

## Repair of Atrial Septal Defect With Eisenmenger Syndrome After Long-Term Sildenafil Therapy

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We report a woman with atrial septal defect and severe pulmonary hypertension with 25.0 Wood unit  $\cdot$  m<sup>2</sup> of indexed total pulmonary vascular resistance. She underwent successful corrective repair of atrial septal defect after 2 years of treatment with sildenafil, and has been monitored for 4 years after repair. This case supports a “treat and repair” approach using advanced pulmonary vasodilator therapy in selected patients with inoperable severe pulmonary hypertension associated with atrial septal defect.

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In patients with left-to-right shunting cardiac lesions and severe pulmonary hypertension, including Eisenmenger syndrome, corrective repair usually has not been a management option after the initial decision of inoperability. Recently, however, the possibility was stated that corrective repair is possible in selected patients with atrial septal defect (ASD) and inoperable severe pulmonary hypertension after advanced therapy with pulmonary vasodilators [1]. This “treat and repair” approach is based on several reports of anecdotal cases [2–4].

We report a patient with ASD and Eisenmenger syndrome in whom successful surgical repair of the defect was possible after 2 years of treatment with sildenafil. This patient has been monitored uneventfully for 4 years after ASD repair.

A 41-year-old Korean woman was referred to our hospital for aggravating exertional dyspnea. She presented with New York Heart Association (NYHA) functional class III. She denied any other specific medical history before age 32 years, when exertional dyspnea was documented. Cyanosis was detected, and percutaneous oxygen saturation was 82%. Echocardiography showed a large secundum ASD and moderate tricuspid regurgitation (TR) with peak velocity of 5.6 m/s. Cardiac catheterization confirmed severe pulmonary hypertension, with body surface area indexed total pulmonary vascular

resistance (PVRI) of 25.0 Wood unit (WU)  $\cdot$  m<sup>2</sup> (Table 1). Vasoreactivity testing performed with oxygen showed a weak response.

It was concluded that corrective repair was impossible and she was conservatively managed for 1 year, but her clinical status did not improve. Sildenafil (25 mg, twice daily) was added to her prescription. Nine months later, the dosage of sildenafil was increased to 50 mg, twice daily.

After 2 years of sildenafil treatment, her symptoms had improved, cyanosis was not observed, and echocardiography showed TR with peak velocity 4.2 m/s. So, in expectation of improvement of PVR, cardiac catheterization was reexamined (Table 1). PVRI was 12.63 WU  $\cdot$  m<sup>2</sup> and the pulmonary/systemic vascular resistance ratio was 0.43. Vasoreactivity testing with oxygen showed a reduction in the ratio to 0.24.

She underwent partial temporary occlusion of the defect with a 34-mm diameter test balloon. Mean pulmonary artery pressure decreased to 56 mm Hg, mean right atrial pressure was maintained, and the cardiac index did not significantly change. She underwent surgical repair of the ASD without significant perioperative problems. An intraoperative open lung biopsy showed “irreversible” hypertensive pulmonary arteriopathy (Fig 1).

At 6 months after repair, she presented in NYHA class I, and echocardiography showed mild TR with peak velocity 3.8 m/s. At 1 year and 8 months after repair, the dose of sildenafil was tapered to 50 mg daily, and at 3 years after repair, all medications were discontinued, including sildenafil. At the last follow-up, 4 years after corrective repair, she had no symptoms, and the result of a 6-minute walk distance test was 550 m.

### Comment

Several cases compatible with the treat and repair approach for patients with ASD and severe pulmonary hypertension have been reported [2–4]. Frost and colleagues [2] described a 29-year-old woman with near-systemic pulmonary hypertension who underwent defect closure after a drop in pulmonary pressure with continuous intravenous prostacyclin. Schwerzmann and colleagues [3] described a 38-year-old woman (PVR of 8.8 WU, reduced to 4.2 WU with adenosine), who showed significant symptomatic and hemodynamic improvement after 1 year of treatment with intravenous prostacyclin, after which the ASD closed percutaneously. Hoetznecker and colleagues [4] described a 71-year-old woman (PVR of 5.8 WU, reduced to 3.0 WU with nitric oxide) who showed a decrease in pulmonary pressure after treatment with bosentan, after which the defect was surgically repaired. However, none of these 3 patients had cyanosis at baseline, and their pulmonary/systemic vascular resistance ratio was not reported. Thus, we cannot be confident that their baseline hemodynamic status was too dangerous to prevent corrective repair. Actually, the hemodynamic cutoff values for ASD repair are peculiar to individual institutions, leading to uncertainties about the operability criteria of ASD.

