Clinical Research

Risk Factors for QRS Prolongation After Repaired Tetralogy of Fallot

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Introduction: Repaired tetralogy of Fallot is usually conducive to a normal and unrestricted lifestyle. However, occasionally, late sudden death occurs due to ventricular tachycardia. This is thought to be due to a combination of factors, including both left and right ventricular dilation, which may be associated with valvular incompetence and residual right ventricular outflow tract obstruction. Several studies have shown that QRS duration >180 ms is a predictor for life-threatening ventricular arrhythmias.

Methods and Results: We recalled our tetralogy population (n=57) to identify risk factors for prolonged QRS duration on the resting ECG. Factors examined included history, demographics, symptoms, surgery, chest X-ray, ECG and echocardiography. Extensive analysis found only a significant positive correlation between QRS duration and degree of residual right ventricular outflow tract obstruction.

Conclusions: Our study suggests that residual right ventricular outflow tract gradients may be a very significant contributor to QRS prolongation. It will be interesting to see if future studies of larger cohorts confirm this finding.

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Most individuals who have had previous repair of tetralogy of Fallot are asymptomatic and lead normal and unrestricted lives. However, right ventricular wall motion abnormalities are common late after tetralogy repair.[1] In addition, residual right ventricular outflow tract incompetence and/or obstruction may cause progressive dilatation of the right ventricle, with dysfunction and a propensity for arrhythmias. Indeed, tetralogy of Fallot is known to be associated with sudden death due to ventricular tachycardia late after complete repair, and factors leading to such arrhythmias include ventricular hypertrophy and/or dilatation, both of which may lead to fibrosis. Myocardial scarring may also occur due to ventriculotomies, coronary artery damage and inadequate myocardial preservation during surgery.[2]

Haemodynamic causes for any tachyarrhythmias should be sought and corrected, and therapy directed towards suppressing the arrhythmia. Treatment strategies include antiarrhythmics, cryoablation, implantable defibrillators and surgical or catheter interventional techniques to alleviate right ventricular outflow tract stenosis or incompetence.[3] Recent changes in the surgical approaches to the repair of the tetralogy at the time of the initial repair may well translate into a reduced incidence of late complications.[4]

Several studies over the past decade, most notably by Gatzoulis et al, have identified risk factors for these events, and one of the most important risk factors appears to be right ventricular dilatation due to surgically induced pulmonary regurgitation. There are several predictors for ventricular arrhythmias after tetralogy repair, but to date QRS duration ≥180 ms on a resting ECG appears to be a highly sensitive predictor of life-threatening ventricular arrhythmias.[5-9] Electrocardiography is a relatively short, cheap and non-invasive investigation that is usually readily available in the outpatient setting.

In this study, we recalled all known surviving Maltese patients with tetralogy of Fallot and attempted to identify risk factors for prolonged QRS duration on the resting ECG.

Methods

All patients with tetralogy of Fallot were identified from the Maltese Paediatric Cardiology Database.[10] Only those patients who had had complete repair of this condition more than one year previous to the study were recalled. Forty-three were lost to follow-up.

Recalled patients were asked to complete a questionnaire. Information collected included demographics, date of birth, symptoms (palpitations, chest pain and syncope) and New York Heart Association class. The following information was obtained from the case notes: whether a shunt was undertaken prior to complete repair, and date shunted; date of total repair; perioperative details, including whether or not the following procedures were undertaken: transannular patch, pulmonary valvotomy, pulmonary ventriculotomy, pulmonary valve excision and pulmonary valve replacement. A standard 12-lead ECG was recorded and the following were identified: presence of sinus rhythm, right bundle branch block and maximum QRS duration. The precautions previously described by Gatzoulis et al were taken.[11] A chest X-ray was obtained and the cardiothoracic ratio was measured.

An echocardiographic examination was also performed and the following were measured: presence and degree of tricuspid regurgitation (graded by distance of jet into the right atrium and base of jet: mild only up to mid right atrium, moderate up the posterior of the atrium and severe extending back to the hepatic veins or inferior vena cava) with measurement of gradient; peak right ventricular outflow tract velocity with continuous wave Doppler; pulmonary regurgitation, graded by presence of retrograde flow detected under the valve only on pulsed-wave Doppler, or further back into the ventricle with retrograde flow also detectable in the pulmonary trunk, or even more severe regurgitation further back into the ventricle with retrograde flow also detectable in the branch pulmonary arteries; the presence or absence of forward diastolic flow in the pulmonary arteries on pulsed wave Doppler; and left and right ventricular dimensions on M-mode Doppler with ECG timing, along with left ventricular septal and posterior wall dimensions in diastole. Chamber dimensions were translated to Z values via reference graphs from a standard text.[12] The ECG was interpreted by one of the authors (OA) who was blind to all other information pertaining to patients.

