Surgical Treatment of Ventricular Tachycardia After Surgical Repair of Tetralogy of Fallot

Relation Between Intraoperative Mapping and Histological Findings

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Background The mechanism of ventricular tachycardia (VT) after correction of tetralogy of Fallot (TF) is poorly understood. The purpose of this study was to examine the histopathology of the arrhythmogenic area detected by intraoperative mapping.

Methods and Results The patients were three men who underwent radical surgery for TF at age 3, 3, or 5 years, respectively. VT developed at 8, 9, or 11 years, respectively, after surgery, and shock developed during VT in every case. The ECG revealed monomorphic VT in two cases and polymorphic VT in one case. Induction of VT resulted in a wide left-axis deviation—pattern QRS with cycle lengths varying between 260 and 330 milliseconds. The VT origin was identified at the right ventricular outflow tract (RVOT). A radical operation was performed with the patient under cardiopulmonary bypass. On epicardial mapping, delayed activation of the RVOT was recorded during sinus rhythm, and clockwise circus movement of the macroreentry current during VT on the right ventricular free wall was documented in each case. The VTs were treated successfully by surgical resection and cryoablation of the myocardium. In every patient, histology of the myocardial specimens showed degeneration, adiposis, fibrosis, inflammatory cell infiltration, and scattered myocyte islets. These lesions corresponded anatomically to the area of myocardium in which delayed activation was evident during epicardial mapping.

Conclusions The results of this study indicate that patients with VT after radical correction of the TF have abnormal histopathological findings at the site of the prior right ventriculotomy scar. These lesions were noted within the region of delayed activation found during epicardial mapping and were found to be a part of the reentrant circuit. (Circulation. 1994; 90:264-271.)

Key Words • tetralogy of Fallot • ventricular tachycardia • mapping • surgery

Methods

Our patient cohort consisted of three men (patients 1 through 3) who were 21, 19, and 26 years old, respectively, and had undergone radical surgical correction of TF at age 3, 3, or 5 years, respectively. In all cases, radical surgery for TF involved a right ventriculotomy incision followed by patch closure of the ventricular septal defect (VSD), excision of the hypertrophied infundibular myocardium, and patch reconstruction of the outflow tract. During follow-up, VT occurred initially at age 12 (9 years after surgery) in patient 1, at age 11 (8 years after surgery) in patient 2, and at age 16 (11 years after surgery) in patient 3. Two of the patients had cardiogenic shock associated with the VT, and the third had a preshock condition. The VT was monomorphic, and patient 1 was treated with eight drugs (disopyramide, ajmaline, procainamide, lidocaine, propranolol, flecainide, verapamil, and mexiteline). Patient 2 required four drugs (lidocaine, procainamide, propranolol, and propafenone), and patient 3 also was treated with eight drugs (disopyramide, procainamide, lidocaine, propranolol, aprindine, cibenzoline, verapamil, and digitalis). However, VT recurred in all patients despite medical therapy, and direct current cardioversion was ultimately required to terminate the VT (Table 1).

Cardiac Catheterization

Right ventriculography revealed aneurysmal dilatation of the right ventricular (RV) outflow tract (RVOT) in two of the patients. In both cases, the dilated area was identical to the incised region at surgery. None of the patients had a residual shunt from a VSD. The RV-pulmonary arterial pressure gradient was 7, 17, and 14 mm Hg in the three patients,
TABLE 1. Clinical Features of Patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, y</th>
<th>Sex</th>
<th>Age at Radical Surgery, y</th>
<th>Status During VT</th>
<th>No. of Drugs</th>
<th>History of DC</th>
<th>Right Ventricle, mm Hg</th>
<th>MPA, mm Hg</th>
<th>LVEF, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>21</td>
<td>M</td>
<td>3</td>
<td>Shock</td>
<td>8</td>
<td>+</td>
<td>32/6</td>
<td>25/5</td>
<td>65</td>
</tr>
<tr>
<td>2</td>
<td>19</td>
<td>M</td>
<td>3</td>
<td>Preshock</td>
<td>4</td>
<td>+</td>
<td>45/8</td>
<td>28/9</td>
<td>59</td>
</tr>
<tr>
<td>3</td>
<td>26</td>
<td>M</td>
<td>5</td>
<td>Shock</td>
<td>8</td>
<td>+</td>
<td>32/4</td>
<td>18/4</td>
<td>79</td>
</tr>
</tbody>
</table>

DC indicates direct current shock; MPA, main pulmonary artery; and LVEF, left ventricular ejection fraction. *Mean value.

respectively. There was evidence of mild tricuspid regurgitation in one patient. The left ventricular (LV) ejection fraction was 65%, 59%, and 79%, respectively (Table 1).

