

# Ventricular arrhythmia in unrepaired and repaired tetralogy of Fallot

## *Relation to age, timing of repair, and haemodynamic status*

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**SUMMARY** Ventricular arrhythmias are common after repair of tetralogy of Fallot and are associated with late sudden death. This study examined the relation of ventricular arrhythmia during normal daily activities to the timing of repair, duration of follow up, and postoperative haemodynamic status. Forty eight hour ambulatory electrocardiographic monitoring was performed in 145 patients: 60 (aged 3 months to 46 years) had not yet undergone repair and 85 were followed from four to 22 (mean 14.6) years after repair. Cardiac catheterisation was performed in 47 (55%) one to 22 (mean 8.9) years after repair. Twelve (20%) of the uncorrected group had ventricular arrhythmia. The incidence increased significantly with age from 0% in patients aged <8 years to 58% in those aged  $\geq 16$  years. In the corrected group 44% had ventricular arrhythmia. The incidence of arrhythmia was associated with older age at repair but not with postoperative haemodynamic status, duration of follow up, or era of surgery.

It is concluded that ventricular arrhythmia is common in older patients with tetralogy of Fallot before repair and that during long term follow up of patients after repair the incidence of ventricular arrhythmia is influenced by the timing of surgery rather than the duration of postoperative follow up, era of surgery, or the haemodynamic result.

Ventricular arrhythmia is common after repair of tetralogy of Fallot.<sup>1,2</sup> Previous studies have investigated the relation of arrhythmia to electrocardiographic conduction defects, postoperative haemodynamic status, and the occurrence of late sudden death.<sup>3-5</sup> The relation of ventricular arrhythmia to the natural history of the condition and to the timing of surgical repair has not, however, been examined.

In this study we determined the incidence of arrhythmia and its relation to age in patients who had not undergone correction. We also assessed the relation of arrhythmia to the age at repair, duration of follow up, era of surgery, and postoperative haemodynamic status in a separate group after correction.

### Patients and methods

We studied 145 patients with a clinical and angiocardiological diagnosis of classical tetralogy of Fallot. Of these, 60 had not yet undergone surgical correction and 85 were studied during long term follow up after correction.

### UNCORRECTED GROUP

The 60 patients (41 male, 19 female) were aged 3 months to 46 (mean 12.6) years. They included 36 children, under the age of 7 years, who were admitted to The Hospital for Sick Children between 1979 and 1980. Twenty of these had undergone palliative surgery (a classical Blalock-Taussig or modified Goretx<sup>6</sup> pulmonary-systemic shunt). The remaining 24 patients, aged  $\geq 8$  years, were studied at the Hammersmith Hospital or at the San Giovanni Hospital over a one year period between 1979 and 1980. They were consecutive patients who had either previously refused corrective surgery or had been referred from

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Accepted for publication 2 February 1984

centres where facilities for cardiopulmonary bypass surgery were not available. All of these older patients had undergone palliative surgery (Blalock-Taussig shunt in 20, Brock operation in two, and two procedures (Brock and Blalock) in three).

#### CORRECTED GROUP

Eighty five consecutive patients (59 male, 26 female) were seen during follow up at the Hammersmith Hospital between 1979 and 1981. Of these, 65 (76%) had previously undergone palliative surgery (Blalock-Taussig shunt in 52 (61%) and Brock operation in 13 (15%)). Complete repair was performed between 1959 and 1978 (1959-1964, 35 patients; 1965-1970, 31 patients; 1971-1978, 19 patients) using standard surgical and cardiopulmonary bypass techniques. The ventricular septal defect was closed with a Teflon-felt patch in 72 patients (83%) and by direct suture in the remainder. In 22 (26%) the right ventricular outflow tract was enlarged with a Dacron or pericardial patch. The age range at corrective surgery was 3-45 (mean 13.6) years. The duration of follow up from surgery to evaluation was 4-22 (mean 14.6) years and was more than 10 years in 66 (78%) patients.

#### INVESTIGATIONS

All the patients underwent 12 lead and 48 hour ambulatory electrocardiography and completed questionnaires related to symptoms. Cardiac catheterisation was performed in 47 (55%) between one and 22 (mean 8.9) years after correction. The remainder were not catheterised for logistic reasons, and no clinical selection criteria were applied.

