ELECTROPHYSIOLOGIC STUDIES

Ventricular Tachycardia After Surgical Repair of Tetralogy of Fallot: Results of Intraoperative Mapping Studies

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Objectives. Four patients with previous repair of tetralogy of Fallot and ventricular tachycardia underwent map-guided surgery to ablate the arrhythmias.

Background. Although patients with repair of tetralogy of Fallot are at increased risk of sudden death due to ventricular tachycardia, little is known of the origin and mechanism of this arrhythmia.

Methods. A customized right ventricular balloon with 112 electrodes was used to record endocardial activation and, where possible, simultaneous epicardial recordings were obtained with a sock electrode array. Three patients had an aneurysm of the right ventricular outflow tract and one had a septal aneurysm. All had moderate to severe pulmonary valve insufficiency. Preoperative electrophysiologic study demonstrated inducible rapid (cycle length 180 to 300 ms) hemodynamically unstable monomorphic ventricular tachycardias.

Results. Intraoperatively, five different tachycardias (two in one patient) were induced and mapped. The sites of earliest activation were located in the subendocardium of the right ventricular outflow tract in all, but they varied widely among the septum, free wall and parietal band and could not be identified by visible scar. All were due to a macroreentrant circuit initiated by a critical delay in activation beyond a functional arc of block. Two patients treated by cryoablation while the heart was beating and perfused at normal temperature had inducible ventricular tachycardia postoperatively. In the two subsequent patients, the application of cryoablation under anoxic cardiac arrest resulted in noninducibility of arrhythmia.

Conclusions. Ventricular tachycardia in tetralogy of Fallot in these four patients was caused by macroreentry in the right ventricular outflow tract. Surgical success depends on detailed mapping and cryoablation under anoxic cardiac arrest. In patients at risk of sudden death, map-directed surgery may offer distinct advantages over either implantable devices or drug therapy.

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Patients who have undergone previous repair of tetralogy of Fallot are at risk of sudden death (1–4). Although some of these deaths have been attributed to the development of late conduction disturbances, specifically complete heart block (5,6), ventricular tachycardia has more recently been identified as an important contributor to this late mortality (7,8). Little is known about either the mechanism or site of origin of the ventricular tachycardia in these patients (9). The development of a customized right ventricular balloon electrode array that conforms to the major anatomic features of the right ventricle (10,11), coupled with an intraoperative mapping system that enables simultaneous recording of 112 endocardial and 112 epicardial electrodes (12,13), has facilitated acquisition of this information. In this study, we report our findings obtained from intraoperative mapping of ventricular tachycardia in four adult patients who had previous surgical correction of tetralogy of Fallot.

Methods

Patient characteristics. Initial surgical correction for tetralogy of Fallot was performed at a mean age of 8 years (range 5 to 11) in the four patients (two male, two female). The clinical presentation with subsequent ventricular arrhythmias occurred from 12 to 28 years after repair and was varied, including cardiac arrest (one patient), syncope (one patient) and palpitation (two patients). Of the latter, one patient had ventricular tachycardia documented on ambulatory electrocardiographic (ECG) monitoring and one was found to have sustained ventricular tachycardia at
220 beats/min on presentation to the hospital. The mean age at the time of presentation with arrhythmias was 30 years (range 23 to 39).

Hemodynamic characteristics. At the time of cardiac catheterization, all four patients had evidence of ventricular outflow tract aneurysmal dilation at the site of previous right ventriculotomy. However, right ventricular function was relatively preserved in all, with a mean right ventricular end-diastolic pressure of 6 mm Hg (range 1 to 11) and a mean ejection fraction determined by radionuclide angiography at rest of 35% (range 26% to 43%). Left ventricular function was normal in three patients, with one patient having grade III left ventricular dysfunction. The mean left ventricular end-diastolic pressure and cardiac output were, respectively, 8 mm Hg (range 5 to 13) and 4.5 liters/min (range 3.8 to 5.4). No patient had evidence of a persistent ventricular septal defect by either angiographic or echocardiographic studies. Three patients had severe pulmonary regurgitation. One patient had moderate and three had mild tricuspid regurgitation.