Electrophysiological Study

Quadrupolar electrode catheters (USCI) with an interelectrode distance of 5 to 10 mm were used for intracardiac recording and programmed stimulation. Under fluoroscopic guidance, four catheters were introduced from the femoral vein to the right atrium. His bundle, RV apex, and RVOT. One to three extrastimuli were used to induce VT at the two sites of the RV. If VT was unable to be induced from the RV, programmed stimulation was performed from the LV. After the induction of monomorphic sustained VT, the site of origin of VT was mapped as the earliest site of activation (Table 2).

Intraoperative Mapping

With the patients under general anesthesia, a median sternotomy was performed. A mat electrode, which included 15 pairs (patient 1) or 24 pairs (patients 2 and 3) of bipolar electrodes with 2-mm interelectrode distances, was placed on the surface of the RV, and local electrograms were recorded simultaneously. A Mingograph 82 (Siemens-Elema AB Sweden) and a Computerized Cardiac Mapping System HPM-7100 (Fukuda Denshi-Electric Co Ltd) were used to record potentials and to process and display the data. The local electrograms and the activation sequence were obtained at the RVOT during sinus rhythm and episodes of VT.

Surgical Procedure

After epicardial mapping was completed, moderate hypothermic extracorporeal circulation was begun via ascending aorta and bicaval cannulation. Cold cardioplegic solution was then infused after aortic crossclamping. Based on the epicardial mapping, the origin of the VT foci within the RVOT was then resected. A cryoprobe was inserted after resection through the myocardial incision, and cryoablation of the surrounding tissue was performed for 2 minutes at ~70°C. In patient 1, the ventricular septum was cryoablated because electrophysiological studies had revealed that the VT foci originated from the ventricular septum close to the RVOT. The myocardial defect was closed using a Gore-Tex (W.L. Gore & Associates, Inc) patch in one patient and directly in the other two patients (Table 3).

Histopathological Examination

Each myocardial specimen removed from the RV was fixed in 10% buffered Formalin. After dehydration and paraffin embedding, complete serial sections 5 or 7 μm thick were obtained and stained with hematoxylin and eosin, azan, and elasta-van Gieson's for microscopic observation.

Results

Preoperative Mapping

In all three patients, VT was induced by programmed extrastimulation. All episodes of inducible VT had a left bundle branch block pattern with a cycle length of 260 to 330 milliseconds. In the two patients who had only one form of VT (patients 2 and 3), the earliest ventricular activation site during VT was RVOT. The other patient (patient 1) had two different forms of VT originating from the RVOT and the RV inflow tract (RVIT).

Epicardial Mapping

In all patients, the VT that was induced at the preoperative electrophysiological study was identical to the clinical VT. In patient 1, however, the VT that seemingly originated from the RVIT was not inducible by electrophysiological study in the operating room.

Delayed activation of the RVOT was recorded during sinus rhythm in all cases. In patient 1, the site of earliest activation during VT was mapped close to the left anterior descending coronary artery. The wave front was conducted down through the RV free wall along the prior right ventriculotomy scar. Subsequently, the wave front spread up along the opposite side of the scar. At the upper border of the scar, diastolic delayed potentials were recorded during VT. Thus, a clockwise macroreentrant circuit was identified around a prior right ventriculotomy scar (Fig 1).

