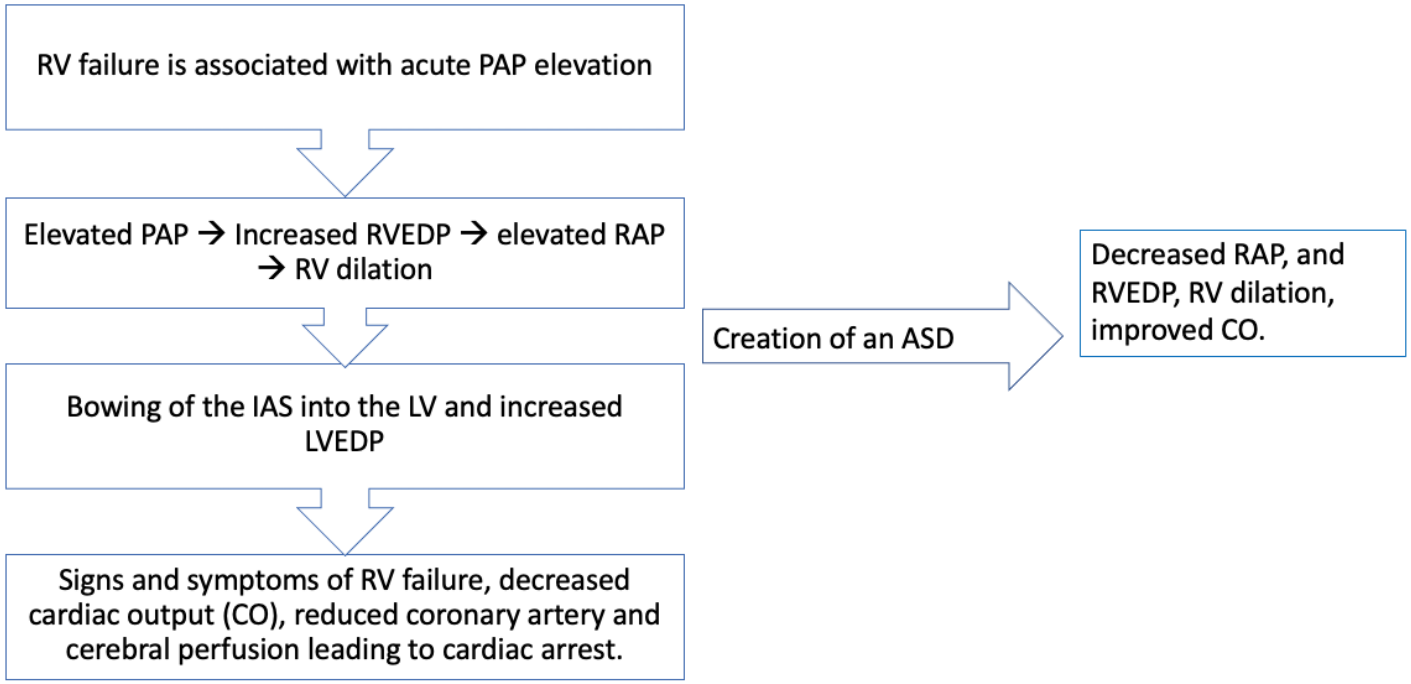
frontiers

Supplementary Material

Supplementary Figure 1. Pathophysiology of the creation of a rescue right-to-left shunt.



Note. ASD, atrial septal defect; CO, cardiac output; IAS, interatrial septum; LV, left ventricle; LVEDP, left-ventricular end diastolic pressure; PAP, pulmonary arterial pressure; RAP, right atrial pressure; RV, right ventricle; RVEDP, right-ventricular end diastolic pressure

Supplementary Table 1. Summary of Data Available in the Literature on Atrial Flow Regulator Implantation for Pediatric Pulmonary Arterial Hypertension Patients

