre-surgical assessment and successful outcome where the absence of such data may have precluded surgical care.

Case Presentation

Two infants with complex univentricular heart disease and atrial septal stents *in situ* were taken to the catheterization laboratory for pre-bidirectional cavopulmonary anastomosis evaluation. We used a standard technique for pressure-sensing wire (St. Jude Medical pressure wire FFR Aeris Agile Tip 0.36mm in width, 175cm in length, St. Paul, MN) measurement [3]. An end-hole guiding catheter (Terumo 4/5-F) was placed proximal to the area of interest. A standard fluid-filled pressure transducer was attached to the catheter system. The sensor of the pressure wire was set to zero *ex vivo*. The wire was then inserted into the guide catheter until the tip extended just beyond the end of the catheter (still in the same vascular structure). In this position, we equalized the pressures registered by both the pressure wire and catheter. The pressure wire was advanced to the area of interest, and pressure was measured. Following measurement, with

the pressure wire back at the tip of the catheter, we confirmed equal pressure signals from the wire and catheter to ensure no significant drift. Values used for predicted oxygen consumption (ml/min/m²) when calculating pulmonary blood flow were taken from tables created by Seckeler et al. using a new predictive equation [4].

Patient 1 had a diagnosis of double inlet left ventricle with atrioventricular and ventriculoarterial discordance and a hypoplastic left-sided right ventricle. A pulmonary artery band was placed at 1 month of age. At 2.5 months of age, he underwent atrial septal stent implant (8 × 18 mm Genesis, Cordis, Ireland) for

a restrictive atrial septum in the context of increasing stenosis of the left atrioventricular valve. At 6 months of age, pre-bidirectional cavopulmonary anastomosis cardiac catheterization demonstrated an elevated mean pulmonary pressure of 23 mmHg. Left ventricular end diastolic pressure was 4 mmHg, and right atrial pressure was 4 mmHg. We obtained a mean pulmonary capillary wedge pressure of 12 mmHg and decided to proceed with obtaining direct left atrial pressure given the importance of an accurate determination of PVR. The obtuse angulation of the atrial stent prevented a fluid-filled hemodynamic catheter from passing into the left atrium (Figure 1A-C). Using a pressure wire,
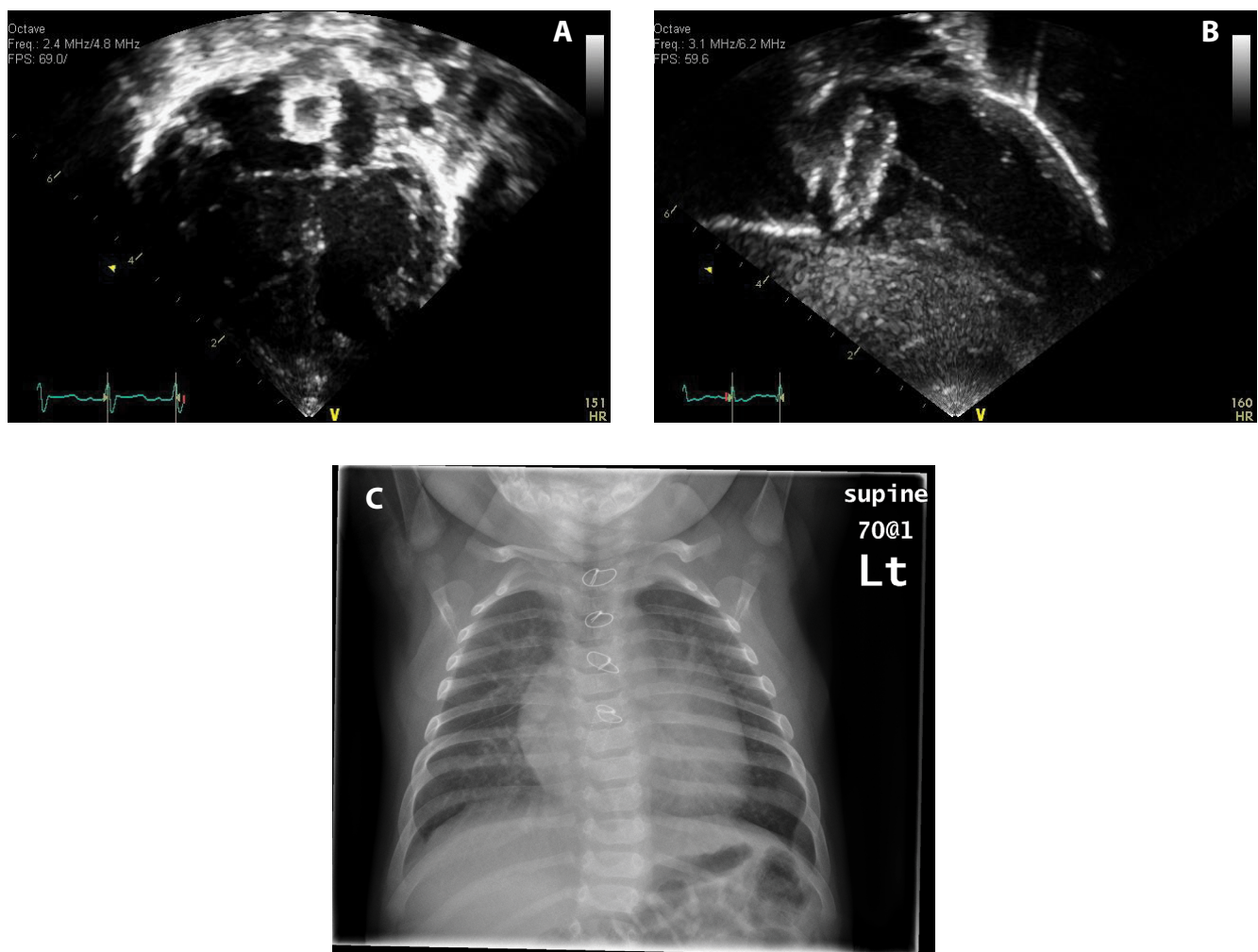

Figure 1. *Panel A*. Two-dimensional echocardiogram, four-chamber apical view. The atrial stent was seen lying in an almost horizontal anterior posterior position. *Panel B*. Two-dimensional echocardiogram, subcostal view directed at the atrial septum. The atrial stent protrudes 2/3:1/3 into the right atrial cavity, precluding passage of a fluid-filled catheter to the left atrium. *Panel C*. Anterior-posterior chest radiograph demonstrating atrial stent position.
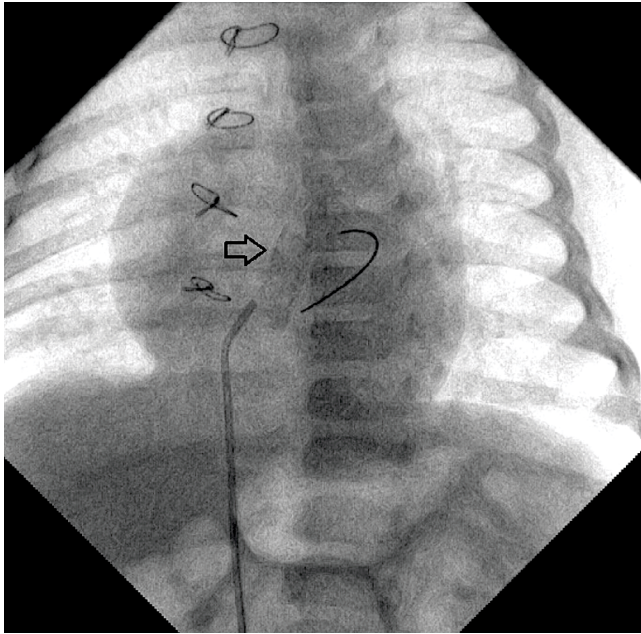
Figure 2. Left anterior oblique, 30°. 4-F terumo angle catheter in right atrium adjacent to a Genesis atrial stent (*open arrow*). Note the acute angulation of the stent compared with the atrial septum. The pressure wire was passed through the body of the stent with the radio-opaque end curled within the left atrium. The pressure sensor was located at the non-opaque-to-opaque junction of the wire.

which easily passed through the side cells of the stent and then traversed to the left atrium, we were able to measure the left atrial pressure at 12 mmHg with a right atrial pressure of 4 mmHg. Using left atrial pressure, the calculated PVR was 1.8 Wood units. As such, we determined that the patient was a satisfactory candidate for bidirectional cavopulmonary anastomosis.

Patient 2 had a diagnosis of atrioventricular and ventriculoarterial discordance, hypoplastic left-sided right ventricle, left atrioventricular valve atresia, and pulmonary atresia. At three days of age, he had a modified right Blalock-Taussig shunt and balloon atrial septostomy for a restrictive atrial septum. He went on to have an atrial septal stent (5 × 16 mm Liberte, Boston Scientific, Marlborough, Massachusetts) placed at six weeks of age. At 3.5 months of age, the patient's pre-bidirectional cavopulmonary anastomosis evaluation showed an elevated mean pulmonary artery pressure of 21 mmHg. Left ventricular end diastolic pressure was 7 mmHg. Similar to the case of Patient 1, a catheter could not be passed through the atrial

septal stent to the left atrium, but a pressure wire was successfully passed through a side cell of the stent into the left atrium, and a direct pressure measurement was obtained (Figure 2). Left atrial pressure was significantly elevated at 16 mmHg compared with a right atrial pressure of 5 mmHg. PVR was calculated as 1.5 Wood units, making the patient a suitable candidate for bidirectional cavopulmonary anastomosis.

Pulmonary pressures were elevated in both patients, but this was in the setting of left atrial hypertension secondary to a restrictive atrial septum (as the lumen of the previously placed stent was now too small for the size of the patient) with normal PVR. Both patients underwent bidirectional cavopulmonary anastomoses and had uneventful postoperative courses. The information obtained using pressure-sensing wires directly contributed to our management decisions and was instrumental in ensuring that the patients were not denied the appropriate next-stage palliative surgery.

Discussion

For children with single ventricle physiology, the accurate assessment of PVR is essential as part of the preoperative evaluation to determine suitability for surgical palliation. For patients in whom measured pulmonary pressure suggests that PVR may be elevated, the perioperative risk becomes difficult to accurately ascertain. The ability to directly measure left atrial pressure in these children to calculate PVR is critical for optimal surgical decision-making. Pulmonary capillary wedge pressure can be used as a surrogate for left atrial pressure. However, there is some error in predicting left atrial pressures using this technique, which can be amplified at higher wedge pressure measurements [5]. Given that such a discrepancy could result in an erroneously low PVR calculation, direct left atrial pressure measurement with a pressure-sensing wire may be more appropriate given the important clinical decision based on these measurements. Future evaluation of the relationship between the pulmonary capillary wedge pressure and left atrial pressure in children with elevated left atrial pressures would be useful.

There is a paucity of published reports of pressure wire use in children with congenital heart disease. However, pressure wires have been safely and successfully used to measure pulmonary artery pressure

via a central or Blalock-Taussig shunt [6]. Zampi et al. also described the role of pressure wires in the setting of hypoplastic left heart syndrome palliated with the hybrid stage 1 procedure [7]. Pressure wires were used to measure distal pulmonary artery pressure and subsequently assess the adequacy of pulmonary bands. Rates of re-operation for pulmonary artery band adjustment were less in the group in which pressure wires were used for this purpose. Pressure wire use has also been reported in the human fetus during aortic balloon valvuloplasty [8].

Pressure-sensing wires are feasible and safe to use in the pediatric setting. We demonstrated how pressure-sensing wires can provide accurate hemodynamic data not otherwise obtainable with conventional catheters in the setting of complex univentricular congenital heart disease.

Conflict of Interest

The authors have no conflict of interest relevant to this publication.

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Retrograde Percutaneous Closure of a Perimemberanous Ventricular Septal Defect with an Occluder Device in a Child with Interrupted Inferior Vena Cava

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Abstract

Femoral venous access is the typical route for the antegrade approach to percutaneous closure of a perimemberanous ventricular septal defect (PM VSD). In this case report, we attempted percutaneous PM VSD closure in a five-year-old child with interrupted inferior vena cava (IVC) using a retrograde arterial approach. The Amplatzer Duct Occluder II was chosen due to its symmetrical design that can be deployed using either a retrograde or antegrade approach. We found the retrograde percutaneous PM VSD closure by off-label use of this device to be an easy and feasible option in this case of interrupted IVC, whereas the use of an antegrade approach would have been imprecise and potentially time-consuming.

Key Words

Ventricular Septal defect • Percutaneous closure • Interrupted inferior vena cava • Amplatzer Duct Occluder II

Introduction

The incidence of congenital interruption of inferior vena cava (IVC) without other visceroatrial situs abnormalities is 0.08–0.1%. Interrupted IVC usually continues via the azygos system to join the superior vena cava [1]. Interrupted IVC is usually an incidental and unexpected finding during cardiac catheterization. Although managing interrupted IVC is challenging, it is not impossible through the use of certain approaches. In particular, previous reports have described the retrograde transcatheter closure of perimemberanous ventricular septal defect (PM VSD) by the off-label use of an Amplatzer Duct Occluder II (ADO II) device (St. Jude Medical, St. Paul, Minnesota) [2, 3, 4].