Electrophysiologic characteristics. Ventricular tachycardia was inducible in the four patients at preoperative electrophysiologic study. The induced ventricular tachycardia was rapid, with the cycle length varying between 180 and 300 ms, and had a strikingly similar configuration in three patients having a left bundle branch block pattern; the fourth patient had both a right and a left bundle branch block tachycardia. In two patients, the tachycardia could be easily terminated by pacing, but in the other two patients, who had a history of syncope, it was hemodynamically unstable and required direct current cardioversion. All patients had inducible tachycardias after the intravenous administration of antiarrhythmic drugs including propafenone, procainamide and quinidine. The predominant indication for surgery was pulmonary regurgitation in three patients and ventricular tachycardia in one patient.

Intraoperative Mapping Technique

Recording electrodes. A customized right ventricular balloon electrode array, previously described (10), was designed to enable endocardial recordings to be obtained from both the body of the right ventricle and the outflow tract. One hundred twelve electrodes were arranged in 14 rows of eight electrodes. Eight rows of electrodes extended from the right ventricular apex to the base and six traversed the outflow tract (Fig. 1). The entire array was depicted in a modified polar projection (Fig. 1B), with the apex at the center. The first four electrodes of rows 11 through 2 monitored the outflow tract and were displayed as if the array was cut along a line between rows 2 and 11. For simplicity, not all electrodes are shown in the rows extending from the tricuspid valve to the apex. C. The array seen as an on-line video display at the time of operation. LAD = left anterior descending artery.

Figure 1. Right ventricular balloon electrode array. A. The array in a right lateral view with the electrodes arranged in rows of 8, extending from apex to base or stretching the outflow extension. B. The entire array in a modified polar projection with the apex at the center and base at the periphery. However, the first 4 electrodes of rows 11 through 2 extend up the outflow tract and are seen as if the array was cut along a line between rows 2 and 11. For simplicity, not all electrodes are shown in the rows extending from the tricuspid valve to the apex. C. The array seen as an on-line video display at the time of operation. LAD = left anterior descending artery.
used to generate an intensity signal that brightened at the time of local activation. All intensity signals were then assembled into a single video format displayed at the time of operation.

In addition, the analog signals were stored for subsequent off-line analysis. Local activation times (defined as the steepest part of the negative deflection from the isoelectric line) were measured from a common reference time and used to generate isochronal maps (12 ms) of endocardial and epicardial activation. When an individual electrogram was not initially interpretable because of broad multiphasic deflections, review of adjacent electrograms often permitted determination of activation times. Although this may have introduced slight inaccuracies in the timing of activation at one or more sites, it should not have precluded satisfactory mapping (14,15). At a paper speed of 250 mm/s, measurements were accurate to ±4 ms. The surface ECG was recorded at the time of operation and stored.

Surgical procedure. Informed consent for map-guided ablative surgery was obtained from each patient before operation. At the time of operation, the patient was placed on normothermic cardiopulmonary bypass. With bicaval cannulation, the right atrium was opened and integrity of the atrial septum ensured. The deflated balloon was introduced into the right ventricle through an incision in the right pulmonary artery or previous ventriculotomy site was used to withdraw the long tip attached to the balloon “finger” or extension, thereby advancing it into the outflow tract for subsequent endocardial recordings. Once in position, the balloon was inflated with dextrose solution to facilitate endocardial contact and stable recordings. The sock was then positioned over the epicardial surface of the heart, such that the first row of electrodes was aligned along the left anterior descending artery. Programmed pacing was performed by using a sutured epicardial electrode on the right ventricular surface.

Cryoablation was performed by delivering two to four contiguous cryolesions at -60°C with use of a 15-mm probe applied for 2 to 3 min.

Results

Induced ventricular tachycardia. Ventricular tachycardia of a configuration similar to that observed clinically or induced at electrophysiologic study, or both, was easily initiated in all patients intraoperatively by using two to four extrastimuli. Three patients had a single tachycardia configuration; the fourth patient had two separate monomorphic tachycardias. All five tachycardias had their site of earliest activation in the right ventricular outflow tract. There was no obvious scar or consistent anatomic landmark to identify this site, which was in the right ventricular free wall in one case, in the right ventricular infundibular septum in three cases and in the parietal band in one case. In each case, the sequence of activation indicated a macroreentrant circuit with the critical return path situated in the subendocardium of the outflow tract. In two cases, application of a cryoprobe to this area during tachycardia terminated the tachycardia. In a third patient, manual pressure over the return path repeatedly terminated the tachycardia.