#### Ambulatory electrocardiography

Ambulatory electrocardiography was performed using Oxford Medilog I cassette recorders and bipolar CM1 and CM5 leads. All the patients who were aged  $\geq 3$  years were studied as outpatients. The tapes were analysed by one of us using a Reynolds Pathfinder I or II high speed analyser system, and the recordings were then reviewed by another of our group. Ventricular arrhythmias were graded using a modification of the Lown criteria<sup>7</sup>: grade 0, no ventricular extrasystoles; grade 1, uniform ventricular extrasystoles with a peak hourly count of  $< 30$ ; grade 2,  $> 30$  uniform ventricular extrasystoles in any hour; grade 3, couplets (two consecutive ventricular extrasystoles) or multiform ventricular extrasystoles with a peak hourly count of  $< 30$ ; grade 4, couplets or multiform ventricular extrasystoles with  $> 30$  in any hour; and grade 5, ventricular tachycardia (defined as  $\geq 3$  consecutive ventricular extrasystoles with a mean rate of  $> 110$  beats/min). In addition, any supraventricular arrhythmia or atrioventricular conduction defect was recorded.

#### STATISTICAL ANALYSIS

The relation of ventricular arrhythmia to age in the uncorrected patients was analysed using Fisher's exact test. In the corrected group, the relation of arrhythmia, age at repair, and duration of follow up was analysed by fitting an additive logistic model using the computer package GLIM.<sup>8</sup>

#### Results

##### UNCORRECTED GROUP

###### Electrocardiogram

All the patients were in sinus rhythm, had electrocardiographic criteria of right ventricular hypertrophy, and had a mean frontal QRS axis of  $+90^\circ$  or greater.

###### Ambulatory monitoring

Twelve (20%) of the 60 patients had ventricular arrhythmias of grade 2 or greater (Fig. 1). There was a significant increase in ventricular arrhythmia with increasing age. No ventricular arrhythmias of grade 2 or greater were detected in the 36 patients who were  $< 8$  years of age. One of five patients aged 8-15 years had a single run of 5 beats of ventricular tachycardia, and three others had infrequent uniform ventricular extrasystoles (grade 1). The highest incidence of ventricular arrhythmia (58%) was found in the 19 patients aged  $\geq 16$  years. Within this older group four patients (21%) had runs of ventricular tachycardia (3-12 beats) of left bundle branch block morphology, consistent with a right ventricular origin.

No significant supraventricular arrhythmias were recorded in the 36 patients aged  $< 8$  years. One patient in the 8-15 year group and three patients over 16 years of age had frequent atrial extrasystoles (a

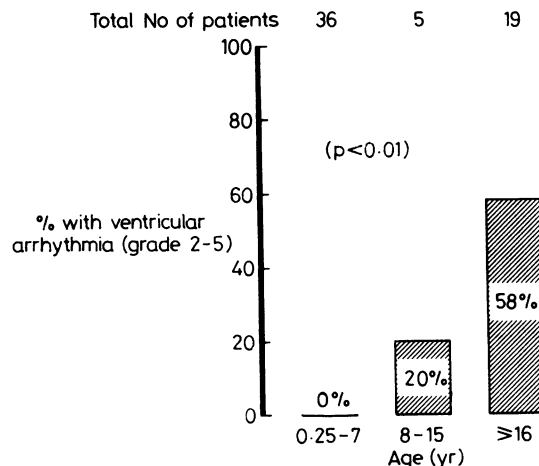


Fig. 1 Relation of ventricular arrhythmia to age in the 60 patients with uncorrected tetralogy of Fallot.

**Ventricular arrhythmia in tetralogy of Fallot**

peak hourly count of >30). Three of these patients also had episodes of supraventricular tachycardia (>180 beats/min). Atrioventricular conduction disturbances were not found.

Six of the patients who had ventricular arrhythmias before operation were restudied after repair. In all, ventricular arrhythmias noted preoperatively were still present at a follow up of 6-12 months.

**Symptoms**

Four patients complained of palpitation. One of these, aged 8 years, had episodes of supraventricular tachycardia during electrocardiographic monitoring. Of the other three in the older group aged ≥16 years, one had recurrent syncopal episodes and ventricular tachycardia during electrocardiographic monitoring in the absence of symptoms, and two had frequent multiform ventricular extrasystoles (grade 4).

**CORRECTED GROUP**

**Electrocardiogram**

Eighty three of the 85 patients were in sinus rhythm and one was in atrial fibrillation. Another had a permanent ventricular pacemaker inserted for sinoatrial and atrioventricular block (shown to be due to His-Purkinje disease during electrophysiological study). Complete right bundle branch block was present in 80 (94%) patients; 12 (14%) also had left axis deviation (mean frontal QRS axis of <-30°). Single uniform

ventricular extrasystoles were present on routine 12 lead electrocardiograms in four patients.

