Persistent fenestration may be a marker for physiologic intolerance after Fontan completion

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Background: We sought to evaluate the medium-term implications of fenestration status.

Methods: Between 1994 and 2012, 326 patients received an extracardiac Fontan (hospital mortality n = 6, 1.8%). A fenestration was routinely created (n = 306, 94%) unless there was technical difficulty. Three hundred patients discharged with an open fenestration were included. The primary end points were death and Fontan failure. Secondary outcomes were Fontan complications such as venovenous collaterals, protein-losing enteropathy, pacemaker requirement, and arrhythmias.

Results: The fenestration was closed in 260 patients: 185 as a catheter intervention (62%) and 75 (25%) spontaneously. Forty patients (13%) had the fenestration open at a median follow-up period of 5.05 years. Of these patients, catheter-based closure failed in 10 (3%). There was no statistically significant difference in pre-Fontan hemodynamic parameters, such as pulmonary artery pressure and pulmonary vascular resistance between the patients with open fenestration and the ones with closed fenestration. Patients with an open fenestration had significantly more late deaths ($P < .001$), Fontan failure ($P = .021$), and Fontan complications ($P = .011$) compared with those with a closed fenestration. Multivariable Cox regression revealed open fenestration ($P < .001$) and indeterminate ventricular morphology ($P = .002$) as risk factors for death/Fontan failure, and ventricular dysfunction ($P = .014$) and open fenestration ($P = .009$) as risk factors for Fontan complications.

Conclusions: Persistent fenestration was a marker for physiologic intolerance as noted by increased rates of mortality and a higher incidence of Fontan failure/complications. The specificity of pre-Fontan physiologic data for fenestration status may not have the fidelity needed for long-term care and thus, the consequences of decision making regarding fenestration status may not be determined until well after the operation. (J Thorac Cardiovasc Surg 2014;148:2532-8)

See related commentary on pages 2538-9.

Surgical creation of a temporary communication between the Fontan pathway and the common atrium, ie, fenestration, was first introduced in the early 1990s as a strategy for high-risk Fontan candidates who had an estimated hospital survival of less than 85%.[1] The rationale for fenestration was to lower the pressure in the Fontan circuit and increase cardiac output, thereby decreasing operative mortality and morbidity.[1] Currently, a strategy of fenestration creation is used worldwide as part of standard Fontan completion.[2,3] Hospital survival for the Fontan operation in the current era is excellent after refinements in surgical strategy including fenestration and improvements in perioperative management.

The impact of fenestration on early clinical outcomes in standard-risk Fontan candidates has been studied in the last 2 decades. There was no survival benefit of fenestration reported and the survival of both fenestrated and nonfenestrated patients with standard-risk profiles was excellent. There were some positive effects of fenestration on secondary outcomes, including chest tube drainage, arrhythmias, and hospital stay,[4-6] although some other retrospective studies showed no clinical benefit of fenestration.[7,8] Much less evidence exists regarding the medium- to long-term effects of persistent fenestration on clinical outcomes. A retrospective study from the Pediatric Heart Network showed no additional benefit of fenestration on functional status and ventricular function at a mean follow-up of 7 to 8 years.[7] A recent cardiac magnetic resonance study from our group showed that not only all inferior vena cava flow but also part of the superior vena cava flow is diverted through the fenestration in two thirds of the study population at a mean follow-up of 12 months,

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Abbreviations and Acronyms
AVV = arterioventricular valve
NYHA = New York Heart Association

raising the possibility of potential adverse effects of persistent fenestration in the medium-term.[9]

Like many North American institutes,[10] Fontan completion with an extracardiac tube graft with fenestration of 3 to 4 mm has been our consistent approach over the past 2 decades. Our intention has been to close the fenestration at 6 to 12 months after Fontan completion; nonetheless, several patients did not tolerate fenestration closure. We hypothesized that persistent fenestration does not have medium-term hemodynamic benefit but failure to close the fenestration may be an indicator of subsequent poor clinical outcomes. Thus, we investigated the impact of persistent fenestration on medium-term mortality and morbidity.

METHODS

A total of 326 patients who underwent extracardiac total cavopulmonary connection for single ventricle palliation at the Hospital for Sick Children between July 1994 and April 2012 were reviewed. Research Ethics Board approval was obtained. Patients who underwent a 1-stage Fontan operation or aortopulmonary connection Fontan operation were excluded. A fenestration was routinely created at our institution unless there was technical difficulty. A total of 306 (94%) patients had a fenestration. Three hundred patients who had an open fenestration at the time of discharge were included in the study.