Cryoaablation. In the first patient to be operated on, cryoaablation was performed during sinus rhythm after mapping. During normothermia, contiguous cryoaablation lesions were delivered to the tachycardia site of earliest excitation on the infundibular septum. No further attempt was made to reinitiate the tachycardia intraoperatively. At postoperative electrophysiologic testing, the tachycardia was still inducible. After clinical recurrences, the patient received an implantable defibrillator.

In the next patient, the site of earliest activation was localized to the parietal band. Despite repeated successful terminations of the tachycardia with manual pressure, four cryoaablation lesions delivered during normothermia to the same area failed to prevent tachycardia reinitiation. There have been no spontaneous occurrences with amiodarone therapy.

In the remaining two cases, pressure over the site of earliest activation also terminated the tachycardia. Because of the previous experience in each case, two contiguous cryoaablation lesions were delivered to that site during anoxic arrest to increase the depth and extent of the cryoaablation lesions. Subsequent stimulation failed to induce the tachycardias then and at later postoperative study.

Epicardial activation sequence. Figure 2 shows the activation sequence in 12-ms isochrones during ventricular tachycardia in the three patients with monomorphic tachycardia. Global epicardial activation is shown in the left three panels and right ventricular endocardial activation in the right three panels. In all three cases, epicardial activation was strikingly similar, with an apparent monofocal origin of activation on a single electrode. This electrode was different in each case (first electrode of row 13, 2 or 0) because of differences in the relation of the sock matrix to the heart. The anatomic sites in each case were the same: high on the right side of the infundibular septum. Despite the apparent monofocal origin at this site, comparison with the simultaneously recorded epicardial right ventricular activation revealed that this was the passive site of epicardial breakthrough. Epicardial activation began 108, 40 and 44 ms, respectively, after earliest endocardial activation in each of the three patients (Fig. 2).
Figure 2. Activation maps during ventricular tachycardia in three patients. Twelve-millisecond isochrones show the global epicardial sequence (left panels) and right ventricular endocardial sequence (right panels). Although the epicardial site of earliest activation (asterisk) was monofocal in each case, it was later (108, 40, and 44 ms, respectively) than the earliest endocardial activation. All three tachycardias originated in the right ventricular outflow tract.

Top right panel. An origin (asterisk) situated on a hypertrophied parietal muscle band. It then proceeded down into the body of the right ventricle and circulated around a functional arc of block between electrode rows 12 and 13. Middle right panel. A tachycardia that originated in the right ventricular septum and then spread around the base of the outflow tract to avoid a longitudinal arc of block between rows 0 and 13. Bottom right panel. Another case with the origin in the septum, with a recirculating front moving around a transverse arc of block (see text). t = time.

The activation sequence of ventricular tachycardia in Patient 3 is shown in the bottom two panels of Figure 2. Each beat of the ventricular tachycardia also started on the right side of the infundibular septum simultaneously at the second electrode of rows 2 and 11, which were immediately adjacent. Subsequent activation spread around the outflow tract and, because of a transverse functional arc of block, could only enter the body of the right ventricle along row 12. The reentrant circuit was completed...
Figure 3. Ventricular tachycardia from the example shown in the top panels of Figure 2. Upper panel, Endocordial unipolar electrograms from electrode row 12 of the balloon array. The top tracing was from the distal outflow tract and each adjacent tracing was from the neighboring electrode on the row ending with the bottom tracing from the right ventricular apex. Although the top and bottom tracings show single activations, the fourth, fifth and sixth tracings show multiphasic deflections. Comparisons with neighboring electrograms from rows 11 and 13 (arrowheads) identified an activation front moving down a parietal band around a line of conduction block between rows 12 and 13. The activation spread into the right ventricular apex then back up into the outflow tract (see text). Bottom panel, Leads I, II and III of the surface electrocardiogram and time code recorded during initiation of the ventricular tachycardia seen in the upper panel. Vertical bar denotes 20 mV; horizontal bar indicates 200 ms.

by ascending activation into the outflow tract along row 2 where, after a 60-ms delay, activation spread from the third electrode back to the origin on electrode 2. In this patient, the tachycardia was repeatedly terminated by pressure at the site of origin. Cryoablation during ischemic cardiac arrest resulted in eradication of the arrhythmias.

