The Fontan operation was designed to provide blood flow in series to the pulmonary and systemic circulation without the requirement for a right ventricular pumping chamber. The operation allows systemic venous blood to flow directly into the pulmonary circulation on the basis of a single ventricular impetus through the arteries, capillaries, and systemic venous system. This arrangement has improved life expectancy for patients with single-ventricle and pulmonary-outflow obstruction compared with previous arterial shunts. The long-term effects of marked single-ventricle preload and inefficient oxygenation via an arterial shunt rarely allowed survival beyond the second or third decade of life. Remarkably, the Fontan operation has become the most common procedure performed for congenital heart disease after the age of 2 years. Over the past 3 decades, the early and intermediate prognoses for patients who have undergone this operation have been improving as a result of useful refinements in the surgical procedure that have been introduced since Fontan’s original direct right atrium–to–pulmonary artery (RA-PA) connection. Furthermore, the indications for the operation have broadened considerably compared with the relatively few patients thought to be eligible in the late 1970s and 1980s.

The ultimate test of any surgical procedure is the long-term status of the postoperative patients. The article by Khairy and associates1 in this issue of Circulation provides insight into the survival of the earliest generation of Fontan patients and allows assessment of the impact of management and surgical variations that have evolved over the past 3 decades on mortality. However, the young adults reported in this study represent the survivors of the early operations and may not reflect the eventual status of today’s infants and children who undergo the modern procedure.

Beyond mortality, it is important to evaluate potential risk factors as they relate to the functional status and quality of life of patients with a Fontan circulation. A recent survey of young children and adolescents who have undergone the Fontan operation attempts to address this issue.2,3 If the factors that lead to a failed Fontan in terms of mortality, current medical status, and quality of life can be understood, it is hoped that the next decade will allow further improvements in the management of patients with a single ventricle.

Mortality

Perioperative and early mortality after the Fontan operation have decreased markedly over the past 3 decades. Among early survivors, late mortality and modes of death can be assessed with the notion that predictors of intermediate or late mortality can be uncovered. In the report by Khairy et al,1 82.6% of the early survivors were alive and had not had a cardiac transplant 15 to 20 years later. It is of interest that this study found no significant difference in life expectancy beyond the postoperative period between the more obsolete, less efficient RA-PA connections and the direct caval–pulmonary artery connections. Among long-term survivors, the data from this series indicated that the 3 most common causes of late death were thromboembolism, heart failure, and sudden death.

Thromboembolic late death was found to be more common than previously documented.4 The predictors of thromboembolic death by multivariate analysis were lack of aspirin/warfarin therapy and intracardiac thrombus. Five of the 6 deaths were in patients who had direct RA-PA connections, which perhaps indicates the modern total cavopulmonary connections are less likely to be associated with thromboembolism; however, less follow-up time is available for the latter group of patients.

The higher risk for heart failure related to the presence of a single morphological right as opposed to left ventricle is consistent with other studies that indicate the same trend.2,3,5,6 This result is to be expected given that the right ventricle is not geometrically suited to be a systemic ventricle. The differences at intermediate follow-up, although significant, are not great between the 2 types of morphological single ventricle, but over the next 15 or 20 years, they are likely to become more prominent.

High right atrial pressures and protein-losing enteropathy are well-established risk factors for heart failure. Sudden deaths were more common earlier after Fontan surgery. Almost all occurred within the first 5 years, were presumed to be related to cardiac arrhythmias, and were not associated with any potential risk factor.

Khairy et al1 have provided excellent data on mortality in the early Fontan patients after 15 to 20 years. The question remains as to the fate of the more modern single-ventricle patients who have undergone the Fontan operation. The majority of present-day patients have hypoplastic left heart syndrome, which indicates that they will be at higher risk.
because of their single right ventricle morphology and physiology.

**Functional Status of Survivors**
Khairy and colleagues\(^4\) assessed early and late mortality after the Fontan operation in patients born before 1985. They did not analyze the functional status of the survivors of these relatively early operations. Recently, over a shorter time span, the Pediatric Heart Network of the National Heart, Lung, and Blood Institute addressed this from a cross-sectional study of Fontan patients from 7 medical centers.\(^2,3\) One aspect of the study was to attempt to delineate the predictors of functional status of Fontan patients.\(^3\) Medical status and physical and psychosocial function were evaluated. A Fontan functional score was developed with the use of (1) ventricular ejection fraction, by echocardiography; (2) percent predicted maximal oxygen consumption; (3) child health questionnaire; and (4) brain natriuretic peptide levels.

A total of 476 patients were evaluated, and multivariate predictors of a poor functional score were determined. These included time since Fontan, right ventricular morphology, pre-Fontan end-diastolic pressure, pre-Fontan oxygen saturation, and parental income. Variables not independently associated with a lower functional score included surgical center, age, weight, fenestration, length of hospital stay at time of Fontan procedures, and post-Fontan surgeries or interventions. A remarkable result of this analysis was that the obvious variables that were analyzed explained only 18% of the Fontan functional score; 82% of the data represented factors still unknown. McCrindle and associates\(^7\) studied the relationship of patient and medical characteristics to health status in children and adolescents after the Fontan procedure in 537 patients (mean age 11.9 years). Both physical functioning and psychosocial functioning scores were lower than those of the US population sample. Visual, speech, hearing, attention, and learning deficits were common. Medical history had some influence on physical and psychosocial function, but noncardiac conditions and socioeconomic status were more important determinants. It is likely that a strategy to address the prevention, detection, and management of noncardiac and psychosocial conditions will be extremely important in addressing quality of life in young Fontan patients.

