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Original Research

Left Pulmonary Artery Occlusion Following Device Closure of Patent Ductus Arteriosus in Premature Infants

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ABSTRACT

Background: Device closure of a patent ductus arteriosus (PDA) is rapidly evolving, with the Amplatzer Piccolo Occluder (Abbott) receiving US Food and Drug Administration approval and becoming the first device approved for PDA closure in patients ≥700 g. We report on the first known cases of complete left pulmonary artery (LPA) occlusion following Piccolo closure of a PDA in premature infants.

Methods: Retrospective chart analysis of PDA closures.

Results: We have performed over 50 cases of Piccolo device closure of the PDA in preterm neonates in the past 2 years, with these 2 cases representing our only complications (4%). This represents a total complication rate similar to or lower than most centers that have published data for this procedure.

Conclusions: Although rare, severe LPA obstruction can be seen in premature infants following device closure of the PDA. The Piccolo device is designed to ideally remain entirely intraductal. Although our device selection appeared to provide a device short enough for the given ductal length, we recommend, whenever possible, giving consideration to using the shortest possible device. We also recommend increasing the frequency of echocardiographic surveillance to weekly studies if at any time the imaging demonstrates an increase in the degree of obstruction/turbulence.

Introduction

Device closure of the patent ductus arteriosus (PDA) has typically been performed outside the neonatal period. For premature infants and neonates, surgical PDA ligation was the standard of care if attempts at medical closure failed. In January 2019, the Amplatzer Piccolo Occluder (Abbott) received US Food and Drug Administration approval and became the first device approved for PDA closure in patients ≥700 g.[1] To date, there have been no reported cases of the Piccolo device causing late obstruction of the pulmonary artery (PA) requiring intervention. Various PDA devices may cause some degree of obstruction of the left pulmonary artery (LPA). Current anecdotal practice is that the relative severity of obstruction seen early on will lessen as the premature infant grows. If the obstruction does not lessen, the infant is at risk of losing the LPA, which historically leads to life-long complications, most commonly, hemoptysis, scoliosis, and recurrent pulmonary infections.[2] We report on development of complete LPA occlusion following Piccolo closure of a PDA in 2 premature infants. To our knowledge, these are the first reported descriptions of this complication.

Patient and device characteristics are listed in Table 1 with comorbidities in Table 2.

We have performed over 50 cases of Piccolo device closure of the PDA in preterm neonates in the past 2 years, with these 2 cases representing our only complications (4%). This represents a total complication rate similar to or lower than most centers that have published data for this procedure.[3]

Table 1. Patient and device characteristics

	Case 1[a]	Case 2
Gestational age, wk, d	26, 2/7	24, 2/7
Birth weight, g	755	785
Sex	Male	Male
Age at procedure, d	30	25
Procedural weight, g	1160	975
PDA narrowest diameter, mm	3.5	3.3
PDA largest diameter, mm	4.5	4.3
PDA length, mm	11.3	12
Device used	5-4 Piccolo	5-4 Piccolo
Suggested device	5-2 Piccolo	5-4 Piccolo

PDA, patent ductus arteriosus.

[a] 5-4 Device embolized and retrieved on initial deployment.

Abbreviations: LPA, left pulmonary artery; NEC, necrotizing enterocolitis; PDA, patent ductus arteriosus; TTE, transthoracic echocardiography.

Keywords: angiography; catheterization; device closure; echocardiography; occlusion; patent ductus arteriosus; Piccolo.

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Table 2. Preprocedural patient comorbidities/concerns.

Case 1	NEC with bowel resection, ileostomy, ventilator dependence, BPD, poor nutrition
Case 2	Persistent metabolic acidosis, ventilator dependence, twin died due to NEC with large PDA, BPD, poor nutrition

BPD, bronchopulmonary dysplasia; NEC, necrotizing enterocolitis; PDA, patent ductus arteriosus.

