Surgical reconstruction of peripheral pulmonary artery stenosis in Williams and Alagille syndromes

Michael C. Monge, MD,[a] Richard D. Mainwaring, MD,[a] Ahmad Y. Sheikh, MD,[a] Rajesh Punn, MD,[b] V. Mohan Reddy, MD,[a] and Frank L. Hanley, MD[a]

Objectives: Peripheral pulmonary artery stenosis is a rare congenital heart defect frequently found in association with Williams and Alagille syndromes. Controversy exists regarding the optimal treatment of peripheral pulmonary artery stenosis, with most centers favoring catheter-based interventions. In contrast, we have preferentially used surgical reconstruction of peripheral pulmonary artery stenosis. The purpose of the present study was to review our experience with surgical reconstruction of peripheral pulmonary artery stenosis.

Methods: We performed a retrospective review of patients who underwent surgical reconstruction of peripheral pulmonary artery stenosis. A total of 16 patients were identified: 7 had Williams syndrome, 6 had Alagille syndrome, and 3 had no identifiable syndrome. Detailed pulmonary angiography was performed in all patients to define stenoses at the main, branch, lobar, and segmental arterial levels. The mean preoperative right ventricular/left ventricular pressure ratio was 0.88 ± 0.07. The surgical approach was a median sternotomy with cardiopulmonary bypass. All peripheral stenoses were augmented with pulmonary artery homograft tissue. The median age at surgery was 14 months, and concomitant procedures were performed in 9 of the 16 patients.

Results: There was 1 operative mortality (6%). The mean right ventricular/left ventricular pressure ratio decreased to 0.40 ± 0.04 postoperatively ($P < .005$), representing a 55% reduction compared with the preoperative values. The patients were followed up for a median of 5 years. No late mortality occurred and reoperation was not required.

Conclusions: The data have demonstrate that this comprehensive surgical approach to the treatment of peripheral pulmonary artery stenosis was associated with low early and no late mortality. Surgical reconstruction of the peripheral pulmonary artery stenosis resulted in a significant decrease in right ventricular pressure. We hypothesize that this reduction in right ventricular pressures will confer a long-term survival advantage for this cohort of patients. (J Thorac Cardiovasc Surg 2013;145:476-81)

CHD

Peripheral pulmonary artery stenosis (PPAS) is a relatively rare form of congenital heart defect found in fewer than 1% of patients with congenital heart disease. Although rare, PPAS is frequently found in association with Williams and Alagille syndromes and is considered a phenotypic hallmark of these 2 genetically mediated syndromes.[1-3] The pulmonary artery stenoses associated with Williams and Alagille syndromes can affect both the central and peripheral pulmonary arteries. However, it is the distal obstruction that typically has the predominant physiologic effect. The result of this obstruction is varying degrees of right ventricular (RV) hypertension, which can be graded from mild to moderate to severe. The adverse physiologic consequences of RV hypertension have been well documented and include hypertrophy, systolic and diastolic dysfunction, and, eventually, can lead to ventricular failure in some cases.[4,5]

Considerable debate has occurred in published studies regarding the natural history of PPAS. Two sources of evidence have suggested that PPAS associated with Williams syndrome might undergo a process of spontaneous regression. Stamm and colleagues[6] noted an inverse correlation between patient age at presentation and the degree of RV hypertension. These data have been interpreted to indicate that RV hypertension decreases over time. In addition, several small series have demonstrated a decrease in RV pressures in patients evaluated by serial cardiac catheterization.[7-10] Most patients who did demonstrate spontaneous regression had mild to moderate PPAS, and spontaneous regression of severe PPAS has been unusual enough to warrant a case report.[11] Currently, no evidence has indicated that PPAS associated with the Alagille syndrome can undergo this same process of spontaneous regression.

It is not surprising that the optimal management algorithm for treating PPAS has yet to be established, with multiple reasons for this ambiguity. First, PPAS and the 2

From the Division of Pediatric Cardiac Surgery,[a] Lucile Packard Children's Hospital/Stanford University School of Medicine, Stanford, Calif; and Division of Pediatric Cardiology,[b] Lucile Packard Children's Hospital/Stanford University School of Medicine, Stanford, Calif.

Disclosures: Authors have nothing to disclose with regard to commercial support.

Read at the 38th Annual Meeting of The Western Thoracic Surgical Association, Maui, Hawaii, June 27-30, 2012.

Received for publication June 17, 2012; revisions received Aug 16, 2012; accepted for publication Sept 20, 2012; available ahead of print Dec 10, 2012.

Address for reprints: Richard D. Mainwaring, MD, Division of Pediatric Cardiac Surgery, Lucile Packard Children's Hospital/Stanford University School of Medicine, 300 Pasteur Dr, Falk CVRC, Stanford, CA 94305 (E-mail: mainwaring@stanford.edu).

0022-5223/$36.00

http://dx.doi.org/10.1016/j.jtcvs.2012.09.102

Abbreviations and Acronyms

PA/VSD/MAPCAs	= pulmonary atresia/ventricular septal defect/major aortopulmonary collateral arteries
PPAS	= peripheral pulmonary artery stenosis
LV	= left ventricular
RV	= right ventricular

genetic syndromes most closely associated with this condition are relatively rare. Second, the possibility that some patients with PPAS will demonstrate spontaneous regression has ameliorated the perceived mandate for intervention. Finally, surgical reconstruction of the lobar and segmental pulmonary arteries has not been a standard part of the armamentarium for most congenital heart centers, rendering PPAS to a nonoperative treatment option in most circumstances.

