Observations on Mechanisms of Ventricular Tachycardia in Man

Hein J. J. Wellens, M.D., Donald R. Düren, M.D., and K. I. Lie, M.D.

SUMMARY Fifty patients with sustained ventricular tachycardia were studied by endocavitary recordings and programmed electrical stimulation. Of 29 patients in whom tachycardia could be initiated, 18 had chronic coronary artery disease and eight had no detectable heart disease. Of 35 patients in whom the tachycardia could be terminated by premature ventricular stimuli, 21 had chronic coronary artery disease and eight had no detectable heart disease.

Initiation of tachycardia was facilitated in 18 of 21 patients by pacing the ventricle at the slowest possible pacing rate. An inverse relation was found between the prematurity of the tachycardia-initiating premature beat and the interval between the premature beat and the first beat of tachycardia, a finding suggestive of a re-entry mechanism. The role of the specific conduction system in initiation and during tachycardia remains unknown. Stimulation site was found to affect initiation and termination of tachycardia and width of tachycardia zone.

PREVIOUSLY WE HAVE REPORTED on the initiation and termination of ventricular tachycardia by timed premature beats during electrical stimulation of the heart.1-4 More recently we have evaluated findings from fifty patients with ventricular tachycardia studied with endocavitary recordings and programmed electrical stimulation of the heart. The present report describes our observations relative to the time of initiation of the tachycardia, with particular emphasis on the effect of basic pacing rate, the coupling interval of the premature beat, and the role of the specific intraventricular conduction system. We have also considered the importance of site of stimulation on initiation and termination of tachycardia.

Material and Methods

Fifty patients were consecutively studied because of ventricular tachycardia (table 1). Twenty-one of these patients had a history of myocardial infarction occurring at least five weeks prior to the onset of tachycardia. Time interval between the first attack of tachycardia and the study varied from two months to five years. None of the 21 patients was in tachycardia at the initiation of the study. In contrast, seven patients developed sustained ventricular tachycardia within the first 24 hours of infarction. All were in tachycardia at the beginning of the study. Three patients developed ventricular tachycardia between the first day and five weeks following acute myocardial infarction; all three entered the catheterization room in tachycardia. The other diagnoses listed in table 1 were made from findings during heart catheterization and cineangiography. The patients in this group were not in tachycardia at the beginning of the study. The time interval between the electrocardiographic documentation of tachycardia and the study varied from three months to 19 years. Patients labeled as unknown had normal findings on heart catheterization and cineangiography (including coronary angiography). None of the patients reported suffered from the Q-T prolongation syndrome, nor did any of them show signs of pre-excitation during sinus rhythm and/or atrial pacing.

In all patients, following informed consent, catheters were passed through the femoral veins using the Seldinger technique. Two bipolar catheters were positioned high on the lateral wall of the right atrium, one for pacing the atrium and the other for recording an intra-atrial electrogram. A triPo1 catheter was positioned in the region of the bundle of His to record a His bundle electrogram. The fourth (bipolar) catheter was placed in the right ventricle and used for ventricular pacing. By using the single test stimulus method during right atrial pacing the electrophysiologic properties of atrioventricular conduction were determined. Thereafter during ventricular pacing single test stimuli were applied at progressively shorter intervals until the ventricular effective refractory period was reached. If the single test stimulus method was not successful in initiating tachycardia, two and then three premature stimuli were applied during ventricular pacing again at progressively shorter intervals until the ventricular effective refractory periods of the first and second premature beats were reached. The zone of premature beat intervals resulting in sustained ventricular tachycardia was carefully determined. In all patients three different basic cycle lengths were used during ventricular pacing. In the last 22 patients stimulation of the ventricle was performed not only from the apex but also from the outflow tract of the right ventricle. A diagnosis of ventricular tachycardia was made if the QRS complex during tachycardia was either not preceded by a His bundle electrogram or was preceded by a His bundle electrogram with an H-V interval shorter than the H-V interval during sinus rhythm.4 It was considered essential that the catheter recording the His bundle electrogram had an identical position during sinus rhythm and tachycardia. All data obtained during the stimulation studies were recorded on tape (Ampex FR 1300) and directly registered on an eight channel Elema recorder. Leads I, II, III, V1, V6, the intracavitary right atrial lead, and the His bundle lead were recorded simultaneously. For recording the His bundle electrogram an Elema EMT 12 was used.

