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EDITORIAL COMMENT

The Fontan Operation

Improved Outcomes, Uncertain Future*

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Since its introduction in 1971, the Fontan operation has become a mainstay of the palliative strategy for infants born with the heterogeneous collection of congenital heart defects characterized by a functional single ventricle (1,2). Over the years, since the initial publications describing this procedure, a number of technical modifications to the surgical strategy have resulted in improved outcomes, allowing generations of children to survive into their adult years (3-5). In the current era, perioperative mortality is low, but there remain questions regarding the long-term viability of this man-made circulation (6).

SEE PAGE 1700

In this issue of the *Journal*, Pundi et al. (7) report the outcomes of the Fontan operation at the Mayo Clinic over a 40-year period, covering almost the entirety of the history of this operation. This important work demonstrates the success of the Fontan operation as part of the palliative strategy but also points to some of the challenges associated with the physiology created by the operation.

Perhaps most striking, but not surprising, is the improvement in short- and long-term outcomes in more recent eras. In this paper, the authors describe a late survival of 95% at 10 years for the cohort that underwent a Fontan operation after 2001. Survival in the initial era (1973 to 1990) was 69%, and survival in the middle era (1991 to 2000) was 89%. Although it is certainly too soon to predict the 20- and 30-year survival rates for the most recent cohort, the 10-year data provide a reason for optimism and suggest that the myriad of small advances in surgical approach and post-operative management over the last 40 years have, in sum, led to important overall improvements in outcomes.

Over time, congenital heart surgeons have moved away from the atriopulmonary connection, instead generally favoring an intra-atrial lateral tunnel or an extracardiac conduit. In the current paper, the extracardiac conduit appeared to have the lowest mortality, although it may be that the lateral tunnel suffered in this comparison due to its use in an earlier era. This paper also documented the increased mortality associated with performing the Fontan operation in "high-risk" patients. Patients who went into the Fontan operation with an elevated pulmonary arterial pressure fared less well than their counterparts with lower pulmonary arterial pressures. Similarly, the need for atrioventricular valve surgery at the time of Fontan procedure conferred increased risk, as did the absence of normal sinus rhythm.

Although the results following Fontan operations have improved substantially, we should remember that a significant number of patients remain for whom the surgery is not the final intervention. The investigators report that 20% of Fontan survivors required a pacemaker, 11% Fontan revision, and 5% an intervention on the atrioventricular valve. Although these numbers are likely inflated by those who received a Fontan early in the Mayo experience, they are useful as a reminder that the Fontan operation often is not the final intervention for many single-ventricle patients.

In addition to surgical reinterventions, there are a significant number of medical complications associated with long-term Fontan physiology. The Fontan operation creates a circulation characterized

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by elevated central venous pressure and diminished cardiac output. These alterations, although generally well tolerated early in childhood, seem to be less well tolerated over time, affecting organ systems outside the heart. In recent years, numerous publications have documented the near universal change to the architecture of the liver that occurs as a result of prolonged exposure to the Fontan circulation (8,9). As investigators have focused on other organ systems, abnormalities have also been identified in bone and muscle structure (10,11), endothelial reactivity (12), and the characteristics of the immune system (13). In the current paper, the authors report a 9% incidence of protein-losing enteropathy, 41% incidence of late arrhythmias, and, although data were available only for a small subset, 21% incidence of liver cirrhosis in those with available imaging or biopsy results. These findings are in line with other reports and reinforce the notion that the Fontan operation does not create a normal physiology. Instead, Fontan physiology can best be thought of as a man-made form of chronic heart failure.

Within the spectrum of abnormalities related to Fontan physiology, plastic bronchitis and protein-losing enteropathy stand out as uniquely problematic. Although the incidence reported in this paper and others suggest that these affect a small minority of patients, the lives of those who experience these complications are substantially altered. The etiology of plastic bronchitis and protein-losing enteropathy are not entirely understood, but both are likely multifactorial, resulting from abnormal lymphatic dilation in the setting of inflammation and perhaps a genetic predisposition (14). Lymphatic interventions hold some promise for the future, particularly for plastic bronchitis, but this approach is not likely to be the final answer because the underlying physiology is generally not altered (15). More work is needed to understand who is most at risk and to continue to work toward therapies successful at achieving long-term remission.

Given the improvements in early and mid-term outcomes described in this paper, focus has rightly turned toward finding new ways to address the morbidities associated with the Fontan circulation. Novel therapies and approaches are needed to improve the durability of the circulation to continue improving on the basic physiological perturbations created by the absence of a subpulmonary ventricle and the reliance on passive pulmonary blood flow. Agents that target pulmonary vascular resistance hold some intuitive promise. By decreasing pulmonary vascular resistance, these agents can potentially improve pre-load and therefore cardiac output, while also lowering central venous pressure. Although a number of short-term studies have shown some potential promise, there has yet to be a conclusive longer study demonstrating safety and efficacy for any single agent, and more work is needed to truly understand whether this class of medications might have a broad role in the long-term care of patients after Fontan operation (16,17).

Ultimately, the Fontan operation was a paradigm-shifting advancement in the care of children born with single-ventricle congenital heart disease. Over the years, technical adjustments and improvements in anesthesia and post-operative care have led to substantial improvements in short- and long-term survival as described in the current paper. However, as a community, our work is not done. We need to maintain our focus on ways to improve the efficiency of this circulation to ensure that outcomes continue to improve for future generations.

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