Comparison of bipolar and unipolar programmed electrical stimulation for the initiation of ventricular arrhythmias: significance of anodal excitation during bipolar stimulation

WILLIAM G. STEVENSON, M.D., ISAAC WIENER, M.D., AND JAMES N. WEISS, M.D.

ABSTRACT To determine if anodal excitation during bipolar stimulation facilitates the initiation of sustained monomorphic ventricular tachycardia, nonsustained polymorphic ventricular tachycardia, or repetitive ventricular responses, both bipolar and cathodal unipolar programmed ventricular stimulation with one to three extrastimuli delivered during ventricular pacing at two rates from the right ventricular apex were performed in 28 patients evaluated for spontaneous sustained ventricular tachycardia or ventricular fibrillation (11 patients), nonsustained tachycardia (eight patients), or syncope (nine patients). In 25 patients a hexapolar pacing catheter was used to record local endocardial activation times adjacent to the cathode and anode and ventricular excitation during bipolar stimulation was defined as predominantly anodal, cathodal, or simultaneous at both anode and cathode. When bipolar and unipolar stimulation were compared there was no difference in the incidence of initiating sustained monomorphic ventricular tachycardia (57% vs 57%), nonsustained polymorphic ventricular tachycardia (14% vs 14%), or repetitive ventricular responses (21% vs 21%), although the response to bipolar vs unipolar stimulation was not concordant in every patient. Evidence of anodal excitation was observed in 11 (44%) patients but did not indicate increased risk of initiation of any ventricular arrhythmia, despite the fact that it was associated with shortening of the ventricular effective refractory period by $5.2 \pm 8.7$ msec ($p < .05$) during bipolar as opposed to unipolar stimulation. We conclude that unipolar and bipolar stimulation produce a similar incidence of initiation of arrhythmia, despite the frequent occurrence of anodal excitation during bipolar stimulation. Thus, the risk of initiation of nonspecific ventricular arrhythmias during programmed stimulation is unlikely to be reduced by the use of unipolar stimulation.

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PROGRAMMED electrical stimulation for the purpose of initiating ventricular arrhythmias in humans is usually performed with a bipolar pair of endocardial electrodes. During bipolar pacing local myocardial excitation may begin at the cathode, the anode, or simultaneously at both sites.\(^1\)\(^2\) The shorter refractory period of anodal as opposed to cathodal ventricular stimulation\(^1\)\(^2\) and changes in the relative contribution of cathode and anode to ventricular excitation during programmed stimulation are factors that could influence the ability of bipolar programmed stimulation to initiate ventricular arrhythmias in humans but that have received little attention.

To determine if anodal excitation during bipolar stimulation facilitates the initiation of either clinically important sustained monomorphic ventricular tachycardia or less specific arrhythmias, such as repetitive ventricular responses and nonsustained polymorphic ventricular tachycardia,\(^5\) we compared the initiation of these arrhythmias and the presence of anodal ventricular excitation as determined from local ventricular electrograms adjacent to the cathode and anode during bipolar and cathodal unipolar programmed stimulation in 28 patients referred for evaluation of documented or suspected ventricular arrhythmias.

Methods

Clinical characteristics of the patients are listed in table 1. All studies were performed in the absence of antiarrhythmic drugs and diazepam was used as needed for sedation. After informed consent was obtained from each patient two or three electrode
catheters were positioned via the femoral and/or internal jugular veins in the high right atrium, across the tricuspid valve (in position to record the His bundle electrogram), and in the apex of the right ventricle. In 25 patients ventricular stimulation was performed with a No. 6F (USCI) hexapolar catheter that allowed recording of ventricular activation times adjacent to the anode and cathode. The middle electrode pair (electrodes 3 and 4) of this catheter had a 1 cm interelectrode distance and all other adjacent electrodes had a 3 mm interelectrode distance. Bipolar stimulation was performed with electrode 3 as the cathode and electrode 4 serving as the anode and bipolar electrograms were recorded from the closely spaced electrode pairs adjacent to the cathode (electrodes 1 and 2) and anode (electrodes 5 and 6).