Case Presentation

A five-year-old boy diagnosed with PM VSD at the age of six months was referred to our hospital for therapeutic intervention. Electrocardiography (ECG) showed left ventricular hypertrophy and cardiomegaly. Pulmonary plethora was shown by chest X-ray. Transthoracic echocardiography showed a moderate-sized PM VSD partially covered by septal aneurysm. The left ventricular opening was 5 mm, and the right ventricular opening was 8 mm. The aortic rim was 6 mm. Pulmonary systolic pressure was 47 mmHg. There was a gradient of 85 mmHg between the left and the right ventricles. The left atrium and ventricle were dilated. There was no aortic regurgitation or any other associated cardiac anomaly. Unfortunately, the subcostal window was obtained without focusing on

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the IVC course.

The procedure was performed under general anesthesia with antibiotic protection (cefotiaxone 100 mg/kg body weight, administered intravenously). During cannulation, right femoral vein entry was attempted; however, the guidewire crossed the midline under fluoroscopy, consistent with inadvertent arterial puncture. A multipurpose catheter MP 2 was inserted, yielding venous waveforms, but an abnormal course was noted on fluoroscopy. Angiography was done by Pigtail 5-F, which showed interrupted IVC with azygous continuation that drained into the left superior vena cava and coronary sinus (Figure 1). After right femoral artery cannulation, one dose of heparin (100 U/kg body weight) was administered intravenously. Left ventricular angiography in LAO/60° cranial view revealed a PM VSD covered by an aneurysm with a 4-mm diameter outlet (Figure 2). The decision was made to proceed with VSD closure via a retrograde route. The procedure was monitored by transesophageal echocardiography (TEE). A guiding Judkin right JR 6-F was used for crossing the PM VSD with an angulated hydrophilic guide wire (0.035-in, Terumo Corporation, Tokyo, Ja-

Figure 2. Angiography in LAO/60° cranial view showing the perimemberanous ventricular septal defect covered by an aneurysm with an outlet diameter of 5 mm.

pan). The guiding JR position was secured in the right ventricle. An ADO II device (9-PDA2-06-04, AGA Medica Corp, Golden Valley, Minnesota, USA) was chosen 1 mm larger than the diameter of the VSD as measured by left ventricolography and TEE. The right disc was deployed in the right ventricle and then drawn until it came into contact with the interventricular septum under fluoroscopy and TEE guidance (Figures 3 and 4). The left disc was then uncovered in the left ventricle. The device was unscrewed and released after TEE confirmed a good device position and no residual shunt (Figure 5). There was no interference with tricuspid or aortic valves. The fluoroscopy time was 24 min, and the procedure time was 90 min.

At two-month follow-up, the child was asymptomatic with no conduction abnormality on ECG. ECG showed good positioning of the device without residual shunt and no change in pre-existent tricuspid regurgitation.

Discussion

VSD is the most common congenital heart defect, comprising approximately 20% of all such defects.

Figure 1. Angiography in the anterior-posterior view shows the course of the pigtail catheter crossing the midline, ascending via azygos continuation, and descending through the left superior vena cava and draining into the coronary sinus.
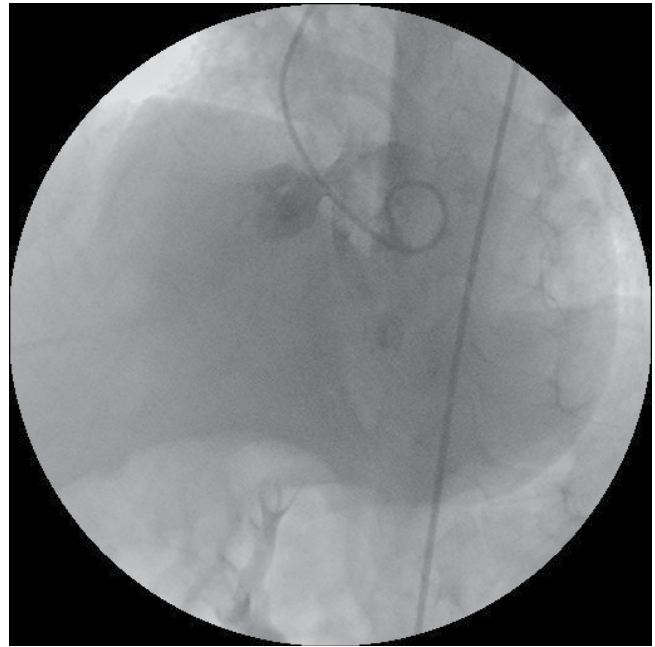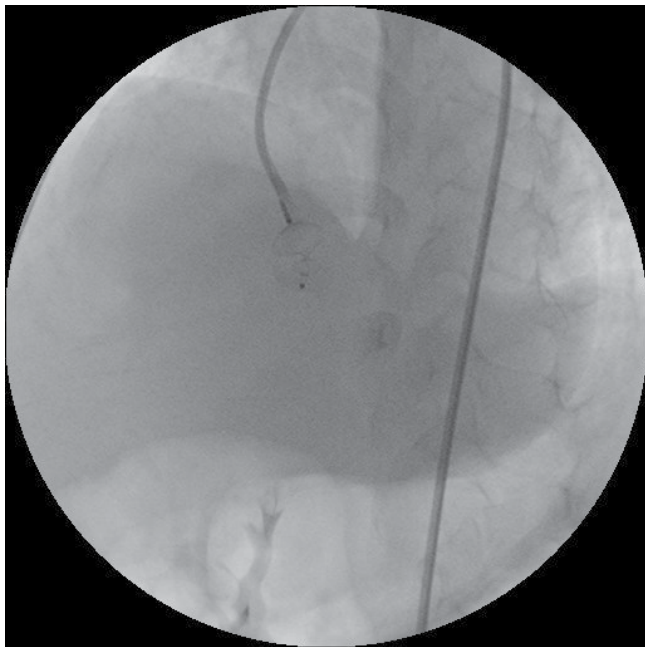
Figure 3. Transesophageal echocardiography in four-chamber view showing the perimemberanous ventricular septal defect partially covered by an aneurysm.

Figure 5. Cineangiography in LAO/60° cranial view showing the device completely deployed and released.
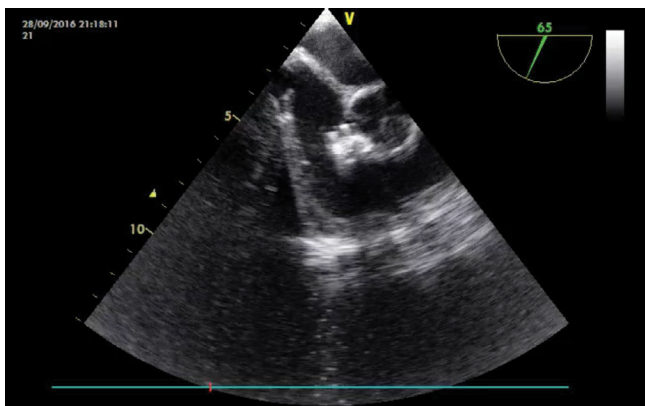

Figure 4. Transesophageal echocardiography in short axis showing good positioning of the ADO II.

With the introduction of Amplatzer devices, transcatheter closure of PM VSDs has become a well-established procedure but is associated with an unacceptable incidence of complete heart block [5]. The routine technique for percutaneous VSD closure is an antegrade approach accomplished by creating an arteriovenous loop. Here, we describe the case of a child who underwent percutaneous closure of a PM VSD using a retograde approach with an off-label ADO II in the presence of interrupted IVC and suitable anat-

omy and diameter of PM VSD for device selection. In this situation, we believed that the transcatheter closure of the PM VSD through internal jugular access would have been imprecise, increased the duration of the procedure, and ultimately been unsuccessful. However, the transcatheter closure of ASD and patent ductus arteriosus has been established using an internal jugular approach in many previously reported cases of interrupted IVC [7, 8]. If the size of the PM VSD had been > 6 mm, we would not have been able to use the ADO II, as the maximum available waist diameter of the device is 6 mm. Therefore, we would have had two options: (1) referring the patient or (2) trialing the use of the azygous vein as alternative route for an antegrade approach. Using an antegrade approach to the percutaneous closure of a PM VSD in a patient with interrupted IVC was previously described by Kawar et al. [6]. Furthermore, our experience with the percutaneous retrograde closure of a MP VSD with interventricular septum aneurysm using the ADO II is consistent with a report by Koneti et al. [2], who described successful retrograde approaches to PM VSD closure in a large group of 57 children with favorable anatomy.

In conclusion, interrupted IVC should be diag-

nosed before planning for cardiac catheterization to choose the preferred alternative route for the procedure. Retrograde percutaneous closure of a PM VSD by off-label ADO II is considered a feasible and alternative to an antegrade approach if the size of the VSD is < 6 mm.

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Conflict of Interest

The authors have no conflict of interest relevant to this publication.

Comment on this Article or Ask a Question

Transcatheter Aortic Valve Replacement for Inoperable Severe Rheumatic Aortic Stenosis with Prior Mitral Valve Prosthesis

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Abstract

Transcatheter aortic valve replacement (TAVR) is traditionally indicated for calcific aortic stenosis. Rheumatic aortic valve disease is treated surgically due to the younger age of patients and a lack of significant calcification that can anchor transcatheter valves. However, severe comorbidities may increase surgical risk, necessitating less invasive therapeutic modalities. Here, we present the first case report of severe rheumatic aortic stenosis with prior mechanical mitral valve prosthesis and liver cirrhosis that was successfully treated by TAVR.

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Key Words:

Aortic stenosis • Rheumatic valve disease • Mitral valve prosthesis • Transcatheter aortic valve replacement

Introduction

Transcatheter aortic valve replacement (TAVR) has become the procedure of choice for treating inoperable and high surgical risk patients with calcific degenerative severe symptomatic aortic stenosis [1, 2, 3, 4, 5, 6]. However, the utilization of TAVR for severe aortic stenosis caused by rheumatic valve disease is uncertain due to the lack of significant calcification necessary to anchor transcatheter valves. Here, we report a case of severe rheumatic aortic stenosis with prior mechanical mitral valve prosthesis and high surgical risk related to liver cirrhosis that was treated successfully with TAVR.

Case Presentation

A 62-year-old woman with rheumatic heart disease and chronic atrial fibrillation underwent mitral valve replacement using a mechanical valve prosthesis in 1991. The surgery was complicated by hepatitis C resulting from the recent development of liver cirrhosis. The patient presented with progressive dyspnea, orthopnea, and severe fluid overload consistent with class IV congestive heart failure. Diagnostic evaluation revealed severe aortic stenosis and tricuspid valve regurgitation, and she was referred for surgical aortic valve replacement and tricuspid valve repair. Hepatology evaluation suggested very high surgical risk due to chronic liver disease. Thus, she was referred for TAVR in the face of high surgical risk [7, 8].

Echocardiography revealed a D-shape septum with a left ventricular ejection fraction of 50%, dilated left atrium and huge right atrium, and mildly dilated right ventricle with hypertrophy and normal systolic function. The aortic valve was fibrotic without significant calcification (consistent with rheumatic disease) with severe aortic stenosis and mild to moderate aortic regurgitation (annulus 20 mm, peak gradient 65 mmHg, mean gradient 42 mmHg, and calculated aortic valve area = 0.8 cm^2). The mechanical mitral valve prosthesis was functioning well, and the tricuspid valve exhibited

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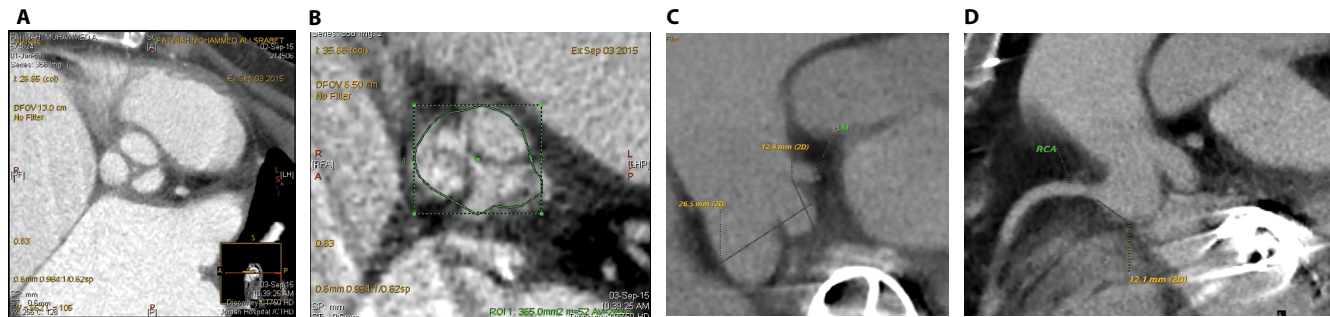Tel.: +962 656 26197; Fax: +962 656 26198; E-Mail: alhaddad63@gmail.com

**Figure 1**. Cardiac computerized tomographic angiography showed a fibrotic aortic valve without significant calcifications (*Panel A*), annular area (*Panel B*), coronary sinus diameter and left main coronary height (*Panel C*), and right coronary height and the distance between the aortic annulus and mitral prosthetic valve = 10 mm (*Panel D*).

severe regurgitation with calculated pulmonary artery systolic pressure of 100 mmHg. Severe pulmonary hypertension appeared to be related to both prior mitral valve disorder and a recent development of congestive heart failure related to severe aortic stenosis.