Patient 4 had two different configurations of ventricular tachycardia that were induced preoperatively and at the time of operation. Figure 4 shows the right ventricular endocardial maps of both tachycardias and leads aVR, aVL and aVF of the surface ECG. In this patient, epicardial mapping with a sock array was precluded by extensive adhesions due to the previous operation. This tachycardia started on the second electrode of row 1 (Fig. 4, left panel). It then formed a reciprocating wave front, moving around a transverse arc of block in the free wall of the right ventricular outflow tract. This region was aneurysmally dilated and, after local resection, this tachycardia could no longer be induced. However, a second tachycardia originating high in the infundibular septum was induced (Fig. 4, right panel). The pattern of activation is suggestive of an incomplete figure eight. Each beat started near of at electrodes 2 and 3 of row 2 and activation spread down toward the right ventricular apex along row 2. Subsequently, two activation fronts moved around a transverse arc of block toward the origin. One wave front attempted to return by row 1 but was preempted by 36 ms by the second wave front, which returned along row 11. Pressure at the site of slow conduction along row 2 reproducibly terminated the tachycardia. Cryoablation during ischemic cardiac arrest at the same site resulted in noninducibility at postoperative electrophysiologic testing.

Mechanism of initiation. In each case, ventricular tachycardia was initiated by programmed extrastimuli. The effect of each premature stimulus was to produce increasing delay in activation of some portion of the distal right ventricular outflow tract. At a critical delay, the activation was able to penetrate a zone of previous functional block and return as the first beat of tachycardia. This is illustrated in Figure 5, which shows initiation of the ventricular tachycardia already shown in the bottom panels of Figure 2. Surface ECG leads I, II, III and aVR showed a sinus beat with right bundle branch block usurped by a sequence of basic stimuli, ending with two premature stimuli that initiated the tachycardia. The top left panel shows right ventricular activation during sinus beats. Earliest activation (asterisks) appeared over a large apical region, but the subsequent spread of activation was forced around an extensive zone of block, extending longitudinally between rows 13 and 0 and transversely across rows 0, 1 and 2. During basic pacing, the sequence was reversed, with activation starting on the opposite side of
Discussion

In patients with previous repair of tetralogy of Fallot, late onset ventricular tachycardia although infrequent, appears to be an important cause of sudden death in these patients (7,8).

Mechanism. Results from experimental studies (16) in a dog model of this condition initially suggested triggered automaticity as the possible mechanism of tachycardia; however, clinical studies appear to support reentry as the primary mechanism. Intraoperative mapping data of Horowitz et al. (9) from four patients demonstrated fractionated low amplitude electrograms, with continuous activity consistent with reentry in all patients. Demonstration of entrainment of the tachycardia in a patient with previous repair of tetralogy of Fallot during electrophysiologic study by Kremers et al. (17) provides additional indirect evidence of reentry as the primary mechanism of ventricular tachycardia in these patients.

Using the right ventricular balloon array in a transthoracic approach allowed us to obtain for the first time simultaneous right ventricular endocardial and global epicardial recordings from the intact ventricles. With 224 electrodes, it was possible to observe the excitation sequence in a detailed manner on a beat-to-beat basis. In all five episodes of ventricular tachycardia, the origin was in the subendocardium of the right ventricular outflow tract. The sock array revealed the epicardium to be merely a passive breakthrough point, with a monofocal activation pattern in all patients. The activation sequence during the tachycardias was always consistent with a macroreentrant circuit.

