Tetralogy of Fallot (TF) is the most common congenital cyanotic heart disease, but it can now be treated with very good long term results.\(^1\) It has been known for many years, however, that patients with surgically treated TF are at risk of sudden cardiac death even many years later, while a large number of these patients exhibit postoperative arrhythmias. What is not entirely clear is the relation between ventricular arrhythmias detected during routine examinations (ECG, Holter) or induced during an electrophysiological study and the risk of sudden cardiac death.

Furthermore, it has become apparent that these patients may suffer from supraventricular arrhythmias at least as often as ventricular arrhythmias. Those arrhythmias also require attention and treatment since they may cause significant morbidity and mortality.

**Supraventricular arrhythmias**

**General remarks**

Chronic right ventricular systolic pressure overload and increased end-diastolic pressure resulting from pulmonary valve insufficiency lead to increased right atrial pressure, hypertrophy and fibrosis. In addition, the atriotomy scar provides an anatomical obstacle, which in combination with haemodynamic disturbances, causes atrial arrhythmias, mainly typical atrial flutter or re-entrant tachycardia around the atriotomy scar.

Roos-Hesselink et al\(^2\) described a series of 53 patients, mean age 23.2 years (range 15-57), who had undergone surgical repair of TF at a mean age of 9.1 years and were followed up for a mean interval of 17.5 years. Nineteen patients (36%) had sinus node dysfunction and 4 needed pacemaker implantation. Atrial fibrillation or flutter developed in 12 patients, while 6 had other types of supraventricular tachycardia. In all, 34% of the patients suffered from supraventricular tachycardia. In comparison, non-sustained ventricular tachycardia (VT) occurred in 10 patients (19%).

Harrison et al\(^3\) analysed a series of 242 patients after repair of TF. They found a 12% incidence of persistent atrial arrhythmias. Compared to the others, patients with atrial tachycardia had been operated on at an older age (25 ± 16 vs. 10 ± 9 years), they were older during follow up, they had larger right atrial dimensions and more pulmonary valve insufficiency. Atrial tachycardia was related with a higher risk of unfavourable events: subsequent development of VT, stroke, or sudden death (69% vs. 30%).

Gatzoulis et al\(^4\), in a multicentre study of 793 patients (mean age 8.2 years, mean postoperative follow up 21.1 years), found that 29 (3.5%) developed atrial flutter or fibrillation. A greater age at the time of repair was related with a higher risk of sudden death and atrial arrhythmia. Tricuspid insufficiency was the main risk factor for development of atrial fibrillation or flutter.

Dietl et al\(^5\) compared the incidence of
atrial and ventricular arrhythmias in patients who underwent transatrial or transventricular repair. Transatrial repair had a highly significant effect in reducing both atrial and ventricular arrhythmias.

One risk factor for the development of atrial arrhythmias is the P wave dispersion in different leads. Hallioglu et al. found that P wave dispersion >35 ms had 83% sensitivity and 89% specificity in predicting the postoperative development of persistent atrial tachycardia in TF patients.

Although intra-atrial re-entrant tachycardia is the most common postoperative atrial arrhythmia, other possible causes should not be overlooked. These include accessory pathways and atrioventricular (AV) nodal re-entrant tachycardia, which are relatively easy targets for treatment with radiofrequency ablation.

**Methods of treatment**

The treatment of postoperative atrial tachyarrhythmias in patients with TF should be based on an assessment of both the patient’s haemodynamic condition and any existing sinus node dysfunction or conduction disturbances. Antiarrhythmic drugs have a moderate degree of success in postoperative atrial tachyarrhythmias, amiodarone being the most effective (78-94% in various studies), followed by sotalol (85%) and digoxin (45%). Class Ic agents should probably be avoided in patients with structural heart disease (such as postoperative TF patients) because of the risk of proarrhythmia and sudden death.

Any patient with significant sinus node dysfunction who needs antiarrhythmic treatment apart from digoxin is a candidate for permanent pacing. The indications for permanent pacing are given in table 1.