Results

Initiation of Tachycardia

As listed in table 2, initiation of tachycardia by premature ventricular stimuli was possible in 29 patients. In two patients three consecutive premature stimuli had to be given to initiate tachycardia. In patients with old myocardial infarction and in those without any etiologic diagnosis it was...
usually possible to initiate tachycardia by appropriately timed premature beats. In the 21 patients in whom a single premature beat elicited tachycardia the width of the tachycardia zone (the zone of premature beat intervals resulting in tachycardia) varied from 20 to 240 msec. In six of these 21 patients the tachycardia zone extended to the effective refractory period of the right ventricle. In three patients, apart from initiation by a single ventricular premature beat during ventricular pacing, a ventricular tachycardia could also be initiated by the ventricular depolarization resulting from A-V conduction of a single atrial premature beat during atrial pacing (fig. 1). In these three patients the tachycardia zone extended to rather late premature beat intervals. This explains why in spite of the time needed for transmission through the A-V junction the supraventricular premature beat arrived in the ventricle in time to initiate tachycardia. Eleven of the 21 patients in whom a tachycardia could be initiated by a single ventricular premature beat showed that the premature beat was followed by a QRS complex similar in shape to subsequent QRS complexes during tachycardia (fig. 1). In five of these eleven patients a His bundle electrogram was found between the extrastimulus and the first QRS complex of tachycardia (fig. 2). Eight of the 21 patients in whom a tachycardia could be initiated by a single ventricular premature beat showed following the premature beat one or two ventricular complexes which differed in configuration from subsequent ones during tachycardia. In four of these eight patients the QRS configuration of

<table>
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<th>Diagnosis</th>
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<th>Age</th>
<th>Male</th>
<th>Female</th>
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<td>47–81</td>
<td>19</td>
<td>2</td>
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<tr>
<td>MI 1 day to 5 weeks old</td>
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<td>38–65</td>
<td>3</td>
<td>—</td>
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<tr>
<td>Within 24 hours of MI</td>
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<td>52–75</td>
<td>6</td>
<td>1</td>
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<tr>
<td>Prolapse MV</td>
<td>3</td>
<td>14–54</td>
<td>3</td>
<td>—</td>
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<tr>
<td>Digitalis intoxication</td>
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<td>76</td>
<td>1</td>
<td>—</td>
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<td>Aneurysm RV</td>
<td>1</td>
<td>61</td>
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<tr>
<td>Cardiomyopathy</td>
<td>3</td>
<td>38–54</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Unknown</td>
<td>11</td>
<td>19–52</td>
<td>8</td>
<td>3</td>
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</tbody>
</table>

Abbreviations: MI = myocardial infarction; MV = mitral valve; RV = right ventricle.

Table 2. Number of Ventricular Premature Beats Needed to Initiate Tachycardia

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Patients</th>
<th>1 VPB</th>
<th>2 VPB</th>
<th>3 VPB</th>
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<tr>
<td>MI older than 5 weeks</td>
<td>21</td>
<td>14</td>
<td>3</td>
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<td>7</td>
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<td>3</td>
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<tr>
<td>Unknown</td>
<td>11</td>
<td>6</td>
<td>2</td>
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</table>

Abbreviations: MI = myocardial infarction; MV = mitral valve; RV = right ventricle; VPB = ventricular premature beat.

Figure 1. Initiation of ventricular tachycardia by a ventricular complex resulting from A-V conduction of an atrial premature beat during atrial pacing (upper part of figure) and a ventricular premature beat during ventricular pacing (lower part). Note that although QRS configuration is different under both circumstances, at the ventricular level the premature beat starts activating the ventricle 500 msec after the last ventricular complex of the basic rhythm. Note also that depending upon the pattern of ventricular activation the interval between premature beat and first QRS of tachycardia varies (in the upper part of the figure this interval measures 430 msec, in the lower part 500 msec).
these beats was similar to the QRS complexes seen during ventricular stimulation (fig. 3). In the remaining four patients, however, the configuration of these beats differed both from the QRS complexes during ventricular pacing and the QRS configuration present during tachycardia (fig. 4). In all four a His bundle electrogram was sandwiched between the premature beat and these QRS complexes, which had the configuration of left bundle branch block.

Lastly, in two patients at long test stimulus intervals a tachycardia was initiated with uniform QRS complexes and no intervening His bundle electrogram, while at shorter test stimulus intervals a QRS complex similar in shape to the paced ventricular complexes followed the test stimulus preceding tachycardia. In these two patients an interval of 100 and 70 msec, respectively, was present between these two zones of premature beat intervals. During that intermediate interval no ectopic ventricular or tachycardia followed the induced ventricular premature beat.