Conduction block. In a surgical series by Harken et al. (18), the mechanism of tachycardia was also reported as reentry, but the ventricular scar was believed to provide the barrier around which the tachycardia could circulate. In our cases, there was no such anatomic barrier. Instead, the circuit was established by a critical delay in activation at a site beyond a functional arc of block, which then became the
site of earliest activation during tachycardia. There was no scar or other visible sign that might have helped direct surgical ablation without mapping. Evidence of this functional block is seen in Figure 5. In sinus rhythm, a transverse line of block separated the 12-ms isochrone from the 96-ms isochrone along electrode rows 1 and 2. With the onset of stimulation (panels S1, S2 and S3), this block disappeared and smooth spread of activation was seen along rows 1 and 2 in a manner inconsistent with a fixed anatomic block. Further evidence of the functional nature of the block is seen in Figure 4. The left panel shows a transverse line of block separating the 0- to 12-ms isochrones from the 120-ms isochrone on electrode row 12. There was no evidence of any conduction block over rows 1 and 2. In contrast, the right panel shows in the same patient a second tachycardia, in which there was no conduction block over row 12. However, a new region of block had appeared, separating the 72-ms isochrone from the 172-ms isochrone along row 1.

Site of earliest activation. Horowitz et al. (9) found that earliest activation occurred consistently in the right ventricular outflow tract. However, in another electrophysiologic study by Kugler et al. (19), the tachycardia was found to originate from the inflow-septal area of the right ventricle. Although our findings are in agreement with those of Horowitz et al. (9), the site of origin within the outflow tract varied widely among patients. Furthermore, in the patient with two configurations of ventricular tachycardia, disparate sites of origin were observed (one in the right ventricular free wall and the other in the right ventricular septum). This belies any a priori assumptions about the origin of a tachy-
cardia based on the presence of visible scar or outflow tract aneurysm and emphasizes the importance of careful mapping to direct surgical ablation.

Cryoaablation and resection. In our patients, resection was feasible in only one case in which the earliest activation site was located in an aneurysmal portion of the free wall of the outflow tract. In the other four cases the site of earliest activation lay deep in structures such as the ventricular septum, with no visible scar to delineate the area to resect. Once the site of earliest activation of a tachycardia is accurately identified, deep cryoaablation should be applied if resection is not feasible. Application of a cryoprobe at −60°C for 2 min to the site of termination by manual pressure proved to be insufficient during normothermia in the perfused heart. To obtain a surgical cure, we found it necessary to expand the cryoaablation lesion by using the cryoprobe during ischemic cardiac arrest.

Right ventricular dysfunction. It has been reported that patients with previous repair of tetralogy of Fallot who have increased right ventricular systolic pressure (7) and right ventricular dimensions by echocardiography (8) have an increased incidence of high grade ventricular arrhythmias. More recent studies have not substantiated this observation. In our patients, global right ventricular function was relatively well preserved; however, all four patients had evidence of aneurysmal dilation of the right ventricular outflow tract or septum, or both, and substantial volume overload from severe pulmonary regurgitation. Although these changes may represent progression of the underlying congenital abnormality, they are more likely the result of the initial surgical correction of the tetralogy of Fallot. Consistent with this view is the recent report by Dietl et al. (20) comparing transatrial versus transventricular approaches to repair of tetralogy of Fallot. Their findings support the suggestion that the transventricular approach may contribute to the late ventricular arrhythmias observed in these patients.

In our patients, it was not possible to obtain histologic data on the arrhythmogenic substrate in the outflow tract. White et al. (21) recently reported that autopsy specimens obtained from patients who died >6 months after repair revealed isolated bundles of myocardial cells surrounded by extensive fibrosis in the region of the scar tissue. This appearance was very similar to that observed in the border zone of myocardial infarction. In our patients, the effects of premature stimuli evoking transient block and critical delays in activation could have been the functional manifestation of such pathologic findings.

Clinical implications. Although our observations are clearly limited by the small number of patients studied, they imply that accurate identification of the arrhythmogenic mechanism is feasible in patients with tetralogy of Fallot. The successful development of a right ventricular balloon array in conjunction with an on-line mapping system should facilitate curative surgical ablation. In these young patients who are known to be at risk of sudden death, map-directed surgery may offer distinct advantages over either implantable devices or drug therapy.

References