Fontan Failure and Death in Contemporary Fontan Circulation: Analysis From the Last Two Decades

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Background. **We sought to evaluate the incidence of Fontan failure or complication and its relation to death in patients having contemporary Fontan strategies over 2 decades.**

Methods. **Five hundred patients who underwent Fontan completion (extracardiac, n = 326; lateral tunnel, n = 174) from 1985 to 2012 were reviewed. Patient characteristics, modes of Fontan failure/complication and death, and predictors for Fontan failure/complication and death were analyzed.**

Results. **There were 23 early deaths (4.6%) and 17 late deaths (3.4%), with no early death since 2000. Survival has improved over time ($p < 0.001$). Twenty-three of 40 patients who died were identified as Fontan failure before death, including ventricular dysfunction (n = 14), pulmonary vascular dysfunction (n = 4), thromboembolism (n = 2), and arrhythmia (n = 4). Mode of death was circulatory failure (n = 18), multiorgan failure (n = 6), pulmonary failure (n = 3), cerebral/renal (n = 5), and sudden death (n = 4). Modes of failure/complication were directly (65%) or conceivably (10%) related to death in 30 of 40 patients (75%). Forty-eight percent of survivors had late Fontan complication(s). Five-year freedom from late Fontan complication was lower among patients who died compared with patients who survived (29.4% versus 53.3%, $p < 0.001$). Ventricular dysfunction ($p = 0.001$) and higher pulmonary artery pressures ($p < 0.001$) after Fontan were predictors for death. Longer cardiopulmonary bypass time ($p = 0.032$) and reinterventions ($p < 0.001$) were predictors for late Fontan complication.**

Conclusions. **Early death in the early era has been overcome. Yet the incidence and causes of late death remain unchanged. There was a strong causative relationship between the mode of Fontan failure/complication and death, indicating the importance of early recognition and treatment of Fontan failure/complication.**

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Innovations in the Fontan operation [1] for patients with functionally single ventricle physiology have dramatically improved survival of this patient group. It becomes increasingly evident that classic Fontan physiology, namely, atriopulmonary connection, has some fundamental limitations, such as significant risk of thrombosis, atrial arrhythmias, and death [2–5]. A recent large clinical series has well documented the modes of death among patients who underwent classic atriopulmonary connection Fontan completion [6]. The contemporary form of Fontan operation, total cavopulmonary connection (TCPC) by creating a lateral tunnel, was introduced in the late 1980s [3, 7]. The latest significant modification was to use an extracardiac conduit as a Fontan pathway in which the atrium is completely isolated from the Fontan circuit. Coupled with the introduction of a three-stage palliation process with bidirectional cavopulmonary shunt as an interim procedure and the concept of fenestrated Fontan completion, the current form of the Fontan operation has yielded substantially higher early and medium-term survival in the last decade [8–11].

Given the striking differences in surgical technique and perioperative and surgical management over 2 decades, we hypothesized that mode of death and Fontan failure/complication would be markedly different. Hence, we sought to describe mode of Fontan failure/complication and cause of death in an attempt to elucidate whether there is any causal relationship between Fontan failure/

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complication and death in a contemporary Fontan cohort over 2 decades.

Patients and Methods

All patients who underwent TCPC as the final stage for single ventricle palliation at the Hospital for Sick Children between March 1985 and February 2012 were included in this study for retrospective chart review. Research Ethics Board approval was obtained. During the study period, 500 children underwent staged Fontan completion with lateral tunnel (n = 174) or extracardiac (n = 326) TCPC. Patients who underwent one-stage Fontan operation, atriopulmonary connection Fontan operation, or initial systemic-to-pulmonary shunt followed by Fontan completion (no bidirectional cavopulmonary shunt performed) were excluded. Patients who did not need neonatal palliation and had bidirectional cavopulmonary shunt as primary palliation were included in the study. The patient diagnoses and preoperative profile are shown in Table 1.

