European Heart Journal (2009) **30**, 1873–1879
doi:10.1093/eurheartj/ehp179

Ventricular arrhythmias and sudden death in adults after a Mustard operation for transposition of the great arteries

Markus Schwerzmann[1], Omid Salehian[2], Louise Harris[3], Samuel C. Siu[4], William G. Williams[3], Gary D. Webb[5], Jack M. Colman[3], Andrew Redington[3], and Candice K. Silversides[3]*

[1]Departement of Cardiology, Grown-up Congenital Heart Disease Program, University of Bern, Inselspital, Bern, Switzerland; [2]Division of Cardiology, McMaster University Medical Center, Hamilton, ON, Canada; [3]Division of Cardiology, Toronto Congenital Cardiac Center for Adults, University of Toronto, University Health Network, Toronto General Hospital, 585 University Avenue, 5 N-521 North Wing, Toronto, ON, Canada M5G 2N2; [4]Division of Cardiology, University of Western Ontario, London, ON, Canada; and [5]Department of Medicine, Philadelphia Adult Congenital Heart Center, Children's Hospital of Philadelphia, University of Pennsylvania, Philadelphia, PA, USA

Received 15 October 2008; revised 16 February 2009; accepted 7 April 2009; online publish-ahead-of-print 22 May 2009

Aims To examine the prevalence of sustained ventricular tachycardia (VT) and sudden death (SD) in adults with atrial repair of transposition of the great arteries (TGA) and to determine associated risk factors.

Methods and results In a single-centre review, we studied the outcome of 149 adults (mean age 28 ± 7 years) who had undergone a Mustard operation for TGA. During a mean follow-up of 9 ± 6 years, sustained VT and/or SD occurred in 9% (13/149) of the cohort. Sustained VT/SD was more likely to occur in patients with associated anatomic lesions [hazard ratio (HR) 4.9, 95% CI 1.5–16.0], with NYHA class ≥III (HR 9.8, 95% CI 3.0–31.6) and with an impaired subaortic right ventricular (RV) ejection fraction (EF) (HR 2.2, 95% CI 1.2–4.0 per 10% decrease in EF). There was an inverse correlation between the RV-EF and both age and QRS duration. Patients with a QRS duration ≥140 ms were at highest risk of sustained VT/SD (HR 13.6, 95% CI 2.9–63.4). Atrial tachyarrhythmia was detected in 66 (44%) patients, but was not a statistically significant predictor of sustained VT/SD in our adult population (HR 2.7, 95% CI 0.6–13.0).

Conclusion Sustained VT/SD in adults after a Mustard operation for TGA are more common than previously described. Age, systemic ventricular function, and QRS duration are interrelated and are associated with VT/SD. A QRS duration ≥140 ms helps to identify the high risk patient.

Keywords Transposition of great vessels • Tachyarrhythmias • Survival

Introduction

Complete transposition of the great arteries (TGA) is one of the most common cyanotic heart defects in newborns and is found in 2–3 of 10 000 live births.[1,2] In the current era, adult patients typically have undergone atrial switch operations, either a Senning or a Mustard procedure.[3,4] These operations confer physiological repair, but the morphological right ventricle (RV) and its tricuspid valve continue to support the systemic circulation. This results in late complications including systemic ventricular failure, systemic atrioventricular valve regurgitation, and rhythm disturbances.[5,6]

In children and adolescents with TGA and atrial switch operations, supraventricular arrhythmias are well described and are shown to be associated with sudden death (SD).[7,8] However, as this population ages, there is further deterioration in systemic ventricular function and ventricular tachycardia (VT) can develop.[9]

We speculated that there may be a different risk profile for adults with VT and/or SD events when compared with children. Therefore, we sought to examine the prevalence of sustained

* Corresponding author. Tel: +1 416 340 3146, Fax: +1 416 340 5014, Email: candice.silversides@uhn.on.ca

VT/SD in adult patients with TGA after an atrial switch operation and to determine risk factors associated with these events.

Methods

After approval from the institutional research ethics board, 149 adults with complete TGA and a Mustard operation performed at the regional paediatric referral hospital (Hospital for Sick Children, Toronto, Canada) and who had regular follow-up at our centre (Toronto Congenital Cardiac Center for Adults, Toronto, Canada) were included. At our centre, only adult patients (age ≥16–18 years) are followed in our clinic.

The study cohort is a subset of a larger cohort of 564 paediatric patients who had undergone an atrial switch operation at the local referring paediatric hospital. Of the 564 operations performed, 512 patients survived to hospital discharge. There were an additional 129 known deaths during paediatric follow-up and 29 children (age <18 years) who had ongoing follow-up at the paediatric hospital at the time of data collection. Therefore, at the time of discharge from paediatric care, there were 354 adult patients with atrial switch operations alive, some of whom did not live locally, others who had moved and others who were lost to follow-up. Of the remaining patients, 149 were followed regularly at our centre and were included in this study.

