Life threatening ventricular tachycardias in late survivors of surgically corrected tetralogy of Fallot

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SUMMARY Electrophysiological tests were performed in three patients with surgically corrected tetralogy of Fallot (mean age at evaluation 25 years, mean age at surgical correction 4 years) who had had either a cardiac arrest or transient neurological disturbances (presyncope, syncope) associated with ventricular arrhythmias. All three patients had an excellent haemodynamic result from surgery as judged by echocardiography and cardiac catheterisation. Ambulatory electrocardiographic monitoring and stress exercise testing were normal in two patients and showed complex ventricular ectopy in one. During invasive electrophysiological evaluation all three patients had inducible ventricular tachycardia (monomorphic QRS in two patients, cycle lengths 230 and 240 ms; polymorphic QRS in one patient, mean cycle length 200 ms) with adverse haemodynamic effects in all three patients.

These findings suggest that rapid ventricular tachycardia with detrimental haemodynamic consequences, similar to that induced during laboratory study, was the basis for the presenting symptoms in each patient. This possibility was confirmed in one patient who had identical QRS morphology during both spontaneous ventricular tachycardia and that induced during the laboratory study. Thus sudden death or symptoms of syncope postoperatively in patients with surgically corrected tetralogy of Fallot appear to be due to rapid ventricular tachycardia, which may occur despite an apparently excellent surgical result.

Sudden death has been reported in 1–4% of patients followed for a decade or more after corrective surgery for tetralogy of Fallot.1–3 Two principal mechanisms of sudden death have been suggested in this group of patients: (a) progressive abnormalities of the atrioventricular conduction system4 and (b) ventricular tachyarrhythmias.5 Although the principal cause of sudden death in these patients has not been established, several risk factors have been identified, including the presence of postoperative right bundle branch block and left axis deviation; residual ventricular septal defect or right ventricular hypertension1 2 6; the presence of ventricular ectopy at rest or during stress exercise testing2 5 6; and older age at operation.3 5

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In patients with surgically corrected tetralogy of Fallot, spontaneous ventricular arrhythmias occur during ambulatory electrocardiographic monitoring and stress exercise testing in 20–40% of patients.5–9 In addition, recent studies using programmed electrical stimulation have shown inducible ventricular tachycardia in patients with surgically corrected tetralogy of Fallot, both with10 11 and without12 spontaneous ventricular tachycardia. These findings5–12 have been interpreted as supporting the view that late sudden death after correction of tetralogy of Fallot may result from ventricular tachyarrhythmias. To date, however, it has not been possible to confirm this view since neither electrocardiographic evidence during spontaneous cardiac arrest nor electrophysiological evaluation of a surgical survivor resuscitated after cardiac arrest has been reported.

In this study we evaluated electrophysiologically a late survivor of surgery for tetralogy of Fallot who was resuscitated after cardiac arrest. We also studied two other patients with syncope and presyncope. All three
Life threatening tachycardias in tetralogy of Fallot

patients had excellent haemodynamic results after surgery for tetralogy of Fallot performed approximately 20 years before the appearance of symptoms due to ventricular tachycardia.

Patients and methods

CLINICAL DATA
Three patients (two men, one woman, aged 28, 22, and 25 years) who had had surgical correction of tetralogy of Fallot at ages 3, 4½, and 4 years were referred for evaluation after cardiac arrest or transient neurological disturbances (presyncope, syncope) associated with ventricular arrhythmias. No patient was taking cardioactive medication when the symptoms from the arrhythmias occurred.

One patient (case 1) had presyncope associated with documented episodes of ventricular tachycardia requiring cardioversion (Fig. 1). One (case 2) had experienced an episode of syncope; he had also had a 10 year history of palpitation. The third patient (case 3) had collapsed at her secretarial job; immediate cardiopulmonary resuscitation was performed, and ventricular fibrillation was evident before successful direct current cardioversion. Retrospectively, she had been aware of palpitation and light headedness for several minutes before collapse.

None of the patients had symptoms of exercise intolerance or congestive heart failure before the development of symptoms. All patients had considered themselves to be in a normal state of health before the appearance of the symptoms.

