Congenital Heart Disease With Associated Pulmonary Arterial Hypertension. Who and When to Operate: A Therapeutic Dilemma

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In countries with easy availability of surgical care for congenital heart disease, most patients undergo surgery at an appropriate age before development of pulmonary vascular disease. However, there is an increasing population of children and young adults with previously undiagnosed or unoperated congenital heart disease. The responsibility of deciding who is operable and whether treatment modalities can reverse vascular changes enough to convert a previously "borderline or inoperable" patient to being a surgical candidate often rests with the pulmonary hypertension specialist.[1-3] Indeed, studies have shown that operating on patients with high pulmonary vascular resistance (PVR) makes the prognosis significantly worse than the natural history of leaving them without surgery.

Cardiac catheterization still remains the gold standard for deciding on operability of these patients.[1,2] One must have a clear mental distinction between elevated pulmonary pressures (as in large left to right post-tricuspid shunts) and elevated PVR, which implies distal vascular changes. Children with large left to right shunts and heart failure symptoms with increased pulmonary blood flow will clearly benefit from early surgery. Patients with large defects and PVR equal to or more than systemic vascular resistance (SVR) will have reversed shunts (Eisenmenger syndrome) and are inoperable. Patients with elevated but subsystemic PVR and therefore smaller left to right shunts are the subjects of the therapeutic dilemma. Must one treat with pulmonary vasodilators first and then recheck hemodynamics and operate if suitable—or just leave them alone and manage as early Eisenmenger syndrome?[3] What is the long-term outcome of survivors of this strategy?

Clinical clues to increasing PVR can be sought by careful history taking. An infant with a large left to right shunt is usually undernourished, has feeding problems and irritability, may become diaphoretic with crying, and may have recurrent respiratory infections. Then, as the child grows, if pulmonary vascular disease develops, these symptoms of increased pulmonary blood flow gradually disappear and the child starts catching up on growth and appetite and becomes less tachypnoec. This is the honeymoon period, when the parents are lulled into a false sense of security that their child is cured of the heart disease, until the shunt reverses as PVR becomes more than the SVR and the child initially gets blue with exercise, and later is cyanosed all the time.

Different defects develop pulmonary vascular disease at different times.[1,3] Complex congenital heart defects like transposition of great arteries, truncus arteriosus, and endocardial cushion defects (especially with Down syndrome) almost always develop increased PVR in infancy.[3] Many children with large defects at the ventricular or great artery level develop vascular changes in the first 2 years of life, unlike atrial defects, where the majority of patients have near normal PVR well into adulthood. Again, there is a subgroup of patients with atrial shunts who present with elevated PVR at a very early age, and are thought to possibly be patients with idiopathic pulmonary arterial hypertension (IPAH) with an associated atrial shunt. The goal in managing patients with left to right shunts is to diagnose these lesions early and intervene before development of irreversible pulmonary vascular disease. Patients with significant shunts (Qp/Qs >2:1) at the ventricular (VSD) or great artery level (PDA or AP Window) should be operated in infancy to prevent vascular disease. Patients with atrial septal defects (ASD) are managed differently. Most patients with moderate secundum ASDs can be treated in the interventional cardiac catheterization laboratory, using devices to close the defect. Careful preprocedure evaluation involves sizing of the defect by prior echocardiography, as well as by balloon sizing using transesophageal echocardiographic guidance during cardiac catheterization, ensuring adequate rims to seat the device and avoiding interference with surrounding structures. A major part of this decision making can be done by transthoracic echocardiogram before taking the patient for the procedure. Patients with sinus venosus, coronary sinus, and primum ASDs are not amenable to transcatheter closure and need to undergo surgical repair. Patients with smaller ASDs with no evidence of right sided volume overload by echocardiogram are usually not at risk for developing PAH, endocarditis, or heart failure and do not need to be closed. The only indications for closure of a small atrial defect or patent foramen ovale would be in an adult with recurrent strokes without other etiologies, or people who train to be deep sea divers (to prevent reverse shunting and catastrophic events).

Evaluation in the cardiac catheterization laboratory should involve very careful assessment of baseline hemodynamics with at least 3 complete right and left heart saturation and pressure runs (Table 1). Hemodynamic calculations include pulmonary and systemic blood flow (Qp and Qs), pulmonary and systemic resistances (PVR and SVR) at baseline, and with acute vasodilator testing (AVT) using inhaled nitric oxide (iNO). [Acute va-

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Table 1: Formulae for calculation of shunts and resistances using hemodynamic data

Qp=VO2/ (PVO2-PAO2)
=VO2/(Pulmonary Vein—Pulmonary Artery Saturation)(Oxygen Capacity);
Qs=VO2/ (Aortic—Mixed Venous Saturation)(Oxygen Capacity);
Qep=VO2/ (Pulmonary Vein—Mixed Venous Saturation)(Oxygen Capacity);
L-R Shunt=Qp-Qep; R-L Shunt=Qs-Qep
Qp/Qs=Aortic—Mixed Venous Saturations/Pulmonary Vein—Pulmonary Artery Saturation.
While breathing 100% O2, one must include dissolved oxygen in the calculation of oxygen content, using the equation "dissolved Oxygen"=0.03*PO2.
PVR=mPAP-mPVP/Qp
SVR=MAoP-MRAP/Qs
Oxygen capacity=13.6*Hemoglobin(gm/dl).

Abbreviations: VO2 = oxygen consumption; Qp = pulmonary blood flow; Qs = systemic blood flow; Qep = effective pulmonary flow; PVO2 = pulmonary vein O2 content; PAO2 = pulmonary artery O2 content; mPAP = mean pulmonary artery pressure; mAoP = mean aortic pressure; mRAP = mean right atrial pressure; mPVP = mean pulmonary venous (or pulmonary artery wedge) pressure; saturation PVR = pulmonary vascular resistance; SVR = systemic vascular resistance.

soresponsiveness is defined as reduction of mean pulmonary artery pressure by at least 10 mm to a value <40 mm with an increased or unchanged cardiac index.][4-6] There are several issues that the clinician has to be aware of while performing and interpreting cardiac catheterization data. Snapshot hemodynamic studies are greatly influenced by sedation, general anesthesia, airway and lung parenchymal issues, stress (of intubation), catecholamines, and variations in acid-base balance, especially in young children under general anesthesia. Several studies have demonstrated benefits of treating Eisenmenger patients with advanced therapies. It is thought that their antiproliferative effects lead to reverse remodeling in the pulmonary circulation and may eventually cause reduction in PVR and improve right ventricular hypertrophy.[1] Perhaps treating borderline patients with pulmonary vasodilators for a finite period of time and reassessing their hemodynamics would reduce their PVR enough to make them candidates for shunt closure. Since short-term improvements in these patients may not translate into long-term survival benefit, partial closure of the defect in highly selective patients with improved hemodynamics on treatment and continuing pulmonary vasodilator therapy seems an attractive prospect and merits further investigation. Larger and longer-term studies using these strategies will be required before one can be sure of the right approach for these patients, but the availability of newer drugs holds a promise for the future.

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