Case 1

The initial angiography demonstrated a long ductus (Figure 1A) with an area of slight narrowing toward the proximal third. During the initial implant of a 5-4 Piccolo, the device embolized to the LPA, was retrieved uneventfully, and repositioned closer to the aortic end. This allowed for a very stable position, making better use of the narrowing in the ductus to better stabilize the device (Figure 1B). Given the embolization on initial attempt of the 5-4, the decision was to not downsize the device to the 5-2 Piccolo as per the manufacturer selection chart (Table 3)[4]. The immediate transthoracic echocardiography (TTE) images showed the device to be intraductal and with laminar flow of both the aorta and the LPA (Figure 2A). The following morning, the TTE was unchanged, and the baby was extubated to high flow nasal cannula.

Five weeks later, a TTE showed the position was unchanged, no residual shunting, laminar flow at the aorta, and only mild turbulence of the LPA with peak velocity of 2.0 m/s (Figure 2B and Table 4). At 9 weeks postprocedure, there was a sudden increase in work of breathing and a new oxygen requirement. A TTE showed a suprasystemic right ventricle and no flow to the LPA. He was taken to the catheterization lab where angiography confirmed absence of flow to the LPA (Figure 3). Fluoroscopically, the position of the device was unchanged, and several revascularization attempts were unsuccessful. He was taken to the operating room for surgical revascularization. In the operating room, the device's proximal disc was intraductal with the LPA below it, completely occluded. The device was left in place and pulmonary arterioplasty was performed. The intraoperative course was complicated by reperfusion injury and pulmonary hemorrhage upon weaning from cardiopulmonary bypass, which resolved over the next 48 hours.

Table 3. Manufacturer suggested sizing chart for Piccolo device.[4]

Occluder sizing for patients >2 kg using extraductal disc placement			
D. mm, in	E. mm, in	E. mm, in	E. mm, in
–	3-4 (0.118-0.157)	4.1-6 (0.161-0.236)	6.1-8 (0.240-0.315)
≤2 (≤0.079)	9-PDAP-03-02-L	9-PDAP-03-04-L	9-PDAP-03-06-L
2.1-3 (0.083-0.118)	9-PDAP-04-02-L	9-PDAP-04-04-L	9-PDAP-04-06-L
3.1-4 (0.122-0.157)	9-PDAP-05-02-L	9-PDAP-05-04-L	9-PDAP-05-06-L
Occluder sizing for patients ≤2 kg using intraductal placement			
D. mm, in	E. mm, in	E. mm, in	
–	3-12 (0.118-0.472)	≥12.1 (≥0.476)	
≤1.7 (≤0.067)	9-PDAP-03-02-L	9-PDAP-03-04-L	
1.8-3.2 (0.071-0.126)	9-PDAP-04-02-L	9-PDAP-04-04-L	
3.3-4 (0.130-0.157)	9-PDAP-05-02-L	9-PDAP-05-04-L	

D, minimal ductus diameter; E, ductus length.

Two weeks postoperatively, there was good flow to the LPA (Figure 4A) with a maximum estimated gradient of only 15 mm Hg, and he was soon thereafter discharged home. At 3 months outpatient follow-up, he had developed severe restenosis, with maximum gradient of 40 mm Hg (Figure 4B). He was again taken to the catheterization lab and underwent successful stent angioplasty using a 6-mm Cook Formula 418 stent (Cook Medical) (Figure 5; Central Illustration), significantly improving flow and reducing the right ventricular pressure from three-quarter to less than one-half systemic pressure. The intervention was performed from the femoral vein using only a Prelude (Merit Medical) 5F low profile short sheath.

Case 2

Unlike case 1, angiography showed a large mostly tubular type F ductus without any central narrowing (Figure 6). Device implant was straightforward, and post release TTE showed it to be well seated with only slight LPA turbulence caused by the proximal disc (Figure 7A) and maximal velocity of only 1.6 m/s. The following morning, there were no changes and no residual PDA.

