The natural and unnatural history of the systemic right ventricle in adult survivors

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Objective: The study objective was to evaluate long-term trends in morbidity and mortality in a national cohort of adult patients with a systemic right ventricle due to the atrial switch for transposition of the great arteries or congenitally corrected transposition of the great arteries.

Methods: We performed a retrospective cohort study from a baseline of 18 years, including life table and Kaplan–Meier analysis for probability of death/transplant, arrhythmia, surgical or percutaneous intervention, and permanent pacemaker insertion.

Results: A total of 97 adults with transposition of the great arteries–atrial switch (Mustard procedure in 80/Senning procedure in 17) and 32 adults with congenitally corrected transposition of the great arteries survived. The median ages at latest follow-up were 29 and 34 years, respectively. At 40 years of follow-up, freedom from death or transplant was 0.90 for those with transposition of the great arteries–atrial switch and 0.84 for those with congenitally corrected transposition of the great arteries ($P = .833$). Freedom from arrhythmia at 40 years of follow-up was 0.51 for those with transposition of the great arteries–atrial switch and 0.93 for those with congenitally corrected transposition of the great arteries ($P = .007$). Freedom from intervention at 40 years of follow-up was 0.33 for those with transposition of the great arteries–atrial switch after initial repair and 0.53 for those with congenitally corrected transposition of the great arteries ($P = .938$). Freedom from pacemaker insertion at 40 years of follow-up was 0.77 for those with transposition of the great arteries–atrial switch and 0.62 for those with congenitally corrected transposition of the great arteries ($P = .161$).

Conclusions: Those patients who survive to adulthood with a systemic right ventricle experience low mortality and good functional status up to 40 years of age. However, there is a substantial burden of atrial tachyarrhythmia, and this occurs significantly earlier in those with transposition of the great arteries–atrial switch. Management of atrial tachyarrhythmia, along with systemic right ventricular dysfunction and systemic atrioventricular valve regurgitation, is likely to be the major challenge for this group of patients over the next decade. (J Thorac Cardiovasc Surg 2013;145:1493-503)

CHD

The morphologic right ventricle (RV) supports the systemic circulation in those individuals with congenitally corrected transposition of the great arteries (ccTGA) and those who have survived atrial switch surgery (the Mustard or Senning procedure) for complete transposition of the great arteries (TGA). Although atrial switch is no longer the gold standard for management of TGA, having been superseded by the arterial switch operation in the late 1980s, many adult patients with TGA will have undergone the older procedure.

Patients with either diagnosis are at risk of a host of complications associated with the systemic RV (SRV), including premature heart failure, regurgitation through the systemic atrioventricular (AV) valve, AV nodal block and a need for permanent pacing, tachyarrhythmia, and sudden cardiac death.

The long-term history of patients with an SRV still needs to be clearly defined. Most of the cohort studies of patients after atrial switch focus on establishing which of the Mustard and Senning procedures was the best procedure to use, and the majority provide follow-up to only 20 years. Patients with ccTGA are the subject of only a handful of cohort studies. Our aim was to establish the natural history of the SRV in both conditions and provide a benchmark to which other treatment approaches for the SRV (eg, placing the morphologic left ventricle [LV] in the systemic circulation) can be compared.

We focused on the group of patients who have survived to at least the age of 18 years, because although this group of patients is of great interest to clinicians engaged in provision of an adult congenital heart disease service, to our

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Abbreviations and Acronyms

AV = atrioventricular
ccTGA = congenitally corrected transposition of the great arteries
LV = left ventricle
MRI = magnetic resonance imaging
PA = pulmonary artery
RV = right ventricle
SRV = systemic right ventricle
TGA = transposition of the great arteries
TR = tricuspid regurgitation
VSD = ventricular septal defect

knowledge there are no studies that assess the prognosis for these survivors.

MATERIALS AND METHODS

We performed a retrospective cohort study, with approval from the regional research ethics committee. We identified 204 patients with TGA-atrial switch or ccTGA (excluding those who had undergone single-ventricle palliation) who had attended the national pediatric or adult congenital cardiac services for Scotland. From this group of patients, we focused on the subset of adult patients (aged at least 18 years) who had an SRV. This resulted in a study population of 129 individuals. Dropout was due to patient death or transplant before the age of 18 years (31 patients), conversion to a systemic LV before the age of 18 years (5 patients), loss of follow-up (16 patients), or age less than 18 years at the time of data collection (23 patients).