Several statistical tests were employed: the Pearson test was used for correlations, the two-tailed t-test was used to compare means of two different populations, analysis of variance was used to compare means of more than two different populations after assigning z-values to chamber and wall dimensions, and the Mann-Whitney U test (nonparametric) was used to compare ranks. A p value <0.05 was considered a statistically significant result.

Results

Fifty-seven individuals were recalled and were assessed as described above. Year of birth ranged from 1946-1999 (mean 1983, median 1987). Only two individuals had QRS duration $\geq$180 ms. None of the cohort complained of any symptoms whatsoever, including palpitations, pain and syncope, and all had normal New York Heart Association scores for exercise.

Perusal of the data revealed that surgical strategies varied with time, with application of new techniques to Maltese patients soon after such techniques were first described.[13] In tetralogy of Fallot, the first operation for the early patients in the series was invariably a shunt procedure. The first classical Blalock-Taussig shunt to augment pulmonary blood supply on a Maltese patient with tetralogy of Fallot was carried out in 1953, eight years after the first report of a successful shunt.[14] The change to a modified Blalock-Taussig shunt, rather than a classical Blalock-Taussig shunt, in the event of shunt being needed prior to total repair came about in the early 1980s. The first total correction was carried out in 1959, four years after the first report of a successful correction.[15] Primary repair became the preferred mode of treatment in the mid-1970s and in 1980, the first transannular patch was undertaken. The first complete transatrial repair was carried out in 1990, and since that period virtually all Fallot repairs have been performed without a right ventriculotomy. To date, all of the above operations have been carried out in tertiary referral centres in the United Kingdom.

A shunt was initially performed in 12 patients at a mean age of 10 months, primary repair was undertaken at a mean of 58 months in those who had had a previous shunt, while the delay to complete repair was longer at 66 months in those individuals who did not have a prior shunt (p=NS). Pulmonary valve replacement was performed in four patients, two at primary repair and

two later at redo tetralogy repair for residual right ventricular outflow tract obstruction.

In the demographic and historical data, there was no significant correlation between QRS duration and year of birth, delay to shunt in those who had a shunt prior to complete repair, time since complete repair, year of complete repair, delay to complete repair, presence of a transannular patch, pulmonary valvotomy, right ventriculotomy or valvectomy (Table 1). However, a longer QRS duration was found in those who had had pulmonary valve replacement (n=4, mean=152.0 ms) as opposed to those who did not (n=53, mean=131.3 ms, p=0.02).

Mean QRS duration was higher (though not statistically significantly) in the group that had not had shunt prior to complete repair than in the group that had had a previous shunt (Table 2).

There was no significant correlation between QRS duration and cardiothoracic ratio on chest X-ray. Similarly, there was no correlation with degree of pulmonary (5=none, 18=mild, 11=moderate, 23=severe) or tricuspid regurgitation (11=none, 38=mild, 8=moderate, 0=severe), right and left ventricular dimensions, tricuspid regurgitation gradient or pulmonary valve diastolic flow. The right ventricular diastolic dimension was elevated in all but two patients. There was no significant association of QRS duration with any chamber or wall dimensions.

Table 1. Correlation of historical and investigational data with QRS duration.

Demographics	r	p
Delay (age) to shunt (n=12, mean delay to shunt=10 months)	-0.480	0.110
Year of total repair (1953 to date)	-0.060	0.630
Delay (age) to total repair Prior shunt, delay=58 months. Primary repair, delay=66 months	-0.100	0.450
Time since total repair (mean 13.9, median 12.5, min 2.5, max 39.6 years)	0.141	0.296
At complete repair	**t**	**p (2-tail)**
Transannular patch performed (n=27)	0.24	0.80
Pulmonary valvotomy performed (n=8)	0.68	0.51
Right ventriculotomy performed (n=19)	-1.17	0.25
Pulmonary valve excision performed (n=7)	0.69	0.51
Pulmonary valve replacement performed (n=4)	3.0	0.02
Chest X-ray	**r**	**p**
Cardiothoracic ratio (mean 0.52, SD=0.06)	-0.100	0.440
Echocardiography	**f**	**p**
Degree of tricuspid regurgitation (11=none, 38=mild, 8=mod, 0=severe)	2.29	0.11
Degree of pulmonary regurgitation (5=none, 18=mild, 11=mod, 23=severe)	0.20	0.90
Pulmonary valvar diastolic flow	0.050	0.717
	r	**p**
Right ventricular outflow tract gradient	0.33	0.013
Tricuspid regurgitation gradient	0.018	0.902
	f	**p**
Left ventricular diastolic dimension	0.85	0.43
Left ventricular systolic dimension	0.28	0.75
Left ventricular posterior wall	0.58	0.56
	t	**p (2-tail)**
Interventricular septum*	1.5	0.15

*T-test used as only 2 values were below the 5th centile.