In 21 patients it was not possible to initiate tachycardia. Diagnoses in these patients are given in table 2.

Effect of Basic Pacing Rate and Site of Stimulation

In all patients data were available during pacing at three different basic cycle lengths. In 18 of the 21 patients in whom only one premature beat was needed to initiate tachycardia, the tachycardia zone was widest, or initiation of tachycardia was possible, only at the slowest of the three pacing rates. In three patients, however, tachycardia could be initiated only at the highest pacing rate.

In ten of the 22 patients in whom stimulation was done both from the apex and the outflow tract of the right ventricle, tachycardia could be initiated by a single ventricular premature beat from both sites of stimulation. When identical basic pacing rates were compared it was found that in five of these ten patients the width of the tachycardia zone was widest during stimulation of the apex, and in two patients during stimulation of the outflow tract (figs. 5 and 6). In the three remaining patients the width of the tachycardia zone stayed the same. In two patients tachycardia could only be initiated during pacing of the apex and in one patient only during pacing of the outflow tract of the right ventricle.

The Interval between the Tachycardia-initiating Premature Beat and the First Beat of Tachycardia

Ten of the 13 patients in whom tachycardia could be initiated by a single ventricular premature beat and who showed onset of tachycardia with complexes of uniform shape immediately following the induced premature beat had a tachycardia zone of 50 msec or more. In eight of these ten patients shortening the interval of the tachycardia-initiating premature beat lengthened the interval between the premature beat and the first QRS complex during tachycardia (fig. 7). In the remaining two patients no relation was found between the prematurity of the induced premature beat and the length of the subsequent interval to the first QRS complex of tachycardia. As shown in figure 1 the interval between the tachycardia-initiating premature beat and the first beat of tachycardia was also affected by the ventricular activation pattern of the premature beat.

![Figure 2](http://circ.ahajournals.org/)

**Figure 2.** Initiation of ventricular tachycardia by a ventricular premature beat during ventricular pacing. Note that a His bundle electrogram follows the premature beat. During tachycardia, 1 to 1 VA conduction is present.

![Figure 3](http://circ.ahajournals.org/)

**Figure 3.** Same patient as figure 1. Initiation of ventricular tachycardia after a ventricular ectopic beat elicited by a ventricular premature beat during ventricular pacing. The His bundle is activated in between the ventricular premature beat and the subsequent QRS complex. It is not possible to decide upon the exact site of origin of the latter QRS complex.
Activation of the Specific Conduction System at Time of Initiation and during Subsequent Beats of Tachycardia

In 20 of the 29 patients in whom a tachycardia could be initiated a His bundle (or right bundle branch) electrogram could be identified between the paced ventricular extrastimulus and the next QRS complex. In 14 of these 20 patients the latter QRS complex was the first complex of tachycardia, while in the remaining six patients one QRS complex of different shape followed the test stimulus and preceded the first QRS complex of tachycardia (fig. 3). In two of the latter six patients two QRS complexes of different QRS configuration preceded tachycardia. As shown in figure 4 these two QRS complexes had a left bundle branch block configuration.

During tachycardia, rapid deflections suggesting His bundle (or right bundle branch) electrograms could be identified in 27 of our 50 patients. In 23 patients these deflections were related to the QRS complex during tachycardia. In three patients they were found to be located at the beginning, in ten patients in the middle and in seven patients at the end or following each QRS complex of tachycardia. In three of the 23 patients a His bundle electrogram followed every second or third QRS complex. In another four patients His bundle activation was found to be related to atrial activation. In two patients His bundle activation followed every atrial complex (both patients had complete A-V block distal to the bundle of His in recordings outside tachycardia) and in another two patients the appearance of a His bundle electrogram depended upon the distance between the ventricular complex and the atrial electrogram, suggesting retrograde concealed penetration from the ventricular complex into the A-V node.

Termination of Tachycardia

As listed in table 3, tachycardia could be terminated by appropriately timed premature beats particularly in the group of patients with old myocardial infarction and those in whom no other cardiac abnormality could be identified. The patients with acute and subacute myocardial infarction were found to be especially resistant to termination of tachycardia by premature stimuli. As for initiation of tachycardia, it was found that site of stimulation played a role in termination of tachycardia. In fifteen of the 22 patients in whom stimulation from the apex and the outflow tract of the right ventricle could be compared, tachycardia could be terminated by timed stimuli. In ten of them this was easier or only possible from the apex. The reverse was true in the other five patients (fig. 8).

