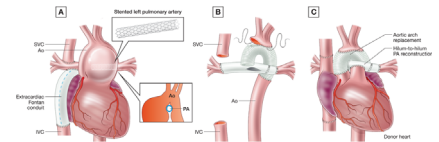




Increasing Complexity of Heart Transplantation in Patients With Congenital Heart Disease

William Y. Shi, MBBS,^{*,†} Pankaj Saxena, PhD, FRACS,[‡] Matthew S. Yong, MBBS,[‡] Silvana F. Marasco, MBBS, PhD, FRACS,[‡] David C. McGiffin, MBBS, FRACS,[‡] Anne Shipp, RN,^{*,†} Robert G. Weintraub, MBBS, FRACP,^{*,†} Yves d'Udekem, MD, PhD, FRACS,^{*,†} Christian P. Brizard, MD,^{*,†} and Igor E. Konstantinov, MD, PhD, FRACS^{*,†}

Owing to improved surgical results, there is a growing population of patients with repaired congenital heart disease (CHD) requiring heart transplantation. The objective of the study was to review our experience in these patients. A retrospective review of the outcomes of heart transplantation in patients with CHD ($n = 77$) between 1988 and 2014 was performed. Outcomes of early (1988-1999) and late (2000-2014) eras were compared. In results, the mean age was 18 ± 14 years (range: 16 days-58 years). Seventy (91%) patients underwent a mean of 2.6 ± 1.3 (range: 1-6) cardiac operations before transplantation, whereas 7 were primary transplants. Univentricular palliation had been performed in 44 (57%) patients. Patients with CHD in the later era had longer mean cardiopulmonary bypass time (early: 190 ± 70 minute vs late: 271 ± 115 minute; $P < 0.001$), ischemic times (early: 222 ± 98 minute vs late: 275 ± 102 minute; $P = 0.039$), and more often required reconstruction of the great arteries at the time of transplantation (8% vs 28%; $P = 0.036$). In those with prior univentricular palliations, the ratio of ischemic to cardiopulmonary bypass time decreased in the later era (early: 1.41 ± 0.60 vs late: 0.99 ± 0.37 ; $P = 0.016$), reflecting increased intraoperative complexity. Following transplantation, hospital mortality was 13% (10/77; 7 due to primary graft failure). There was no difference in in-hospital mortality between the 2 eras ($P = 0.52$); however, patients in the later era more often required postoperative extracorporeal membrane oxygenation (early: 8%, 3/38 vs late: 28%, 11/39; $P = 0.036$). In patients with prior univentricular palliations, those in the late era



Aortic and pulmonary artery reconstruction during cardiac transplantation.

Central Message

Patients with CHD undergoing cardiac transplantation in the recent era were more complex. They had a greater number of prior cardiac operations, and more often underwent complex vascular reconstructions and required more prolonged intraoperative preparation.

Perspective

Patients with CHD represent an increasing proportion of heart transplant recipients. Judging from the trends identified in our study and the foreseeable growth in the number of CHD patients with end-stage heart failure, it is essential that surgeons adjust their transplantation practice to deal with these complex patients.

See Editorial Commentary pages 498-499.

^{*}Department of Cardiac Surgery, Royal Childrens Hospital, University of Melbourne, Melbourne, Australia

[†]Department of Cardiology, Royal Children's Hospital, University of Melbourne, Melbourne, Australia

[‡]Department of Cardiothoracic Surgery, The Alfred Hospital, Monash University, Melbourne, Australia

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Address reprint requests to Igor E. Konstantinov, MD, PhD, FRACS, Cardiac Surgery Unit, Royal Children's Hospital, Parkville, Victoria 3052, Australia. E-mail: igor.konstantinov@rch.org.au

were more likely to experience postoperative renal impairment (early: 1/21, 5% vs late: 9/23, 39%; $P = 0.01$). Patients with CHD had higher 30-day mortality (CHD: $n = 8$, 10% vs non-CHD: $n = 17$, 3.8%; $P = 0.021$), but similar survival at 10 years ($67\% \pm 12\%$ vs $70\% \pm 4.7\%$; $P = 0.87$) compared to those without CHD. In conclusion, patients with CHD undergoing cardiac transplantation in the recent era were more complex. They had a greater number of prior cardiac operations, and more often underwent complex vascular reconstructions and required more prolonged intraoperative preparation.