SURGICAL HISTORY
No patient had undergone a previous palliative operation (for example, systemic to pulmonary artery anastomosis). The original surgical reports were reviewed in all three patients. The surgical procedure for correction of tetralogy of Fallot was similar in each patient and used cardiopulmonary bypass with right ventriculotomy for patch closure of ventricular septal defect and resection of right ventricular infundibular hypertrophy. Two patients (cases 2 and 3) had transannular patches for the relief of severe valvular pulmonary stenosis. One patient (case 2) underwent surgical revision of his right ventricular outflow tract four and six years after his initial corrective operation.

CURRENT HAEMODYNAMIC STATUS
Chest radiographs were normal in one patient and showed mild cardiomegaly in two. Echocardiography suggested an excellent surgical result, showing a mildly enlarged right ventricle but normal left ventricular size and function in the three patients. On the
Dunnigan, Pritzker, Benditt, Benson

Table 1 Results of electrocardiography and electrophysiological testing of three late survivors of repair of tetralogy of Fallot

<table>
<thead>
<tr>
<th>Case Nos</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at symptoms (yr)</td>
<td>28</td>
<td>22</td>
<td>25</td>
</tr>
<tr>
<td>12 lead ECG Ambulatory monitoring</td>
<td>SR, RBBB VE, AE</td>
<td>SR, RBBB Couplets, multimorphic VE</td>
<td>SR, RBBB (left axis) No arrhythmias</td>
</tr>
<tr>
<td>Exercise testing: Arrhythmias</td>
<td>Normal</td>
<td>VE diminished but not suppressed</td>
<td>Normal</td>
</tr>
<tr>
<td>Time (mins)</td>
<td>12</td>
<td>12</td>
<td>6-6</td>
</tr>
<tr>
<td>Peak heart rate (beats/min)</td>
<td>193</td>
<td>156</td>
<td>163</td>
</tr>
<tr>
<td>Sinus cycle length (ms)</td>
<td>1040</td>
<td>875</td>
<td>705</td>
</tr>
<tr>
<td>Conduction intervals (ms): PA</td>
<td>55</td>
<td>35</td>
<td>40</td>
</tr>
<tr>
<td>AH</td>
<td>40</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>HV</td>
<td>40</td>
<td>65</td>
<td>58</td>
</tr>
<tr>
<td>Atrioventricular conduction (ms)*: Effective refractory period</td>
<td>420</td>
<td>420</td>
<td>350</td>
</tr>
<tr>
<td>Functional refractory period</td>
<td>510</td>
<td>600</td>
<td>435</td>
</tr>
<tr>
<td>Shortest CL with 1:1 atrioventricular conduction</td>
<td>400</td>
<td>500</td>
<td>280</td>
</tr>
<tr>
<td>Induced ventricular tachycardia (extrastimuli†)</td>
<td>S2S3S4</td>
<td>S2S3S4</td>
<td>S2S3</td>
</tr>
</tbody>
</table>

*Pacing cycle length (CL) 600 ms. †S, 500 ms in all patients. VE, ventricular extrasystoles; AE, atrial extrasystoles; RBBB, right bundle branch block; SR, sinus rhythm.

basis of the physical examination, echocardiogram, and angiocardiogram all three patients had evidence of mild to moderate pulmonary regurgitation. At cardiac catheterisation the right ventricular pressures were 35/2, 34/9, and 24/6 mm Hg in the three patients with no evidence of residual intracardiac shunting. On the basis of these findings all three patients were considered to have had an excellent result from surgery.

ELECTROPHYSIOLOGICAL EVALUATION

Standard 12 lead electrocardiograms, modified maximal treadmill exercise tests using the Bruce protocol, and 48 hour continuous ambulatory electrocardiographic monitoring were performed in each patient. After informed consent had been obtained the electrophysiological tests were performed in the fasting state. Diazepam was given for sedation. Three pacing wires were inserted via the femoral vein and positioned in the high right atrium, His bundle recording site, and right ventricular apex under fluoroscopic control; the femoral artery was cannulated to monitor arterial pressure. Stimulation was performed from either the high right atrium or right ventricular apex using square wave stimuli of 2 ms duration at twice diastolic current threshold from a custom made programmable stimulator. Atrioventricular and ventriculoatrial conduction characteristics were assessed by both incremental pacing and the extrastimulus technique from the high right atrium and right ventricular apex.