Reference	Study details	n	Symptoms	Complications	Follow-up	Outcomes
Patel et al. (2015) (1)	Implantation of an AFR for a patient with PAH	1	- NYHA class III - Impaired 6MWT - Progressive ascites and pedal edema	None	6 weeks	- Improvement in 6MWT - Relief of ascites and pedal edema - Subjective symptomatic improvement - Mean resting saturation 98%
Rajeshkumar et al. (2017) (2)	AFR devices implanted in patients with severe PAH presenting with syncope and right heart failure	12	- NYHA class III (9/12) - NYHA class IV (3/12) - Syncope or presyncope (12/12) - Angina (3/12) - Palpitations (3/12)	- Preprocedural atrial flutter (1/12) - Postprocedural hypoxia warranted continued oxygen supplementation for 48–72 hours (6/12)	Median 189 (range 10–296) days	- Improvement in NYHA class (12/12) - Relief of syncope (12/12) - Subjective symptomatic improvement in 6MWT - Preserved device patency (12/12) - Mean resting saturation 92%
Dąbrowska-Kugacka et al. (2019) (3)	AFR for severe, drug-resistant PAH after CHD correction	1	- WHO class IVa - Recurrent syncope - Ascites and pedal oedema	None	6 weeks	- Improved WHO class - Relief of syncope - Relief of edema

Janus et al. (2020) (4)	AFR as a bridge to lung transplant in a young patient with drug-resistant, idiopathic PAH	1	- WHO class IV - Impaired 6MWT - Ascites and pedal edema	Postprocedural hypoxia warranting O_2	8 weeks	- Improved WHO class - Improved 6MWT
Hansmann et al. (2022) (5)	Implantation of AFR devices in 3 children (age 6–13 years)	3	- WHO FCs of III–IV - 1 patient had dyspnea on exertion, edema, and ascites - 1 patient was listed for heart transplantation for 2 years prior - All patients had group 2 PH secondary to RCM	Unknown: not reported, short follow-up time	1–3 months	Improved left-atrial dilation, postcapillary pulmonary hypertension, and heart failure symptoms
O'Callaghan et al. (2022) (6)	Implantation of AFR devices in 15 patients with greatly varying age	6 pediatric, 9 adult	- Failing Fontan (5/6) - 1 patient had Shone's complex and extensive surgical history; unable to wean from ventilation and had left atrial hypertension	- 3/15 died (1 after major hemorrhagic stroke on ECMO) - 2/15 patients with CHD and PH died from complications related to right heart failure	5 weeks (3-8)	- O_2 saturations increased in all Fontan patients - Improvement in NYHA classification - All patients survived to follow up

Note. 6MWT, six-minute walk test; AFR, atrial flow regulator; CHD, congenital heart disease; ECMO, extracorporeal membrane oxygenation; NYHA, New York Heart Association; PAH, pulmonary arterial hypertension; PH, pulmonary hypertension; RCM, restrictive cardiomyopathy

Supplementary Table 2. Patient-level Demographic and Clinical Characteristics at Baseline

No.	Device: size	Sex	Age (years)	Weight (kg)	Primary diagnosis	Clinical indication for devices	PH classification	Genetics	PH therapy	Anticoagulants/ other medications
1	FASD: 21 mm (5 mm fenestration)	F	9.35	70.0	APAH-CHD (large secundum ASD)	Orthopnea, effort intolerance	1.4	Nil	Tadalafil	Aspirin, Coumadin
2[1]	FASD: 24 mm (6 mm fenestration)	M	10.03	28.0	IPAH (incidental large ASD)	Dyspnea, fatigue, unable to augment vasodilator therapy	1.1	Nil	Ambrisentan, selexipag, tadalafil	Aldactazide, clopidogrel
3	AFR: 4 mm Occlutech	M	3.52	15.0	Fontan (DORV/MA)	Reduction in fenestration	5.4	Nil	Sildenafil	Amlodipine, Coumadin, enalapril
4[2]	AFR: 6 mm	F	4.38	13.9	Fontan (HLHS: AS/MA)	Fontan failure	5.4	Nil	Sildenafil	Aspirin, enalapril, enoxaparin, furosemide, spironolactone
5	AFR: 4 mm	M	14.59	19.9	Fontan (HLHS: AS/MA)	Occlusion of Fontan fenestration	5.4	Nil	Tadalafil	Coumadin
6	AFR: 6 mm	F	4.76	20.8	Fontan (HLHS: AS/MA)	Occlusion of Fontan fenestration	5.4	Nil	Ambrisentan, tadalafil	Coumadin
7	AFR: 6 mm	M	6.29	22.7	IPAH	Syncopal events, PH crises	1.1	Nil	Ambrisentan, tadalafil, remodulin	Aldactazide, aspirin, clopidogrel, Keppra
8	AFR: 4 mm	F	6.15	17.8	Fontan (HLHS: AS/MS)	Elevated PVRI	5.4	Nil	Ambrisentan, tadalafil	Coumadin
9	FASD: 10.5 mm	F	0.31	6.8	APAH-CHD (large PDA, moderate-to-large ASD)	CLD, persistent NIV requirement	1.4	T21	Tadalafil	Nil