TABLE 2. Preoperative Electrophysiological Findings

<table>
<thead>
<tr>
<th>Patient</th>
<th>ECG Pattern</th>
<th>VT Origin</th>
<th>CL, ms</th>
<th>Preoperative EPS</th>
<th>Intraoperative EPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>LBBB+RAD</td>
<td>RVOT</td>
<td>330</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>LBBB+RAD</td>
<td>RVIT</td>
<td>300</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>LBBB+RAD</td>
<td>RVOT</td>
<td>290</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

VT indicates ventricular tachycardia; CL, cycle length; EPS, electrophysiological study; LBBB, left bundle branch block; RAD, right-axis deviation; LAD, left-axis deviation; RVOT, right ventricular outflow tract; and RVIT, right ventricular inflow tract.
In patient 2, epicardial mapping revealed that the wave front also revolved around the scar in a clockwise fashion during VT (Fig 2).

In patient 3, aneurysmal dilatation was noted along the horizontal incision line of the RV. During VT, diastolic delayed potentials were recorded in this area, and a clockwise macroreentrant circuit was mapped around the prior right ventriculotomy scar (Fig 3).

**Surgical Results**

There were no surgical or postoperative deaths. Three months after surgery, one patient developed VT that was slow and had a different configuration from the previous preoperatively documented clinical VT. In this patient, VT was easily controlled with the combined drug therapy of mexiletine (300 mg/d) and propranolol (60 mg/d). No recurrence of VT was noted after medical therapy. In the other two patients, VT did not recur after surgical resection and cryoablation. During a mean follow-up of 40 months, there were no episodes of recurrent VT or other cardiac events.

**Histopathological Findings**

The sizes of RV free wall specimens resected during the operations ranged from 8×20 to 34×38 mm. In patient 1, the RVOT wall around the scarred suture line of the previous operation showed diffuse endocardial fibroelastosis, transmural prominent adiposis, and mild fibrosis, which invaded the myocardium and replaced almost 50% of the myocytes. The surviving myocytes formed isletlike groups that were connected to each other with a few small myocyte branches and were irregularly scattered in the middle layer of the RV wall (Fig 4). The myocytes showed swelling, myofibrillolysis, vacuolation, focal necrosis, disarray, and hypertrophy, and there was focal infiltration of lymphocytes, plasma cells, eosinophil leukocytes, macrophages, and polynuclear giant cells around the myocyte islets (Fig 5).

The RV wall of patient 2 showed histological features around the operation scar similar to those of patient 1, i.e., adiposis, fibrosis, cell infiltration, myocyte islet formation, degeneration, disarray, and hypertrophy (Fig 6).

The kinds of infiltrating cells were almost the same as for patient 1, but eosinophilic leukocytes were more numerous, and some of them showed degeneration. At the site of midsystolic activity, both degenerated and normal myocytes were surrounded by fibrous and fatty...
tissue, showing many isletlike conformations. On the contrary, the site with diastolic activity during VT corresponded only to myocyte groups with degeneration.

In patient 3, histological features similar to those of patients 1 and 2 were seen. Myocytes in the islets, surrounded by thick fibrous and/or fatty tissue, showed severe degeneration such as edematous swelling, vacuolation, and deposition of protein debris. Endocardial and subendocardial fibroelastosis and fibrosis were most prominent in patient 3 (Fig 7).

Discussion

Patients who undergo surgical repair for TF are known to be at increased risk of sudden death in the late postoperative period. VT, which occurs with higher frequency in patients after surgical repair of TF, is considered to be the major cause of sudden death in this patient population.1-5,15

In a multicenter study of 359 surgically treated patients with TF,16 sustained VT was noted in 33 patients (9.2%). These patients differed significantly from the VT-free patients with respect to their age at the time of surgical repair of TF (VT, 6.9±3.8 years; VT free, 4.2±3.0 years). In our patients, VT occurred at an average of 8.7 years after surgical repair of TF. The radical surgical correction was performed at a mean age of 3.7 years, slightly younger than that of the patient group studied by Chandar et al.16

It has also been noted that the risk of sudden death after surgical correction of TF was related to postoperative hemodynamics. Garson et al15,17 reported that 38% of patients with premature ventricular contractions on routine ECGs died suddenly between 1 and 10 years after the operation, and 100% of patients who died suddenly had both RV systolic pressure of >60 mm Hg and RV end-diastolic pressure of >8 mm Hg.