Routine care for these patients includes an annual clinical evaluation with an electrocardiogram (ECG) and transthoracic echocardiography. In the current era, cardiac magnetic resonance (CMR) imaging or radionuclide angiography (in patients with pacemakers) is performed every 2–4 years. A 24 h Holter ECG was performed at the discretion of the treating cardiologist. Typical indications for performing a Holter included marked bradycardia, symptomatic bradycardia, palpitation, and presyncope/syncope. In some instance, they were performed as part of routine surveillance.

The patients' medical records were reviewed to collect demographic information, medical and surgical details including age at the time of the atrial switch operation or pacemaker implantation, current clinical status, ECG findings, Holter recordings, and results from imaging studies. Patients were classified as simple transposition if they had concordant atrioventricular and discordant ventriculoarterial connections with an intact ventricular septum or only a small, haemodynamically not important ventricular septal defect. Simple transposition also included patients with isolated patent ductus arteriosus or aortic coarctation. Complex transposition was defined by the presence of an associated ventricular septal defect requiring closure at the time of the Mustard procedure or other lesions, such as a ventricular outflow tract obstruction. We studied the occurrence of events (arrhythmias, death) after the transition of care from the paediatric to the adult congenital clinic based on the clinical records and the findings at the time of the last clinical visit.

The majority of patients had their last echocardiogram done at the time of their last follow-up. Right ventricular systolic function was assessed echocardiographically in all patients. Right ventricular systolic function was graded by visual assessment as normal [RV-ejection fraction (EF) ≥50%], mildly (RV-EF 40–49%), moderately (RV-EF 30–39%), or severely hypokinetic (RV-EF <30%). We previously demonstrated a statistically significant correlation between visually assessed RV function on echocardiography and RV-EF derived from CMR in our laboratory.[10] Tricuspid regurgitation was assessed echocardiographically and graded qualitatively by an experienced reader as mild (Grade 1), moderate (Grade 2), moderately severe (Grade 3), or severe (Grade 4). Right ventricular function was quantitatively assessed using CMR or radionuclide imaging in a subset ($n = 111$) of patients. The CMR and radionuclide methods used at our centre to assess the systemic RV have been previously described and a good correlation has been shown for ventricular EF by these two techniques with 95% limits of agreement within 16%.[10,11] QRS duration was measured in the widest complex on the ECG.

Outcomes

Arrhythmias were classified as atrial tachycardia or VT based on documentation from a 12-lead ECG or Holter monitor recording. Atrial tachycardia included atrial fibrillation, typical isthmus-dependent atrial flutter and other intra-atrial tachycardias. Atrial tachycardia was further divided into paroxysmal or persistent arrhythmias. Ventricular tachycardia was classified as non-sustained (three or more consecutive beats of ventricular origin, heart rate >100 b.p.m., lasting <30 s) or sustained (lasting >30 s). Sudden death was defined as an unexpected death due to cardiovascular collapse within 1 h of the initial symptoms. Cause of death was determined from hospital record review. An adverse arrhythmic event was defined as an episode of sustained VT or SD. Earlier outcomes for some of the patients in this series have been previously reported.[5,7,9,12]

Statistical analysis

Data were analysed using STATA 8.2 statistical software (Stata Corporation, College Station, TX, USA). Data are expressed as mean ± SD for normally distributed variables and as median with inter-quartile range (IQR) for non-normal data. The IQR indicates the lower and upper quartile of ordered observations and is essentially the range of the middle 50% of the data. It is a measure of variation of non-normally distributed data. Between-group comparisons were performed using a Student's *t*-test or a Mann–Whitney test for normally and non-normally distributed data, respectively. Between-group comparison of categorical data was performed using the Pearson χ^2 test or the Fisher's exact test as appropriate. Comparison of normally distributed data over multiple patient groups was done by an analysis-of-variance model followed by a Bonferroni correction. To depict the relationship between age, QRS duration, and systemic RV systolic function, patients were categorized into age-related quartiles. However, in the univariate analysis, age is presented as a continuous variable. Survival of patients was analysed using Kaplan–Meier curves. Survival curves were for calculated for the duration of follow-up at our centre (age at the last visit or age at death minus age at the first clinic visit). Follow-up time was defined as time in years after first presentation to the adult congenital cardiac clinic. Hazard ratios for univariate predictors of outcome were calculated with a Cox proportional hazard model for the duration of follow-up. Owing to the small number (<20) of outcome events (sustained VT and/or SD), no multivariate analysis was performed. Receiver operating characteristic (ROC) curve analysis was used to determine the optimal QRS duration to differentiate between patients with and without VT and/or SD. A *P*-value <0.05 was considered statistically significant.

