Long-term outcomes after first-onset arrhythmia in Fontan physiology

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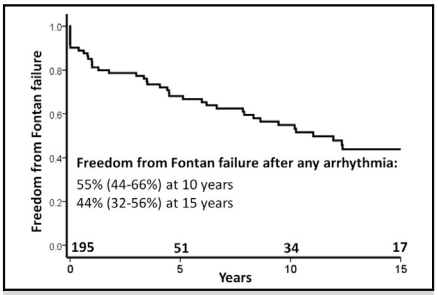
ABSTRACT

Objectives: Patients living with a Fontan circulation are prone to develop arrhythmias. However, their prognostic impact has been seldom studied. As such, we aimed to determine the incidence and predictors of arrhythmias after the Fontan procedure and the long-term outcomes after the first onset of arrhythmias.

Methods: Of the 1034 patients who have undergone a Fontan procedure as recorded in the Australian and New Zealand Fontan Registry, we identified those in whom a tachyarrhythmia or bradyarrhythmia developed. We evaluated the incidence and predictors of developing arrhythmias and their prognostic impact on late outcomes.

Results: Arrhythmia developed in 195 patients. Tachyarrhythmia was present in 162 patients, bradyarrhythmia was present in 74 patients, and both forms were present in 41 patients. At 20 years, freedom from any arrhythmia, tachyarrhythmia, and bradyarrhythmia was 66% (95% confidence interval [CI], 59-72), 69% (95% CI, 62-75), and 85% (95% CI, 80-90), respectively. On multivariable analyses, patients with an extracardiac Fontan (hazard ratio [HR], 0.23; 95% CI, 0.10-0.51; $P < .001$) were less likely to develop an arrhythmia, whereas those with left atrial (HR, 3.18; 95% CI, 1.45-6.95; $P = .004$) and right atrial (HR, 4.00; 95% CI, 2.41-6.61; $P < .001$) isomerism were more likely to have an arrhythmia. After onset of any arrhythmia (tachyarrhythmia or bradyarrhythmia), 10- and 15-year survivals were 74% (65%-83%) and 70% (60%-80%), respectively, and freedom from Fontan failure was 55% (44%-64%) and 44% (32%-56%), respectively. The development of any arrhythmia (HR, 2.20; 95% CI, 1-44-3.34; $P < .001$), tachyarrhythmia (HR, 2.56; 95% CI, 1.60-4.11; $P < .001$), and bradyarrhythmia (HR, 1.85; 95% CI, 1.16-2.95; $P = .01$) were all independent predictors of late Fontan failure on multivariable analyses.



Freedom from Fontan failure after onset of arrhythmia.

Central Message

The development of an arrhythmia is associated with a heightened risk of subsequent failure of the Fontan circulation. Current treatment strategies prevent Fontan failure in approximately half of these patients at 10 years.

Perspective

Arrhythmias are associated with an increased risk of failure of the Fontan circulation. Timing of surgery, such as transplantation and Fontan conversion, remains difficult to identify because current medical management (medications, DCCV, and ablation) provides relief to half of patients for 10 years.

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Abbreviations and Acronyms
CI = confidence interval
DCCV = direct current cardioversion
HR = hazard ratio
IQR = interquartile range

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Conclusions: The development of an arrhythmia is associated with a heightened risk of subsequent failure of the Fontan circulation. (J Thorac Cardiovasc Surg 2016;152:1355-63)

Long-term survival after the Fontan procedure has improved, but these patients remain at risk of arrhythmias, thromboembolic events, and failure of their circulation.[1-4] Arrhythmias have been described to occur in 13% to 54% of patients over the course of the first 2 decades after Fontan surgery.[1,5,6] They seem to predominantly occur in the patients who have undergone the atriopulmonary connection, with arrhythmias occurring as a response to progressive atrial stretch.[7,8]

There are limited data on the type of arrhythmias encountered and their prognostic impact on late outcomes. As such, we sought to use the Australian and New Zealand Fontan Registry to evaluate our experience with arrhythmias in patients with a Fontan circulation and determine their prognostic impact on long-term outcomes.