**Ambulatory monitoring**

Thirty eight (44%) patients had ventricular extrasystoles of grade 2 or greater (Table). There were six (7%) with ventricular tachycardia of left bundle branch block morphology consistent with a right ventricular origin. Seven (8%) patients had frequent atrial extrasystoles (>30 in any hour), and three had episodes of supraventricular tachycardia. None had second or third degree atrioventricular block.

**Symptoms**

Eleven (13%) patients complained of palpitation. Of these, five had ventricular arrhythmia of grade 2 or greater, including one with ventricular tachycardia during electrocardiographic monitoring. Four (5%) patients had syncope: of these, two had multiform ventricular extrasystoles and one had asymptomatic ventricular tachycardia during electrocardiographic monitoring.

**Age at repair and duration of follow up**

Patients were divided into three groups according to their age at repair. Ventricular arrhythmia of grade 2 to 5 was detected in three (17%) of the patients in whom repair was performed between 2 and 7 years of age, in 19 (42%) of patients operated on between 8 and 15 years of age, and in 16 (73%) of patients whose age at operation was ≥16 years (Fig. 2). Five of the six patients with ventricular tachycardia were more than 10 years old at the time of repair. Using an additive logistic model, the effect of age at repair on the influence of ventricular arrhythmia was highly significant ( $\chi^2$  (2 df)=17.5, p<0.001). The relation of

Table Grade of ventricular arrhythmia in 85 patients in corrected group

Grade:	0-1	2	3	4	5
No of patients	47	2	17	13	6

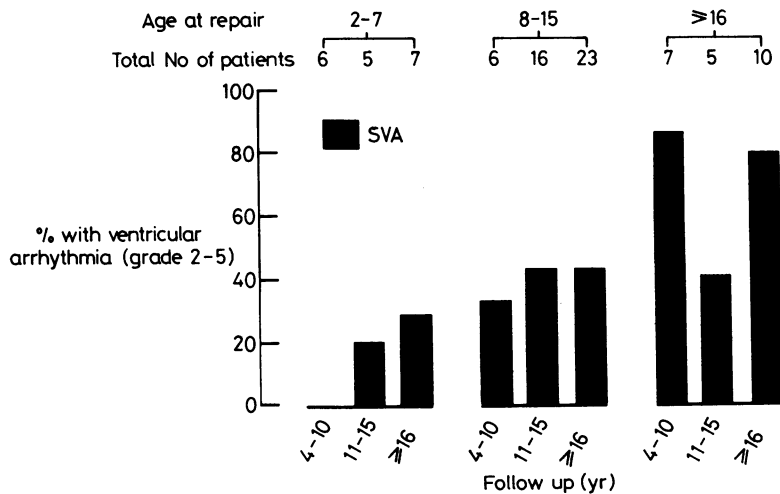


Fig. 2 Relation between significant ventricular arrhythmia (SVA) (grade 2 or greater), age at repair, and duration of follow up in the 85 patients after repair.

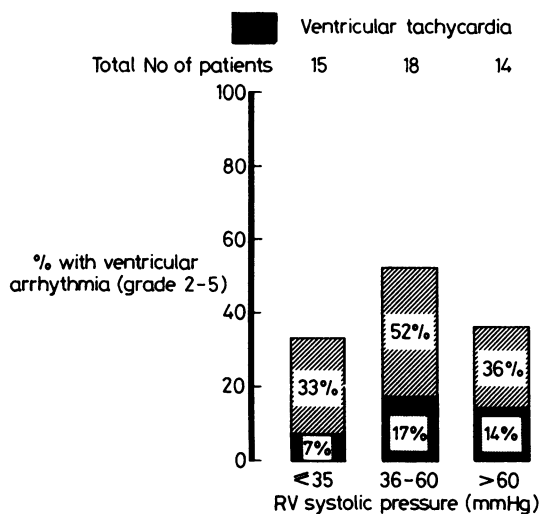


Fig. 3 Relation of right ventricular (RV) systolic pressure and ventricular arrhythmia (grade  $\geq 2$ ) in the 47 patients at follow up catheterisation.

ventricular arrhythmia to the interval between repair and electrocardiographic monitoring was also studied. As monitoring was performed over a short period of time (two years) in relation to the follow up duration this interval between monitoring and repair also corresponds to the era of surgery. There was no relation between the age at operation and the era of surgery. The duration of follow up or era of surgery did not have a significant effect on the incidence of ventricular arrhythmia ( $\chi^2$  (2 df) = 0.28,  $p > 0.90$ ).