Computerized tomographic angiography (CTA) showed the following: fibrotic aortic valve without significant calcification (Figure 1A), annular area = 365 mm^2 (Figure 1B), coronary sinus diameter = 26.5 mm and left main coronary height =12.9 mm (Figure 1C), right coronary height = 12.1 mm, and distance between the aortic annulus and mitral prosthetic valve = 10 mm (Figure 1D).

The procedure was performed in the catheterization laboratory under general anesthesia and transesophageal echocardiography (TEE) guidance. Percutaneous access was performed through the left common femoral artery with two ProGlide closure devices (Abbott Vascular Inc., Redwood City, California) pre-deployed to achieve homeostasis. Aortic valvuloplasty was performed using a 20-mm diameter balloon during rapid pacing, which showed full expansion and stability without displacement related to prior mitral valve prosthesis. Next, a 23-mm valve (Edwards Sapien XT, Edwards Lifesciences, Irvine, California) was introduced through the e-sheath and positioned across the aortic valve (Video 1). The valve was implanted using the rapid pacing technique and balloon inflation (Video 2). Post-procedural angiography revealed a well-positioned prosthesis without significant aortic regurgitation (Video 3), and TEE revealed a well-functioning aortic valve. A 23-mm valve provided 14% annular area oversizing, which was adequate

to anchor and stabilize the valve in the absence of significant calcification. The patient was ambulated six hours after the procedure and discharged from the hospital three days later. At follow-up evaluation two weeks later, the patient showed a lack of symptoms, a well-functioning aortic valve, and improved pulmonary hypertension to 70 mmHg. The patient remained asymptomatic and stable 15 months after the procedure.

Discussion

To our knowledge, this is the first reported case of TAVR for rheumatic aortic stenosis with prior mechanical mitral valve prosthesis. This case has many unique features. In particular, rheumatic aortic valve disease usually lacks significant calcifications that are necessary to anchor the implanted valve and prevent its embolization. Also, the presence of prior mechanical mitral valve prosthesis could potentially complicate TAVR implantation by causing displacement, malposition, or even embolization. There are several usual recommendations for implanting a balloon-expandable transcatheter heart valve in patients with prior mitral valve prosthesis. First, the valve should be positioned more ventricularly due to anticipated aortic shift during deployment to prevent embolization. Second, stepwise and slow inflation of the valve is advised for proper and controlled implantation. Third, the implantation should be guided by aortography and TEE to evaluate interaction with the mitral prosthesis. We also believe that balloon valvuloplasty is mandatory in such cases prior to valve implantation for
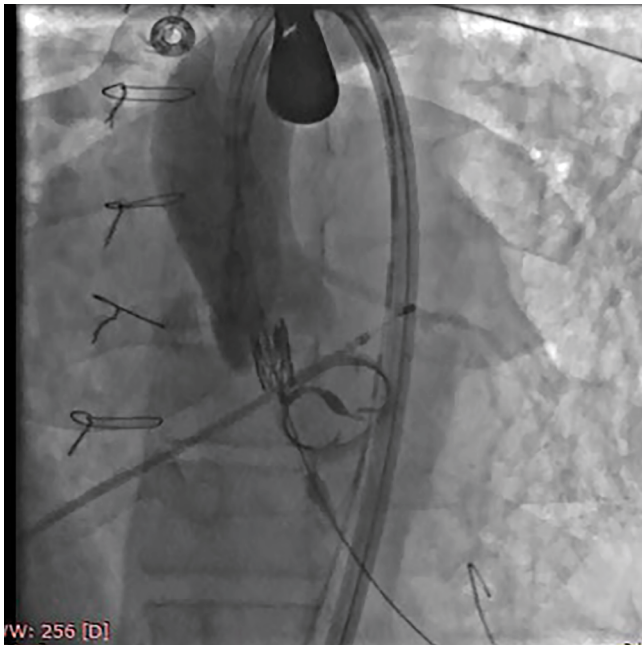
**Video 1**. Valve positioning prior to implantation. View supplemental video at https://doi.org/10.12945/j.jshd.2017.015.16.vid.01.
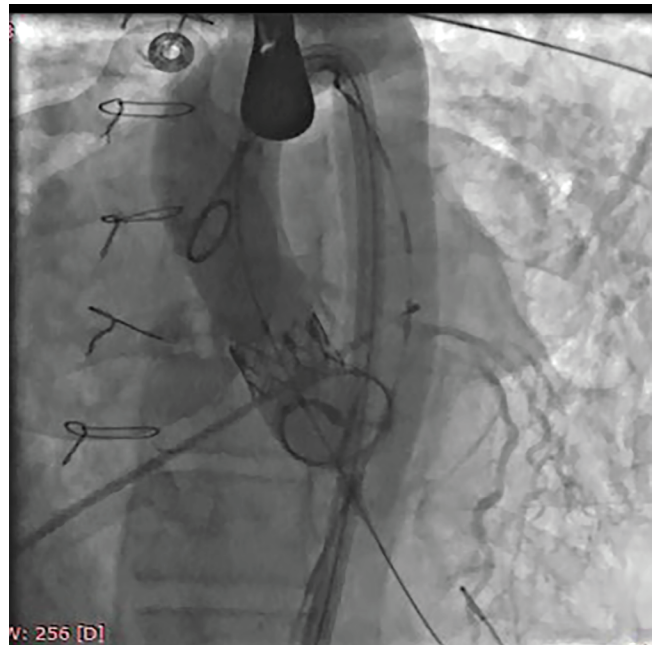
Video 2. Aortic valve implantation during rapid pacing. View supplemental video at https://doi.org/10.12945/j.jshd.2017.015.16.vid.02.

the following reasons. First, an inflated balloon can confirm full expansion of the fibrotic aortic valve leaflets. Second, balloon stability during inflation can indicate good anchoring, suggesting that the implanted valve is less likely to embolize. Third, it can allow examination of the interaction between the aortic valve and mitral prosthesis that could potentially cause displacement or malposition.

Rheumatic valve disease usually inflicts younger patients, and surgical valve replacement is the procedure of choice for these patients. However, the presence of comorbidities (i.e., liver cirrhosis) and prior mitral valve prosthesis makes TAVR a potentially excellent solution for severe aortic stenosis.

Review of the literature revealed several case reports of TAVR in rheumatic heart disease. Bilge et al. described two patients with rheumatic aortic stenosis and high surgical risk who ultimately underwent TAVR [9]. Akujuo et al. presented a case in which TAVR was combined with transcatheter mitral valve implantation in a patient with both aortic and mitral valves affected by rheumatic valve stenosis [10]. Chainani et al. reported a case of left main percutaneous coronary intervention and TAVR in a patient with rheumatic heart disease and porcelain aorta
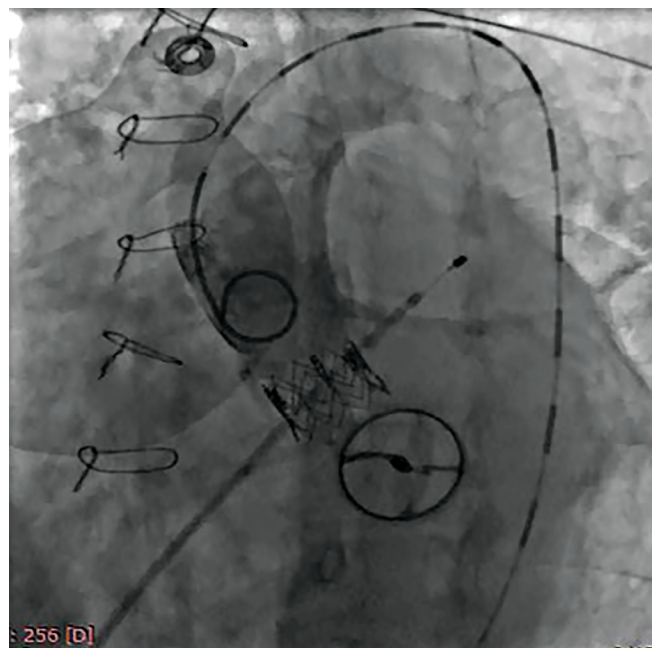
Video 3. Post trans-catheter aortic valve replacement angiography showing well-positioned valve without significant aortic regurgitation. View supplemental video at https://doi.org/10.12945/j.jshd.2017.015.16.vid.03.

[11]. However, our case is unique because TAVR was performed in the presence of prior mitral valve prosthesis. On the other hand, several reports have been published on TAVR in the presence of prior mitral valve prosthesis [12, 13, 14, 15, 16], although aortic stenosis in these reports was related to calcific aortic stenosis and not rheumatic disease as in our case. Thus, this is the first report of TAVR for rheumatic aortic stenosis with prior mitral valve prosthesis.

In conclusion, the indications for TAVR are evolving to include a wider range of patients and different valvular disorders. This is the first case demonstrating the feasibility of TAVR for rheumatic aortic stenosis with prior mitral valve prosthesis in the presence of high-risk features for surgical valve replacement. A registry of such patients with longer-term follow-up is necessary to establish the role of TAVR in rheumatic aortic stenosis.

Conflict of Interest

The authors have no conflict of interest relevant to this publication.

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Continuous Assessment of a Stented Coronary Artery Using a Pressure Wire During Percutaneous Pulmonary Valve Implantation

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Abstract

A 52-year-old woman with tetralogy of Fallot status post-complete surgical repair with infundibular resection, pulmonary valvotomy, and patch closure of the ventricular septal defect presented with severe pulmonary regurgitation and depressed right ventricular function. During intended percutaneous pulmonary valve implantation (PPVI), multiple stenotic lesions were discovered in her left anterior descending (LAD) coronary artery, and the procedure was aborted. She underwent treatment of these lesions using drug-eluting stents by our adult interventional colleagues and returned to the congenital catheterization laboratory for PPVI 18 months following her initial procedure. Given the potential risk of crush injury to the coronary arterial stents, the distal LAD artery was continuously monitored during the procedure via a pressure wire with the capability of re-expanding the stent if needed.

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Key Words

Congenital catheterization • Intervention • Valve implantation

Introduction

Percutaneous pulmonary valve implantation (PPVI) is an effective method for treating right ventricular outflow tract (RVOT) obstruction and regurgitation in patients with congenital heart disease [1, 2, 3]. A rare but catastrophic complication of PPVI is mechanical coronary artery compression due to implantation of a stent and/or valve within the RVOT [4]. Coronary artery testing is recommended during balloon angioplasty of the RVOT to assess coronary artery compression or distortion. However, the presence of an existing coronary artery stent may render coronary artery testing with balloon angioplasty/compliance testing a higher risk procedure. Here, we report the first use of a pressure wire within a stented left anterior descending (LAD) coronary artery in close proximity to the RVOT during PPVI to assess for coronary artery stent compromise and to maintain access for treatment of compression with redilation of the stent or re-stent if necessary.