Results

Patient characteristics

We identified 149 adult patients with regular clinical follow-up. Demographic and clinical data are shown in *Table 1*. Echocardiographic assessment was available for all patients and most patients had the study performed at the time of their last clinic visit (IQR 0–8 months). Quantitative assessment of systemic ventricular was available in 111 patients. Right ventricular-EF was calculated

Table 1 Patient characteristics

Characteristic	Overall n = 149
Female gender, n	52 (35%)
Body surface area (m^2)	1.8 ± 0.2
Mean age at first follow-up (year)	19 ± 2 (range 17–31)
Mean age at last follow-up (year)	28 ± 7 (range 18–53)
Mean duration of follow-up at the adult congenital clinic (year)	9 ± 6 (range 0–28)
Mean time since atrial repair (year)	26 ± 6 (range 13–41)
Documented baffle stenosis, n	16 (11%)
Surgical history	
Simple transposition, n	107 (72%)
Previous balloon atrial septostomy, n	122 (82%)
Previous surgical atrial septectomy, n	72 (48%)
Median age at atrial repair (year)	1.2, IQR 1.0–2.1
Re-intervention for haemodynamic residue, n[a]	15 (10%)
Arrhythmia history	
Atrial tachycardia, n	66 (44%)
Sustained ventricular tachycardia, n	7 (5%)
ICD-implantation, n	10 (7%)
Pacemaker implantation, n	35 (23%)
Functional class at last follow-up	
NYHA class I, n	113 (76%)
NYHA class II, n	22 (15%)
NYHA class III, n	8 (5%)
NYHA class IV, n	5 (3%)
Medication at last follow-up[b]	
ACE-inhibitors or angiotensin-receptor blockers, n	45 (30%)
Beta-blockers (excluding Sotalol), n	27 (18%)
Diuretics, n	7 (5%)
Digoxin, n	8 (5%)
Amiodarone, n	8 (5%)
Sotalol, n	5 (5%)
Systemic ventricular function	n = 111
RV ejection fraction ≥50%, n	25 (23%)
RV ejection fraction 40–49%, n	36 (32%)
RV ejection fraction 30–39%, n	32 (29%)
RV ejection fraction <30%, n	18 (16%)

ICD, implantable cardioverter-defibrillator; RV, right ventricular; NYHA, New York Heart Association.
[a]Re-intervention included percutaneous intervention for baffle stenosis/leak (n = 7), re-do surgery for baffle stenosis/leak (n = 6), surgical removal of an infected pacemaker lead and subsequent baffle reconstruction (n = 1), re-do surgery to close a residual VSD (n = 1).
[b]Medications are not mutually exclusive.

by magnetic resonance imaging in 81 patients (median time interval to the last follow-up or death was 9 months, IQR 0–24 months) and by radionuclide angiography in 30 patients (median time interval to last follow-up or death 19 months, IQR 10–34 months). In four non-survivors, no quantitative assessment of subaortic RV function was available.

Arrhythmias

Sustained VT was documented in seven (5%) patients. All episodes of sustained VT were documented on a 12-lead-ECG or on intraoperative ECG monitors. Sustained VT was more frequently documented in patients who were older (32 ± 6 vs. 28 ± 7 years, $P = 0.04$) and who had lower functional class (NYHA class ≥III, 71 vs. 6%, $P < 0.001$). Patients with sustained VT had lower subaortic RV-EF (20 ± 7 vs. 42 ± 10%, $P < 0.001$) and broader QRS complexes (170 ± 27 vs. 110 ± 25 ms, $P < 0.001$) compared with patients without sustained VT. In all but one patient with sustained VT, systemic RV-EF was <30%. Fifty-seven percent (four of seven) of the patients with sustained VT had complex TGA compared with 27% (38/142) of patients without sustained VT ($P = 0.09$).

Sixty-two (42%) patients had episodes of paroxysmal atrial tachyarrhythmias and four (3%) patients were in persistent atrial fibrillation. Patients with atrial tachyarrhythmia were older (30 ± 7 vs. 26 ± 6 years, $P < 0.001$), had lower RV-EF (39 ± 12 vs. 43 ± 11%, $P = 0.052$), and had more significant tricuspid regurgitation (more than moderate tricuspid regurgitation in 41 vs. 18%, $P = 0.002$) compared with patients without atrial tachyarrhythmias. Six of the 62 patients with atrial tachyarrhythmias also had sustained VT during follow-up.

In 35 patients, a pacemaker had been implanted at a mean age of 19 ± 10 years. Pacemakers were implanted for sick sinus syndrome in 23 patients, complete heart block in six patients and to permit medical therapy of atrial arrhythmias in six patients. Eight patients exhibited permanent ventricular pacing on the last available 12-lead-ECG. Ten patients had implantable cardioverter defibrillator (ICD) placement at a mean age of 30 ± 6 years. In seven patients, the ICD implantation was performed after an episode of VT. Three other ICDs were implanted prophylactically in patients with bradyarrhythmias (two with sick sinus syndrome and one with complete heart block) and severe systemic RV dysfunction.