One week later, TTE showed a slight increase in maximal velocity of 2 m/s (Figure 7B) but overall, still reassuring. One month later, 5 weeks following the procedure, there was a further increase in maximal velocity, now up to 2.7 m/s (Figure 7C). With the belief this would improve

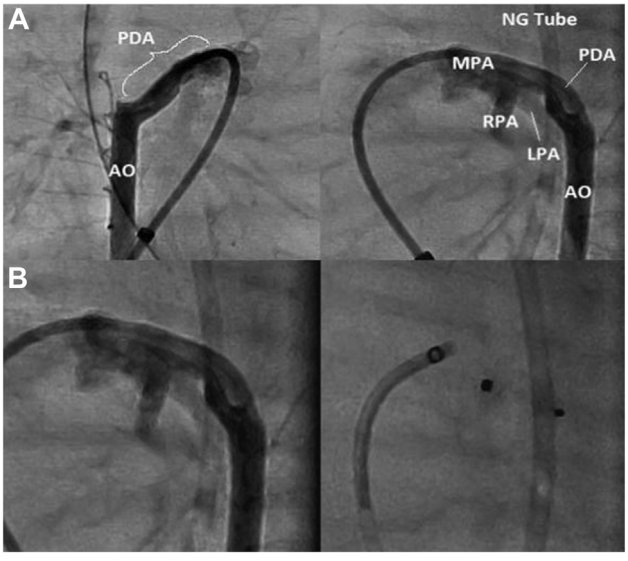


Figure 1.
(**A**) Case 1 initial angiogram with frontal RAO projection (left panel) and straight lateral (right panel). Note the slightly anterior position of the nasogastric tube relative to the descending aorta in the lateral projection. (**B**) Device position demonstrated post release in the right panel compared with the initial angiogram on the left panel. Positioned as distal as safely possible due to the initial embolization. AO, aorta; LPA, left pulmonary artery; MPA, main pulmonary artery; NG, nasogastric; PDA, patent ductus arteriosus; RAO, right anterior oblique; RPA, right pulmonary artery.

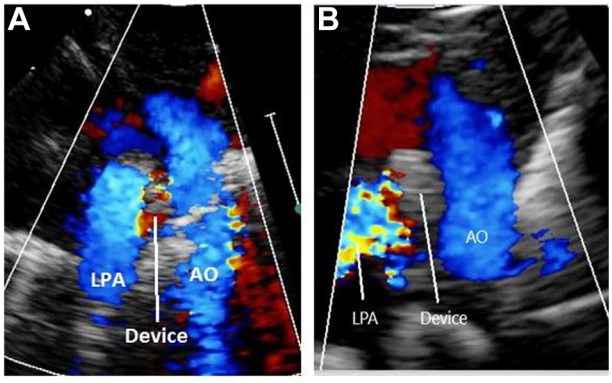


Figure 2.
Progression of LPA stenosis in case 1. (**A**) TTE immediately post device placement showing max gradient of 14 mm Hg. (**B**) TTE at 5 weeks post placement showing mildly increased turbulence in LPA with maximum gradient of 20 mm Hg. AO, aorta; LPA, left pulmonary artery; TTE, transthoracic echocardiography.

Table 4. Timing of surveillance transthoracic echocardiograms and maximum gradient recorded at the left pulmonary artery.

Echo timing	Case 1	Case 2
Echo 1 timing (max gradient, mm Hg)	1 d (14)	1 d (10)
Echo 2 timing (max gradient, mm Hg)	5 wk (20)	1 wk (16)
Echo 3 timing (max gradient, mm Hg)	9 wk (no flow)	5 wk (29)
Echo 4 timing (max gradient, mm Hg)	–	6 wk (26)
Echo 5 timing (max gradient, mm Hg)	–	7 wk (31)
Echo 6 timing (max gradient, mm Hg)	–	8 wk (30)
Echo 7 timing (max gradient, mm Hg)	–	9 wk (27)
Echo 8 timing (max gradient, mm Hg)	–	10 wk (32)
Echo 9 timing (max gradient, mm Hg)	–	11 wk (31)
Echo 10 timing (max gradient, mm Hg)	–	12 wk (50) no flow