Discussion

As reported earlier in patients suffering from recurrent ventricular tachycardia in the presence of an old myocardial infarction, initiation (and termination) of the arrhythmia can usually be accomplished by the application of appropriately timed ventricular premature stimuli, and occasionally, depending upon the width of the tachycardia zone, by atrial premature stimuli. In this study the same was found in the majority of patients with no identifiable cause for their tachycardia. This was in contrast to patients with ventricular tachycardia in the setting of acute or recent myocardial infarction or in the few patients with prolapsing mitral valve and cardiomyopathy. We have previously discussed the possibility that these differences may be related to

| Table 3. Number of Ventricular Premature Beats Needed to Terminate Tachycardia |
|---------------------------------|--------|--------|--------|
| Patients                        | 1 VPB  | 2 VPB  | 3 VPB  |
| MI older than 5 weeks           | 21     | 14     | 6      | 1      |
| MI 1 day to 5 weeks old         | 3      | 2      | —      | —      |
| Within 24 hours of MI           | 7      | 2      | —      | —      |
| Prolapse MV                     | 3      | —      | —      | —      |
| Digitalis intoxication          | 1      | —      | —      | —      |
| Aneurysm RV                     | 1      | 1      | —      | —      |
| Cardiomyopathy                  | 3      | 1      | —      | —      |
| Unknown                         | 11     | 5      | 2      | 1      |

Abbreviations: MI = myocardial infarction; MV = mitral valve; RV = right ventricle; VPB = ventricular premature beat.
differences in electrophysiologic mechanisms of tachycardia. The findings of initiation and termination of tachycardia by premature stimuli given within well defined timing intervals have been considered as suggestive of re-entry. Recent experimental observations by Cranefield et al. question these suppositions. These authors described, in preparations with a highly abnormal ionic environment or following digitalis poisoning, initiation of a supposedly focal tachycardia by a single stimulus during pacing. In evaluating data from patients in whom a tachycardia could reproducibly be initiated and terminated during cardiac pacing, we have observed other, not previously published, characteristics which play a role in initiation of tachycardia and which may be of help in determining the mechanism of tachycardia.

Effect of Basic Pacing Rate

In the majority of our patients (18 of 21) in whom tachycardia could be initiated by a single premature beat, we found that initiation was accomplished by pacing the heart at the slowest possible rate, although in some patients this was only possible at the highest pacing rate used. Cranefield and Wit noted in their preparation initiation of focal tachycardia by the extrastimulus method; no description is given of the effect of premature stimulation at different basic cycle lengths. In an earlier publication Wit et al. reported on the relation between basic pacing rate and initiation of re-entrant arrhythmias and showed that their occurrence was accomplished by either pacing the preparation at very slow rates or at much faster rates. Other factors like supraventricular excitability may also be affected by heart rate and rhythm. We conclude that at the present time the discriminative value of basic pacing rate in the differentiation between re-entrant and focal mechanisms in man needs further study.

Figure 5. Initiation of ventricular tachycardia by a single premature beat during pacing of the outflow tract of the right ventricle. The tachycardia zone ranged from 310 (upper part of figure) to 260 msec (lower part of figure).

Figure 6. Same patient as figure 5 during pacing of the apex of the right ventricle. Note that during pacing at the same basic cycle length as figure 5 the tachycardia zone measured only 20 msec.
Effect of Site of Stimulation

Initiation of tachycardia is influenced not only by the basic pacing rate but also by the site of stimulation. As shown in some patients, tachycardia could be initiated by premature beats given at one stimulation site and not at the other. This finding indicates that failure to initiate tachycardia during programmed stimulation may not be used as an argument against re-entry being the mechanism of the arrhythmia. It demonstrates that both distance from and approach to the area of abnormal impulse formation play a role in the genesis of arrhythmias by premature stimuli. Site of stimulation also affected termination of tachycardia. In patients with the Wolff-Parkinson-White syndrome it was demonstrated that proximity to the re-entry circuit influenced the possibility of termination of tachycardia by premature stimuli. This suggests that in patients with ventricular tachycardia the site of stimulation which terminates tachycardia may be important for localization of the site of abnormal impulse formation. It also stresses the necessity of careful selection of the optimal stimulation site if treatment of ventricular tachycardia by a chronically implanted pacemaker is considered.