Case Presentation

A 52-year-old woman with tetralogy of Fallot presented to our adult congenital cardiology program for evaluation. She underwent complete surgical repair at 8 years of age consisting of infundibular resection, pulmonary valvotomy, and patch closure of a ventricular septal defect. Her residual atrial septal defect was closed with a CardioSEAL™ Occlusion Device (Nitinol Medical Technologies, Ind., Boston, Massachusetts) at 38 years of age. Past medical history was also significant for diabetes mellitus and hypertension. As a result of her surgical palliation, the patient had severe pulmonary valve regurgitation with decreased right ventricular function and was referred for PPVI.
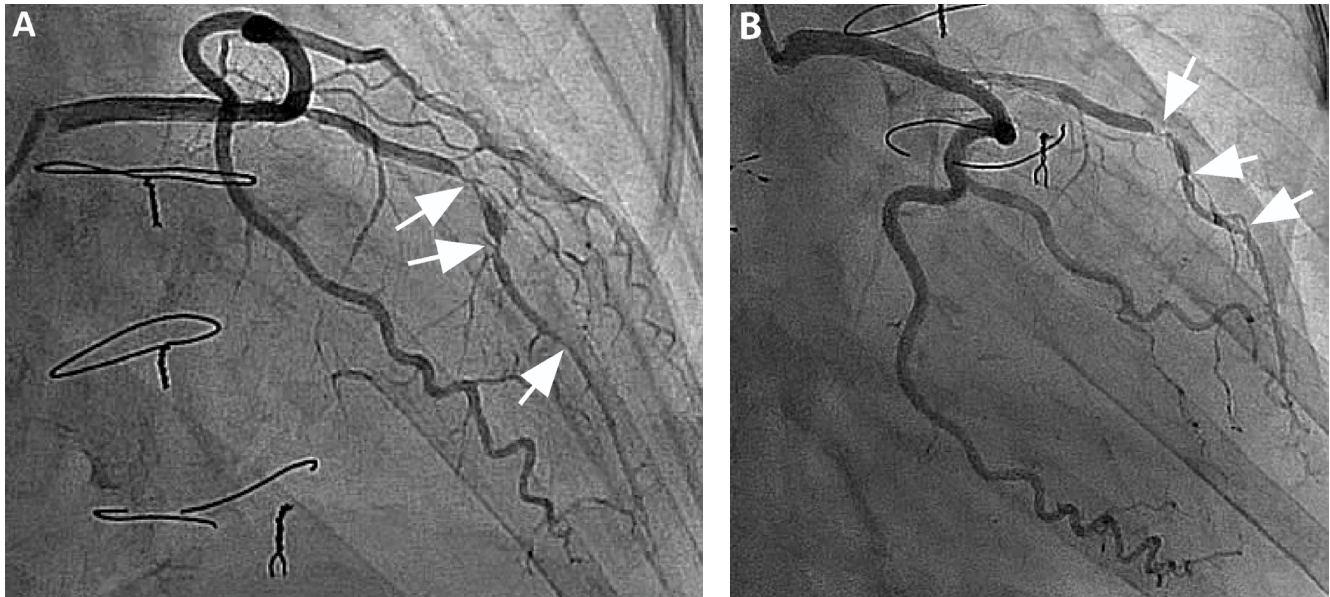
Figure 1. Selective left coronary angiography performed during the first catheterization in anteroposterior (*Panel A*) and right anterior oblique/caudal (*Panel B*) projections. There were a total of three stenotic lesions (**arrows**) along the left anterior descending (LAD) artery with near occlusion of the vessel.

Prior to RVOT intervention, multiple stenotic lesions were discovered within her LAD, and the procedure was aborted (Figure 1). Over the next few months, the patient underwent percutaneous coronary intervention by our adult interventional colleagues with a total of three drug-eluting stents placed along her proximal, mid, and distal LAD. After surveillance coronary angiography revealed no residual coronary arterial narrowing, the now 54-year-old patient was referred back to the congenital cardiac catheterization laboratory for PPVI.

Following hemodynamic evaluation, three-dimensional rotational angiography was performed for the RVOT with simultaneous selective left coronary angiography to delineate the spatial relationship between the RVOT and left coronary artery (Videos 1 and 2 Figure 2). The course of the left main coronary artery was immediately posterior to the RVOT but superior to the intended transcatheter valve landing zone at the level of the native pulmonary valve annulus. The stented LAD was anterior and leftward to the RVOT. Angiography of the RVOT showed a dilated RVOT that narrowed to 16.7 × 20.1 mm at the level of the native pulmonary valve (Video 3, Figure 3). We next planned on performing
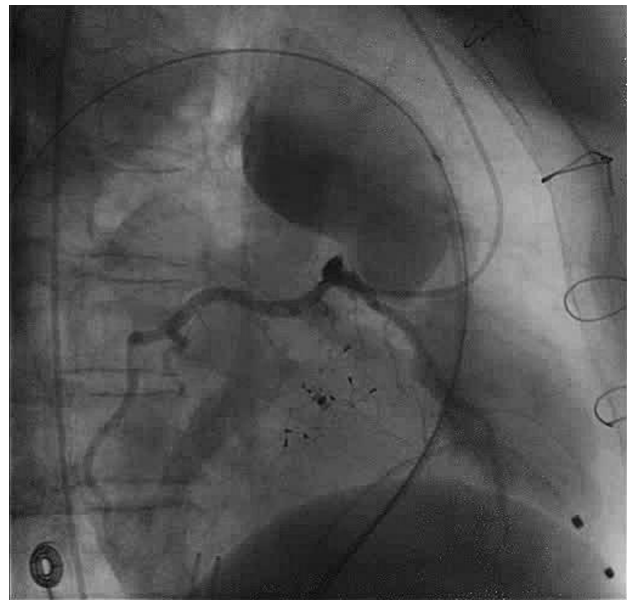
Video 1. Three-dimensional rotational angiography performed via a simultaneous power injection in the right ventricular outflow tract and hand injection of the left main coronary artery. The narrowing of the right ventricular outflow tract was located at the native pulmonary valve annulus with the left main coronary artery running immediately behind the right ventricular outflow tract. The stented LAD coursed leftward and posterior to the right ventricular outflow tract. View supplemental video at https://doi.org/10.12945/j.jshd.2017.017.17.vid.01.

Video 2. Three-dimensional rotational reconstruction of the right ventricular outflow tract (**yellow**) and left coronary artery (**blue**) from dual injection three-dimensional rotational angiography. The left main coronary artery ran posterior to the outflow tract and was superior to the intended valve implantation site at the level of the native pulmonary valve annulus. The LAD coursed leftward and posterior to the right ventricular outflow tract. View supplemental video at https://doi.org/10.12945/j.jshd.2017.017.17.vid.02.

balloon sizing of the RVOT with a low-pressure balloon. Given the risk of coronary stent compression with balloon angioplasty, stent implantation, and PPVI within the RVOT, we decided to continuously monitor distal LAD pressure during the intervention. This plan was discussed with our adult interventional colleagues, who were prepared to provide support as needed.

A 6-F JL-4 Guiding catheter (Cordis®, Milpitas, California) was used to cannulate the left main coronary artery, and a 0.014" PrimeWire Prestige® PLUS pressure guide wire (Volcano Co., San Diego, California) was positioned in the distal LAD (Video 4, Figure 4). The measured pressure from the pressure wire was calibrated with the proximal coronary arterial pressure measured from the guide catheter. A 2.5 × 15 mm Maverick coronary balloon (Boston Scientific Co., Marlborough, Massachusetts) was prepped and ready for use in the case of a crush injury to a coronary artery stent during RVOT intervention.

Sizing of the RVOT was performed using a 25 mm × 4 cm Tyshak II balloon (B. Braun Medical Inc., Bethlehem, Pennsylvania) inflated to 1 atm. Selective left coronary angiography and continuous LAD pressure monitoring was performed during balloon sizing of the RVOT. Both the proximal left coronary
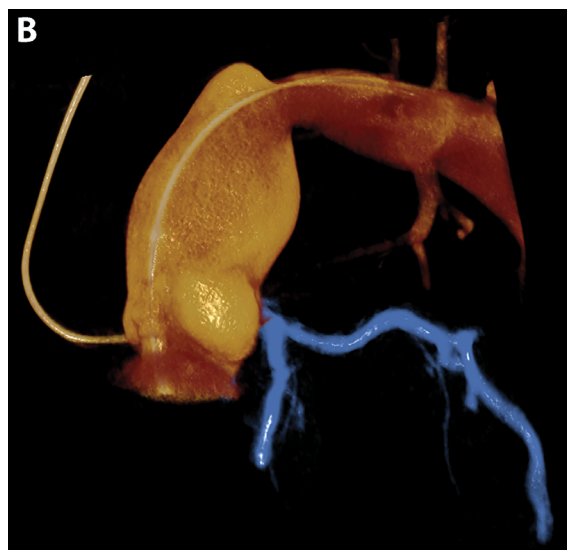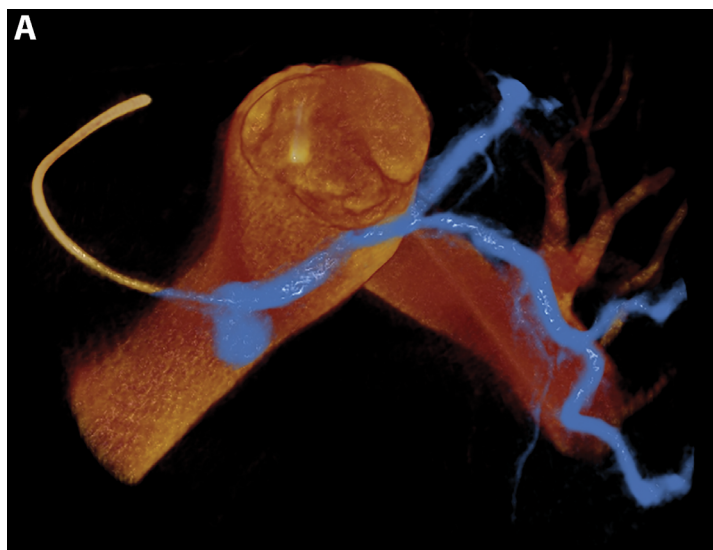

Figure 2. Three-dimensional rotational reconstruction of the right ventricular outflow tract (**yellow**) and left coronary artery (**blue**) in steep caudal (*Panel A*) and left anterior oblique (*Panel B*) projections from a dual injection three-dimensional rotational angiogram. The left main coronary artery ran posterior to the outflow tract and was superior to the intended valve implantation site at the level of the native pulmonary valve annulus. The LAD coursed leftward and posterior to the right ventricular outflow tract.
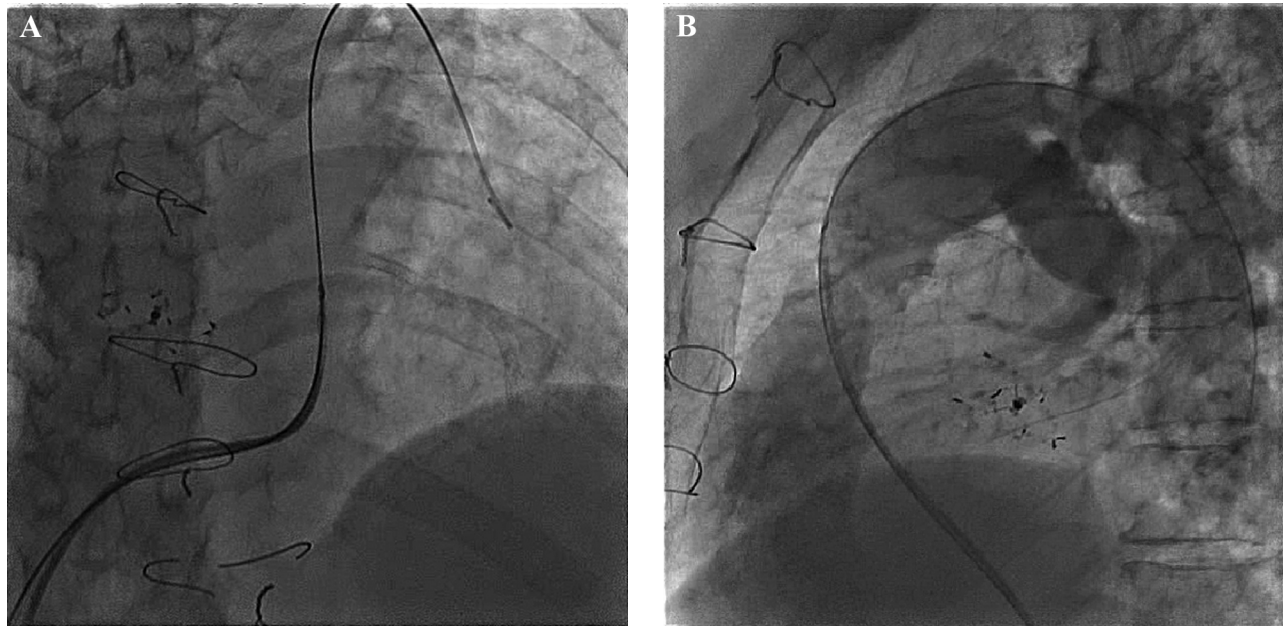
Video 3. Angiography of the right ventricular outflow tract in the anteroposterior (*Panel A*) and lateral (*Panel B*) projections. The narrowing of the right ventricular outflow tract occurred at the 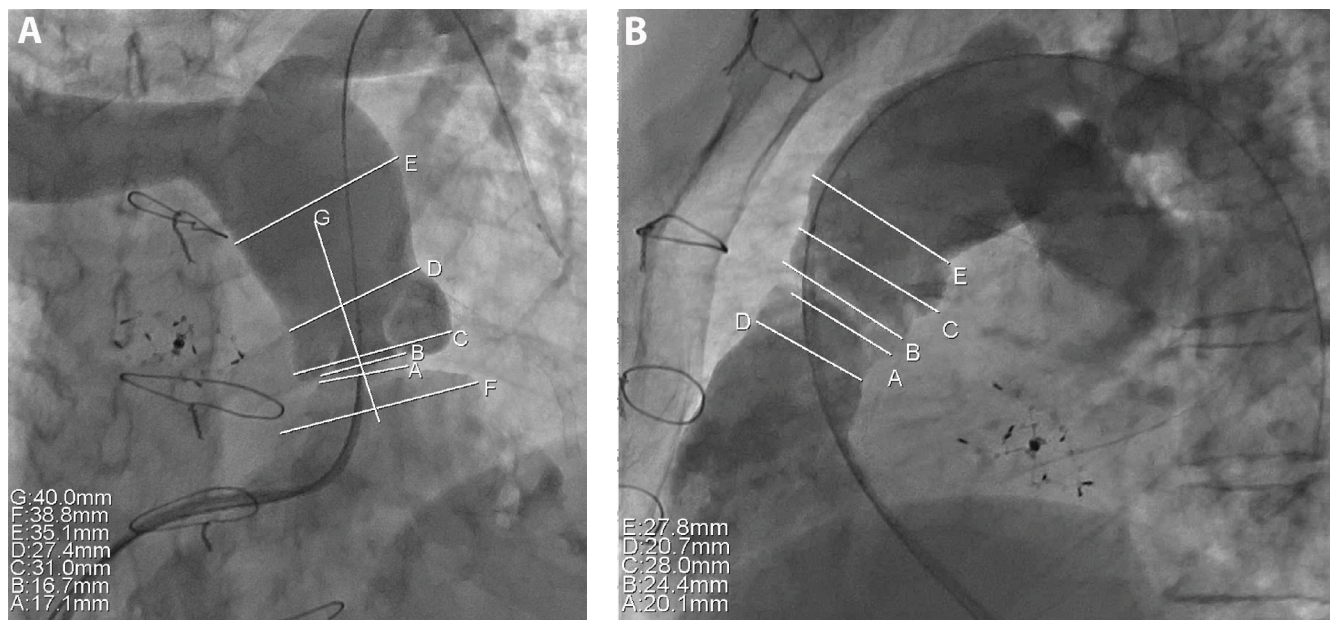native pulmonary valve annulus. View supplemental video at https://doi.org/10.12945/j.jshd.2017.017.17.vid.03A and https://doi.org/10.12945/j.jshd.2017.017.17.vid.03B.