Operative Technique and Fenestration Closure

The surgical techniques for the Fontan operation have been described elsewhere.[11] Briefly, standard normothermic or mild hypothermic cardiopulmonary bypass was used. Extracardiac total cavopulmonary connection was typically performed in an on-pump beating state without cardioplegic cardiac arrest unless other intracardiac procedures were required. A transverse 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 incision was made on the tube graft as well as on the right atrial lateral wall, and a fenestration was created between the Fontan graft and the atrium by means of a direct side-by-side anastomosis without a bridging graft. A polytetrafluoroethylene tube (n = 254), aortic homograft (in the 1990s; n = 67), or another conduit (n = 5) was used as the external conduit. The average conduit size was 20 ± 1 mm (median, 21 mm; range, 20-22 mm). The median size of the fenestration was 4 mm (range, 3.5-5 mm).

Catheter-based fenestration closure was performed electively at 6 to 12 months if physiologically tolerated. After initial assessment at the outpatient clinic, patients were taken to the cardiac catheterization-laboratory. Suitability for fenestration closure was decided based on changes in the central venous pressure (Fontan pressure), systemic blood pressure, and arterial oxygen saturation with test occlusion of the fenestration. Fenestration closure was performed with an Amplatzer septal occluder (AGA Medical, Golden Valley, Minn).

Outcome Assessment

All patient charts were independently reviewed by 3 investigators (YK, AS, and JZ). Echocardiography was used to assess whether or not the fenestration was open at latest follow-up and patients were divided into 2 groups: closed fenestration and open fenestration. Outcomes were compared between the 2 groups. Primary end points were death and Fontan failure, defined as Fontan takedown/revision, need for mechanical circulatory support, or transplantation.[12-14] Secondary outcomes were Fontan complications, including venovenous collaterals, protein-losing enteropathy, pacemaker requirement, arteriovenous malformation, and arrhythmias. Echocardiographic images were reviewed and qualitative assessments of ventricular function and degree of arterioventricular valve (AVV) regurgitation were performed using a method described previously.[15] Ventricular function was graded as normal, mildly reduced, moderately reduced, or severely reduced. The degree of AVV 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). Differences between the groups were analyzed with the Mann-Whitney U test. Event frequencies were compared with the χ^2 or Fisher test. Freedom from death/Fontan failure and Fontan complications were analyzed by Kaplan-Meier analysis and the log-rank test. Univariable predictors for death/Fontan failure and Fontan complications were analyzed with a Cox regression model. Variables that were significant at the $P \leq .05$ level in univariable analysis were included in a multivariable Cox regression model. Statistical analysis was performed using SPSS version 17.0 statistical software (IBM Corporation, Armonk, NY).

RESULTS

Seventy-five (25%) patients were identified as having a fenestration that closed spontaneously. A total of 195 (65%) patients were brought to the catheterization laboratory for assessment of fenestration closure. Thirty (10%) patients were considered too high risk for fenestration closure and were not assessed by test occlusion. Ten (3%) of 195 patients failed balloon test occlusion because of high pulmonary artery pressure (n = 7) or hemodynamic instability (n = 3). As a result, at a follow-up period of 5.05 (2.37-10.26) years, the fenestration was closed in 260 patients: 75 (25%) by spontaneous closure and 185 (62%) by catheter-based closure. Forty patients (13%) had an open fenestration. There was no statistical difference between those with open and closed fenestration with respect to pre-Fontan status, including diagnosis, dominant ventricle, ventricular and AVV function, pulmonary artery pressure, and pulmonary vascular resistance (Table 1).

Death and Fontan Failure

Nine (3%) patients died after discharge. Cause of death included circulatory failure in 2 patients, respiratory failure in 1 patient, multiorgan failure in 1 patient, thromboembolism in 1 patient, and unknown in 4 patients. Freedom from death in patients with a closed fenestration was significantly higher than that in patients with an open fenestration (99.2% vs 74.5% at 5 years, $P < .001$; Figure 1, *A*). A comparison of 3 groups (catheter-based closure, n = 185; spontaneous closure, n = 75; and open, n = 40) showed that the mechanism of fenestration closure was not important but the presence of an open fenestration was associated with the lowest survival (spontaneous closure,