Survival

In our clinical cohort, there were 13 deaths at a mean age 26 ± 7 years. The mean period of follow-up in our clinic was 9 ± 6 years. *Table 2* lists the clinical details pertaining to the cause of death. Of these, 11 were classified as cardiac-related deaths, including eight SD or deaths due to intractable VT. Two deaths were due to neurological events. After 10 and 20 years of follow-up and after transition of care to the adult clinic, 93% (95% CI 86–96%) and 73% (95% CI 48–87%) of patients were alive, respectively.

Right ventricular function

By quantitative measurement of resting systemic ventricular function, the oldest quartile of patients (age >32 years) had a significantly lower RV-EF compared with patients <28 years of age (*Table 3*). In the oldest quartile of patients with quantitative measurements of RV-EF, only two of thirty-three (6%) patients had normal RV-EF (≥50%). There was an association between depressed RV systolic function and increasing severity of tricuspid regurgitation (*Table 3*). Patients with lower functional capacity had lower subaortic RV-EF; RV-EF was 43 ± 10% in patients with

Table 2 Deaths during follow-up

No.	Complex TGA	Age at death (years)	RV function[a]	QRS duration (ms)[a]	Clinical notes
1	Yes	37	RV-EF 19%	180	Sudden death, heart failure
2	Yes	25	RV-EF 39%	170	Sudden death
3	No	29	RV-EF 21%	180	Sudden death, heart failure, coronary anomaly, previous myocardial infarction
4	No	18	Severe RV dysfunction on echo	140	Previous stroke, heart failure
5	Yes	18	Severe RV dysfunction on echo	220	Heart failure
6	No	24	RV-EF 42%	100	Status epilepticus
7	Yes	38	RV-EF 18%	140	Intractable VT after PA banding, heart failure, large baffle leak
8	Yes	35	RV-EF 23%	170	Sudden death
9	Yes	29	RV-EF 15%	170	Perioperative death (heart transplantation), heart failure
10	No	21	Severe RV dysfunction on echo	220	Intractable VT during ICD placement, heart failure
11	Yes	23	RV-EF 51%	120	Sudden death, heart failure, severe pulmonary hypertension
12	Yes	24	RV-EF 47%	—	Cerebral abscess
13	No	19	Mild RV dysfunction on echo	100	Sudden death, atrial fibrillation

ICD, implantable cardioverter-defibrillator; PA, pulmonary artery; VT, ventricular tachycardia; RV-EF, right ventricular ejection fraction.
[a]Assessment of RV function and QRS duration at last clinic visit prior death.

Table 3 Characteristics of the cohort by age-related quartiles

	Quartile 1 (age 18–23)	Quartile 2 (age >23–28)	Quartile 3 (age >28–32)	Quartile 4 (age >32–53)	*P*-value
Total, *n*	36	38	36	39	
QRS duration, ms (*n*)	114 ± 30 (36)	105 ± 20 (38)	110 ± 26 (35)	125 ± 32 (33)[†]	0.03
Supraventricular tachycardia, *n*	8 (22%)	14 (37%)	18 (50%)*	26 (67%)*[†]	
Degree of tricuspid regurgitation[a]	1.2 ± 0.6	1.3 ± 0.6	1.6 ± 0.8	1.5 ± 0.7	0.10
Grade of subaortic RV dysfunction[a]	1.7 ± 0.8	1.9 ± 0.5	2.2 ± 0.5[†]	2.1 ± 0.6	0.01
RV-ejection fraction, % (*n*)	45 ± 12 (17)	45 ± 9 (29)	40 ± 11 (32)	36 ± 12 (33)[†‡]	0.003

RV, right ventricular.
*$P < 0.05$ compared with Quartile 1.
[†]$P < 0.05$ compared with Quartile 2.
[‡]$P < 0.05$ compared with Quartile 3.
[a]Degree of tricuspid regurgitation and grade of RV dysfunction assessed echocardiographically.

NYHA class I ($n = 83$), 41 ± 13% in patients with NYHA class II ($n = 20$), and 23 ± 7% in patients with NYHA class III or IV ($n = 8$; $P < 0.001$ for NYHA class I vs. III/IV and for NYHA class II vs. III/IV). There was an inverse linear correlation between RV-EF and age [RV-EF (%) = 55 − 0.50 × age in years: $P = 0.001$; *Figure 1*], QRS duration and age [QRS duration (ms) = 92+0.74 × age; $P = 0.02$] at the time of assessment, and RV-EF and QRS duration [QRS duration = 157 ms − 1.1 × RV-EF (%); $P < 0.001$; *Figure 2*].