Figure 3. Angiography of the right ventricular outflow tract in the anteroposterior (*Panel A*) and lateral (*Panel B*) projections with measurements. The narrowing at the native pulmonary valve annulus measured 17.1 × 20.1 mm in both projections.

arterial and distal LAD coronary arterial pressures decreased equally and simultaneously during inflation of the sizing balloon and completely recovered to baseline with balloon deflation (Figure 5).

No coronary arterial compression was demonstrated by angiography. There was a 19.8-mm waist on the sizing balloon, and pre-stenting of the RVOT was completed with two Palmaz 3110 XL stents (Cordis®,
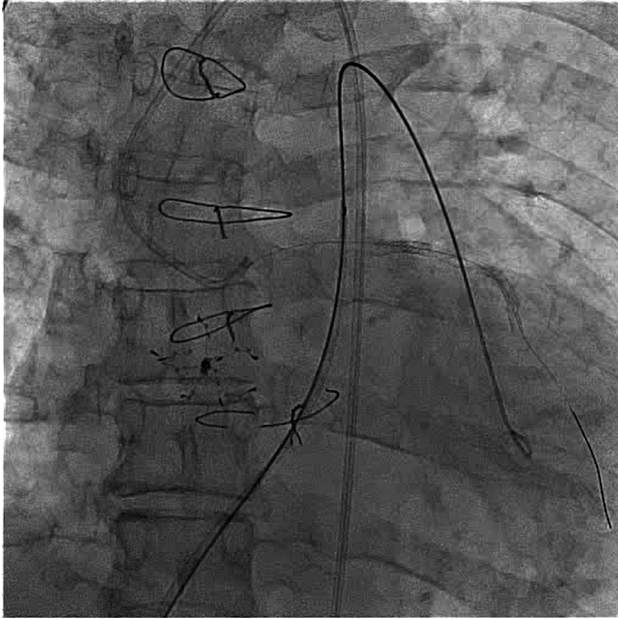
Video 4. Selective left coronary angiography showing the tip of the pressure wire positioned in the LAD distal to the previously placed stents. View supplemental video at https://doi.org/10.12945/j.jshd.2017.017.17.vid.04.

Milpitas, California) delivered on 22 mm × 3.5 cm BIB balloons (NuMED, Inc., Hopkinton, New York) without a significant pressure difference across the LAD stent. The stents overlapped at the RVOT narrowing, which was the intended landing zone for the valve. A PB1018 Melody Transcatheter Pulmonary Valve® (TPV) (Medtronic, Minneapolis, Minnesota) was delivered via a 22-mm Ensemble® Transcatheter Valve Delivery System (Medtronic) coaxially within the Palmaz stents. Distal LAD coronary arterial pressure remained stable during the RVOT intervention. Repeat selective left coronary arterial angiography was performed following Melody TPV implantation, which showed no compression of the coronary artery (Video 5, Figure 6). The pressure wire and JL guide catheter were then removed. Intracardiac echocardiographic evaluation of the Melody TPV revealed trivial central valvar regurgitation and no paravalvar leak (Video 6). The patient tolerated the procedure without complication and was discharged home on Aspirin 325 mg and Clopidogrel 75 mg daily.
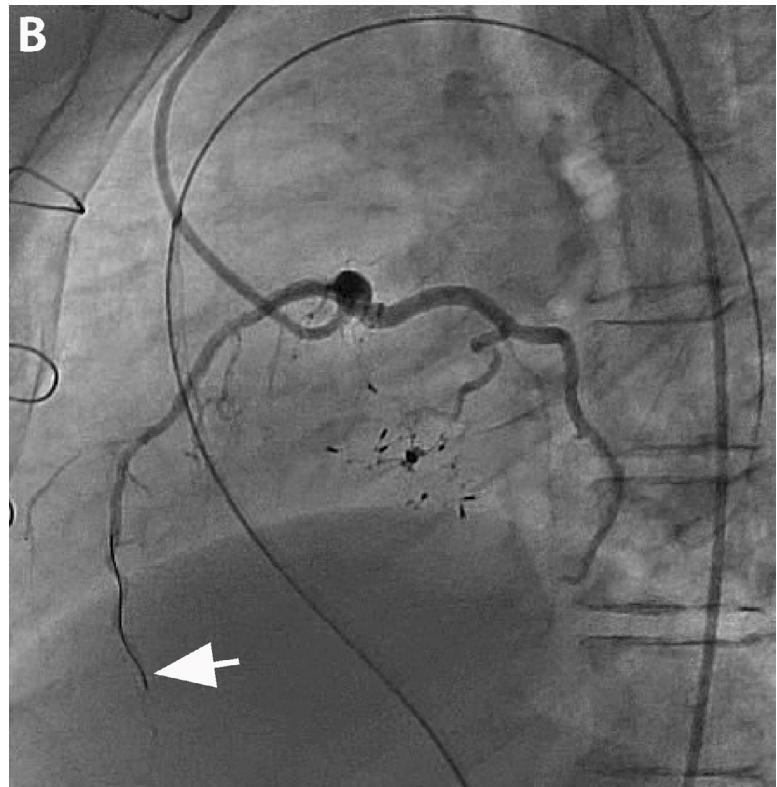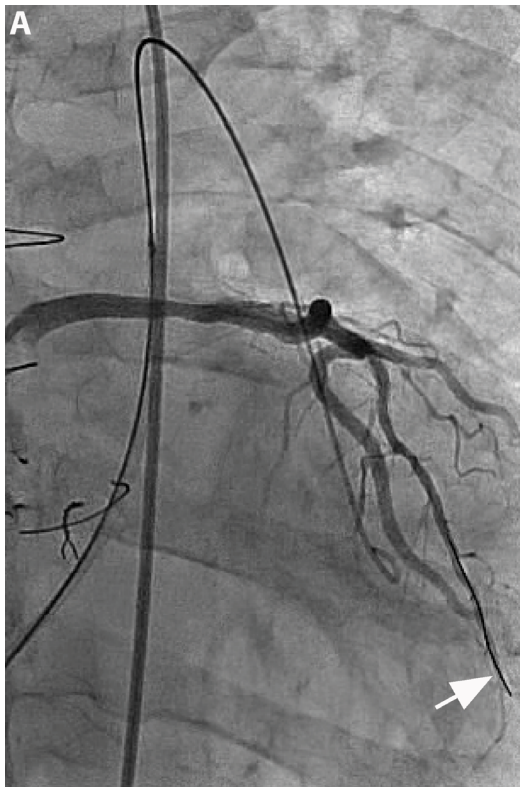

Figure 4. Anteroposterior (*Panel A*) and lateral (*Panel B*) projections of selective left coronary angiography showing the pressure wire (**arrow**) positioned in the distal LAD artery distal to the previously placed drug-eluting coronary stents.
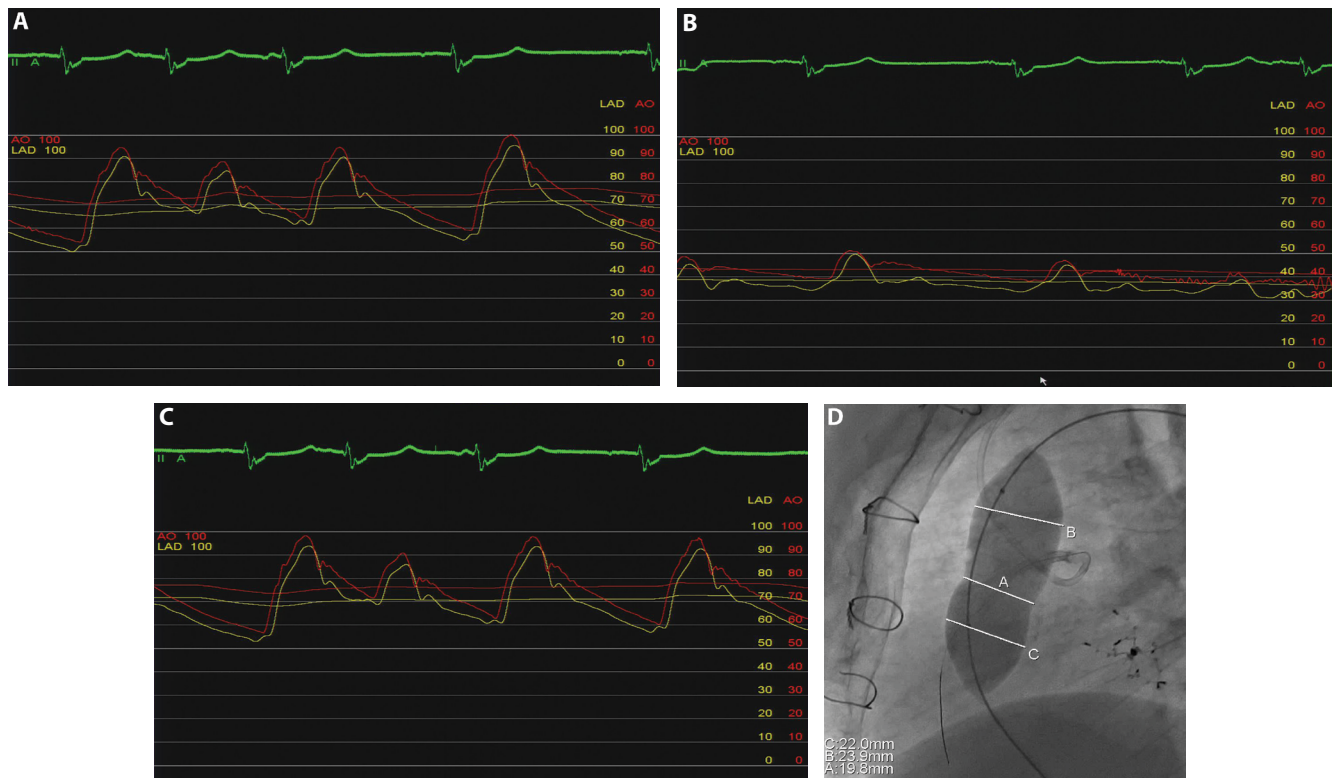
Figure 5. Continuous pressure monitoring of the proximal left main coronary artery (**red**) and distal LAD artery (**yellow**). At baseline (*Panel A*), the pressure in the LAD was slightly lower than the left main pressure. With balloon sizing of the RVOT (*Panel B*), both pressures decreased equally and returned to baseline upon deflation of the sizing balloon (*Panel C*). The lateral projection of the balloon sizing (*Panel D*) showed a balloon waist of 19.8 mm in diameter inferior to the left main coronary artery.