Table 2. Comparison of shunted with unshunted group

	Statistic	p	Shunted (n=12)		Unshunted (n=45)	
Mean delay to total repair	t=–0.42	0.68	58 months		66 months	
Mean QRS duration	t=–1.81	p=0.09	120.8 ms		136.4 ms	
Transannular patch	chi=1.4	0.24	Yes n=8	No n=4	Yes n=19	No n=26
Pulmonary valvotomy	–	1 (Fisher's test)	Yes n=1	No n=11	Yes n=7	No n=38
Right ventriculotomy	–	1 (Fisher's test)	Yes n=4	No n=8	Yes n=15	No n=30
Pulmonary valve excision	–	0.63 (Fisher's test)	Yes n=2	No n=10	Yes n=5	No n=40
Pulmonary valve replacement	–	0.28 (Fisher's test)	Yes n=2	No n=10	Yes n=2	No n=43
Cardiothoracic ratio	t=–0.22	0.82	Mean	0.52	Mean	0.52
Presence of right bundle branch block	–	0.22 (Fisher's test)	Yes n=8	No n=4	Yes n=37	No n=6
Tricuspid regurgitation gradient	t=–1.1	0.29				
Degree of tricuspid regurgitation			4=none, 6=mild, 2=moderate		7=none, 32=mild, 6=moderate	
Degree of pulmonary regurgitation	t=–0.78	0.44	1=none, 4=mild, 4=moderate, 3=severe		4=none, 14=mild, 7=moderate, 20=severe	

A significant positive correlation was found between continuous wave forward flow Doppler of the right ventricular outflow tract and QRS duration (mean gradient 22.8 mmHg, median 19.5 mmHg, range 4-83 mmHg; r=0.33, p=0.013).

The shunt group was compared with the group that did not have shunt prior to surgery (Table 2). No significant difference could be found between the two groups. Specifically, there was no statistically significant difference in pulmonary regurgitation between the two groups (Mann-Whitney U test: p=0.1).

Discussion

This paper is limited by the relatively small number of patients involved and by the inhomogeneous study population, resulting from the different surgical eras and medical and surgical techniques over the relatively long span of time reviewed by the paper (1950s to date). Forty percent of our tetralogy population have been lost to follow-up and all of the remainder report excellent subjective exercise tolerance (NYHA questionnaire class 1 – exercise testing was not undertaken). This may be an indicator of attrition due to sudden death with automatic selection of 'good patients'. However, this factor is unlikely to account for a substantial number of deaths, since the remainder include a significant number of patients with right ventricular dilatation, a known risk factor for tachycardias.

In the majority of cases, the mechanism of sustained ventricular tachycardia late after tetralogy repair is a macro-reentry. QRS prolongation (along with QT and JT dispersion) are signs of depolarisation and repolarisation abnormalities that are related to the altered mechanical properties of the right ventricle in repaired tetralogy.[11]

The lack of correlation between pulmonary regurgitation and QRS duration in this study may be due to the relatively small numbers involved. Right ventricular dysfunction is also known to be caused by right ventricular outflow tract obstruction,[3] and may in turn also prolong QRS duration, as we found in our cohort.

In this study, pulmonary valve replacement was shown to predispose to QRS prolongation and this may be due to a variety of factors. These include perioperative factors that necessitate the insertion of a replacement valve, such as a small pulmonary valve root that may, in some cases, almost lead to functional pulmonary atresia. The replacement of the pulmonary valve in this setting usually necessitates the insertion of a transannular patch in order to widen an excessively small pulmonary root, a factor that in itself is known to predispose to pulmonary regurgitation. Postoperative factors that may lead to prolongation of the QRS in this setting include valve deterioration with stenosis and/or regurgitation.[16]

In other studies, we have shown that in Malta, as in other developed countries, there has been a declining age at presentation for all congenital heart disease lesions,[17] and that this has been associated with a declining age at diagnosis for all such conditions.[18] Such trends are associated with earlier age at intervention and declining mortality for all conditions,[13] including tetralogy of Fallot.[19]

It has been shown that Blalock-Taussig shunt insertion prior to corrective surgery predisposes to cardiorespiratory dysfunction.[20] This study – perhaps due to the small size of the sample population – failed to demonstrate shunt insertion prior to complete repair as a risk factor for QRS widening.

The conventional treatment strategy appears to be complete repair for children with tetralogy of Fallot who are symptomatic, with moderate or severe cyanosis or cyanotic spells, if the infant is large enough. This latter factor depends on the individual surgeon and centre, and if the infant is deemed too small, a shunt is inserted to tide the child over until complete repair is carried out. The conventional approach is to wait until the child begins to outgrow the shunt, usually after 2-4 years depending on the growth rate, and when cyanosis begins to worsen, to elect for complete repair.

Our study suggests that residual right ventricular outflow tract gradients may be very significant contributors to QRS prolongation. It will be interesting to see if future studies confirm this finding.

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