To assess susceptibility to inducible ventricular tachycardia the following programmed ventricular stimulation protocol was performed14: (a) one to four ventricular extrasystoles were introduced after eight beats of ventricular pacing at cycle lengths of 600, 500, and 400 ms; and (b) ventricular burst pacing was performed at cycle lengths from 400 to 250 ms. A similar stimulation protocol was used with a single right ventricular pacing wire inserted percutaneously at the time of subsequent studies to assess the efficacy of antiarrhythmic drugs.

Results

Table 1 summarises the electrocardiographic and electrophysiological data in the three patients.

ELECTROCARDIOGRAPHIC DATA

During normal sinus rhythm all three patients had a QRS morphology of right bundle branch block, but only one (case 3) had left axis deviation. One patient (case 2) had occasional monomorphic ventricular extrasystoles before, during, and after a maximum graded exercise treadmill examination, whereas two (cases 1 and 3) had no arrhythmias. During ambulatory electrocardiographic monitoring, major abnor-
Life threatening tachycardias in tetralogy of Fallot

Fig. 2 Electrocardiograms obtained during 48 hour ambulatory monitoring (case 2). The two tracings ((a) and (b)) were recorded simultaneously as were those in (c) and (d). The ventricular extrasystoles are polymorphic; a four beat salvo of ventricular tachycardia is evident in (c) and (d).

malities were noted in only one patient (case 2) as episodes of polymorphic ventricular extrasystoles occurring singly and in couplets with a short (four beat) episode of non-sustained ventricular tachycardia (Fig. 2).

ELECTROPHYSIOLOGICAL DATA
During invasive electrophysiological assessment of atrioventricular (antegrade) conduction (Table 1), two patients (cases 2 and 3) had HV intervals >55 ms; however, this interval was not prolonged during either incremental atrial pacing or assessment of atrioventricular conduction during refractory period determinations. In each patient the effective and functional refractory period of the atrioventricular node always exceeded that of the distal His-Purkinje system. The effective and functional refractory periods of the atrioventricular node were prolonged in two patients (cases 1 and 2). During ventricular pacing 1:1 ventriculoatrial (retrograde) conduction was present to a cycle length of 380 ms in one patient (case 1); the other two (cases 2 and 3) had ventriculoatrial dissociation at all cycle lengths.

ELECTROPHARMACOLOGICAL TESTS
Ventricular tachycardia initiation was achieved in all patients at a S1 cycle length of 500 ms (Table 1). Two patients required three extrastimuli (S2, S3, S4) for ventricular tachycardia initiation, whereas one had inducible ventricular tachycardia with only two extrastimuli (S2, S3). Two patients (cases 1 and 3) had a regular tachycardia (cycle lengths 230 and 240 ms) with uniform QRS morphology (Fig. 3a and b). One patient (case 2) had a polymorphic ventricular tachycardia with a mean cycle length of 200 ms (Fig. 4a and b)—that is, a beat to beat variation in QRS morphology as opposed to pleomorphic ventricular tachycardia. In one patient (case 1) the QRS morphology of induced tachycardia was identical to that which occurred spontaneously (Fig. 1). In all patients the tachycardia had adverse haemodynamic results and required termination within 30 s of induction.
Fig. 3  Electrocardiograms and electrogams showing initiation of ventricular tachycardia in (a) case 1 and (b) case 3. (a) Programmed ventricular stimulation with eight paced beats (S₁, 500 ms), and three premature stimuli (S₁S₂ 280 ms, S₂S₃ 230 ms, S₃S₄ 200 ms) resulted in induction of a rapid monomorphic ventricular tachycardia. The cycle length of the tachycardia varied in the first few seconds after induction then became regular as in Fig. 1(b). Programmed ventricular stimulation with eight paced beats (S₁, 500 ms) and two premature stimuli (S₁S₂ 230 ms, S₂S₃ 220 ms) induced a rapid monomorphic ventricular tachycardia. I, II, III, surface electrocardiograms; FAP, femoral artery pressure (mm Hg); HBE, His bundle electrogram; RA, right atrial electrogram; RV, right ventricular electrogram; S₁S₄ stimulus artefacts.
Life threatening tachycardias in tetralogy of Fallot

