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EDITORIAL COMMENTARY

Primary pulmonary vein stenosis: Can we expect different results?

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See related article on pages 181-8.

Much has been written on the topic of acquired pulmonary vein stenosis (PVS) after repair of total anomalous pulmonary venous return (which still is an enigma); even less is known about primary PVS. In this issue of the *Journal*, Shi and colleagues¹ from Shanghai, China, present their experience from the surgical treatment of 18 patients with primary PVS (in fact, 26 patients had been referred to their institution, but 7 in 8 did not undergo operation because of family refusal or mild severity of disease, and their long-term outcomes are unknown), making this one of the larger reports to date.

What we do know is that primary PVS is rare, often presenting in the setting of other defects with significant left to right shunting. There have been rare reports of its presentation in adults in isolation.² In general, our knowledge of

pulmonary vein biology lags that of the arterial side. This is changing rapidly, however, in part due to continuing rapid advances in molecular biology. Recently, a French group identified the EI-F2AK4 (also known as GCN2) gene as the culprit for a form of veno-occlusive disease.³ The same gene was subsequently found to be responsible for another closely related pathology, pulmonary capillary hemangiomatosis.⁴ In both, a form of uncontrolled endothelial and smooth muscle proliferative response leads to specific pathology on the venous side of the pulmonary circulation, not too dissimilar as seen in PVS.

Shi and colleagues report their outcomes after 3 different surgical procedures: patch venoplasty, endarterectomy, and the technique of marsupialization, or “sutureless” repair. Although the results are inconclusive, Shi and colleagues suggest that perhaps the marsupialization procedure is the most effective surgical solution. The median age of their patients was 20 months (survival of the fittest?), and their mean follow-up time was only 33 months. Finally, one of their figures (Figure 3, A) shows the sobering statistic that nearly all the patients in their series had development of restenosis. We all know how that story will end.

There is much we still don’t know about this disease. For instance, as seen in this series, both prevalence and severity

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of this disease appear to be greater on the left side. Even in catheter-based intervention reports, the left-sided veins are seen to be affected more frequently.⁵ It has been hypothesized that the enlarged left atrium and left ventricle lead to rotation of the heart on its base, in turn leading to compression of the left (particularly left lower) pulmonary veins. Perhaps with some degree of obstruction on the left side, further excess flow is redirected to the right side, leading to injury to right-sided pulmonary veins. This hypothesis, however, may be contradicted by the fact that many infants have PVS present quite early, even in the first months of life, and some are seen with the disease first manifesting on the right side. Also, the disease has a more aggressive course in babies with prematurity or a history of lung disease. A third of the infants in the current series of Shi and colleagues were born prematurely. How either prematurity or lung disease plays a role remains unclear.

Finally, echocardiography is the primary tool used to follow up these children. In Shi and colleagues' report, computed tomographic angiography was used selectively to assess for evidence of recurrence. We now know that echocardiography can underestimate the degree of stenosis. Doppler flow patterns are dependent on the type of stenosis and the degree of flow in the pulmonary venous bed. In the presence of critical stenosis with severe reduction in flow, it thus may be difficult to make a diagnosis, because lack of flow may be more difficult to appreciate than a jet of turbulent flow. In a recent follow-up study, the authors from Toronto have shown that magnetic resonance imaging identified inevitable restenosis even after marsupialization. Echocardiography often missed or underestimated the magnitude of the problem.⁶

The last notable finding from the report of Shi and colleagues, affirming previous reports, is that the milder the disease at presentation, the better the outcome. This has also been reported with catheter-based interventions, for which an effective stent diameter of 7 mm is seen as the cutoff to give the best long-term outcomes. One could ask, however, whether these milder stenoses need to be addressed at all as long as the underlying shunt lesions are addressed.

These observations naturally lead to questions. Given the poor outcomes and the inevitable restenosis, is PVS actually a surgical disease? Should we be expecting a different outcome while trying the same solution time after time? Thus far, however, no medical therapy has been shown to

be effective. An alternative strategy is lung transplantation. Not infrequently, however, patients are referred for consideration of a lung transplant after attempts at marsupialization and even after reoperative marsupialization, increasing the morbidity of a "reoperative" transplant and the odds of having preformed reactive antibodies, which affect long-term transplant outcomes.

Although the outcomes of lung transplants leave much to be desired, they can readily stand up to current surgical results for PVS. According to the International Society for Heart and Lung Transplantation, the 50% conditional survival for infants after a lung transplant is nearly 12 years. This means that if an infant undergoes a transplant and survives the first year, he or she has a 50% chance of survival to 12 years with the same graft.

In short, there is much that we still don't know, but perhaps we are asking the wrong question. Should we really wonder whether one surgical technique is better than another, or should we be asking why this disease occurs in the first place? Perhaps it is time to create a registry for patients with PVS (either acquired or primary) and bring everyone (surgeons, cardiologists, and basic science colleagues) to the table to answer what we don't know. The Congenital Heart Surgeons Society has created a biorepository under the direction of Dr Peter Gruber exactly for this purpose.⁷ Perhaps we can do something different and expect a different outcome.

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