Data were collected and anonymized for each individual from our electronic database and hospital case notes between January 2011 and 2012. Patient-specific timelines allowed calculation of survival curves for mortality, atrial arrhythmia, surgical or catheter intervention, and pacemaker insertion. Follow-up was from the age of 18 years. Patients were censored at the time of their last clinic review, date of death, date of cardiac transplant, or date of surgery to restore the morphologic LV to the systemic circulation (a Senning–Rastelli or arterial switch operation).

During long-term follow-up, patients underwent regular clinical review that included establishment of New York Heart Association status and ascertainment of occurrence of cardiovascular events, such as arrhythmia, hospital admission, and intervention.

Tachyarrhythmia was defined as any supraventricular or ventricular tachyarrhythmia captured on ambulatory or 12-lead electrocardiograph recording that was clinically significant (ie, caused symptoms or required treatment). We excluded cases in which tachyarrhythmia occurred exclusively within 30 days of cardiac surgery. Reintervention was defined as any cardiac surgical or percutaneous cardiac procedure occurring after baseline. Pacemaker insertion was defined as any permanent epicardial or endocardial pacemaker, and included those with cardiac resynchronization therapy.

Regular imaging with transthoracic echocardiography and, when no contraindications existed, cardiac magnetic resonance imaging (MRI) was performed (Table 1). This was used to establish the degree of tricuspid regurgitation (TR) and SRV dysfunction. A total of 50 patients underwent formal cardiopulmonary exercise testing, and peak oxygen uptake (measured in $mL \cdot kg \cdot min^{-1}$) was recorded if the test was maximal (Table 1). Since 2010, cardiac MRI and cardiopulmonary exercise test have been performed routinely on both groups of patients regardless of functional status or presumed need for surgery to clarify anatomy and provide more accurate assessment of ventricular function, and we believe the values obtained from these data provide an accurate cross-sectional assessment of the cohort at the time of data collection.

Data were described as frequencies, means and standard error, and medians and interquartile range. Means were compared with the independent samples *t* test, and medians were compared with the independent samples median test. Chi-square test using linear-by-linear association was used to assess the relationship between severity of TR and severity of SRV impairment.

Cumulative probability of survival was estimated using the Kaplan–Meier and life table method, and differences between groups were evaluated via the log-rank test. We performed analysis for survival from death or transplant, atrial tachyarrhythmia, surgical intervention after baseline, and pacemaker therapy.

Cox proportional hazards models were used to identify predictors for death or cardiac transplant. All analyses were performed using PASW Statistics v18.0.3 (IBM corporation, New York, NY).

RESULTS

We first identified the 204 patients in the pediatric population (Figure 2). Patients were censored at the time of their last review, when they died, when they received a cardiac transplant, or when they underwent surgery that restored the morphologic LV to the systemic circulation and the RV to the pulmonary circulation (ie, a double switch or Senning–Rastelli). Although a clear survival advantage up to 10 years was experienced by those with TGA-atrial switch, mortality between the 2 cohorts was remarkably similar after this time (log-rank $P = .657$). Of 133 patients with TGA-atrial switch (89 male, 44 female), 88 had ongoing follow-up, 23 died, 19 were lost to follow-up, 2 underwent cardiac transplantation, and 1 underwent a subsequent arterial switch procedure. Of 71 patients with ccTGA (46 male, 25 female), 49 had ongoing follow-up, 14 died, 3 were lost to follow-up, 1 underwent cardiac transplantation, 1 underwent an atrial and arterial double switch operation, and 3 underwent Senning–Rastelli repair.

The red line indicates the period from 18 years of follow-up and the major area of interest for this study. There were 97 adult survivors of atrial switch surgery for TGA and 32 adult survivors of ccTGA. The characteristics are outlined in Table 1.

Most of the patients undergoing atrial switch had undergone a Mustard repair, with only 17% undergoing the Senning procedure. More coexistent lesions were present in those patients with a diagnosis of ccTGA. By the end of the follow-up period, the majority of patients had good functional status, normal or only mild impairment of SRV function, and no or mild TR, with only 2 patients with ccTGA proceeding to tricuspid valve replacement and only 3 patients with severe regurgitation.

We assessed the relationship between SRV impairment and severity of TR. The 2 patients who underwent tricuspid valve replacement were excluded from the analysis. The chi-square value for linear-by-linear association between SRV impairment and severity of TR was 10.064