10	AFR: 4 mm	F	1.86	7.9	APAH-CHD (hemitruncus: RPA from AA, large PDA to LPA)	PH crises requiring reliable atrial shunt	1.4	VOUS	Ambrisentan, tadalafil, treprostinil	Aspirin, clopidogrel, furosemide, spironolactone
11	FASD: 10.5 mm	M	1.92	9.5	Fontan (PA/IVS/MAPCA)	Multiple fenestrated ASD, hypoxemia	5.4	Nil	Tadalafil	Atenolol, enoxaparin
12	AFR: 6 mm	F	17.94	47.8	IPAH	Syncopal events, PH crises	1.1	DiGeorge syndrome	Ambrisentan, selexipag, tadalafil	Amlodipine, aspirin, enoxaparin
13[3]	[Failed due to iliac vessel occlusion; surgical closure]	F	0.40	5.3	APAH-CHD (large ASD)	Large shunt and prolonged intubation period	1.4	CNV *12p11.21*	Bosentan, tadalafil	Nil
14[3]	[Failed; 7.5 mm FASD embolized]	M	0.42	4.0	BPD-PH (moderate ASD, PDA)	Prolonged respiratory support, FTT	3.7	Nil	Ambrisentan, tadalafil	Lasix, spironolactone

Note. AA, ascending aorta; AA/MS, aortic atresia/mitral stenosis; AFR, atrial flow regulator; AP, aortopulmonary collateral; APAH-CHD, PAH associated with congenital heart disease; AS/MA, aortic stenosis/mitral atresia; AS/MS, aortic stenosis/mitral stenosis; ASD, atrial septal defect; BPD, bronchopulmonary dysplasia; CHD, congenital heart disease; CLD, chronic lung disease; CNV, copy number variation; DORV/MA, double outlet right ventricle/mitral atresia; F, female; FASD, fenestrated atrial septal defect; FTT, failure to thrive; HLHS, hypoplastic left heart syndrome; IPAH, idiopathic pulmonary arterial hypertension; IVS, interventricular septum; LPA, left pulmonary artery; M, male; MAPCA, major aortopulmonary collateral artery; NIV, noninvasive ventilation; PA/IVS, pulmonary atresia/intact ventricular septum; PAH, pulmonary arterial hypertension; PDA, patent ductus arteriosus; PH, pulmonary hypertension; PM, pacemaker; PS, pulmonary stenosis; PVRI, pulmonary vascular resistance index; RPA, right pulmonary artery; T21, trisomy 21; VOUS, variant of unknown significance

[1] Patient 2 has two cardiac catheterization events: the first device embolized and the second was deployed successfully six months later.

[2] Patient 4 had two cardiac catheterizations one month apart: the first attempt used a 4 mm AFR that was undersized for the atrial shunt while the second used a 6 mm AFR and was successful.

[3] Patients 13 and 14 did not receive anticoagulants after the procedure as devices were unable to be implanted.

References

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