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Table 1. Hemodynamic Data

Variable	Initial Study		2 Years of Sildenafil Therapy		
	Baseline	O <sub>2</sub> (10 L/min)	Baseline	O <sub>2</sub> (10 L/min)	Balloon Occlusion Test
mRAP, mm Hg	1	2	10	8	8
mLAP, mm Hg	1	2	10	8	
mPAP, mm Hg	87/20, 55	85/20, 55	128/32, 75	110/34, 65	99/26, 56
mSAP, mm Hg	140/80, 100	140/83, 105	137/71, 98	131/75, 95	133/68, 95
Svco <sub>2</sub> , %	69	74	76	68	79
PaO <sub>2</sub> , %	75	80	86	89	
SaO <sub>2</sub> , %	89	92	94	99	99
Qp (L/min/m <sup>2</sup> )	2.16	2.24	5.15	4.7	
Qs (L/min/m <sup>2</sup> )	2.49	2.72	2.98	1.75	2.83
Qp/Qs ratio	0.87	0.82	1.73	2.68	
PVRI (WU · m <sup>2</sup> )	25.0	23.7	12.63	12.1	
SVRI (WU · m <sup>2</sup> )	39.8	37.8	29.53	49.7	30.73
PVRI/SVRI	0.63	0.63	0.43	0.24	

mLAP = mean left atrial pressure; mPAP = mean pulmonary arterial pressure; mRAP = mean right atrial pressure; mSAP = mean systemic arterial pressure; PVRI = body surface area indexed pulmonary vascular resistance; PaO<sub>2</sub> = partial pressure of arterial oxygen; Qp = body surface area indexed pulmonary blood flow; Qs = body surface area indexed systemic blood flow (cardiac index); SaO<sub>2</sub> = arterial oxygen saturation; Svco<sub>2</sub> = oxygen saturation in the superior vena cava; SVRI = body surface area indexed systemic vascular resistance; WU = Wood unit.

The criteria used to determine the operability of patients with congenital heart disease and pulmonary arterial hypertension include the presence of cyanosis from right-to-left shunting, hemodynamic change after balloon test occlusion, and pulmonary vasoreactivity [1]. Cyanosis from right-to-left shunting, a drop in cardiac output, or an increase in right ventricular filling pressure with test balloon occlusion are all indicative of a low likelihood of benefit from permanent closure [1]. According to the Inhaled Nitric Oxide as a Preoperative Test (INOP I), a pulmonary/systemic vascular resistance ratio of less than 0.42 with oxygen alone or a ratio of less than

0.27 with oxygen plus nitric oxide have been identified as the optimal cutoff values for determining operability [5]. Steele and colleagues [6] suggest that surgical treatment can be advised in patients with ASD if the PVRI is less than 15 WU · m<sup>2</sup>. According to these criteria, the baseline hemodynamic findings in our patient were absolutely against corrective repair.

In conclusion, we experienced a definite case compatible with the treat and repair approach for patients with ASD and severe pulmonary hypertension. Our case suggests that sildenafil treatment in some selected patients with ASD and severe pulmonary hypertension can result in significant improvements in pulmonary hypertension, which may allow corrective repair of ASD.

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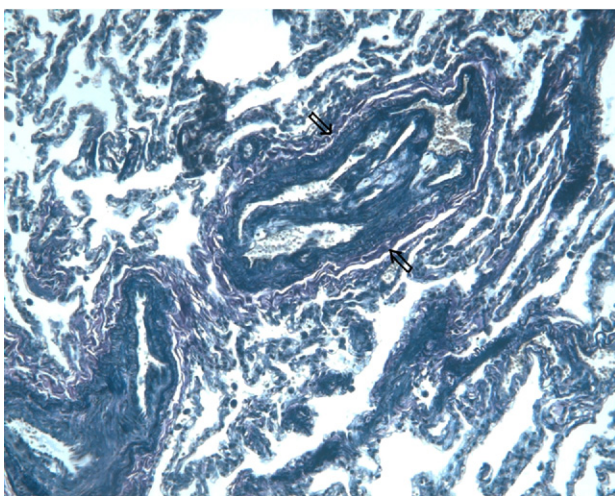


Fig 1. A photomicrograph of an open lung biopsy specimen during corrective repair shows one branch of a small muscular artery (arrows) with a plexiform lesion with intimal fibrosis and medial hypertrophy. It conforms to a grade 4/6 Heath Edwards or a grade 5/6 Wagenvoort pulmonary hypertensive change (Van Gieson stain, original magnification × 200).