Surgical Techniques

The surgical techniques for Fontan operation have been described elsewhere [8]. Briefly, standard mild hypothermic cardiopulmonary bypass was used. With the lateral tunnel technique, a semicylindrical polytetrafluoroethylene baffle was anastomosed to the inferior vena cava. The suture line was carried anterior to the atrial septum to avoid pulmonary venous obstruction. Extracardiac Fontan operation was typically performed in an on-pump beating heart state without cardioplegic cardiac arrest. A large incision was made on the inferior aspect of the central branch pulmonary artery, and a tube graft was anastomosed. The inferior end of the graft was then anastomosed to the inferior vena cava. A fenestration was created between the Fontan graft and the atrium. An aortic homograft (in the 1990s [n = 67]), polytetrafluoroethylene tube (n = 254), or another conduit (n = 5) were used as the external conduit. The average conduit size was 20 ± 1 mm (median 21 mm; range, 20 to 22 mm). A fenestration was used in 411 patients (82%). The median size of the fenestration was 4 mm (range, 3.5 to 5 mm). Operative data are shown in Table 1.

Change in Fontan Strategy

By the mid 1990s, the surgical strategy had shifted from lateral tunnel to extracardiac with routine fenestration based on our experience [8]. Patient selection and surgical indications were also modified. Currently, any anatomic issues including significant atrioventricular valve regurgitation, pulmonary vein stenosis, or hypoplastic branch pulmonary arteries are addressed before Fontan completion either at stage II bidirectional cavopulmonary shunt or as an interim stand-alone procedure. These changes have made the Fontan operation very simple and efficient. In the recent era (1999 to 2012), concomitant procedures (31% versus 53%, $p < 0.001$) are required less often compared with the early era (1985 to 1998). Consequently, cardiopulmonary bypass time (63 versus 126 minutes, $p < 0.001$), the use of aortic cross clamp (31% versus 73%, $p < 0.001$), and cross-clamp time (33 versus 58 minutes, $p < 0.001$) are significantly shorter in the current era.

Assessment of Mode of Fontan Failure or Complication and Death

All patient charts were independently reviewed by three investigators (Y.K., J.Z., and A.S.). Each physician made an independent assessment of the modes of Fontan failure and death. If the assessments were different, the patient was re-reviewed until consensus was reached. After the data were collected and summarized, analysis and interpretation of the data were discussed. As defined by The Society of Thoracic Surgeons, Fontan failure is significant physiologic failure of cavopulmonary connection leading to inhospital death (death during the hospitalization of Fontan creation), Fontan takedown/revision, need for mechanical support, or transplantation [12, 13]. As there were a substantial number of complications seen during follow-up, we have grouped these relatively minor late complications as "late Fontan complication" for the purpose of analysis.

The Fontan failure and late Fontan complication included all complications as follows: ventricular dysfunction, ventricular systolic or diastolic dysfunction or both documented by echocardiography; pulmonary vascular dysfunction, increased pulmonary vascular resistance; mechanical problem, anatomic pathway obstruction (eg, conduit stenosis); thromboembolism, arrhythmia, protein-losing enteropathy, arteriovenous fistula, arteriovenous malformation, and plastic bronchitis. If a patient had more than one mode of Fontan failure/complication, the most severe mode was documented. Mode of death was classified as (1) circulatory failure; (2) multiorgan failure; (3) pulmonary failure; (4) cerebral issues; (5) renal failure; 6) sudden death; and (7) unknown, based on previous studies describing causes of death (Appendix) [6, 14]. The onset of Fontan failure/complication and time to death (from Fontan operation) were documented. The causal relationship between Fontan failure/complication and death was analyzed. The mode of failure/complication and its impact on mortality was assessed clinically by performing root cause analysis. The strength of causal link to each patient's course was estimated as follows: (1) no link to death; (2) possible link to death; and (3) direct relation to death. Echocardiographic images were reviewed, and qualitative assessments of ventricular function and degree of atrioventricular valve regurgitation were also reviewed. Ventricular function was graded as normal, mildly reduced, moderately reduced, or severely reduced. The degree of atrioventricular valve regurgitation was graded as none/trivial, mild, moderate, or severe.

Statistical Analysis

Continuous data are presented as median (interquartile range). Discrete data are presented as frequency (percentage). The level of statistical significance was set at