Discussion

Coronary artery compression during PPVI has been reported in multiple case series with outcomes varying from symptomatic acute coronary syndrome to cardiac arrest [5, 6, 7, 8, 9, 10, 11]. Morray and colleagues retrospectively evaluated coronary artery testing in 404 patients referred for PPVI in a multi-institutional study [4]. The risk of coronary artery compression in the study was 4.7% for all patients, with a risk of 71% for patients with abnormal coronary artery anatomy (i.e., left coronary artery arising from the right coronary artery, status post-Ross procedure). Additional risk factors for coronary artery compression included tetralogy of Fallot and transposition of the great arteries. Given this potential catastrophic outcome, coronary arterial testing with a balloon of equal size to the intended pre-stent implantation balloon is recommended and is the standard of care during PPVI. Although coronary artery testing provides good in-formation about the relationship of the coronary arteries to the RVOT, it cannot completely predict the final interaction between the patient's anatomy, pre-stents, and TPV. A recent study used three-dimensional rotational angiography to improve our understanding of coronary artery anatomy during PPVI [12]. In our case, both two-dimensional and three-dimensional angiography were used to evaluate the relationship between the stented left coronary artery and the RVOT prior to any intervention.

The accepted technique of coronary artery testing during balloon angioplasty of the RVOT is effective if the compression or distortion of the coronary artery is relieved by deflation of the balloon. However, with a stent already present in the at-risk LAD, deflating the balloon may not relieve the coronary artery compression. A stent implanted within the RVOT or coronary artery may prevent reversible coronary arterial compression. Here, we describe the first PPVI in a patient with coronary arterial stents that were
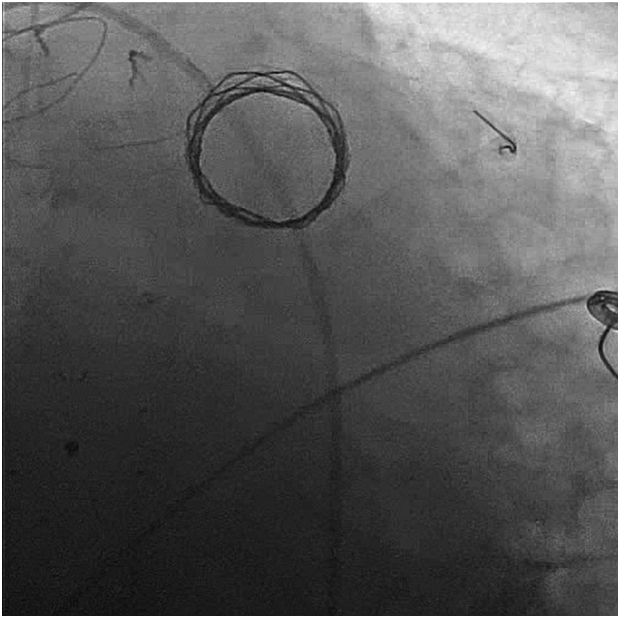
Video 5. Selective left coronary angiography following Melody TPV implantation at steep caudal projections showing no significant coronary arterial narrowing after PPVI. The pressure wire was positioned in the distal LAD. View supplemental video at https://doi.org/10.12945/j.jshd.2017.017.17.vid.05.
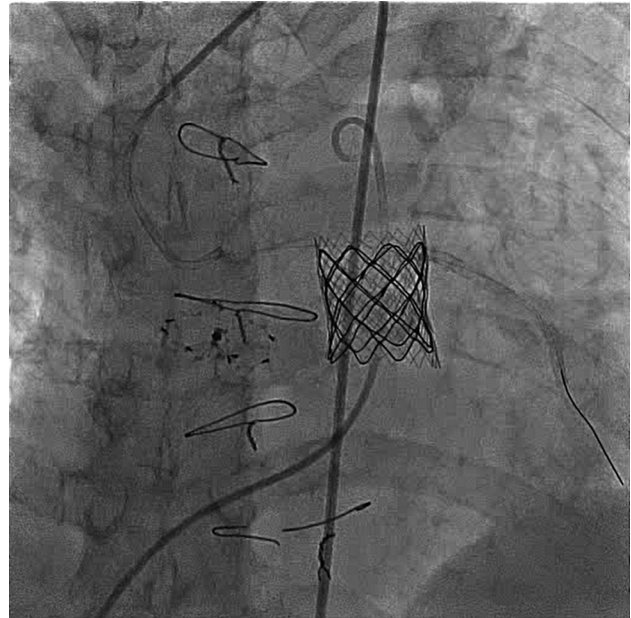
Video 6. Main pulmonary artery angiography following Melody TPV implantation demonstrating trivial central valvar regurgitation with a catheter through the valve and no paravalvar leak. View supplemental video at https://doi.org/10.12945/j.jshd.2017.017.17.vid.06.
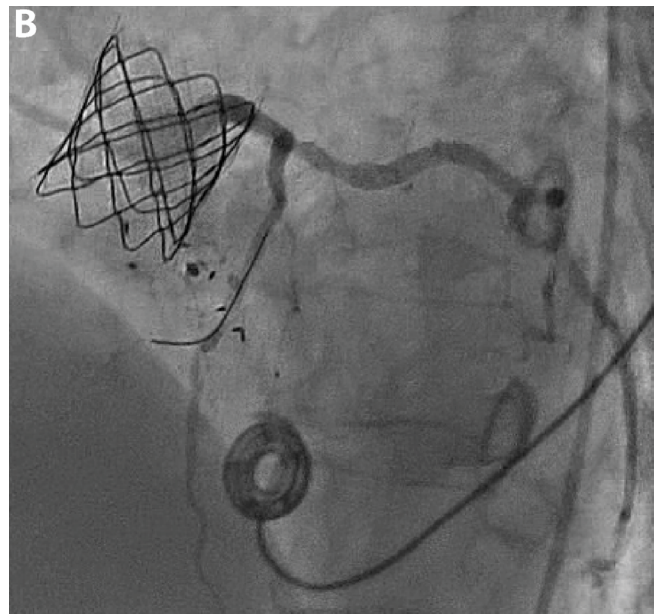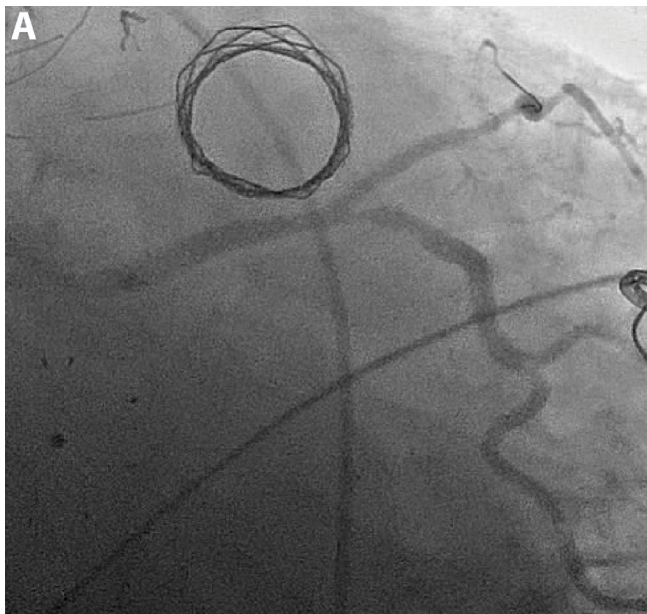

Figure 6. Selective left coronary angiography following Melody TPV implantation at steep caudal (*Panel A*) and left anterior oblique (*Panel B*) projections. No significant coronary arterial narrowing was seen following PPVI.

continuously monitored via a pressure wire during the intervention. Although the left coronary artery appeared remote from the implantation site, there were potential masses (e.g., calcification, scar tissue) in addition to the pre-stents that could result in coronary artery compression. Continuous distal LAD pres-

sure monitoring provided a constant assessment of coronary perfusion during the intervention and not just during angiographic balloon testing of the RVOT. As expected, pressures in both the proximal left main and distal LAD coronary arteries equally decreased with obstruction of the RVOT during balloon compliance testing, stent implantation, and PPVI, which resulted in a temporary decrease in left ventricular preload. In addition, both pressures recovered equally upon deflation of the balloons. Coronary artery stent compression would have been identified if either of the two following scenarios were present following balloon deflation: (1) a discrepancy between the two pressure waveforms indicating coronary artery stenosis or (2) both pressures not returning to baseline values as a result of acute left ventricular dysfunction. Had there been evidence of coronary artery compression, the JL guide catheter positioned in the left main coronary artery would have allowed us to advance the prepped coronary balloon over the pressure wire to re-expand the stent.

Currently, the estimated number of adults with congenital heart disease in the United States is greater than 1 million [13]. As the congenital heart disease patient population ages, there will be an increasing number of patients with combined acquired cardiovascular disease in addition to their underlying congenital heart disease. With technological advancements in transcatheter therapies, a greater proportion of this patient population will receive percutaneous treatment in the catheterization laboratory. The interventional cardiologist must be mindful of both types of heart disease in the older patient. This procedure was performed in the congenital cardiac catheterization laboratory given the need for biplane imaging during PPVI. Our adult interventional colleagues were prepared to provide any assistance in the event of a coronary intervention. Adult congenital heart disease programs have bridged the gap between pediatric and adult cardiac care and can often assist in the planning of complicated interventional procedures in adult congenital heart disease patients. Close collaboration between congenital and adult interventional cardiology is needed to provide the best care to this patient population.

In conclusion, coronary artery compression is a risk of PPVI and should be routinely evaluated. Continuous coronary arterial pressure monitoring via a pressure wire can facilitate PPVI in high-risk patients with coronary arterial stents. Given the risk of coronary artery stent compression, these high-risk procedures should be performed with support from adult interventional cardiology.

Conflict of Interest

The authors have no conflict of interest relevant to this publication.

> **Comment on this Article or Ask a Question**

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Transcatheter Retrograde Device Closure of an Isolated Pulmonary Valve Stump Using a Deflectable Sheath Technique

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Abstract

Patients with a single ventricular heart physiology may have a persistent egress through one of the semilunar valves that was surgically closed during the palliative operations. This semi lunar patency results in a blind ending pulmonary artery stump. Consequently, the patient is at risk for thrombus that can then result in a paradoxical embolic event and potentially an ischemic stroke. Patients therefore must undergo a reoperation to close the stump or remain on anticoagulation for lifetime. This report demonstrates the use of a retrograde arterial approach and a deflectable delivery sheath to obliterate the proximal pulmonary valve with a vascular device.

Key Words

Stroke • Pulmonary valve • Device closure • Single ventricle • Embolic events

Introduction

The surgical palliation of children with univentricular hearts without obstruction to pulmonary outflow consists of either Damus-Kaye-Stansel anastomosis of the two great vessels in the setting of potentially obstructed systemic outflow or division of the pulmonary artery leaving the aorta as the sole outflow pathway if there is no potential for subaortic obstruction [1]. If the latter approach is elected, the technique of pulmonary artery division must minimize the potential for thrombus formation in the blind ending pulmonary artery stump and subsequent risk for systemic embolic events [2, 3, 4]. In the event that such a stump is present, anticoagulation may be employed [5, 6, 7], but if thrombus develops within the stump or embolism occurs, an intervention to exclude the stump may be required. Here, we describe a novel management strategy in such a circumstance and present long-term follow-up information.

Case Presentation

The original cardiac anatomy of our patient was that of a functionally univentricular heart. There was (right-sided) mitral atresia, a large secundum atrial septal defect, and a large outlet ventricular septal defect. The aorta arose from the anterior and leftward (morphologic right) ventricle and was unobstructed, as was the aortic arch. The pulmonary artery arose from the rightward and posterior (morphological left) ventricle and had significant valvar and subvalvar obstruction, such that the patient had prostaglandin-dependent pulmonary blood flow (Figure 1).

As a neonate, via sternotomy, the patient underwent construction of a right-sided modified Blalock-Taussig shunt using a 4-mm-diameter graft. The ductus arteriosus was not ligated at that time
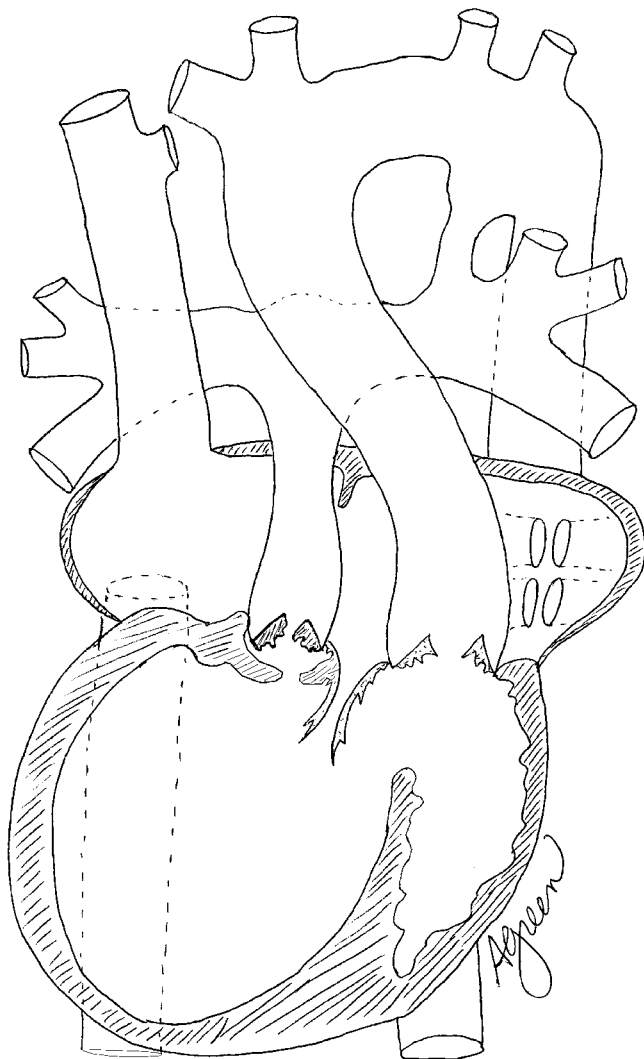
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Figure 1.   Schematic of the single ventricle anatomy prior to surgical intervention.