**Specific Issues and Controversies**

**Lateral Versus External Conduit Repair**
Total cavopulmonary connections have the advantage of saving energy compared with the original RA-PA connections, eliminating less effective blood flow via a large, turbulent atrium that sends blood directly to the pulmonary artery. The external conduit approach has been advocated because the resultant sutureless atrium may decrease the incidence of atrial arrhythmias. Advocates of the intra-atrial lateral tunnel approach are concerned about the possible increased likelihood of thrombosis or stenosis in an external conduit. Insufficient long-term data are available to differentiate the outcome between these 2 approaches.

**Stage 2 Intervention**
At the present time, the vast majority of patients who have undergone a Fontan operation have had a 3-stage procedure: an early Norwood or shunt operation, followed by a “stage 2” bidirectional Glenn (or hemi-Fontan) procedure, and finally, the Fontan operation, which totally separates the systemic and pulmonary venous return and provides pulmonary blood flow without a ventricular pumping chamber. The rationale for the intermediate bidirectional Glenn operation is to protect the single ventricle from a large volume load for the first few years of life. For infants with hypoplastic left heart syndrome, the procedure is mandatory, because the initial Norwood shunt will not provide adequate oxygenation before the age when a full Fontan operation can be performed. However, many patients who are being followed up did not have a stage 2 operation, and at this time, no evidence indicates that this has been detrimental in terms of mortality. It has been reported that late exercise performance may be enhanced when a volume-unloading operation has been performed before the Fontan procedure.\(^2\) Nevertheless, there may be patients in whom oxygenation is acceptable and the Fontan operation may be performed directly, which would eliminate the intermediate surgical procedure.

**Fenestration**
Provision of a surgical fenestration between the total cavopulmonary connection and the right atrium is a part of Fontan operation management at most centers. In the immediate postoperative period after the Fontan operation, a fenestration allows adequate cardiac output, albeit with lower than normal oxygen saturation. A number of reports have indicated a more uneventful postoperative course, with smaller pleural effusions and earlier discharge from the intensive care unit and the hospital. For many centers, all Fontan operations include a fenestration regardless of the preoperative risk assessment; however, more recently, external conduits have not always been fenestrated, given the more technical challenge of keeping the anastomosis open at an optimal size. If one accepts the advantages of fenestration for many patients in the early postoperative period, the question must be asked as to whether a persistent fenestration becomes a risk factor in the presence of late right-sided thrombus formation and possible paradoxical embolization. Most centers will close residual significant-sized fenestrations, as determined by arterial oxygen saturation, by percutaneous device placement. It is likely that low-risk Fontan patients can be managed surgically without fenestration initially, thereby eliminating the need to close the fenestration if it persists over many years.

**Protein Losing Enteropathy**
The development of protein-losing enteropathy is associated with a poor clinical course in patients after a Fontan operation. Despite all measures, mortality is 50% within the first 5 years after the diagnosis is made.\(^8\) Multiple treatment modalities exist for protein-losing enteropathy, and this reflects the absence of definitive management principles based on its cause. Protein-losing enteropathy remains one of the greatest
challenges in the management of post-Fontan single-ventricle patients.

Anticoagulation Therapy
The present findings by Khairy and associates\(^1\) address the controversial aspects of whether anticoagulation/antiplatelet therapy should be administered routinely to all Fontan patients. The significant incidence of thromboembolic death in this series suggests that morbidity from thromboembolism is higher than previously reported. It would seem prudent to institute daily antiplatelet therapy for most Fontan patients. There has been no consensus on the requirement for coumadin anticoagulation therapy. Most centers will provide anticoagulation therapy for patients whom they consider to be at higher risk (eg, RA-PA connection, external conduit, sluggish venous circulation, or low cardiac output).

Fontan Conversion and Antiarrhythmic Surgical Intervention
As patients who had RA-PA connections in early life reach young or middle adulthood, the incidence of hemodynamic deterioration and arrhythmias increases. In recent years, a number of these patients have undergone conversions to total cavopulmonary connection and at the same time have undergone a Maze procedure to treat intractable atrial arrhythmias. The indications for surgical revision usually are a combination of exercise intolerance and refractory arrhythmias. With time, more and more patients may be expected to be candidates for this type of surgery. Eventually, because direct RA-PA anastomoses are no longer being performed, the issue of conversion will disappear. Although the indications may vary from center to center, it is generally agreed that revision has been very helpful in a significant number of symptomatic patients.

The Fontan operation has given the patient with a single ventricle a longer and better-quality life than was previously possible. The effects of a 1-ventricle circulation are becoming more clearly delineated after 3 decades, but much remains to be learned. Conventional management regimens must always be challenged, and new approaches considered. The clinical course of Fontan patient survivors beyond 15 to 20 years will undoubtedly present an increasingly difficult challenge.

Disclosures

None.

References


Key Words: Editorials | follow-up studies | mortality | Fontan procedure
Fontan Operation After 3 Decades: What We Have Learned
Welton M. Gersony

doi: 10.1161/CIRCULATIONAHA.107.748566

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