The Interval between the Tachycardia-initiating Premature Beat and the First Beat of Tachycardia

An inverse relation was found between the prematurity of the tachycardia-initiating premature beat and the interval between this beat and the first QRS complex of tachycardia. This finding resembles observations in patients with re-entrant A-V nodal tachycardia in whom increasing the prematurity of the atrial test pulse results in an increasing A-H interval, without change in the H-atrial echo interval leading to a net increase in echo time (the interval between the atrial test stimulus and the atrial echo). An illustration of this inverse relation between prematurity of the test pulse and interval to the next beat in the canine Purkinje fiber is given in figure 7 of the article on re-entry by Wit et al. The presence of this phenomenon in the majority of our patients seems highly suggestive that re-entry was the mechanism responsible for initiation of tachycardia.

Activation of the Specific Conduction System

Recently Akhtar et al. reported re-entry in the His-Purkinje system as a possible basis for a ventricular ectopic beat (V) following timed ventricular stimuli. They showed that the appearance of V was related to a critical time interval between the ventricular test stimulus and retrograde activation of the bundle of His (a critical V-H interval). Twenty of our 29 patients in whom a tachycardia could be initiated by timed ventricular stimuli showed a His bundle electrogram between the ventricular test stimulus and the next QRS complex. In those patients in whom the latter QRS complex was the first complex of the tachycardia, the appearance of a His bundle electrogram seemed to be related to the prematurity of the test pulse. For instance, in patients with a wide tachycardia zone late premature beats.
initiating tachycardia were not followed by a His bundle electrogram (His bundle activation probably being hidden in the QRS complex) in contrast to early premature beats which initiated tachycardia. This finding suggests that activation of the bundle of His may be a concomitant phenomenon and not helpful in delineating the re-entry circuit during tachycardia. In six patients the QRS complex \( (V_3) \) following the test stimulus differed from subsequent QRS complexes during tachycardia. In two of these patients the configuration of \( V_3 \) looked like QRS configuration during ventricular pacing, whereas in four \( V_3 \) had a typical left bundle branch block configuration. In all six patients, increasing the prematurity of the test pulse initially produced a retrograde His bundle electrogram followed later (at shorter premature beat intervals) by complex \( V_3 \). To differentiate between local re-entry (at the site of stimulation) and re-entry in the bundle branch system, in the genesis of \( V_3 \), stimulation at different ventricular sites seems to be of great value. Unfortunately pacing from both the apex and the outflow tract of the right ventricle was done in only two of these six patients. In both patients \( V_3 \) and tachycardia only occurred during pacing of the apex of the right ventricle. A more thorough study on relation between pacing site and QRS configuration of \( V_3 \) and on the significance of the timing of His bundle activation in the genesis of \( V_3 \) is needed, to define whether \( V_3 \) is generated close to the stimulation site or caused by re-entry in the His-Purkinje system. It seems appropriate at the present time to conclude that a single ventricular complex \( (V_2) \) following an early ventricular test pulse is a common phenomenon but that perpetuation of the mechanism leading to \( V_3 \) and resulting in tachycardia is uncommon.

Activation of the specific conduction system cannot only be observed at the time of initiation but also during subsequent beats of tachycardia. The timing of activation of the His bundle in relation to the QRS complex has been considered helpful in locating the site of impulse formation in the ventricle. If the His bundle activation precedes or is located at the beginning of the QRS complex an origin in the specific intraventricular conduction system has been suggested. Unfortunately the timing of the activation of the bundle of His during ventricular tachycardia will be influenced by several factors such as ability to invade the specific conduction system and the conduction velocity in...
antegrade and retrograde direction in the His-Purkinje system. This makes the location of the His bundle electrogram of questionable value for identification of the site of origin of ventricular tachycardia. We conclude that identification of site of origin and pathway of tachycardia (the bundle branches, the Purkinje system, fibrotic ventricular muscle or combinations of these) is usually not possible during programmed electrical stimulation of the heart. Only under exceptional circumstances, such as initiation of a ventricular tachycardia by a supraventricular impulse which is blocked in one of the bundle branches or termination of a ventricular tachycardia by a supraventricular premature beat which is not conducted to the ventricular myocardium, is it possible to prove that the re-entry circuit incorporates the bundle branches. In patients suffering from ventricular tachycardia, myocardial excitation mapping is needed for exact identification of site of origin and pathway of tachycardia.

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