Figure 2.   Schematic of the single ventricle anatomy after the Fontan operation.

and later closed spontaneously. At 6 months of age, via re-do sternotomy, the patient underwent shunt takedown and construction of a bidirectional Glenn anastomosis. The main pulmonary artery was not divided but was suture-ligated proximally. Follow-up echocardiography revealed persistent patency of the main pulmonary artery. At 30 months of age, via third-time sternotomy, an extracardiac Fontan operation was performed using a 20-mm conduit. The main pulmonary artery was again suture-ligated but not divided, leaving a blind end pulmonary outflow stump (Figure 2).

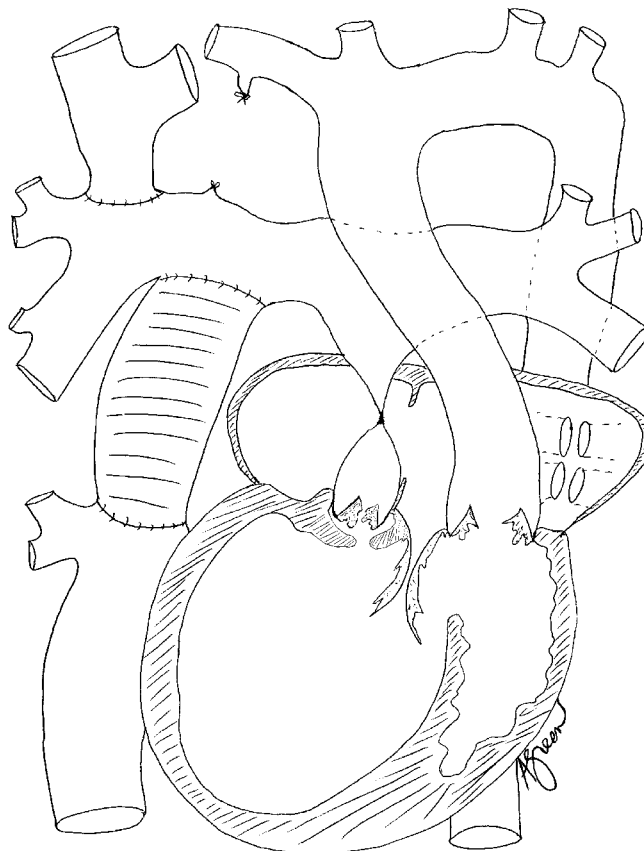An echocardiogram performed on post-operative day 5 demonstrated persistent to-and-from flow into the proximal pulmonary artery but no antegrade flow into the pulmonary arteries or Fontan circuit (Figure 3). Although no thrombus was appreciated within the pulmonary valve sinuses or proximal pulmonary artery, the patient was started on warfarin therapy. A follow-up echocardiogram two months later demonstrated a moderate-sized mobile thrombus within the pulmonary stump despite an international normalized ratio of 3.3. Although there was no evidence of systemic embolism, it was deemed necessary to proceed with obliteration of the pulmonary stump, as the presence of thrombus was felt to indicate failure of anticoagulation therapy. Because of the patient's recent surgery and multiple prior procedures, transcatheter obliteration was proposed.

At nearly 3 years of age and a weight of 18 kg, the patient proceeded to the cardiac catheterization laboratory. The procedure was performed under general anesthesia guided by transesophageal echocardiog-
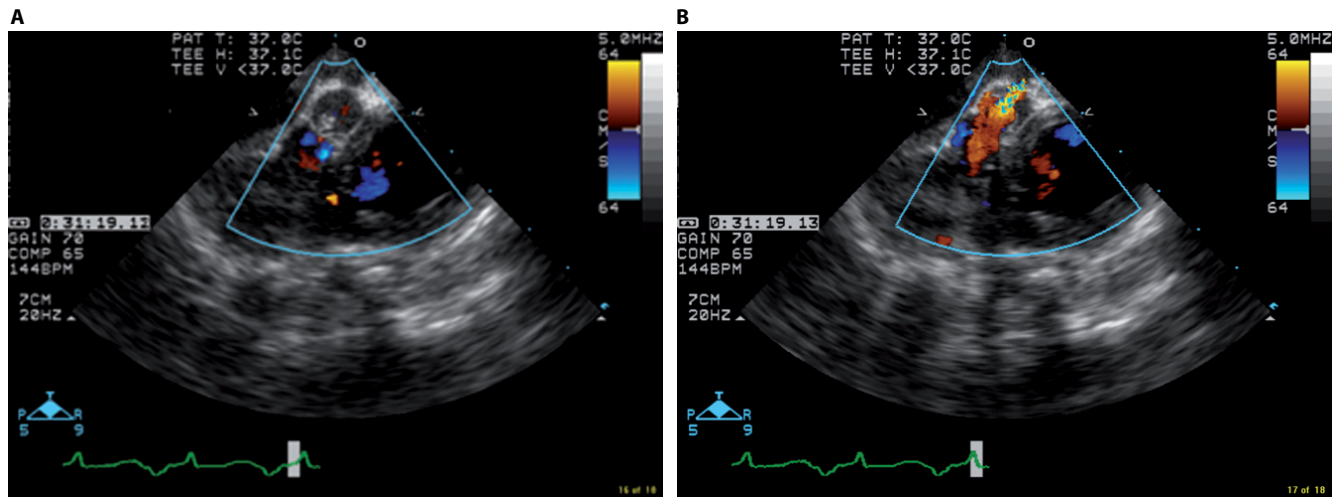
Figure 3. Transthoracic echocardiogram color-flow Doppler image on post-operative day 5 after the Fontan operation. (*Panel A*) Evidence of persistent to-and-from flow into the proximal pulmonary artery stump. (*Panel B*) No evidence of significant antegrade flow across the sutured main pulmonary artery into the Fontan circuit.

raphy and fluoroscopy. Vascular access consisted of a 5-F percutaneously-placed sheath in the left femoral artery. Angiography of the femoral arterial system confirmed an appropriate vessel diameter of 4.2 mm for upsizing the arterial sheath. From the left femoral artery sheath, a 5-F pigtail catheter was positioned using a 0.035-in J wire across the aortic valve and through the ventricular septal defect into the right-sided morphologic left ventricle. Subsequently, a 0.032-in J wire was positioned through the 5-F pigtail, and an 8.5-F (internal diameter) Agilis steerable sheath (St. Jude Medical, St. Paul, Minnesota) was positioned over the 0.032-in J wire and into the mid-right-sided morphological left ventricular cavity. The Agilis sheath was deflected to allow an angle directly toward the pulmonary valve (Figure 4). During this maneuver, there was a brief (< 3 s) episode of transient complete heart block with no hemodynamic changes. Subsequently, a 6-F multi-purpose A-1 catheter was advanced through the Agilis sheath and positioned immediately distal to the pulmonary valve apparatus for an angiogram (Figure 5). Subsequently, a 0.038-in standard J-wire was advanced into the proximal pulmonary artery, and the 6-F multi-purpose catheter was removed. A 6-F JL 3.5 coronary guide catheter was inserted over this wire into the pulmonary valve stump. This wire was removed, and the coronary guide catheter was used to position a 12-mm Amplatzer Vascular Plug (St. Jude Medical) across the pulmonary valve apparatus. The device was fully deployed with a waist in the mid-portion (Figure 6), suggesting engagement with the pulmonary valve annulus. A ventriculogram demonstrated a well-positioned device and no evidence of flow into the pulmonary valve or pulmonary artery (Figure 7). Subsequent angiography and transesophageal echocardiography demonstrated no significant leak around the device but a trivial leak through the device mesh. The previously noted thrombus material remained within the pulmonary outflow stump, with thrombus egress prevented by the device. The femoral arterial sheath was removed, periprocedural antibiotics were administered, aspirin and warfarin were restarted, and there were no unanticipated adverse events.

The patient was maintained on warfarin and aspirin post-procedure. An early pre-discharge transthoracic echocardiogram demonstrated that the vascular occlusion device was in a good position across the pulmonary valve with elimination of leaflet motion. A trace amount of prograde flow by color-flow Doppler was observed through the device mesh without reflux back across the valve leaflets. The previously noted thrombus remained along the posterior wall of the pulmonary stump. After 6 months, warfarin was discontinued, and aspirin was continued indefinitely. No evidence of thrombus recurrence or propagation was detected, nor was there any sign of systemic embolism.
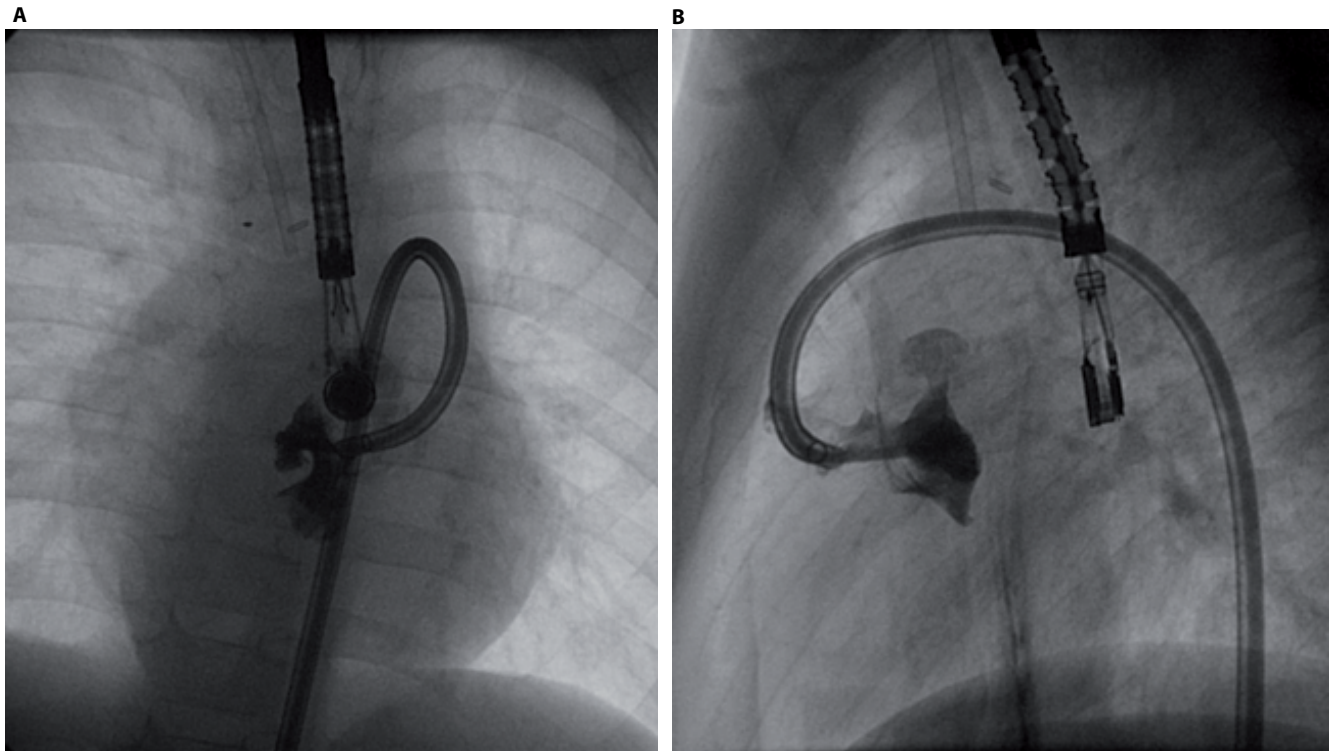
A

