Role of Purkinje Fibers in Post-Infarction Ventricular Tachycardia

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OBJECTIVES
The objective of this study was to assess the role of Purkinje fibers in monomorphic, post-infarction ventricular tachycardia (VT).

BACKGROUND
Ventricular fibrillation and polymorphic VT in the setting of acute myocardial infarction (MI) may be triggered by ectopy arising from Purkinje fibers.

METHODS
From among a group of 81 consecutive patients with post-infarction monomorphic VT referred for catheter ablation, 9 patients were identified in whom the clinical VT had a QRS duration ≤145 ms. Mapping was performed focusing on areas with Purkinje potentials.

RESULTS
A total of 11 VTs with a QRS duration ≤145 ms were induced and mapped in the 9 patients; 9 of the 11 VTs had a right bundle branch block/left-axis morphology that mimicked left posterior fascicular VT. The mean VT cycle length was 402 ± 82 ms. Eight of 9 patients had a history of inferior MI involving the left ventricular septum. One patient had an anterior wall MI with septal involvement. Mapping during VT demonstrated re-entry involving the inferior left ventricular wall. In each of the VTs, a Purkinje potential was present at the exit site of the VT re-entry circuit. Single radiofrequency catheter ablation lesions were successful in eliminating these VTs in all patients.

CONCLUSIONS
The Purkinje system may be part of the re-entry circuit in patients with post-infarction monomorphic VT, resulting in a type of VT with a relatively narrow QRS complex that mimics fascicular VT. (J Am Coll Cardiol 2006;48:2500–7) © 2006 by the American College of Cardiology Foundation

Characteristics of subjects. Eighty-one consecutive patients with prior MI referred for VT ablation between 1996 and 2005 underwent left ventricular (LV) endocardial mapping during sinus rhythm and during VT whenever feasible (Table 1).

In 9 of 81 patients, the clinical VT had a QRS width ≤145 ms (Fig. 1). These 9 patients are the subjects of this study. Data were gathered retrospectively in 7 patients and prospectively in 2 patients. Eight of the 9 patients had a prior inferior wall MI that involved the LV septum. One patient had an anterior wall MI with septal involvement. The infarctions occurred a mean of 4.7 ± 4.1 years earlier (range 3 months to 10 years). The clinical characteristics of these 9 patients and the 72 other patients who had VT with QRS durations >145 ms are described in Table 1. Eight of the 9 patients had an implantable cardioverter-defibrillator.

In 7 patients, the VT had a right bundle branch block morphology with left-axis deviation. In one patient, the VT had a right bundle branch block with right-axis deviation, and, in one patient, the VT had a left bundle branch block morphology with left-axis deviation.

Electrophysiology study. The electrophysiology procedures were performed in the fasting state after informed consent was obtained. A quadripolar catheter was positioned in the right ventricle, and programmed stimulation was performed with up to 4 extrastimuli at 2 basic drive cycle lengths. A quadripolar catheter with 5-mm interelectrode spacing was positioned at the His bundle to rule out bundle branch re-entry tachycardia. The mapping catheter was positioned in the LV using either a retrograde aortic or trans-septal approach. A bolus of 5,000 U of heparin was administered followed by an infusion of 1,000 U/h adjusted to maintain an activated clotting time of approximately 300 s.

Mapping and ablation. A 3-dimensional mapping system with a 4-mm-tip ablation catheter (Navistar, CARTO, Biosense Webster Inc., Diamond Bar, California) was used to create a voltage map during sinus rhythm in 6 of 9 patients and for activation mapping during VT in 4 of 9 patients. Bipolar electrograms were recorded between the 4-mm-tip electrode and a 2-mm ring electrode separated by 1 mm. In 3 of 9 patients, a quadripolar electrode catheter...
(EP Technologies, Mountain View, California) with a 4-mm-tip electrode and 2-5-2 mm interelectrode spacing was used for mapping and ablation. The bipolar electrograms were filtered at 50 to 500 Hz. Bipolar pacing was performed from the distal electrode pair of the mapping catheter at twice the diastolic threshold, with a pulse width of 2 ms.

A voltage map was generated in all patients in whom electroanatomic mapping was performed. Scar was defined as a site with an electrogram voltage ≤1.0 mV (6).