Fig. 4 Electrocardiograms and electrograms showing initiation of ventricular tachycardia (case 2). (a) Programmed ventricular stimulation with eight paced beats ($S_1$ 500 ms), and three premature stimuli ($S_2S_2$ 260 ms, $S_2S_3$ 200 ms, and $S_2S_4$ 190 ms) resulted in induction of a rapid polymorphic ventricular tachycardia. (b) Continuous recording from (a). Note polymorphic nature of tachycardia with apparent dissociation of septal and apical ventricular electrograms. I, II, III, surface electrocardiograms; RV, right ventricular electrogram; RA, right atrial electrogram; HBE, His bundle electrogram; FAP, femoral artery pressure (mm Hg).

I, II, III, surface electrocardiograms; RV, right ventricular electrogram; RA, right atrial electrogram; HBE, His bundle electrogram; FAP, femoral artery pressure (mm Hg).
either by intracardiac burst ventricular pacing or direct current cardioversion. After the administration of procainamide, however, one patient (case 1) had an increase in his ventricular tachycardia cycle length to 270 ms, which allowed successful right and left ventricular endocardial mapping. The earliest endocardial activity recorded in this patient was from the anterior mid-right ventricle. In the other patients (cases 2 and 3), however, pharmacological manipulation did not result in a lengthening of tachycardia cycle length, and endocardial mapping during ventricular tachycardia was not possible.

In an attempt to select a pharmacological regimen that would prevent recurrences of ventricular tachycardia serial electropharmacological testing was performed (Table 2). Oral procainamide administration in two patients (cases 1 and 3) resulting in steady state trough serum concentrations of 9 and 12 mg/l was successful in preventing recurrent tachycardia in only one (case 3). In the patient in case 1 a procainamide serum concentration of 17.6 mg/l after intravenous administration during catheterisation resulted in the suppression of inducible ventricular tachycardia. Nevertheless, the oral dose of procainamide required to achieve this serum concentration produced unpleasant side effects, and the patient in case 1 was treated with amiodarone (600 mg daily for 5 out of 7 days). This patient (case 1) has had no recurrences of previously frequent episodes of ventricular tachycardia in nine months of follow up. The patient in case 2 had no inducible ventricular tachycardia after an oral loading dose of the investigational antiarrhythmic drug, bethanidine sulphate; he has been free of palpitation and syncope while taking this drug, although follow up ambulatory electrocardiographic recordings showed a persistence of polymorphic ventricular extrasystoles with couplets.

### Table 2 Effect of drugs on ventricular tachycardia (VT)

<table>
<thead>
<tr>
<th>Case No</th>
<th>Drug regimen</th>
<th>Serum concentration (mg/l)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Procainamide</td>
<td>9.8*</td>
<td>Inducible, sustained VT</td>
</tr>
<tr>
<td></td>
<td>Procainamide</td>
<td>17.6†</td>
<td>VT not inducible</td>
</tr>
<tr>
<td></td>
<td>Amiodarone (600 mg/day, 5/7 days)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Procainamide</td>
<td>11.6†</td>
<td>Inducible, sustained VT</td>
</tr>
<tr>
<td></td>
<td>Quinidine</td>
<td>3.5*</td>
<td>Inducible, sustained VT</td>
</tr>
<tr>
<td></td>
<td>Phenytoin</td>
<td>11.0*</td>
<td>VT not inducible</td>
</tr>
<tr>
<td></td>
<td>Bethanidine sulphate (20 mg/kg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Procainamide</td>
<td>9.3*</td>
<td>Inducible, sustained VT</td>
</tr>
<tr>
<td></td>
<td>Procainamide</td>
<td></td>
<td>VT not inducible</td>
</tr>
<tr>
<td></td>
<td>Procainamide</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Steady state concentration after oral administration.
†After intravenous drug administration before electropharmacological testing (in case 1 the patient was simultaneously taking maintenance oral procainamide).
‡Electropharmacological testing after acute oral dose (see text).