Atrial antitachycardia pacing has a place in the treatment of atrial arrhythmias that are not treatable by catheter or surgical ablation, or are closely related with bradycardias. In a recent study of 15 postoperative patients there was adequate sensing of arrhythmias in 14, for a total of 167 episodes of which 90 (54%) were terminated successfully.

Radiofrequency ablation of atrial arrhythmias has been reported in all categories of congenital heart disease, including patients with TF. Because of the high incidence of atrial tachyarrhythmias around atrial incisions and isthmus-dependent atrial flutter, electro-anatomical mapping has an important role in the identification of reentry circuits, as well as in verifying the creation of a complete line of block. Often, the discovery of rather narrow channels between scars allows blocking of the circuit with a relatively small number of lesions. The cavotricuspid isthmus may participate in the tachycardia, either as the sole mechanism or as part of a figure-of-eight re-entrant circuit. Successful ablation of all atrial tachycardia circuits is feasible in the majority of patients, although there is a recurrence rate of 20-30%. A large number of patients remain free of arrhythmias after catheter ablation, thus avoiding the need for antiarrhythmic drug therapy and its possible side effects. Although catheter ablation has satisfactory results in patients with good haemodynamic parameters, surgical treatment is the method of choice when there are significant residual lesions. During surgery, the right atrial or biatrial MAZE operation may be performed in combination with correction of the anatomical problems.

**Ventricular arrhythmias and sudden death**

**General remarks**

Postoperative ventricular arrhythmias are very common in TF patients. They have been found in 5-10% of patients on the 12-lead ECG and in 40-60% on 24-hour Holter monitoring in older series of patients who underwent surgery at a more advanced age. Newer techniques and repair at a younger age have led to a significant reduction in the incidence of arrhythmias. In a series of patients who had surgical repair before the age of 18 months, Walsh et al found that only 1 of 41 patients with adequate 24-hour Holter data had ventricular arrhythmias more severe than Lown grade I, while there was no late mortality attributable to arrhythmias over a mean follow up period of 60 months.

Transatrial repair has been proved to have a beneficial effect on the incidence of ventricular arrhythmias. Dietl et al compared the incidence of arrhythmias in

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**Table 1. Indications for pacing in disturbances of sinus node function.**

<table>
<thead>
<tr>
<th>Class</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1) Symptomatic bradycardia.</td>
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<tr>
<td></td>
<td>2) Marked exercise intolerance or reduced chronotropic response.</td>
</tr>
<tr>
<td></td>
<td>3) Congestive heart failure and chronic bradycardia.</td>
</tr>
<tr>
<td>II</td>
<td>1) Brady-tachy syndrome, need for antiarrhythmic drugs apart from digitalis (IIa).</td>
</tr>
<tr>
<td></td>
<td>2) Resting heart rate &lt;35 min⁻¹, pauses &gt;3 s (IIa in children, IIb in teenagers).</td>
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2 groups of patients who underwent transventricular (n=28) or transatrial (n=36) repair. In the former group 28 patients (39.4%) had significant ventricular arrhythmias (≥ Lown II), while in the latter group only 1 patient (2.8%) had significant arrhythmias (this patient had severe pulmonary valve insufficiency). When electrophysiological studies were performed they were positive in 8/28 (26.8%) of the transventricular group and in 0/5 patients of the transatrial group.

Sudden cardiac death has been reported in 1.5-5% of patients after repair of TF and ventricular arrhythmias have been implicated as an aetiologic factor in many studies.22,23 Garson et al20 reported that ventricular arrhythmias were found on the ECG in 100% of patients who later died suddenly, compared to 12% of those who did not (p<0.01). However, other studies have cast doubt on a direct relation between ventricular arrhythmias on 24-hour Holter and sudden death. Cullen et al22 followed 47 patients with surgically corrected TF and similar haemodynamic parameters prospectively for 12 years after an initial 24-hour Holter recording. They found no correlation between the degree of ventricular arrhythmias and sudden death (2 sudden deaths in the group with low grade arrhythmias compared to 1 non-sudden death in the group with severe arrhythmias).