with patient growth, he was followed closely with weekly echocardiograms for the next 6 weeks, which remained relatively unchanged. Then, on week 12 postprocedure, there was an increase to a peak of 3.6 m/s, with minimal flow by color doppler (Figure 7D). This coincided with the infant acutely requiring additional respiratory support. He was taken to the catheterization lab where angiography confirmed severe obstruction to the LPA (Figure 8). The device appeared unchanged in position from previous fluoroscopy. Several attempts to revascularize the LPA were unsuccessful. The patient was taken to the operating room and underwent uncomplicated surgical revascularization. This included the proximal disc being excised entirely to relieve the obstruction. The intraoperative findings showed the device seated mostly intraductally, with the proximal disc up against the roof of the PA but protruding down and entirely blocking the LPA orifice. The device was also compressing the LPA, further compromising flow. Postoperatively, there were no complications. He has since been discharged from the hospital, and at 3-month follow-up, he had excellent flow to the LPA with only mild turbulence (Figure 9).

Discussion

Currently, there are only anecdotal and few published reports of LPA stenosis caused by device closure of PDAs in severely premature infants. These cases are typically described as not needing intervention. In most scenarios, the LPA grows with the patient, and in time, the degree of stenosis improves.

The 2 cases we present here are somewhat different. In the first case, initial echocardiographic imaging was very reassuring. Different from all other cases described so far, the subsequent echocardiogram at 2 months showed total absence of the LPA. In a 2020 publication from Taiwan, Chien et al[5] described a suspected mechanism for the occasional stenosis that develops. They demonstrated echocardiographic findings that suggested the device may become compressed and elongated, therefore protruding more into the LPA. In our patients, we did not experience any changes in the device position. Echocardiographic and fluoroscopic measurements showed no evidence of any elongation. In fact, during surgery, the device was noted to still be

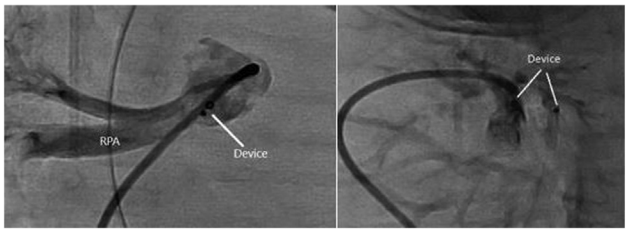


Figure 3.
Case 1 posteroanterior and lateral angiogram at 9 weeks postprocedure demonstrating absent left pulmonary artery. RPA, right pulmonary artery.

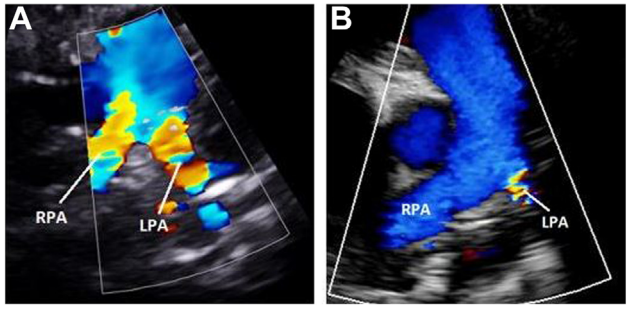


Figure 4.
(**A**) Case 1 TTE image showing normal LPA flow 2 weeks postoperatively from arterioplasty. (**B**) TTE performed at 3 months follow-up postoperatively showing restenosis of the LPA with a max gradient of 40 mm Hg. LPA, left pulmonary artery; RPA, right pulmonary artery; TTE, transthoracic echocardiography.

within the ductus with the LPA occluded below the device from what appeared to be compression caused by the mass effect above it. The LPA required a patch arterioplasty extending from the bifurcation back to just beyond the distal end of the device. We theorize one possible mechanism to be residual ductal tissue extending into the LPA, which constricted, creating a severe LPA coarctation post device placement. Another theory could be the natural history of a PDA to shorten over time, and given that the Piccolo is designed to stay completely intraductal, using a shorter device when possible may mitigate this complication. In our case the embolization of the device in case 1 led us to not trying a smaller device, although, in retrospect, it may have been worth an attempt. In case 2, the device was chosen based on the manufacturer's guidelines, but moving forward, a greater emphasis should be placed on clinical judgment and using the shortest possible device for the desired effect.