Risk factors for sustained ventricular tachycardia and/or sudden death

Sustained VT and/or SD occurred in 13 patients (9% of the cohort; five patients with sustained VT, two patients with intractable VT, six patients with SD). The Cox proportional hazard ratios for the predictors of sustained VT/SD during follow-up in a univariate analysis are shown in *Table 4*. Ventricular tachycardia/SD was more likely to occur in patients with later repair (median age at the time

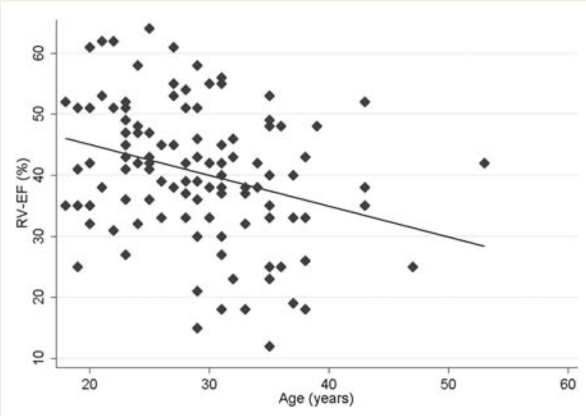

Figure 1 Inverse correlation between subaortic RV-ejection fraction (EF) and age at the time of quantitative assessment of systemic ventricular function [RV-EF (%) = 55 − 0.50 × age (years), *P* = 0.001].

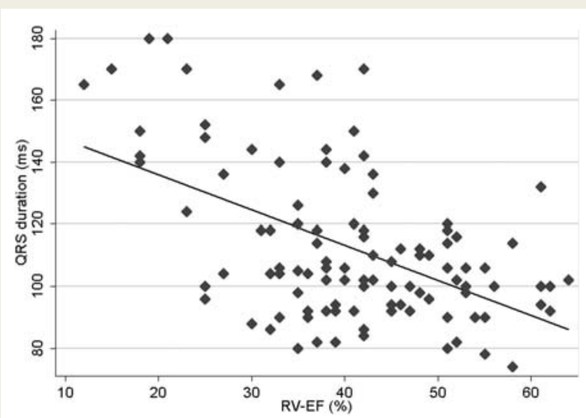

Figure 2 Inverse correlation between RV-ejection fraction (EF) and QRS duration (QRS duration = 157 ms—1.1 × RV-EF (%), *P* <0.001).

of operation 3.0, IQR 1.5–4.0 years vs. 1.2, IQR 0.9–2.0 years for patients without adverse event, *P* = 0.003), with complex transposition or with NYHA class ≥III. A history of atrial tachyarrhythmia was not a statistically significant predictor of an event in this population. Patients with more than moderate tricuspid regurgitation or more than moderately depressed RV function (measured by echocardiography) were more likely to have had a VT/SD. The mean RV-EF was lower in patients with events compared with those without (26 ± 13 vs. 42 ± 10%, *P* = 0.007).

Figure 3 depicts the QRS duration in individual patients with and without VT/SD. The maximal non-paced QRS duration was 165 ± 34 ms in the 13 patients with a serious arrhythmic event compared with 107 ± 21 ms in 128 event-free survivors (*P* <0.001). The ROC analysis showed that a QRS duration ≥140 ms had the best ability to differentiate between these two groups of patients with a sensitivity of 85% and specificity of 90%. The area under the ROC curve was 0.92 (95% CI 0.82–1.00). Eighteen percent (25/141) of patients without permanent ventricular pacing had a QRS duration ≥140 ms and 11 of these patients had an arrhythmic event during follow-up. Only 2 of 116 patients with QRS duration <140 ms had a serious arrhythmic event during follow-up (negative predictive value 98%).

Discussion

In this study, we have explored the changing clinical profile of aging patients with atrial switch procedures for complete TGA. We found that sustained VT/SD occurred in 9% of our cohort during a mean follow-up of 9 years after transition of care from the paediatric to the adult clinic. Subaortic RV systolic dysfunction was increasingly common in this aging population. Age, systemic ventricular function, and duration of the QRS complex were interrelated and all were associated with sustained VT/SD. Patients with a QRS duration ≥140 ms had a >10-fold risk for SD or sustained VT compared with those with QRS duration <140 ms.

Sustained VT is rarely observed during childhood after a Mustard or Senning operation. Gelatt *et al.*[7] observed non-sustained VT in only 14 of 482 children (3%) and there was no episode of sustained VT during a median follow-up period of 11.5 years. In another retrospective study comparing 47 children after an atrial switch procedure with SD events to 93 matched controls (same operation and no SD event), there was only one documentation of a VT prior to the event in the entire cohort.[8] The mean age at the SD event was 12 years with an average post-surgery interval of 11 years. Previously recorded Holter ECGs in 66 of 140 children did not show any VT. By comparison, in our adult TGA population, 5% of patients had sustained VT.