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Figure 4. Agilis sheath retrogradely placed into the left ventricle and deflected toward the pulmonary valve. (*Panel A*) Anterior-posterior projection. (*Panel A*) Lateral projection.
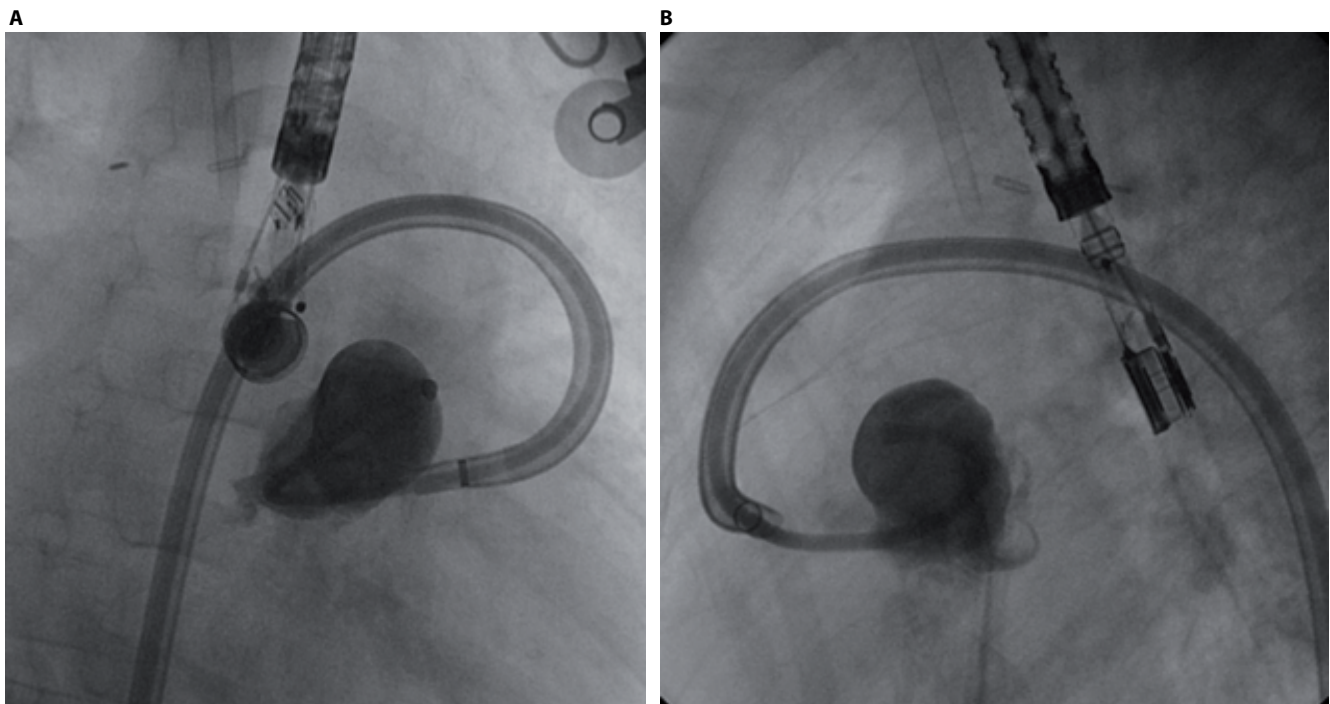
A

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Figure 5. A 6-F multipurpose A-1 catheter advanced through the Agilis sheath and positioned immediately distal to the pulmonary valve apparatus for an angiogram. (*Panel A*) Right anterior oblique projection. (*Panel B*) Lateral projection.
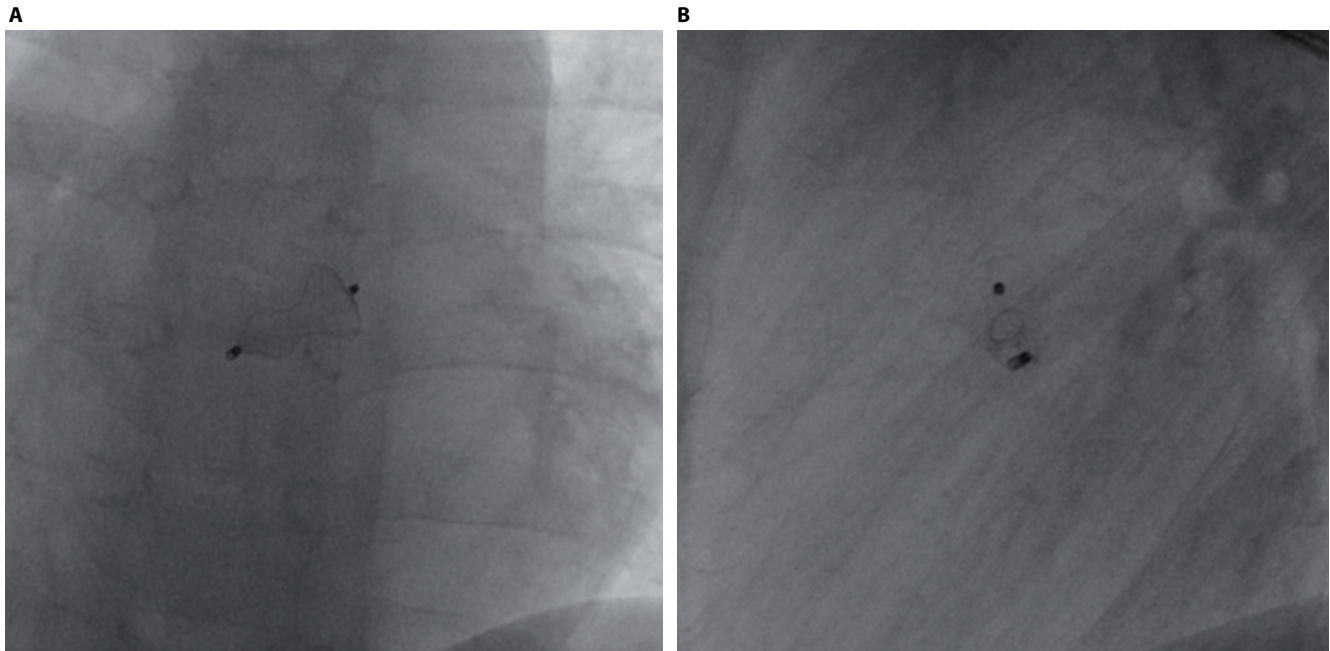
A

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Figure 6. A 12-mm Amplatzer Vascular Plug fully deployed with a waist in the mid-portion across the pulmonary valve apparatus. (*Panel A*) Anterior-posterior projection. (*Panel B*) Lateral projection.
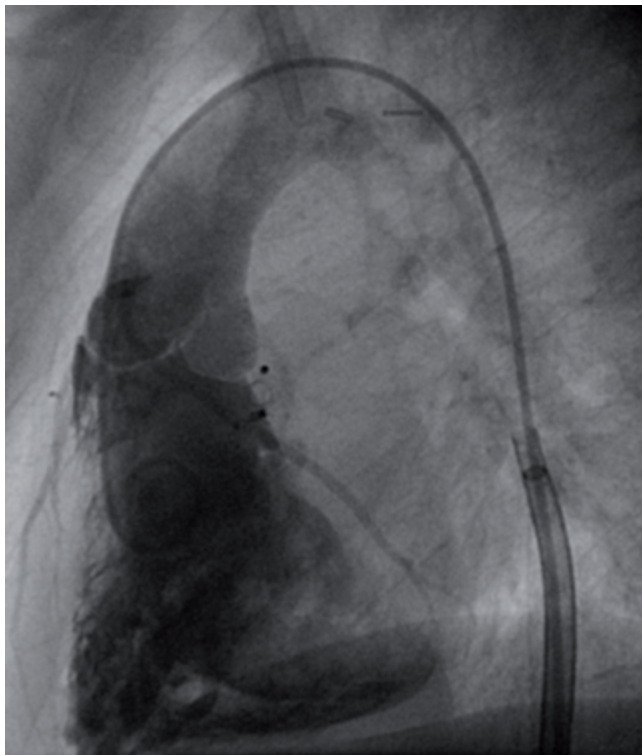

Figure 7. Ventriculogram demonstrating a well-positioned Amplatzer Vascular Plug and no evidence of flow into the pulmonary valve or pulmonary artery.

The echocardiogram at the most recent follow-up of 7 years demonstrated a well-positioned vascular device and no residual flow into or out of the proximal pulmonary artery (Figure 8). This finding was confirmed by magnetic resonance imaging angiography with and without contrast, though the images were partially obscured by an artifact related to the occlusion device. In addition, at the most recent follow-up, there was no leg length discrepancy and normal femoral pulses bilaterally.

Discussion

We believe this to be the first report of the use of a percutaneous retrograde deflectable sheath technique and vascular occluder to obliterate the proximal pulmonary artery in this setting. There are reports of perventricular approaches to close the pulmonary artery stump [8] as well as multiple publications describing vascular occluders for other indications including AV malformations, aorto-pulmonary collaterals, and coronary fistula [9].

This indication should be relatively rare, as the pulmonary valve is often resected and the proximal pulmonary trunk obliterated with suture lig-
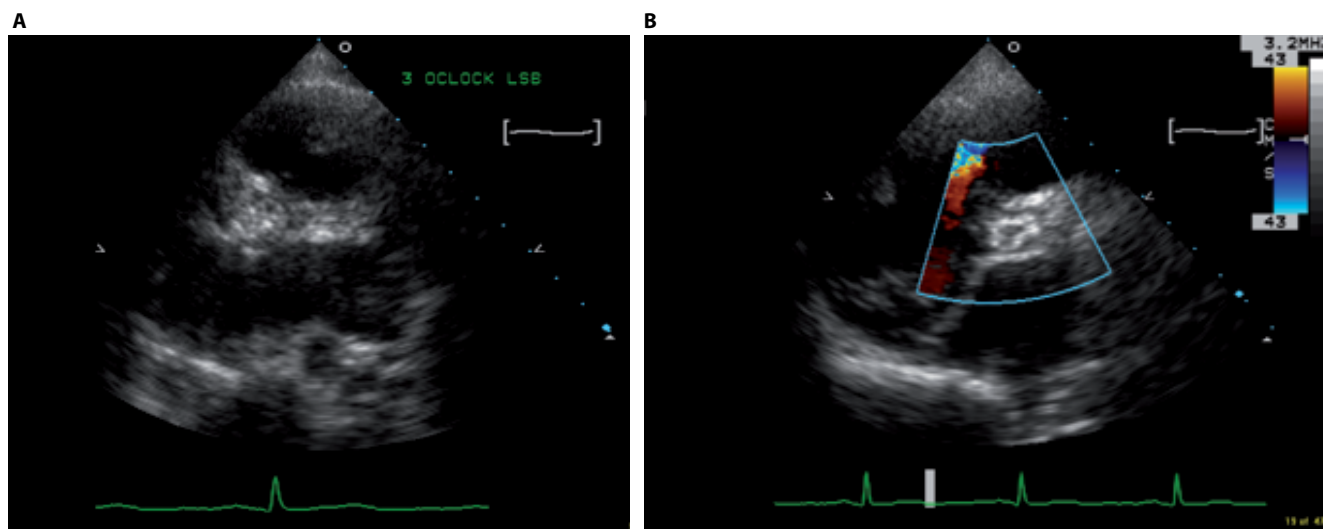
Figure 8. Transthoracic echocardiogram with color-flow Doppler at 7-year follow-up demonstrated a well-positioned vascular device and no residual flow into or out of the proximal pulmonary artery. (*Panel A*) Two-dimensional imaging. (*Panel B*) Color-flow Doppler imaging.

ature during staged palliation. However, in some cases, the surgeon may not perform these maneuvers, perhaps because of the presence of important coronary artery branches around the pulmonary annulus or the wish to preserve additional pulmonary blood flow at the time of the Glenn operation. In such circumstances, thrombus may develop within the proximal pulmonary artery immediately distal to the pulmonary valve apparatus [7]. If this is recognized, the patient may be treated with long-term anticoagulation [5]. With valve patency, and particularly to-and-from flow across the pulmonary valve, a thrombus may dislodge into the systemic circulation [2, 3, 4] and result in stroke [2, 3], with significant consequent morbidity and even mortality [7]. When thrombus is identified or suspected, the most aggressive approach would include surgical thrombectomy and patch closure of the pulmonary annulus. As this would require what in most children would be fourth sternotomy, as well as the use of cardiopulmonary bypass, a trial of medical therapy may be undertaken. If that fails or is felt unlikely to be successful, we have demonstrated an effective alternative to surgery. Also, perventricular techniques should be considered if the femoral arterial system is deemed inadequate for the large deflectable sheath.

In conclusion, this report demonstrates the use of a retrograde arterial approach and a deflectable delivery sheath to obliterate the proximal pulmonary valve with a vascular device, thus precluding the need for reoperation, perventricular technique, or lifetime anticoagulation and associated risks. Transcatheter obliteration of a blind ending pulmonary artery stump is feasible and durably effective.

Conflict of Interest

The authors have no conflict of interest relevant to this publication.

> **Comment on this Article or Ask a Question**

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