Unipolar pacing was performed with electrode 3 as the cathode and a surface electrode patch as the anode. In three patients a standard No. 6F quadrupolar catheter with 1 cm interelectrode distances was used and bipolar and unipolar pacing was performed with the distal electrode (electrode 1) serving as the cathode and electrode 2 serving as the anode during bipolar pacing. Both bipolar and unipolar stimulation were performed at twice the late diastolic threshold for that electrode configuration from the right ventricular apex. Stimuli of 2 msec duration were delivered by a programmable stimulator (Bloom Associates, Ltd.). Three to five surface electrocardiographic leads and intracardiac electrograms filtered at 30 to 500 Hz were recorded on an Electronics for Medicine VR-12 chart recorder at a paper speed of 150 mm/sec.

Extrastimuli were delivered after an 8 beat basic drive at a "slow" (600 msec) and "fast" (450 msec) cycle length. In five patients the slow cycle length was increased to 550 (two patients) or 500 msec (three patients) and the fast cycle length was increased to 400 msec to avoid sinus competition with a slower basic drive. The stimulation protocol proceeded in a stepwise manner, as follows. (1) During bipolar stimulation at the slow basic drive a single extrastimulus (S2) scanned early diastole in 10 msec decrements until reaching ventricular refractoriness and was then positioned 10 to 20 msec beyond refractoriness to allow scanning of diastole with a second extrastimulus (S3) in 10 msec decrements starting at S2S3 = S1S2 + 50 msec. (2) Bipolar stimulation was performed at the fast basic drive with single and double extrastimuli. (3) Unipolar stimulation was performed at the slow basic drive with single and double extrastimuli. (4) Unipolar stimulation was performed at the fast basic drive with single and double extrastimuli. (5) Bipolar stimulation was performed at the slow basic drive with S2 and S1 fixed 10 to 20 msec beyond their effective refractory periods and early diastole scanned with a third extrastimulus (S3). (6) Unipolar stimulation was performed at the slow basic drive with triple extrastimuli. (7) Bipolar stimulation was performed at the fast basic drive with triple extrastimuli. (8) Unipolar pacing was performed at the fast basic drive with triple extrastimuli.

The stimulation protocol was terminated for the initiation of a sustained ventricular arrhythmia requiring direct-current countershock for termination or for the reproducible initiation of hemodynamically tolerated sustained ventricular tachycardia by both bipolar and unipolar stimulation. If hemodynamically tolerated sustained ventricular tachycardia was initiated with one electrode configuration, the same step in the protocol was completed with the use of the other electrode configuration. In five patients the protocol was terminated prematurely because of repeated initiation of supraventricular tachycardia (one patient) or use of only up to two extrastimuli (the initial four patients studied). Only one patient failed to receive the same number of extrastimuli during unipolar and bipolar pacing because of the initiation of ventricular tachycardia requiring countershock during bipolar pacing.

Ventricular excitation was considered to arise predominantly at the anode when the activation time recorded adjacent to the anode was 5 msec or more earlier than the activation time adjacent to the cathode. A less than 5 msec difference in activation times adjacent to the cathode and anode was considered to represent simultaneous ventricular excitation at both the cathode and anode. Previous analysis of local electrograms recorded with this hexapolar catheter during bipolar and unipolar ventricular pacing with single extrastimuli strongly suggests that simultaneous or early ventricular activation adjacent to the anode is the result of an anodal contribution to ventricular excitation.

**Definitions**

**Ventricular effect refractory period.** The longest stimulus coupling interval that fails to capture the ventricle.

**Sustained monomorphic ventricular tachycardia.** A regular ventricular rhythm with rate greater than 100 beats/min and consistent beat-to-beat QRS morphology lasting more than 29 sec or requiring an intervention for termination due to syncpe.

**Nonsustained polymorphic ventricular tachycardia.** Six beats to 30 sec of ventricular tachycardia displaying frequent beat-to-beat changes in QRS morphology.

**Repetitive ventricular response.** One or five beats of intraventricular reentry following the last stimulated beat, excluding macroreentry via the His-Purkinje system.