The incidence of sudden death appears to increase with the length of follow up. Nollert et al22 studied a series of 490 patients with TF who survived the first postoperative year and found that the annual mortality increased from 0.24% during the first year of the study to 0.94% after 25 years. The most common cause of death was sudden death (n=13), followed by congestive heart failure (n=6). Greater age at repair, elevated right ventricular systolic pressure postoperatively and preoperative polycythemia were risk factors for sudden death.22,23

Since 1995 efforts have been made to discover non-invasive ECG indices of the risk of VT and sudden death. Gatzoulis et al found that a QRS duration >180 ms was a very sensitive and quite specific index for the development of VT and sudden death.24 In addition, in a multicentre study of 793 patients, the use of a transannular patch in combination with severe pulmonary valve insufficiency and a rapid change in the QRS over time were correlated with an increased risk of VT and sudden death.4

QT dispersion has also been correlated with sustained VT. A QT dispersion >60 ms in correlation with a QRS duration >180 ms improved the stratification of adult patients with TF and VT.22 In another study, Berul et al found that a QRS duration >180 ms and increased JT dispersion were the most sensitive and specific indexes for VT and sudden death. Brili et al proposed the signal-averaged ECG as a non-invasive method for the assessment of the risk of ventricular arrhythmias.27 A filtered QRS duration >148 ms, a low potential duration ≥32 ms and RMS-40 ≤23 mV were found to have significant sensitivity in predicting sustained VT in patients with TF.

The place of electrophysiological studies (EPS) in the treatment of VT following repair of TF continues to be the subject of debate. In the current era of implantable defibrillators and radiofrequency ablation, EPS are used only rarely to assess the efficacy of antiarrhythmic medications. In an older study by Chandar et al15 the inducibility of VT during an EPS was correlated with the presence of complex ectopic ventricular activity on a Holter recording or syncope. None of the patients who died suddenly had inducible VT during the EPS, but all had other risk factors, such as a high degree of ventricular ectopic activity or abnormal haemodynamic findings. Also, none of the patients with normal Holter findings or normal haemodynamic parameters had inducible VT.

Alexander et al studied a group of 130 patients with congenital heart disease who underwent an EPS, 33% of whom had TF.29 According to univariate analysis a positive EPS was associated with a six-fold greater risk of decreased survival. However, the positive prognostic value of a positive EPS for sudden death was only 20% and there was a high rate of false negatives (33%).

A more recent multicentre study of 252 postoperative TF patients showed that a positive EPS is a very powerful prognostic factor for clinical VT and sudden death.30 The patients were followed for 18.5 ± 9.6 years after surgical repair and for 6.5 ± 4.5 years after the EPS. Clinical VT or sudden death occurred in 24.6%. Sustained monomorphic VT was induced in 30.2% and polymorphic VT in 4.4%. The inclusion of polymorphic VT in the definition of inducibility increased the sensitivity with a marginal reduction in specificity. The positive and negative prognostic value of the EPS were 55.2 ± 5.3% and 91.5 ± 2.2%, respectively. Independent predictive factors for inducibility were age ≥18 years during the study (odds ratio, OR 3.3), palpitations (OR 2.8), previous palliative surgery (OR 3.1), arrhythmia ≥ Lown II (OR 5.6) and cardiothoracic index ≥0.6 (OR 3.3). Arrhythmia-free survival at 1, 5, 10 and 15 years was 97.9%, 92.8%, 89.3% and 89.3% in the non-inducible patients and 79.4%, 62.6%, 58.7% and 50.3% in the inducible patients, respectively (p<0.0001). Inducible monomorphic VT (relative risk, RR 5.0, p<0.0002), and
polymorphic VT (RR 12.9, p<0.0001) both successfully predicted the future development of VT and sudden death.