The reported incidence of systemic ventricular dysfunction in patients with atrial switch operations for TGA has varied from 10 to 61%.[7,13–15] The large variation in reported RV function may partly be attributed differing ages between study populations and differences in imaging modalities used to assess systemic ventricular function. Relying on quantitative RV function measurement, we observed a steady decline in RV-EF as our patients grew older. This decline was more evident in patients over age 30 years. There was a large variation in RV-EF for any given age, but RV-EF was severely reduced in one-third and normal in <10% of the oldest quartile of our patients (i.e. patients >32 years). This observation is in keeping with a study from the Netherlands, assessing RV function by echocardiography 14 and 25 years after a Mustard procedure.[15] Sixty-one percent of patients showed moderate-to-severe RV dysfunction 25 years after surgery, although all patients had good RV function 11 years earlier. Our findings support the concern that RV systolic performance will be a major factor for the aging TGA patient following an atrial switch operation.

Previously identified risk factors for death in survivors (>30 days) of an atrial switch operation include cardiac morphology (i.e. complex TGA),[16,17] surgery in an earlier decade,[7,15] operative period arrhythmias,[7] a history of supraventricular arrhythmias during follow-up,[8,18] and advanced NYHA functional class.[8,18,19] These risk factors were derived predominantly from paediatric cohorts. Similar to this study, SD was the predominant mode of late death with an incidence of ≈0.5%/year. As reported in prior

Table 4 Univariate Cox regression hazard ratios for serious arrhythmic advents

	Sustained VT/SD		Hazard ratio (95% CI)	P-value
	Yes (n = 13)	No (n = 136)		
Medical history				
Complex TGA (n = 42), n	8 (62%)	34 (25%)	4.9 (1.5–16.0)	0.008
NYHA class ≥III (n = 13), n	8 (62%)	5 (4%)	9.8 (3.0–31.6)	<0.001
Atrial tachycardia (n = 66), n	11 (85)%	55 (40%)	2.7 (0.6–13.0)	0.21
Cardiac imaging				
≥Moderate tricuspid regurgitation (n = 42), n	10 (77%)	32 (24%)	5.4 (1.5–20.0)	0.01
RV-ejection fraction decrease/10%			2.2 (1.2–4.0)	0.01
>Moderate RV dysfunction assessed echocardiographically (n = 34), n	8 (62%)	26 (20%)	3.6 (1.1–11.2)	0.03
Electrocardiographic features				
QRS duration ≥140 ms (n = 25), n	11 (85%)	14 (10%)	13.6 (2.9–63.4)	<0.001
Per 10 ms increase in QRS duration			1.3 (1.1–1.5)	<0.001

TGA, transposition of the great arteries, NYHA, New York Heart Association, RV, right ventricular.

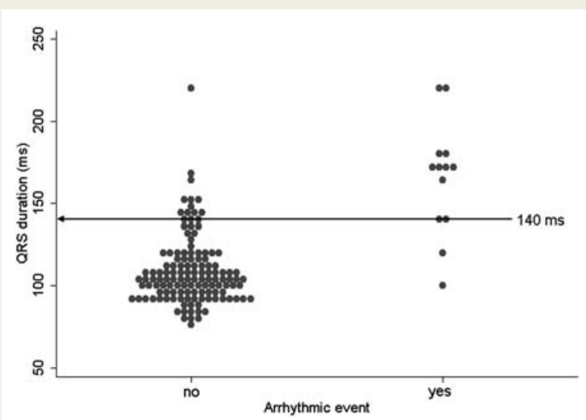

Figure 3 The QRS duration in patients with (n = 13) and without (n = 128) serious arrhythmic event (sustained VT and/or SD).

studies, we also frequently observed atrial tachyarrhythmias in patients with sustained VT/SD, but this association did not reach statistical significance. Our findings suggest that with increasing age, atrial arrhythmias may be less predictive of SD than systemic RV dysfunction and a broad QRS complex. In paediatric series, significant RV systolic dysfunction and/or broad QRS complexes are probably too uncommon to allow for recognition as markers of an adverse outcomes. For instance, in the study of Kammeraad *et al.*,[8] RV systolic function was severely impaired in five (26%) SD cases and one (3%) control, whereas in our study all but one patient with sustained VT had a systemic RV-EF <30%. Similarly, QRS duration was 99 and 94 ms in paediatric patients with and without SD, whereas our adult patients with adverse arrhythmic events had a QRS duration of 165 ms compared with 108 ms in adults without event. In addition, adults with a TGA and atrial switch operations can be considered a selected group of 'paediatric survivors' and may therefore have a different clinical profile and attrition rate compared with the original paediatric patient cohort. Hence, predictors of an adverse outcome may vary not just as a function of time between adult and paediatric TGA patients but also due to a selection bias.