The cumulative probability of initiation of repetitive ventricular responses and nonsustained polymorphic ventricular tachycardia for unipolar vs bipolar stimulation at each step in the protocol were compared by life table analysis and the log-rank test. Nonsustained arrhythmias that were elicited only once at a given step were not included for analysis. Paired and unpaired Student’s t tests and chi-square tests were used as appropriate. Data are expressed as mean ± SD.

**Results**

**Unipolar vs bipolar stimulation.** Electrophysiologic characteristics of unipolar compared with bipolar pacing for all 28 patients are shown in table 2. There were no differences between unipolar and bipolar stimulation with respect to the late diastolic threshold or refractory periods of the basic drive, first, or second extrastimuli. Sustained monomorphic ventricular ta-
TABLE 2
Comparison of electrophysiologic data for unipolar vs bipolar programmed stimulation

<table>
<thead>
<tr>
<th></th>
<th>Unipolar</th>
<th>Bipolar</th>
<th>p value</th>
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<tbody>
<tr>
<td>n</td>
<td>28</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Threshold (mA)</td>
<td>0.91 ± 0.94</td>
<td>0.71 ± 0.39</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Slow BCL ERP</td>
<td>258 ± 19</td>
<td>256 ± 23</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Slow S1, ERP</td>
<td>203 ± 25</td>
<td>200 ± 22</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Slow S2, ERP</td>
<td>199 ± 24</td>
<td>184 ± 16</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Fast BCL ERP</td>
<td>235 ± 16</td>
<td>235 ± 18</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Fast S1, ERP</td>
<td>183 ± 23</td>
<td>184 ± 23</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Fast S2, ERP</td>
<td>170 ± 19</td>
<td>170 ± 14</td>
<td>&gt; .05</td>
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<tr>
<td>RVR</td>
<td>57%</td>
<td>57%</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>NSPVT</td>
<td>14%</td>
<td>14%</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>SMVT</td>
<td>21%</td>
<td>21%</td>
<td>&gt; .05</td>
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BCL = basic cycle length; ERP = effective refractory period; NSPVT = nonsustained polymophic ventricular tachycardia; RVR = repetitive ventricular response; SMVT = sustained monomorphic ventricular tachycardia. All times are in msec.

Chyocardia was initiated in six patients. Tachycardia was initiated by both bipolar and unipolar stimulation with the same number of extrastimuli in four patients (figure 1), by unipolar stimulation only in two patients, and by bipolar stimulation only in one patient. In one additional patient, unipolar stimulation was not performed at the step in the pacing protocol that initiated ventricular tachycardia during bipolar pacing because termination of tachycardia required countershock. There was no statistical difference in the risk of initiation of sustained monomorphic ventricular tachycardia between unipolar and bipolar pacing at any step in the stimulation protocol.

Nonsustained polymorphic ventricular tachycardia was initiated in six patients. In three of these patients, who had presented with sustained monomorphic ventricular tachycardia (one patient), ventricular fibrillation (one patient), and syncope (one patient), sustained

![FIGURE 1](https://example.com/image1.png)

FIGURE 1. Initiation of sustained monomorphic ventricular tachycardia during bipolar (A) and unipolar (B) stimulation. Illustrated in each panel, from the top, are the surface electrocardiographic leads V1 and V5, intracardiac recordings from the high right atrium (HRA), His bundle (HIS), right ventricular electrodes adjacent to the cathode (RVA1,2), and right ventricular electrodes adjacent to the anode (RVA5,6) during bipolar pacing, and the 50 msec time lines (T). Only the last beat (S3) of the basic drive train with a 600 msec cycle length is shown. A. Two extrastimuli (S2, S3) at coupling intervals of 310 and 380 msec during bipolar pacing initiate sustained monomorphic ventricular tachycardia. Local ventricular activation is earliest adjacent to the cathode for both extrastimuli. B. Sustained monomorphic ventricular tachycardia with the same morphology and cycle length (420 msec) is initiated by two extrastimuli at coupling intervals of 310 and 390 msec during unipolar pacing.
monomorphic ventricular tachycardia was also initiated. A sustained arrhythmia was not initiated in the remaining three patients. One of these had idiopathic cardiomyopathy and was resuscitated from an episode of ventricular fibrillation, and the remaining two had spontaneous nonsustained ventricular tachycardia and coronary artery disease without spontaneous sustained arrhythmias. Nonsustained polymorphic ventricular tachycardia was initiated by both unipolar and bipolar stimulation in two patients, by bipolar stimulation only in two patients, and by unipolar stimulation only in two patients (figure 2). As shown in figure 3, there was no difference in the risk of initiation of repetitive ventricular responses or nonsustained polymorphic ventricular tachycardia with bipolar and unipolar stimulation at any step in the pacing protocol.