Radiofrequency energy was delivered during VT only at sites where there was concealed entrainment. Applications of radiofrequency energy were titrated to maintain a target temperature at the electrode-tissue interface of 60 °C. The radiofrequency energy application was continued for at least 30 s if adequate heating at the electrode-tissue interface was achieved. If VT terminated within 30 s, the energy application was continued for 60 s, then repeated for another 60 s. If the VT did not terminate in the first 30 s, the energy application was discontinued and other target sites were sought.

We assessed the presence or absence of Purkinje potentials whenever the area of scar involved the LV septum. After-depolarizations described by Ouyang et al. (7) and Nogami et al. (8) were sought at sites where Purkinje potentials were recorded. In areas of scar, pacing was performed during sinus rhythm to identify the VT exit site. Inducible VTs that were felt to be non-clinical were not targeted in a systematic manner because of changing ablation strategies over the time the data were collected.

Evidences of participation of Purkinje fibers. The following criteria were used to demonstrate participation of Purkinje fibers in the VT re-entry circuit:

1. Absence of a His depolarization preceding the QRS complex during VT at a site where a His depolarization was recorded during sinus rhythm. This was the case in 8 of 9 patients (Fig. 5).
2. In 1 of 9 patients, a His depolarization was recorded 50 ms before the QRS complex during VT that had a left bundle branch block configuration. In this patient, pacing at the right ventricular apex resulted in a post-pacing interval of 90 ms, ruling out bundle branch re-entry.

Fascicular and interfascicular VT were ruled out by demonstrating concealed entrainment from a myocardial site distant from the septum and the fascicles. Furthermore, matching stimulus-QRS and electrogram-QRS intervals were required to demonstrate that this site participated in the re-entry circuit (Fig. 6).

When Purkinje potentials were recorded within a region of scar, we assessed whether there was evidence of slow conduction at contiguous sites within the region until reaching sites where a Purkinje potential was no longer detected (Fig. 7). This was compared to conduction in regions of normal voltage (Fig. 7).

The 2 patients (Patients #1 and #8 in Table 2) who were enrolled prospectively did not differ from the retrospectively enrolled patients with respect to QRS width during VT or any other measured variables.

Follow-up. The patients were seen in follow-up every 3 to 6 months. The mean duration of follow-up was 12 ± 8 months. Treatment with sotalol was continued in 4 patients who were taking sotalol before the ablation procedure. The other patients were not treated with antiarrhythmic medications during follow-up.

Statistical analysis. Continuous variables are expressed as mean values ± 1 SD and were compared using the Student t test. Categorical variables were compared by chi-square analysis or with the Fisher exact test if a cell size was <5. A p value of <0.05 was considered significant.

Table 1. Characteristics of Patients Identified by QRS Duration of Clinical VT of ≤ and >145 ms

<table>
<thead>
<tr>
<th>Parameter</th>
<th>QRS ≤145 ms</th>
<th>QRS &gt;145 ms</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>9</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>Number of VTs</td>
<td>11</td>
<td>175</td>
<td></td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>67 ± 11</td>
<td>67 ± 9</td>
<td>1.0</td>
</tr>
<tr>
<td>Women/men</td>
<td>2/7</td>
<td>10/62</td>
<td>0.6</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>0.33 ± 13</td>
<td>0.25 ± 11</td>
<td>0.09</td>
</tr>
<tr>
<td>QRS during VT (ms)</td>
<td>139 ± 7</td>
<td>197 ± 34</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>VT morphology</td>
<td></td>
<td></td>
<td>0.1</td>
</tr>
<tr>
<td>LBBB</td>
<td>1/11</td>
<td>100/175</td>
<td></td>
</tr>
<tr>
<td>RBBB</td>
<td>10/11</td>
<td>75/175</td>
<td></td>
</tr>
<tr>
<td>VT cycle length (ms)</td>
<td>402 ± 82</td>
<td>448 ± 110</td>
<td>0.17</td>
</tr>
<tr>
<td>Infarct localization</td>
<td></td>
<td></td>
<td>0.2</td>
</tr>
<tr>
<td>Inferior</td>
<td>8/9</td>
<td>52/72</td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>3/9</td>
<td>42/72</td>
<td></td>
</tr>
<tr>
<td>Amiodarone therapy</td>
<td>0/9</td>
<td>40/72</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

LBBB = left bundle branch block; RBBB = right bundle branch block; VT = ventricular tachycardia.
RESULTS

Patient characteristics. The mean LV ejection fraction in the 9 patients with VT that had a QRS duration ≤145 ms tended to be greater than in the other 72 patients (Table 1). Eleven different VTs with a QRS duration ≤145 ms were induced in the 9 patients. In 4 of the 9 patients, a VT that had a QRS duration ≥145 ms also was induced. These VTs were not targeted for ablation.