#### Cardiac catheterisation

The right ventricular systolic pressure was  $< 35$  mm Hg in 15 (32%) patients, 36–60 mm Hg in 18 (38%), and  $> 60$  mm Hg in 14 (30%) as a result of a residual right ventricular outflow gradient. The pulmonary artery pressure was normal ( $< 30$  mm Hg) in all patients, and only one had evidence of a small inter-ventricular shunt (Qp:Qs ratio 1.6:1). There was no significant association between the level of right ventricular systolic pressure (Fig. 3) or end diastolic pressure and the presence of ventricular arrhythmia (mean (SD) end diastolic pressure 7 (3.7) mm Hg in the patients with ventricular arrhythmia compared with 6.2 (2.6) mm Hg in those without).

#### Discussion

The long term survival and symptomatic status of patients who have undergone repair of tetralogy of Fallot are excellent.<sup>9</sup> Retrospective studies, however,

have reported an incidence of late sudden death of up to 4% and have suggested that these deaths may result from ventricular arrhythmia.<sup>1,3,10,11</sup> In our study, 44% of patients after repair of tetralogy of Fallot had ventricular arrhythmias of grade 2 or greater during their normal daily activities. This raises two questions. What clinical or haemodynamic factors are associated with these arrhythmias? Do they contribute to long term morbidity and mortality?

Previous reports have focused on the relation of ventricular arrhythmia to the haemodynamic status of the patient after repair. Garson *et al* found a significant association between the presence of ventricular extrasystoles and an increased right ventricular systolic pressure,<sup>3</sup> and Rosing *et al* reported high grade ventricular arrhythmias in patients with increased right ventricular dimensions on echocardiography.<sup>4</sup> We were unable to show an association between any grade of ventricular arrhythmia and residual increase in right ventricular systolic or end diastolic pressure. This applied equally to the patients with very frequent ventricular extrasystoles (grades 2 and 4) and to those with ventricular tachycardia (grade 5). Furthermore, in a separate study using radionuclide angiography there was no significant relation between right or left ventricular ejection indices and the presence of ventricular arrhythmia.<sup>12</sup> In contrast, we found a strong association between late ventricular arrhythmia and older age at the time of repair, which was independent of the duration of follow up and therefore in turn independent of the era in which cardiac surgery was performed. It is legitimate in this instance to equate duration of follow up with era of operation since all patients were studied electrocardiographically during a narrow time span. In our study the age at which surgery was performed was not related to the era of surgery. Our findings suggest that late ventricular arrhythmias are related to the timing of surgery rather than to the operation itself or to residual haemodynamic abnormalities. This is supported by the results of electrocardiographic monitoring in the 60 patients who had not yet undergone repair. In this group, a high incidence of ventricular arrhythmias was already present in the older patients. Katz *et al* analysed symptoms of arrhythmia rather than electrocardiographic recordings and reached similar conclusions about the importance of the age at repair.<sup>9</sup>

Necropsy studies have shown extensive myocardial fibrosis in adults with uncorrected tetralogy of Fallot, which is not detected in hearts of younger patients.<sup>13</sup> An increase in right ventricular fibrosis with age may be the substrate for the high incidence of ventricular arrhythmia which we found in both older uncorrected patients and patients whose repair was carried out at an older age. Generalised fibrosis may result in mul-

tiple micro re-entry circuits. This is supported by the results of electrophysiological studies of both Garson *et al*<sup>14</sup> and Kugler *et al*,<sup>15</sup> which indicate that ventricular arrhythmias may arise from many areas of the right ventricle. In addition, the ventriculotomy may be the site of macro re-entry arrhythmias,<sup>16</sup> and these may be particularly important in the presence of generalised fibrosis.

Despite the high incidence of ventricular arrhythmia in patients after repair of tetralogy of Fallot symptoms are infrequent and long term prognosis is good.<sup>9</sup> Thus ventricular arrhythmias cannot all be specific markers of poor prognosis. Prospective studies are needed to determine which features of arrhythmia are related to sudden death so that a therapeutic guideline can be established. It may well be that arrhythmias become life threatening only in the presence of poor ventricular function or significant residual structural abnormality or both. This could explain why patients who died suddenly, as reported by Garson *et al*, Gillette *et al*, and Fuster *et al*, had both arrhythmia and haemodynamic abnormalities.<sup>3 5 17</sup>

We were unable to assess the effect of the operation itself on ventricular arrhythmia as the same patients were not studied before and after repair; we have, however, shown that the incidence of ventricular arrhythmia during long term follow up is related to the age at repair and not to the postoperative haemodynamic status. Although many of our patients underwent repair at an older age than is the current practice, our findings support the trend towards early correction, which may reduce the incidence of late ventricular arrhythmia.

We thank Professor M Healy, Department of Medical Statistics, University of London, for his advice.

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