In patients with acquired heart disease and left heart dysfunction, prolongation of the QRS due to left-sided intraventricular conduction delay is associated with lower functional NYHA class, worse left ventricular function and higher mortality rates.[20,21] Prolongation of QRS and severely decreased left ventricular function secondary to ischaemic and non-ischaemic events have an additive effect on mortality.[22] In our patients, QRS duration ≥140 ms was associated with lower functional NYHA class, worse subaortic RV function and higher mortality, and may be an equally important prognostic marker as it is in left-sided heart failure. Increasing QRS duration in adult TGA patients correlates with the extent of late gadolinium enhancement on CMR,[23] and with the decline in RV function and functional capacity over time.[15] It is unknown, if QRS duration in the setting of a failing systemic RV is associated with mechanical RV dyssynchrony or if there would be a favourable response to cardiac resynchronization therapy in this population. Finally, the indications for ICD implantation in adult patients with TGA and subaortic RV dysfunction are not known. Other issues, such as the complexities and risks associated with lead placement to achieve adequate defibrillation thresholds need to be factored into decision making.[24]

Limitations

Because our centre is a regional referral centre, the population may represent a more complex group of patients compared with those followed at local or regional centres. Thus, the prevalence of VT/SD could be overestimated. By exclusively studying late outcome in adult TGA patients previously followed at our local regional paediatric centre, we intended to minimize the referral bias of complex adult patients referred to us from other centres.

Overall, the prevalence of patients with simple TGA[1,2] or QRS duration in our TGA patients were comparable to prior studies.[15,25] Alternatively, the prevalence of SD could be underestimated, if the lost to follow-up cohort of patients are simply non-survivors (having suffered VT or SD). Difference in definition of SD could also affect the prevalence estimates as well as the predictors of outcome. Thus, systematic follow-up of this population may help to detect earlier structural or electrophysiological problems, initiate earlier decision making for interventions and perhaps result in better outcomes.

One of the most consistent reported markers of VT/SD in paediatric patients is atrial tachycardia.[7,8] The small number of events (VT/SD) remains a limitation of this study. We cannot exclude the possibility that our study was underpowered to identify this association in the adult population. The increasing prevalence of atrial arrhythmias as patients age post-repair may reduce its predictive value for the adverse events studied in our paper. Furthermore, because only adult patients were included in this study, there exists a potential selection bias. Children who had died were not included in this cohort. Nonetheless, this bias is unlikely to significantly change the impact of our findings that provide insight into the clinical features associated with VT/SD in adult patients after Mustard operations.

Our routine clinical surveillance does not always include Holter monitoring and therefore we were unable to reliably assess the prevalence of non-sustained VT. Because of missing data, we were not able to analyse serial changes in RV-EF or QRS duration in the same patient over several years. Further studies may be necessary to determinate, if the rate of changes in RV function and QRS duration over time is more predictive of an adverse event.

Conclusions

Sustained VT/SD occurred in 9% of our adult cohort of patients with TGA and a Mustard operation. Age, systemic ventricular function, and duration of the QRS complex were interrelated and these factors were associated with sustained VT and/or SD. These variables can be used to help identify the high-risk patient.

Funding

This work was supported by a grant from the Swiss National Science Foundation, Bern, Switzerland (M.S.) and a grant from the Heart and Stroke Foundation of Ontario, Canada (C.K.S.).

Conflict of interest: none declared.