Most patients with Williams syndrome have supravalvar aortic stenosis, a subject that has garnered an enormous amount of attention during the past several decades. Dozens of reports have focused on the surgical management of supravalvar aortic stenosis, debating the merits of single, dual, or 3-sinus repair.[12-14] In contrast, very limited information exists on the treatment of patients with both systemic and pulmonary outflow tract obstruction,[6,15] with most centers advocating a "multimodality approach." This strategy includes catheter-based interventions to address the PPAS[16,17] and reserving surgery to repair the supravalvar aortic stenosis and central pulmonary arterial stenoses.

Our center has acquired extensive experience in the treatment of pulmonary atresia with a ventricular septal defect and major aortopulmonary collateral arteries (PA/VSD/MAPCAs). This work frequently requires reconstruction of PPASs at the segmental and lobar levels. Because of this significant surgical experience with peripheral vessel reconstruction in PA/VSD/MAPCAs, we have applied these same techniques to the reconstruction of PPASs associated with Williams and Alagille syndromes. The present report summarizes the surgical approach and the results of our surgery-based approach to PPAS.

MATERIALS AND METHODS

The institutional review board at Stanford University approved the study protocol. Patients undergoing surgical reconstruction of the PPAS were identified from the cardiac database. A written questionnaire and Health Insurance Portability and Accountability Act authorization form were sent to the families. A returned questionnaire signified consent by the parents for a review of the medical records. A review of the medical records, along with the questionnaire, provided the basis for ascertaining the current health status of the children.

The present study summarizes our surgical experience from 2002 to 2012 with 16 consecutive patients who had PPAS with severe RV hypertension. We defined "severe" RV pressures as RV pressures that exceeded two thirds of the systemic pressure. Of the 16 patients, 7 had Williams syndrome, 6 had Alagille syndrome, and 3 had no identifiable syndrome; 9 were female and 7 were male. The median age at surgery was 14 months (range, 2 months to 13 years), and the median weight at surgery was 8.7 kg (range, 3.3 to 28.5 kg). Six patients underwent preoperative balloon dilation of the PPAS, with an average decrease in RV pressure of 10 mm Hg.

All 16 patients underwent cardiac catheterization for evaluation of the hemodynamics and to provide a "roadmap" for reconstruction of the pulmonary arterial system. The mean RV/left ventricular (LV) pressure ratio was 0.88 ± 0.07 (range, 0.72-1.00). For the patients with Williams syndrome who had supravalvar aortic stenosis, the descending thoracic aortic pressure measurement was substituted for the LV pressure. The pulmonary angiogram (Figure 1, *A*) demonstrated diminutive, but confluent, central branch pulmonary arteries. The ostial stenoses of the right upper lobe segments can be faintly seen. Separate right (Figure 1, *B*) and left (Figure 1, *C*) pulmonary angiograms highlighted the multiple lobar and segmental branch stenoses affecting the right upper, middle, and lower lobes and left upper lobe. This preoperative anatomy has been recapitulated in an artist's illustration (Figure 2, *A*).

Surgical reconstruction was performed by way of a median sternotomy and used cardiopulmonary bypass support. All stenoses identified by angiography were augmented using pulmonary artery homograft tissue. The surgical technique we use includes external dissection of the affected arterial branch to obtain distal vascular control. This dissection can lead to the edge of the lung parenchyma, which can be safely brushed back to achieve distal access for reconstruction of the lobar and segmental branches. The entirety of this dissection is performed with electrocautery and before heparinization, because dissection near the lung tissue after heparinization can result in significant intraparenchymal hemorrhage. After cardiopulmonary bypass has been established, both sides of the heart are decompressed (a LV vent is inserted through the right superior pulmonary vein), which greatly facilitates surgical exposure. The affected arteries are incised longitudinally through the area of stenosis and onto the normal distal vessel for at least 1 cm beyond the endothelial abnormality (Figure 2, *B*). The median number of reconstructed peripheral arterial stenoses was 7 (range, 5-10). The main pulmonary artery and central branch pulmonary arteries were enlarged to achieve a normal size for the patients' body surface area (Figure 2, *C*).

Of the 16 patients, 9 had associated cardiac anomalies (Table 1). Of the 7 patients with Williams syndrome, 6 had supravalvar aortic stenosis. The median LV outflow tract gradient was 65 mm Hg (range, 45-100 mm Hg). Aortic cross-clamping was performed only to address these associated cardiac lesions.

Statistical analysis was performed using a paired *t* test.

RESULTS

The 16 patients in the present series underwent 17 surgical reconstructions of the PPAS, with 1 operative mortality. The sole death occurred in 1 patient with Williams syndrome. That patient had concomitant repair of supra-aortic valvar stenosis and PPAS and postoperatively demonstrated profound LV dysfunction, progressed to multisystem organ failure, and subsequently died. The median cardiopulmonary bypass time for the entire group was 209 minutes (range, 78-312 minutes), and the median cross- clamp time for the 9 patients with associated cardiac malformations was 35 minutes (range, 7-51 minutes). The median duration hospital stay for the 15 survivors was 14 days (range, 8-40 days).

The RV/LV pressure ratios decreased from 0.88 ± 0.07 preoperatively to 0.40 ± 0.04 (range, 0.24-0.54) in the immediate postoperative period, representing a 55% reduction