### Discussion

The major finding of our study is that rapid sustained ventricular tachycardia was induced by programmed stimulation in three patients who had excellent haemodynamic results after surgical repair of tetralogy of Fallot but who suffered transient neurological disturbances or cardiac arrest. The rapid ventricular tachycardia with adverse haemodynamic effects, similar to that induced during the laboratory study, was presumably the basis for the presyncope, syncope, and cardiac arrest; this was confirmed in one patient. Our results support the idea that ventricular tachycardia with consequent haemodynamic compromise results in cardiovascular collapse in these patients after surgical correction of tetralogy of Fallot, a finding analogous to that reported in patients with other forms of heart disease who survived life threatening ventricular arrhythmias.

The difficulties inherent in the diagnosis and management by non-invasive electrocardiographic testing of patients with symptoms of presyncope, syncope, and cardiac arrest are indicated by our patients, two of whom had normal ambulatory electrocardiograms and stress exercise tests. These findings emphasise the need for invasive provocative electrophysiological testing in diagnosing arrhythmias in symptomatic patients after repair of tetralogy of Fallot. Additionally, standard doses of conventional antiarrhythmic drugs were successful in suppressing inducible ventricular tachycardia in only one of three patients, stressing the role of drug testing using programmed ventricular stimulation as an aid in the management of these patients with ventricular tachycardias.

All our patients had minimal atrioventricular conduction abnormalities, but none was sufficiently severe to explain symptoms of presyncope or syncope.
Life threatening tachycardias in tetralogy of Fallot

The clinical significance of atrioventricular conduction abnormalities in patients after repair of tetralogy of Fallot has not been fully determined.\textsuperscript{21} Since first suggested as a mechanism of late sudden death in surgical survivors,\textsuperscript{4} abnormalities in atrioventricular conduction in asymptomatic patients after repair with excellent haemodynamic results have been frequently reported.\textsuperscript{22,23} Deanfield \textit{et al}, however, suggested that conduction abnormalities may not play a role in sudden death since they found a structurally intact atrioventricular conduction system at histological examination in three patients after sudden death.\textsuperscript{24}

Recent reports have emphasised the presence of inducible ventricular tachycardia in patients who have had surgical correction of tetralogy of Fallot. Horowitz \textit{et al} studied four patients with documented ventricular tachycardia after surgery for tetralogy of Fallot.\textsuperscript{10} The ventricular tachycardia had a similar QRS morphology in each of their patients (left bundle branch block), and endocardial mapping showed the earliest ventricular activity to be in the right ventricular outflow tract, suggesting that the ventricular tachycardia in their patients originated at the site of the previous ventriculotomy. Kugler \textit{et al} reported their findings in three asymptomatic patients after surgery for tetralogy of Fallot who had not had documented tachycardia.\textsuperscript{12} All three patients had inducible ventricular tachycardia, and in contrast to the results of Horowitz \textit{et al},\textsuperscript{10} they found the earliest endocardial activity to be in the inflow-septal portion of the right ventricle rather than the outflow tract. Our results suggest that the pathophysiological basis for ventricular tachycardia may not be the same in each patient with ventricular tachycardia after repair of tetralogy of Fallot. In two of the patients we studied a uniform QRS morphology during tachycardia was present, suggesting an identical site of initiation for each cycle of tachycardia; in one of these patients endocardial mapping showed the earliest endocardial activity to be in the mid-right ventricular free wall. The third patient had polymorphic ventricular tachycardia, suggesting a continuous change in the pattern of ventricular activation. In the necropsy study by Deanfield \textit{et al} several focal regions of extensive fibrosis were identified in the right ventricle in five of six patients after sudden death after surgery for tetralogy of Fallot; the fibrosis was confined to the ventriculotomy site in three patients, to the ventricular septum in one, and to the outflow tract patch in one.\textsuperscript{24} These necropsy findings provide an anatomical basis for the variable electrocardiographic characteristics of ventricular tachycardia in the patients we studied as well as those reported by Horowitz \textit{et al}\textsuperscript{10} and Kugler \textit{et al}.\textsuperscript{12}

Previous reports have emphasised that residual haemodynamic abnormalities in patients after repair of tetralogy of Fallot predispose to an increased risk of sudden death.\textsuperscript{1,2,6,22,23,25} Nevertheless, our results show that even patients with normal or only mildly abnormal haemodynamic indices may develop serious ventricular arrhythmias. In all our patients cardiac function was normal and they were considered to have had an excellent haemodynamic result from surgery.

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References

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