The mean cycle lengths of the VTs with QRS durations ≤145 ms and >145 ms did not differ significantly (Table 1).

Mapping results. A Purkinje potential that preceded the QRS complex by a mean of 13 ± 16 ms was recorded...
during sinus rhythm at the VT exit site in each of the 9 patients. After-depolarizations similar to the potentials described in previous reports (7,8) were not present in any patient at effective ablation sites where Purkinje potentials were recorded during sinus rhythm, either before or after ablation. The exit site was located within a region of scar in all patients. There was significantly slower conduction where contiguous Purkinje potentials were recorded during sinus rhythm in regions of scar as compared with regions where the voltage was >1 mV (0.7 ± 0.24 m/s vs. 3.0 ± 0.92 m/s, p < 0.001).

A Purkinje potential preceding the QRS complex during VT by 10 ms was observed in only 1 of 175 VTs among the 72 patients with VTs that had a QRS duration >145 ms. Pacing at this site during VT failed to demonstrate concealed entrainment. The potential preceding the QRS complex was validated as being a Purkinje potential by demonstrating a Purkinje potential preceding the QRS complex during sinus rhythm. Furthermore, the exit site of this VT did not show Purkinje potentials during sinus rhythm.

In 22 of the 175 VTs, there was evidence by pace mapping and/or entrainment mapping that the septum, but

Figure 3. An example of spontaneous variation in the ventricular tachycardia (VT) cycle length, with changes in the interval between Purkinje potentials preceding the changes in RR interval. Displayed are 2 panels recorded at different times during the same VT. Leads V1 and V6 and intracardiac recordings from the mapping catheter (Map) and the right ventricular apex (RVA) are shown. The Purkinje potential intervals and RR intervals are indicated.

Figure 4. Recordings from the distal poles of the mapping catheter (Map dist) located at a site in the posteroseptal left ventricle where a Purkinje potential precedes the QRS complex by 20 ms during sinus rhythm (A) and by 35 ms during ventricular tachycardia (VT) (B). Pace mapping performed at this site during sinus rhythm (C), shows a match with the VT morphology (D).
not Purkinje fibers, was involved in the re-entry circuit. The QRS width of these VTs was 190 ± 26 ms. This was significantly broader than the QRS width of the VTs in which Purkinje fibers did participate (139 ± 7 ms, p < 0.001).

In 6 of 9 patients, concealed entrainment was demonstrated at the VT exit site, and there was a match between the stimulus-QRS interval during concealed entrainment and the Purkinje potential-QRS interval during VT. In all patients with spontaneous variation in the VT cycle length (8 of 9 patients), changes in Purkinje potential intervals preceded changes in RR intervals. In 8 of 9 patients, pacing during sinus rhythm reproduced the VT morphology at a site where a Purkinje potential was present.

In 2 of 4 patients in whom activation mapping (in conjunction with entrainment mapping) was performed with an electroanatomic mapping system, an isthmus between the infarct scar and the mitral annulus was also involved in the VT re-entry circuit.

In 2 patients, the inferior wall scar was part of the re-entry circuit. In each of the 4 patients, the exit site was located in the posteroseptal left ventricle at sites where Purkinje potentials were recorded during VT and during sinus rhythm. In Patients #5 and #8 (Table 2), 2 different branches of the Purkinje network, both in the posteroseptal area, appeared to be involved in the re-entry circuit. The effective ablation sites displayed Purkinje potentials during both VT and sinus rhythm and were located 11 mm and 31 mm from each other, respectively.

In 4 of 6 patients in whom a voltage map was performed during sinus rhythm, the LV scar involved both the inferior wall and parts of the septum. In 1 of 6 patients, the scar involved the entire septum and inferior wall, and in another

Figure 5. Continuous recording showing termination of ventricular tachycardia (VT) (left) and resumption of sinus rhythm (right) with a catheter at the His position (arrows). A His bundle depolarization is present during sinus rhythm but not VT, ruling out bundle branch re-entry.