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INTRODUCTION

Patients with congenital heart disease (CHD) represent an increasing proportion of heart transplant recipients.^{1,2} Data from the United Network of Organ Sharing demonstrated that the frequency of cardiac transplantation among adults with CHD had increased from 5.6%-10.5% in the recent decade.¹ When compared with non-CHD patients, patients with CHD are generally younger and have fewer comorbidities.³ However, these patients continue to have inferior early outcomes when compared with non-CHD patients.^{1,3-5}

Prior surgical procedures, prolonged ischemic times, complex anatomy, and pulmonary vascular abnormalities, as well as immune sensitization from the use of blood products have been described as contributors to mortality.^{2,4,6,7} The complexity of this patient group is increasing as more patients with CHD are surviving after multiple cardiac operations. We describe the changing spectrum of complexity and the outcomes of patients with CHD undergoing heart transplantation.

METHODS

From April 1988 to January 2014, 817 patients underwent orthotopic heart transplantation in Melbourne, Australia, including 125 (43%; $n = 54$ with CHD) patients at the Royal Children's Hospital and 692 (3.3%; $n = 23$ with CHD) at the Alfred Hospital. Altogether, there were 77 patients with CHD.

The study was approved by Human Research Ethics committees of both hospitals. As patients with heart failure reached 18 years, their care was transitioned from the Royal Children's Hospital to the Alfred Hospital. Follow-up was 100% complete with a mean of 7.5 ± 7.3 years (range: 1.0-22.5 years) up to February 1, 2015. Patients with CHD ($n = 77$) were compared to 442 patients without CHD of the same age range and undergoing cardiac transplantation during the same time period.

Definitions

Outcomes of transplantation were reviewed for 2 arbitrarily defined eras: early (1988-1999) and late (2000-2014). Hospital mortality was defined as death before hospital discharge or within 30 days of surgery. Primary graft dysfunction was defined as evidence of ventricular dysfunction with hemodynamic instability requiring high-dose inotropic support, a mechanical-assist device within 24 hours after transplantation. Stroke was defined as a focal neurologic deficit of central origin that persisted beyond 24 hours, which was associated with positive

imaging findings. Renal impairment was identified by pretransplant or posttransplant serum creatinine of greater than $100 \mu\text{mol/L}$. Post-operative renal failure was defined as the need for dialysis or doubling of pretransplant serum creatinine levels.

A composite end point of "any postoperative event" encompassing in-hospital death, stroke, renal failure, primary graft failure, postoperative extracorporeal membrane oxygenation (ECMO), and postoperative intra-aortic balloon pump was also analyzed.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics for Windows Version 21.0 (Armonik, NY) and R statistical package (R Core Team, www.R-project.org). Descriptive statistics for continuous variables were expressed as a mean \pm standard deviation and compared using the independent *t*-test and Wilcoxon sum-rank test. Binary variables were summarized as frequencies and percentages and comparisons were made using the chi-squared test. The Kaplan-Meier method was used to analyze and compare survival between patients with and without CHD. The log-rank test was used to determine statistical significance between Kaplan-Meier curves. Univariate and multivariate logistic regressions were performed to identify predictors of inhospital outcomes. We also performed regression on the year of surgery to identify temporal trends. We calculated the ratio of ischemic time to bypass time to evaluate duration of bypass in relation to ischemic time. Locally weighted scatter plot smoothing (Loess smooth curves) was constructed for selected factors at intervals of 5 years to graphically evaluate temporal trends. All tests were 2 tailed and $P < 0.05$ were considered significant.

RESULTS

Outcomes of Transplantation in Patients With CHD

Of the 77 patients with CHD, the mean age was 18 ± 14 years (range: 14 days-58 years). There were 48 (62%) males and 29 (38%) females. Preoperative and intraoperative data are presented in [Table 1](#). Patient characteristics that were associated with later year of surgery on logistic regression are shown in [Table 2](#).

Most (91%, 70/77) patients underwent a mean number of 2.6 ± 1.3 (range: 1-6) cardiac operations before transplantation. Only 7 patients underwent primary transplantation.

Univentricular physiology was present in 44 (57%) patients. Most of these 44 patients with

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