The mechanism described by Chien et al[5] could possibly describe what occurred with our second patient, although we were unable to detect any change in the device length, position, or appearance. Another less likely theory may simply be that the LPA always was, and simply destined to be, stenotic, and that is why we had to perform the stent angioplasty even after surgery. In a 2007 publication, Javois et al[6] described pre-existing LPA stenosis masked pre-device by increased ductal flow leading to worsening LPA stenosis after closure. This phenomenon could help explain the findings in the cases reported.

Unlike the patient in case 1, this second patient began to demonstrate more significant obstruction earlier but remained stable for nearly 6 weeks before becoming clinically problematic (Table 4). Intraoperatively, the proximal disc was in fact hanging down and obstructing the orifice to the LPA. Although we were unable to appreciate a change in position either by echocardiography or fluoroscopy, it is possible there was some device elongation as described by Chien et al.[5]

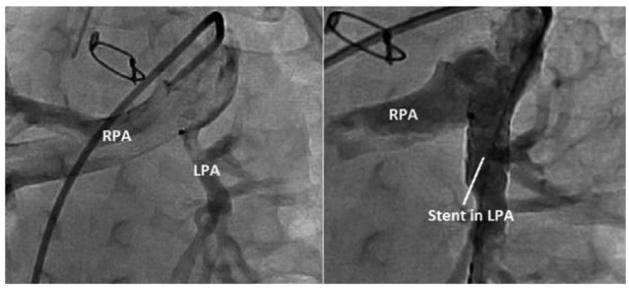
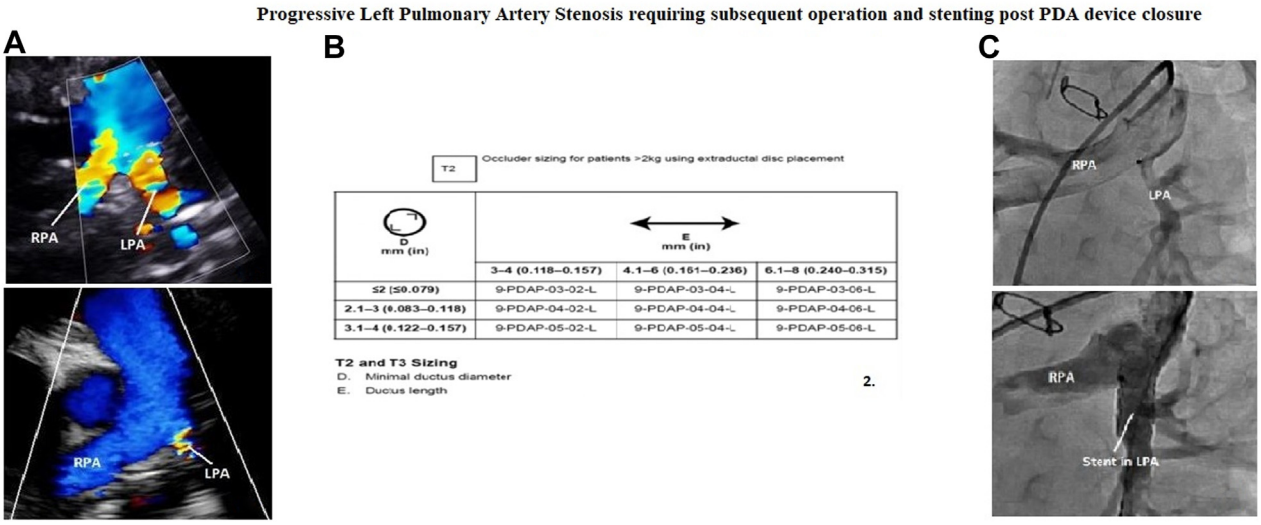


Figure 5.
Catheterization #3 of case 1. Posteroanterior and lateral angiograms showing stent angioplasty of the LPA with Cook Formula 418 bare metal with preserved flow to left upper lobe branch which is crossed in this angiogram. LPA, left pulmonary artery; RPA, right pulmonary artery.