Electrophysiological Findings

VT after surgical correction of TF has been classified into two types: VT originating from the RVOT, as reported by Horowitz et al,9 and VT originating from the RVIT septum, as reported by Kugler et al.10 The former type of VT was considered to be related to prior right ventriculotomy or reconstruction of the RVOT, whereas the latter type was believed to be related to closure of the VSD.

Using intraoperative mapping, Horowitz et al9 and Downar et al13 identified the site of origin of VT at the RVOT. In two cases reported by Horowitz et al,9 the origin of VT was within the free wall. Of the five episodes of VT in the four patients reported by Downar et al,13 VT originated from the free wall in one episode, from the septum in three episodes, and from the parietal band in one episode. In all three of our patients, epicardial mapping during VT showed diastolic activity within the free wall of the RVOT and reentrant loops around the prior right ventriculotomy scar, similar to the report of Horowitz et al.9 Patient 1 had VT originating from the RVIT septum. This VT, however, was unable to be induced during surgery, and thus the site of the VT foci was not identified. Kugler et al10 reported that the origin of the VT was at the RVIT in which the local electrogram was recorded earliest. However, detailed mapping or resection of the VT foci was not performed in their study. Thus, no detailed intraoperative electrophysiological studies of VT originating from the RVIT have been performed.
Surgical Procedure

When VT is unable to be controlled by drug therapy, surgical resection of the VT origin or catheter ablation should be considered. Before surgery or catheter ablation, precise mapping of the origin of VT is essential. Our three patients were treated surgically by a combination of myocardial resection and cryoablation. This combination was initially used clinically by our group in 1980 to treat patients with nonischemic VT. Successful methods of radical treatment of VT include incision of scarred regions, as reported by Horowitz et al., and resection of the aneurysmatically dilated RVOT, as reported by Campbell et al. Downar et al. also attempted cryoablation for radical treatment of VT in four patients. However, the procedure was unsuccessful in two patients in whom ischemic cardiac arrest was not incorporated. Based on these results, Downar et al. pointed out the importance of aortic crossclamping before cryoablation. Cryoablation was performed after aortic crossclamping, and cardioplegic solution was administrated to ensure a freezing effect, similar to the methods of cryoablation used for nonischemic VT.

Histopathology

The present study revealed that the site of the presumed origin of VT showed significant abnormalities such as fibrosis, adiposis, and degeneration of the myocardium. Specifically, the site of the presystolic activation consisted of degenerating myocytes surrounded by fibrosis and adiposis. The site showing delayed conduction along the reentrant circuit showed scattered myocyte islets in the extensive adiposis and/or fibrosis, which could form an electrical maze around the surgical suture area.
FIG 5. Photomicrograph of right ventricle of patient 1 at the area adjacent to the previous suture for radical repair. Original magnification ×100. Hematoxylin and eosin stain. Myocyte disarray, hypertrophy, and degeneration with inflammatory cell infiltration are seen.

FIG 6. Photomicrograph of right ventricle of patient 2. Original magnification ×40. Hematoxylin and eosin stain. Islet formation of survived myocyte is surrounded by fibrosis.
the development of reentrant circuit. Hegerty et al reported that the amounts of myocardial fibrosis of the RVOT in patients with TF younger than 1 year did not differ from those in healthy control subjects but that the patients more than 5 years old had significantly increased fibrosis. Transatrial approach and early radical treatment of TF were recommended to circumvent the histopathological change. From histological examination of our cases, we considered fibrosis and adiposis in RVOT to be closely related to the mechanism of VT.

**Therapeutic Option**

An alternative to surgical resection for the treatment of VT is catheter ablation. However, radiofrequency catheter ablation can create only small areas of injury (<2-mm diameter). Thus, treatment of VT with this technique is limited and generally used only after surgical repair of TF. Although direct current electrical shock has been used for ablation in certain cases, it is occasionally associated with serious complications. Garson reported patients developing shock and dying due to electromechanical dissociation immediately after ablation.

Downar et al reported on the implantation of an implantable cardioverter-defibrillator to treat VT in this patient population. This therapy appears, however, to be a final resort in patients who were unable to be treated by other direct interventions.

In conclusion, our study suggests that surgical resection is a reliable form of therapy for patients developing VT after surgical repair of TF.

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**References**


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