References

1. Ferencz C, Rubin JD, McCarter RJ, Brenner JI, Neill CA, Perry LW, Hepner SI, Downing JW. Congenital heart disease: prevalence at livebirth. The Baltimore-Washington Infant Study. *Am J Epidemiol* 1985;**121**:31–36.
2. Grabitz RG, Joffres MR, Collins-Nakai RL. Congenital heart disease: incidence in the first year of life. The Alberta Heritage Pediatric Cardiology Program. *Am J Epidemiol* 1988;**128**:381–388.
3. Senning A. Surgical correction of transposition of the great vessels. *Surgery* 1959; **45**:966–980.
4. Mustard WT. Successful two-stage correction of transposition of the great vessels. *Surgery* 1964;**55**:469–472.
5. Oechslin E, Jenni R. 40 years after the first atrial switch procedure in patients with transposition of the great arteries: long-term results in Toronto and Zurich. *Thorac Cardiovasc Surg* 2000;**48**:233–237.
6. Warnes CA. Transposition of the great arteries. *Circulation* 2006;**114**:2699–2709.
7. Gelatt M, Hamilton RM, McCrindle BW, Connelly M, Davis A, Harris L, Gow RM, Williams WG, Trusler GA, Freedom RM. Arrhythmia and mortality after the Mustard procedure: a 30-year single-center experience. *J Am Coll Cardiol* 1997; **29**:194–201.
8. Kammeraad JA, van Deurzen CH, Sreeram N, Bink-Boelkens MT, Ottenkamp J, Helbing WA, Lam J, Sobotka-Plojhar MA, Daniels O, Balaji S. Predictors of sudden cardiac death after Mustard or Senning repair for transposition of the great arteries. *J Am Coll Cardiol* 2004;**44**:1095–1102.
9. Puley G, Siu S, Connelly M, Harrison D, Webb G, Williams WG, Harris L. Arrhythmia and survival in patients >18 years of age after the mustard procedure for complete transposition of the great arteries. *Am J Cardiol* 1999;**83**:1080–1084.
10. Salehian O, Schwerzmann M, Merchant N, Webb GD, Siu SC, Therrien J. Assessment of systemic right ventricular function in patients with transposition of the great arteries using the myocardial performance index: comparison with cardiac magnetic resonance imaging. *Circulation* 2004;**110**:3229–3233.
11. Hornung TS, Anagnostopoulos C, Bhardwaj P, Kilner PJ, Davlouros PA, Bailey J, Francis JM, Pennell DJ, Underwood SR, Gatzoulis MA. Comparison of equilibrium radionuclide ventriculography with cardiovascular magnetic resonance for assessing the systemic right ventricle after Mustard or Senning procedures for complete transposition of the great arteries. *Am J Cardiol* 2003;**92**:640–643.
12. Gatzoulis MA, Walters J, McLaughlin PR, Merchant N, Webb GD, Liu P. Late arrhythmia in adults with the mustard procedure for transposition of great arteries: a surrogate marker for right ventricular dysfunction? *Heart* 2000;**84**:409–415.
13. Hurwitz RA, Caldwell RL, Girod DA, Brown J. Right ventricular systolic function in adolescents and young adults after Mustard operation for transposition of the great arteries. *Am J Cardiol* 1996;**77**:294–297.
14. Wilson NJ, Clarkson PM, Barratt-Boyes BG, Calder AL, Whitlock RM, Easthope RN, Neutze JM. Long-term outcome after the mustard repair for simple transposition of the great arteries. 28-year follow-up. *J Am Coll Cardiol* 1998;**32**:758–765.
15. Roos-Hesselink JW, Meijboom FJ, Spitaels SE, van Domburg R, van Rijen EH, Utens EM, McGhie J, Bos E, Bogers AJ, Simoons ML. Decline in ventricular function and clinical condition after Mustard repair for transposition of the great arteries (a prospective study of 22–29 years). *Eur Heart J* 2004;**25**:1264–1270.
16. Williams WG, McCrindle BW, Ashburn DA, Jonas RA, Mavroudis C, Blackstone EH. Outcomes of 829 neonates with complete transposition of the great arteries 12–17 years after repair. *Eur J Cardiothorac Surg* 2003;**24**:1–9.
17. Lange R, Horer J, Kostolny M, Cleuziou J, Vogt M, Busch R, Holper K, Meisner H, Hess J, Schreiber C. Presence of a ventricular septal defect and the Mustard operation are risk factors for late mortality after the atrial switch operation: thirty years of follow-up in 417 patients at a single center. *Circulation* 2006;**114**: 1905–1913.
18. Dos L, Teruel L, Ferreira IJ, Rodriguez-Larrea J, Miro L, Girona J, Albert DC, Goncalves A, Murtra M, Casaldaliga J. Late outcome of Senning and Mustard procedures for correction of transposition of the great arteries. *Heart* 2005;**91**:652–656.
19. Sarkar D, Bull C, Yates R, Wright D, Cullen S, Gewillig M, Clayton R, Tunstill A, Deanfield J. Comparison of long-term outcomes of atrial repair of simple transposition with implications for a late arterial switch strategy. *Circulation* 1999; **100**:II176–II181.
20. Murkofsky RL, Dangas G, Diamond JA, Mehta D, Schaffer A, Ambrose JA. A prolonged QRS duration on surface electrocardiogram is a specific indicator of left ventricular dysfunction. *J Am Coll Cardiol* 1998;**32**:476–482.
21. Sandhu R, Bahler RC. Prevalence of QRS prolongation in a community hospital cohort of patients with heart failure and its relation to left ventricular systolic dysfunction. *Am J Cardiol* 2004;**93**:244–246.
22. Horwich T, Lee S-J, Saxon L. Usefulness of QRS prolongation in predicting risk of inducible monomorphic ventricular tachycardia in patients referred for electrophysiologic studies. *Am J Cardiol* 2003;**92**:804–809.
23. Babu-Narayan SV, Goktekin O, Moon JC, Broberg CS, Pantely GA, Pennell DJ, Gatzoulis MA, Kilner PJ. Late gadolinium enhancement cardiovascular magnetic resonance of the systemic right ventricle in adults with previous atrial redirection surgery for transposition of the great arteries. *Circulation* 2005;**111**:2091–2098.
24. Michael KA, Veldtman GR, Paisey JR, Yue AM, Robinson S, Allen S, Sunni NS, Kiesewetter C, Salmon T, Roberts PR, Morgan JM. Cardiac defibrillation therapy for at risk patients with systemic right ventricular dysfunction secondary to atrial redirection surgery for dextro-transposition of the great arteries. *Europace* 2007;**9**:281–284.
25. Neffke JG, Tulevskill, van der Wall EE, Wilde AA, van Veldhuisen DJ, Dodge-Khatami A, Mulder BJ. ECG determinants in adult patients with chronic right ventricular pressure overload caused by congenital heart disease: relation with plasma neurohormones and MRI parameters. *Heart* 2002;**88**:266–270.