Central Illustration.
(**A**) Anatomic heart model showing Piccolo device, which is designed to remain intraductal. (**B**) shows typical catheter course through femoral vein and out into the pulmonary artery. (**C**) shows the Amplatzer Piccolo device attached to the delivery catheter. LPA, left pulmonary artery; PDA, patent ductus arteriosus; RPA, right pulmonary artery. Central Illustration figure acquired through Abbott Laboratories; www.cardiovascular.abbott.

In retrospect, there was no great alternative to surgery at the time we discovered the flow to be totally occluded. The devices had been in place too long to allow for safe retrieval, thereby necessitating a sternal approach and arterioplasty to revascularize the PA. Although we developed restenosis postoperatively in the first patient, necessitating stent placement, this was performed 4 months later when the patient size allowed for placement of the 6-mm Formula 418 stent (Cook Medical). Therefore, attempt at stent angioplasty rather than surgery, had we intervened sooner, would not have been possible with anything more than a coronary stent, which is far from ideal. The 6-mm Formula stent will have a good possibility of allowing for a purely transcatheter periodic rehabilitation moving forward, with anything smaller such as a coronary stent having required yet additional interventions to fracture the stent, or possibly additional surgery. Additionally, for the stent placement, we used a 5F Prelude (Merit Medical) low profile sheath, which offers an external diameter equivalent to a standard 4F sheath. With very clear landmarks provided by the PDA device, a long sheath with larger diameter is unnecessary for proper positioning. Additionally, the 6-mm Formula stent can be safely dilated to 12 mm, allowing for ample growth.[7]

Conclusion

Although rare, severe LPA obstruction can be seen in premature infants following device closure of the PDA. The Piccolo device is designed to ideally remain entirely intraductal. Although our device selection appeared to provide a device short enough for the given ductal length, we recommend, whenever possible, giving consideration to using the shortest possible device. We also recommend increasing the frequency of echocardiographic surveillance to weekly studies if at any time the imaging demonstrates an increase in the degree of obstruction/turbulence. Clinicians should have a low threshold for alternative imaging modalities such as computed tomography or more invasive options if a pattern of increased obstruction is detected. This may allow for a transcatheter based

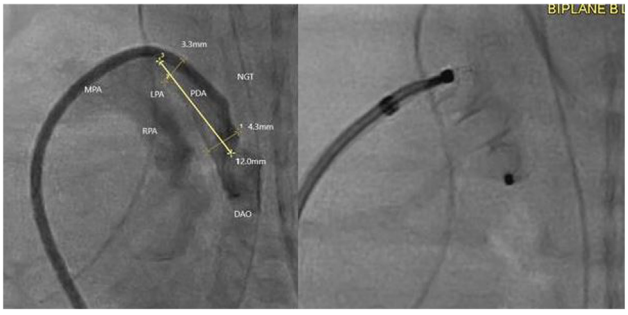


Figure 6.
Case 2. Straight lateral view angiogram of patent ductus arteriosus.