MATERIALS AND METHODS

The Australian and New Zealand Fontan Registry was commenced in 2008 and includes patients who underwent the Fontan procedure in both countries. All 8 pediatric and 7 adult centers overseeing the care of patients with congenital heart disease in Australia and New Zealand participated in this study.

The clinical characteristics and early and late outcomes of the patients have been reported by d'Udekem and colleagues.[1] Data for this study were extracted from the Australia and New Zealand Fontan Registry for the patients who consented to the Registry. For those who had not provided consent, data were obtained from hospital databases.[1,9] Patients who died before discharge after the Fontan procedure and those who underwent Fontan takedown in the same admission were excluded. This study was approved nationally and by the Hospital Research Ethics committees of the participating centers.

Tachyarrhythmias were defined as a documented supraventricular tachycardia, atrial flutter, atrial fibrillation, or intra-atrial reentry tachycardia. Bradyarrhythmias were defined as a documented complete heart block, sinus node dysfunction, or bradycardia (defined as a resting heart rate of <50 beats/min). The presence of arrhythmia was determined using cardiologist clinical review documentation and hospital medical documentation. We identified the time point at which an arrhythmia was first recognized and analyzed freedom from late end points.

To determine the prognostic impact of arrhythmia on long-term outcomes, we examined 3 late end points: death, death or cardiac transplantation, and Fontan failure. The composite end point of Fontan failure was defined as death, heart transplantation, Fontan takedown or conversion, protein-losing enteropathy, plastic bronchitis, or New York Heart Association functional class III or IV at follow-up.

Echocardiogram reports were reviewed to assess the onset of a decrease in ventricular function. Because patients were investigated across several centers, no single quantitative measurement of ventricular systolic function could be obtained, and these echocardiographic reports retain a degree of subjectivity. Generally, patients were deemed to have reduced ventricular function if their echocardiogram showed evidence of at least moderate systolic dysfunction on visual assessment. We analyzed the time point at which patients were first found to have reduced ventricular function, because we deemed this to represent an important point in patients' clinical trajectory, which may potentially herald an increased risk of subsequent late events.

Statistical Analysis

Data were analyzed using SPSS Version 23.0 (IBM Corp, Armonk, NY). Continuous variables were compared using the unpaired *t* test, Wilcoxon signed-rank test, and 1-way analysis of variance. Categoric variables were compared using the Fisher exact and chi-square tests.

The Kaplan–Meier method and log-rank statistic were used. We determined freedom from arrhythmias since the date of the initial Fontan procedure. Separate analyses were performed for any arrhythmia, tachyarrhythmia, and bradyarrhythmia. As such, patients who experienced both a tachyarrhythmia and bradyarrhythmia formed part of both the tachyarrhythmia and bradyarrhythmia subgroup analyses.

In addition, we also determined the freedom from late events from the time of the first onset of an arrhythmia. In these Kaplan–Meier analyses, t = 0 referred to the time of the arrhythmia. Again, separate analyses were performed for any arrhythmia, tachyarrhythmia, and bradyarrhythmia.

Multivariable Cox regression was used to determine the independent predictors of developing arrhythmias after the Fontan procedure. The covariates entered into the regression model are shown in Table 1.

To determine the impact of an arrhythmia on long-term outcomes, the time of the first onset of an arrhythmia was inserted into the multivariable Cox regression model as a time-varying covariate, and its associated hazard ratio (HR) was calculated. In essence, patients' follow-up was split into 2 periods: before and after the onset of arrhythmia. As such, the association between the development of an arrhythmia and the subsequent late end points could be established.

RESULTS

Occurrence of Arrhythmia

From 1975 to 2014, a total of 1034 patients were discharged alive after the Fontan procedure across Australia and New Zealand. There were 210 atriopulmonary, 269 lateral tunnel, and 555 extracardiac conduit Fontan variants.

An arrhythmia was present in 195 patients. Of these, tachyarrhythmia was present in 162. These tachyarrhythmias were diagnosed as supraventricular tachycardia in 96 patients, atrial flutter in 34 patients, atrial fibrillation in 17 patients, junctional tachycardia in 10 patients, and ventricular tachycardia in 5 patients. A bradyarrhythmia occurred