Methods of treatment

From the above considerations it appears that the decision concerning the treatment of ventricular arrhythmias in postoperative TF patients is a complex process in which clinical manifestations, the 12-lead ECG, the 24-hour Holter recording, the haemodynamic and electrophysiological data, must all be taken into account. Patients with significant residual haemodynamic defects (especially severe pulmonary valve insufficiency and severe obstruction of the right ventricular outflow tract) and VT should undergo surgery for pulmonary valve replacement and relief of any significant outflow tract obstruction, together with intraoperative cryoablation of the VT whenever this is possible. Therrien et al.,30 in a study of 70 patients who underwent pulmonary valve replacement and intraoperative VT ablation, reported that the incidence of VT decreased from 22% to 9% (p<0.001) during a mean follow up of 4.7 years.

The usefulness of the implantable cardioverter-defibrillator has been proven in several series of patients with congenital heart disease, including TF.31,32 It is certainly the indicated therapy in patients who have suffered cardiac arrest, unstable VT, or syncope of unknown aetiology with inducible VT.

Radiofrequency ablation may be employed as primary therapy in selected patients who have excellent haemodynamic findings and sustained VT.33-36 Ablation has been performed successfully even in patients with multiple forms of tachycardia.33 It can also be used for reduction of the arrhythmiological burden in patients with frequent discharges after defibrillator implantation. Electroanatomical mapping can be particularly useful in the identification of an arrhythmiological circuit and in the verification of conduction block after critical isthmus ablation.35,36

The use of antiarrhythmic drugs, popular in the past, is now limited to the following cases: a) patients with high grade ectopic ventricular activity and poor haemodynamic condition who are not candidates for corrective surgery and do not have severe enough symptoms to justify defibrillator implantation; b) patients with a defibrillator and frequent episodes of VT, in order to reduce the number of shocks; and c) patients with well-tolerated VT and good haemodynamic data, who are unwilling to undergo ablation or in whom ablation has been unsuccessful and the efficacy of the medication has been documented by an EPS. Drugs that have been described as effective are the Ib agents (phenytoin, mexiletine), β-blockers and amiodarone.21,37 Drug treatment of asymptomatic ventricular arrhythmias, even of high degree, in patients with good haemodynamic parameters is not recommended.

Disturbances of atrioventricular conduction

Disturbances of atrioventricular conduction are very common in patients with surgically corrected TF, and usually take the form of right bundle branch block, which is seen in 80% of patients. The combination of right bundle branch block and left axis occurs in 11% and the combination of right bundle branch block, left axis and first degree AV block in 3% of patients. Although this combination was implicated in the past as predictive of complete AV block, this was not confirmed by subsequent studies and should not be considered in itself as an indication for pacing. Most patients with right bundle branch block after ventriculotomy have a benign prognosis, even though theoretically they remain at risk of complete AV block should left bundle branch block develop as a result of degenerative changes. Patients with second degree type II AV block, or complete AV block that persists for more than 2 weeks after surgery, should undergo permanent pacemaker implantation. Syncopal patients with a long HV interval (>100 ms), or AV block below the His bundle during atrial pacing at rates <120 min⁻¹ are also candidates for pacing. In asymptomatic patients with these electrophysiological findings close monitoring every 6 months is recommended, with 24-hour Holter monitoring and stress testing.38 The indications for pacing for disturbances of AV conduction are summarised in table 2.

Table 2. Indications for pacing in disturbances of atrioventricular (AV) conduction.

Class I:
1) Complete AV block persisting for >2 weeks postoperatively.
2) Second degree AV block, type II or high degree (2:1, 3:1, etc.).

Class II:
1) Syncope and long HV interval (> 100 ms).
2) Symptomatic patients with AV block below the His bundle during atrial pacing at rates <120 min⁻¹.
Conclusions
Cardiac arrhythmias comprise one of the most common postoperative problems in patients with TF. Both atrial and ventricular arrhythmias may cause significant morbidity and mortality. Treatment should always be given in conjunction with an attempt to improve haemodynamic parameters, and often involves a combination of therapeutic methods, including medication, pacing, ablation, defibrillator implantation and surgical treatment.

References


