Dependence on an expanded polytetrafluoroethylene graft for provision of pulmonary blood flow is a common yet precarious interval through which a population of patients with congenital heart disease must pass. The goals of the systemic-to-pulmonary artery shunt are to relieve cyanosis and to provide time before establishing in-series circulation by either complete repair of 2-ventricle lesions or, in the case of the single-ventricle patient, a bidirectional Glenn shunt. In the case of patients with single-ventricle anatomy, this period of parallel circulation is necessary to permit the lung maturation and the reduction in pulmonary vascular resistance that are necessary for subsequent palliation. For patients who will ultimately achieve a 2-ventricle repair, the goals of a preliminary shunt may include increasing the size of the pulmonary artery size or having a larger, older patient at the time of repair. This period of parallel circulation is tenuous, and the patient remains at increased risk during this period of altered circulation.

With parallel circulation, cardiac output from the heart is partitioned to the lungs and body based on the relative resistances of the pulmonary and systemic circulations. If the shunt is large, the patient will experience excessive pulmonary blood flow and congestive heart failure. Furthermore, with a large shunt, diastolic pressure is low and coronary circulation may be impaired. With stress, autonomic reflexes will result in an acute increase in sympathetic tone. The elevation of systemic vascular resistance leads to acute increase in the ratio of pulmonary to systemic flow. In the face of limited cardiac output, this acute increase in the ratio of pulmonary to systemic flow can result in a critical reduction in systemic oxygen delivery. Therefore, autonomic reflexes aimed at maintaining vital organ perfusion with in-series circulation have an adverse effect in patients with parallel circulation and can result in a critical reduction in oxygen delivery. This is likely to be one mechanism of death for patients with parallel circulation. Alternatively, if the shunt is sufficiently limiting, then increasing pulmonary blood flow in response to increased metabolic demands such as may occur with fever or exercise will not be possible, increased cyanosis results, and again a critical reduction in oxygen delivery will occur. Additional limitations of parallel circulation include the potential for parenchymal lung disease, anemia, and decreased cardiac output to result in worsening cyanosis. Decreased cardiac output from the single ventricle may be the result of myocardial dysfunction, atrioventricular valve regurgitation, or arrhythmias. In addition, dehydration will result in decreased preload with decreased cardiac output and may occur in the course of an acute illness resulting from decreased fluid intake, gastrointestinal loss, and/or fever. Diuretic use is common in this patient population and will limit the ability of the patient to autoregulate fluid status in the face of an acute illness. Small expanded polytetrafluoroethylene grafts generally are used for these systemic-to-pulmonary artery shunts despite their thrombogenicity. The lumen of the grafts develops a neointima. Both the coagulation system and the inflammatory processes contribute to the development of this neointima, which is a proliferation of myofibroblasts with endothelial cell in-growth. The neointima is associated with organizing thrombus and tends to be most severe at the anastomotic sites. Furthermore, these patients are uniformly cyanotic, and other growth factors such as vascular endothelial growth factor have increased expression in this patient group, potentially intensifying neointimal growth. As a result of this luminal in-growth, the caliber of the shunt is reduced over time even as the patient continues to grow. The patient with shunt-dependent pulmonary blood flow survives in an environment marked by both physiological and anatomic vulnerabilities.

To identify patients with parallel circulation at risk of life-threatening complications, we developed a home monitoring program. In addition to routine use of aspirin, parents were discharged with a pulse oximeter and a suitably sensitive infant scale. They were directed to obtain twice-daily arterial saturations and daily weights. Parents were instructed to call in case of an arterial saturation <75% or an acute weight loss of ≥30 g. An increase in cyanosis can be the result of a reduction in shunt caliber, a decrease in single-ventricle cardiac output, pulmonary disease, or anemia. Acute weight loss is a sensitive indicator of dehydration, which can result in decreased total cardiac output, increased blood viscosity, and an increased risk of shunt occlusion. In our single-center experience, home monitoring proved successful in limiting the mortality of patients with shunt-dependent pulmonary blood flow.
In this issue of *Circulation*, Li and colleagues report the results of a prospective observational study looking at the impact of aspirin on the outcome of patients with various diagnoses undergoing systemic-to-pulmonary artery shunts. Aspirin is an accepted treatment for a number of vascular diseases, including coronary artery, cerebrovascular, and peripheral arterial disease. Aspirin is a nonselective cyclooxygenase (COX) inhibitor, blocking both COX-1 and COX-2 pathways. COX-1 inhibition results in decreased platelet adhesion and aggregation, whereas COX-2 inhibition decreases inflammation. Both of these actions would be expected to limit neointimal formation and to have a favorable impact on shunt patency and durability. Aspirin use was associated with a >7-fold reduction in the risk of shunt thrombosis and a decreased risk of death among patients undergoing a systemic-to-pulmonary shunt, including the Norwood procedure.

This large, prospective observational study by Li et al involving >1000 patients is the largest study to examine the impact of aspirin on systemic-to-pulmonary artery shunts. There are, however, a few shortcomings. The study was not randomized. Aspirin use may have been associated with other factors that minimized shunt occlusion and death. Nonuse of aspirin may have been collinear with other factors such as low surgical volume and small shunt size that may have affected outcome. Aspirin use is associated with bleeding complications, and no data concerning aspirin-related complications were collected. Although overall aspirin use was associated with improved survival, it would be helpful to know if a subgroup of patients sustained aspirin-related complications. All 954 patients undergoing a modified Blalock-Taussig-Thomas shunt had either a 3.0- or a 3.5-mm shunt. These shunt sizes would be typical for a Norwood procedure, but it seems surprising that not a single patient with tetralogy of Fallot, pulmonary atresia, or tricuspid atresia received a ≥4.0-mm shunt. Could the use of small shunts have increased the complication rate? Furthermore, the end points are somewhat arbitrary. Recent data from our institution obtained from the home monitoring program suggest a flattening of the growth curve for patients with hypoplastic left heart syndrome at ~4 months of age. We have therefore targeted 4 months of age as the optimal timing of a bidirectional Glenn shunt. Li and colleagues have defined an early bidirectional Glenn as occurring before 4 months of age. Our current population of patients undergoing an elective bidirectional Glenn shunt would straddle this 4-month age cutoff. Furthermore, an early bidirectional Glenn shunt may be undertaken for poor growth with congestive heart failure, physiological evidence of a large rather than a small shunt. Finally, the authors chose to include patients undergoing the right ventricular to pulmonary artery conduit modification of the Norwood procedure; these larger expanded polytetrafluoroethylene grafts seem less likely to develop critical caliber reduction during the interstage period. Nonetheless, the inclusion of these 2 groups, the early bidirectional Glenn patients with heart failure and the right ventricle to pulmonary artery conduit modification patients, would only bias the outcome to a less dramatic effect of aspirin.

These criticisms are minor. The primary conclusion of the study by Li and colleagues, that aspirin use is associated with improved survival of shunt-dependent patients, is clear and well supported by the data. Aspirin is inexpensive, readily available, easily administered, and reasonably well tolerated. The findings of the study strongly suggest that aspirin should be part of the management strategy for all patients with a systemic-to–pulmonary artery shunt. The impressive impact of aspirin mandates clinical trials of other antiplatelet and anticoagulant strategies and improved thromboresistant graft materials. Efforts to improve shunt durability and increased monitoring of high-risk patients have the potential to limit morbidity and mortality of patients with complex congenital heart disease during their highly vulnerable period of shunt-dependent pulmonary blood flow and parallel circulation.

Disclosures

None.

References


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