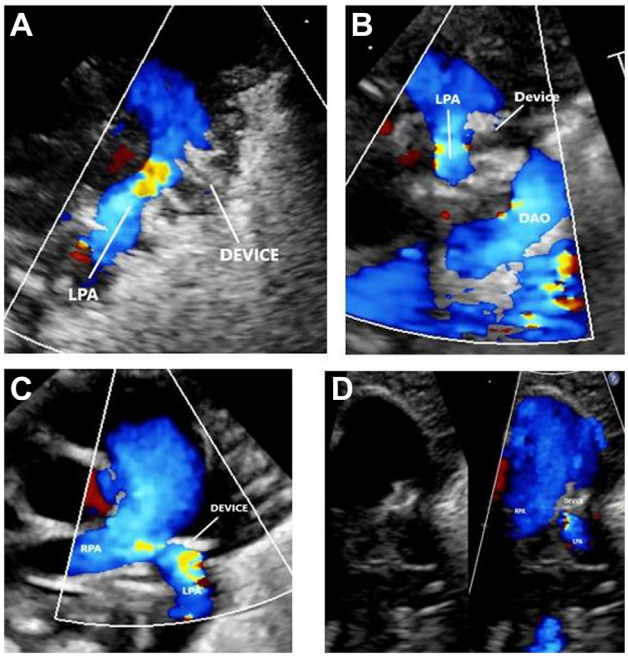


Figure 7.
(**A**) Mild LPA turbulence most notable between the discs immediately after device release. (**B**) 1-week postprocedure. Slight increase in maximal velocity of LPA. (**C**) 5 weeks post procedure. Vmax 2.7 m/s. (**D**) 12 weeks postprocedure 2D and color doppler demonstrating near total LPA obstruction. DAO, descending aorta; LPA, left pulmonary artery; MPA, main pulmonary artery; NGT, nasogastric tube; RPA, right pulmonary artery.

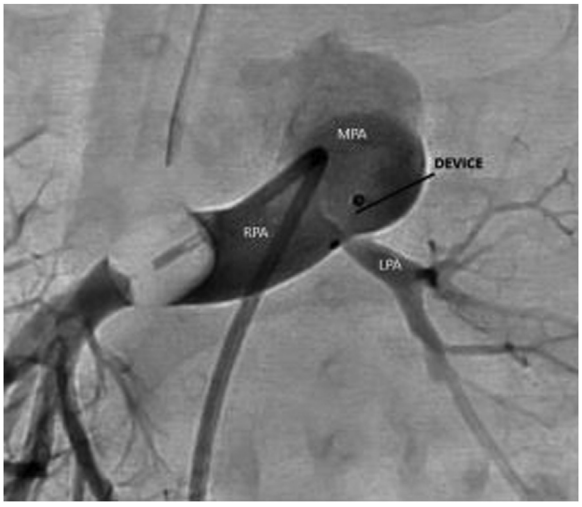


Figure 8.
Frontal angiogram demonstrating severely diminished flow to the LPA. LPA, left pulmonary artery; MPA, main pulmonary artery; RPA, right pulmonary artery.

intervention to either retrieve the device, if relatively soon, or stent the LPA, if patient size allows.

Declaration of competing interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethics statement and patient consent

The research reported has adhered to the relevant ethical guidelines and patient consent has been obtained from legally authorized representatives. There was no institutional review board approval required for this retrospective case series.

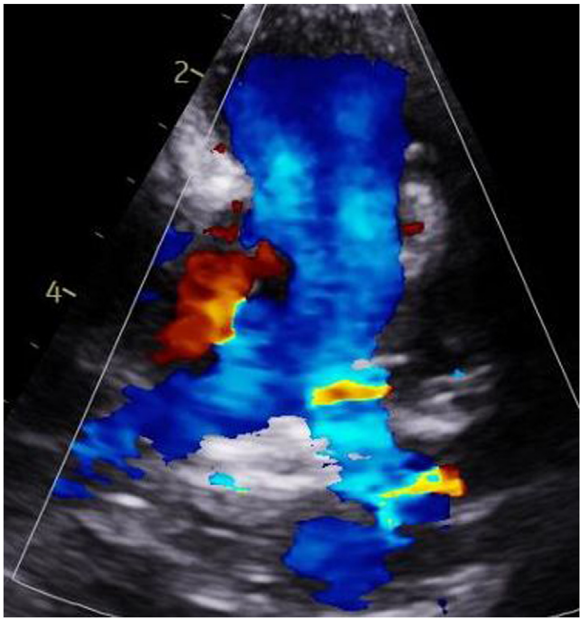

Figure 9.
Postoperative echocardiogram showing nonobstructive left pulmonary artery flow.

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