Figure 6. Demonstration of concealed entrainment at a site remote from the Purkinje system. (A) Electrogram during sinus rhythm without Purkinje potentials. (B) Mid-diastolic isolated potential at this site during ventricular tachycardia (VT). The electrogram-QRS interval measured from the isolated potential is 160 ms. (C) Entrainment mapping performed at this site shows a matching stimulus-QRS interval of 160 ms during concealed entrainment. The catheter moved and ablation was not attempted at this site. This VT was ablated at a site displaying Purkinje potentials during both VT and sinus rhythm.
Radiofrequency ablation. Radiofrequency ablation was performed at the exit site of the re-entry circuit in 7 patients (during 9 different VTs) and at another site within the common pathway of the re-entry circuit in 2 patients (during 2 VTs). In one of the latter 2 patients, concealed entrainment was documented at a posteroseptal site where a Purkinje potential was recorded; however, the catheter moved before delivery of radiofrequency energy. This VT was successfully ablated in the isthmus between the infarct scar and the mitral valve annulus. In the other patient, the VT was successfully ablated within an inferior wall scar distant from the mitral annulus and the septum. Pace mapping during sinus rhythm showed a matching QRS morphology with the targeted VT at a site where Purkinje potentials were recorded. In 1 patient, concealed entrainment was demonstrated in the isthmus between an inferior wall scar and the mitral annulus. Delivery of radiofrequency energy in this area failed to terminate the VT, and radiofrequency energy delivery at the exit site displaying Purkinje potentials resulted in successful ablation.

In 1 patient, the target site was on the LV septum, immediately below where a His bundle depolarization was recorded. In another patient, the effective ablation site was at the anterior part of the septum where a Purkinje potential

Table 2. Characteristics of Patients and Mapping Sites

<table>
<thead>
<tr>
<th>Patient #</th>
<th>VTCL (ms)</th>
<th>Number of Other VTs</th>
<th>Identification of Exit Site</th>
<th>RF Effect Site</th>
<th>Septal Involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>415</td>
<td>1</td>
<td>PM SR</td>
<td>CP</td>
<td>IW + lower septum</td>
</tr>
<tr>
<td>2</td>
<td>540</td>
<td>0</td>
<td>CE</td>
<td>CP</td>
<td>IW + upper septum</td>
</tr>
<tr>
<td>3</td>
<td>380</td>
<td>0</td>
<td>CE, PM SR</td>
<td>Exit</td>
<td>N/A</td>
</tr>
<tr>
<td>4</td>
<td>250</td>
<td>0</td>
<td>CE, PM SR</td>
<td>Exit</td>
<td>IW + septum</td>
</tr>
<tr>
<td>5</td>
<td>400</td>
<td>1</td>
<td>CE, PM SR</td>
<td>Exit</td>
<td>IW + upper septum</td>
</tr>
<tr>
<td>6</td>
<td>390</td>
<td>1</td>
<td>CE, PM SR</td>
<td>Exit</td>
<td>N/A</td>
</tr>
<tr>
<td>7</td>
<td>380</td>
<td>0</td>
<td>CE, PM SR</td>
<td>Exit</td>
<td>N/A</td>
</tr>
<tr>
<td>8</td>
<td>380</td>
<td>3</td>
<td>PM SR</td>
<td>Exit</td>
<td>IW + septum</td>
</tr>
<tr>
<td>9</td>
<td>380</td>
<td>0</td>
<td>PM SR</td>
<td>Exit</td>
<td>AW, upper septum</td>
</tr>
</tbody>
</table>

AW = anterior wall; CE = concealed entrainment; CP = common pathway; IW = inferior wall; N/A = not applicable; PM SR = pace-map during sinus rhythm; RF = radiofrequency ablation; VTCL = ventricular tachycardia cycle length.
from the anterior fascicle was recorded. This patient's VT had a right bundle branch block morphology with right-axis deviation.

Radiofrequency ablation resulted in termination and non-inducibility of all 11 VTs with a QRS duration $\leq 145$ ms in the 9 patients. A total of $2.4 \pm 1.8$ radiofrequency energy applications per patient (range 1 to 5) were delivered to eliminate the targeted VTs. There were no complications of ablation. None of the patients had any new conduction abnormalities after ablation.

**Follow-up.** During a mean follow-up of 12 $\pm$ 8 months, none of the ablated VTs recurred. One patient died from trauma 2 months after the ablation procedure.

**DISCUSSION**

**Involvement of the Purkinje system.** The results of this study demonstrate that Purkinje fibers may participate in the re-entry circuit of post-infarction VT. Involvement of the Purkinje system accounts for the relatively narrow QRS complexes ($\leq 145$ ms) during these VTs. In all but 2 patients, the VT had a right bundle branch block morphology and a superior axis, suggesting that the left posterior fascicle was activated when the VT wave front exited the re-entry circuit. In 1 patient, the VT had a right bundle branch block configuration with right axis deviation and a Purkinje potential was recorded at the effective ablation site in the anterobasal septum, consistent with involvement of the left anterior fascicle. In the 1 patient in whom the VT had a left bundle branch block morphology, the effective target site was near the His bundle. This suggests that a proximal portion of the His-Purkinje system, before the branch point of the right and left bundle branches, was involved.

Purkinje potentials alone are not a specific indicator of participation within the re-entry circuit, as illustrated in one patient who had a QRS duration $> 145$ ms during VT. The presence of both a Purkinje potential and concealed entrainment during VT is required to indicate involvement of the Purkinje fibers in the re-entry circuit. The other diagnostic criteria used in this study also provided evidence of Purkinje fiber involvement in the VT re-entry circuit.

Although surviving Purkinje fibers can be identified in post-infarction scars in conjunction with surviving myocardial cells (3), a role for the Purkinje system in re-entrant VTs in the setting of healed infarction has been thought unlikely because of the rapid conduction properties of Purkinje fibers (12). However, in this as well as another study (13), slow conduction was demonstrated in Purkinje fibers that were present within regions of scar. It is unclear whether the conduction delay was present only in the Purkinje fibers or also at the Purkinje-myocardial tissue interface.

It is important to note that classic bundle branch re-entry was excluded by the absence of His deflections preceding the QRS complexes during VT in most cases and/or by entrainment mapping. Furthermore, concealed entrainment with matching stimulus-QRS and electrogram-QRS intervals was demonstrable at sites without His-Purkinje potentials, which also is strong evidence against bundle branch re-entry and fascicular tachycardia. The absence of late potentials (7,8) after effective ablation at sites with Purkinje potentials argues against re-entry confined to the Purkinje fibers alone.

**Mapping and ablation.** Entrainment mapping documented that the re-entry circuit in all patients was macro-re-entrant and involved mainly the infarct scar. Radiofrequency ablation was effective at sites other than the exit site where a Purkinje potential was recorded. In 2 of 9 patients, the effective ablation site was within the common pathway where a Purkinje potential was not present. However, the exit sites of these VTs did display Purkinje potentials. Figure 8 illustrates the proposed re-entry circuit involving Purkinje fibers in the septum.

Although the ablation procedure did not result in any conduction abnormalities, caution is required because ablation at a proximal site in the Purkinje system could result in left bundle branch block or high-degree atrioventricular block.

**Study limitations.** The possibility that Purkinje fibers were very close to the re-entrant circuits but not actually critical to re-entry cannot be completely excluded. Although our criteria are very suggestive of involvement of Purkinje fibers in post-infarction VT, high-resolution mapping would be needed to confirm the role of the Purkinje system in post-infarction VT. A second limitation is that most of the data in the study were gathered retrospectively.

None of the patients in this study were being treated with amiodarone. However, many other patients with implantable cardioverter-defibrillators and recurrent VT were treated with amiodarone. It is possible that amiodarone suppressed VT that involved the Purkinje system in some patients, thereby resulting in an underestimate of the prevalence of this type of VT.

The conduction velocity of the Purkinje fibers was calculated based on recordings from adjacent sites displaying Purkinje potentials. This provided at best a rough estimate of conduction velocity. However, our findings are plausible because similar findings have been demonstrated in an experimental preparation (13).

**Figure 8.** Schematic illustration of a re-entry circuit around an inferoseptal scar. Surviving muscle bundles within the myocardium and in the Purkinje system are components of the re-entry circuit.
REFERENCES