Anodal excitation. Evidence of an anodal contribution to ventricular excitation was observed during bipolar stimulation during at least one step in the stimulation protocol in 11 (44%) of the 25 patients in whom local ventricular electrograms adjacent to the anode and cathode were recorded. This consisted of early or simultaneous activation during the basic drive and predominantly cathodal stimulation during extrastimuli in four patients, anodal excitation during the basic drive and premature stimuli in four patients, and cathodal

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**FIGURE 2.** Bipolar (A) and unipolar (B) stimulation in the same patient at the same basic drive cycle length. Illustrated in each panel, from the top, are time lines T, surface electrocardiographic leads I, II, aVF, V₁, and V₅, and intracardiac recordings from the high right atrium (HRA), His bundle (HIS), right ventricular electrodes 1 and 2 (RVA₁,₂) adjacent to the cathode (electrode 3), and right ventricular electrodes 5 and 6 (RVA₅,₆) which are adjacent to the anode (electrode 4). All times are in msec. A, During bipolar pacing at a basic drive cycle length of 600 msec, three extrastimuli (S₂, S₃, S₄) elicit one repetitive ventricular response. Ventricular activation is more than 5 msec earlier adjacent to the cathode (RVA₁,₂) than adjacent to the anode (RVA₅,₆) during the basic drive and the extrastimuli. B, In the same patient, stimulation is unipolar, with electrode 3 serving as the cathode and a skin electrode serving as the anode. Only the last stimulus of the basic drive train (S₁) of 600 msec is shown. Three extrastimuli at identical coupling intervals as in A initiate nonsustained polymorphic ventricular tachycardia, the first 7 beats of which are shown.
excitation during the basic drive and anodal excitation during a critical range of extrastimuli in seven patients (figure 4). When predominantly cathodal excitation was present during the basic drive during bipolar pacing, anodal excitation was more common with two or three extrastimuli (22% and 25%) than with one extrastimulus (8.3%), although this difference did not reach statistical significance.

Although patients who had evidence of anodal excitation during bipolar pacing as a group had shorter ventricular refractory periods than patients without evidence of anodal excitation (table 3), unipolar cathodal refractory periods were also shorter in the patients with than in those without anodal excitation. This suggests that the differences in refractory periods were due to variability of myocardial refractoriness and were unrelated to the anodal contribution to excitation. However, when anodal excitation was present during bipolar extrastimuli or the basic bipolar drive the refractory periods were $5.2 \pm 8.7$ msec shorter than the unipolar refractory periods in the same patient receiving the same number of extrastimuli at the same basic drive ($p < .05$). This difference is at the limits of the accuracy of the technique.

There was no difference in the incidence of initiation of sustained monomorphic ventricular tachycardia, polymorphic ventricular tachycardia, or repetitive ventricular responses in the groups with and without evidence of anodal excitation during bipolar pacing (table 3). In five patients local ventricular electrograms were recorded during the initiation of sustained monomorphic ventricular tachycardia by bipolar pacing. Evidence of anodal excitation was present during the stimuli initiating tachycardia in only one patient (20%), and this patient also had ventricular tachycardia initiated by unipolar stimulation with the same number of extrastimuli.

Local ventricular electrograms were recorded in four patients during the initiation of nonsustained polymorphic ventricular tachycardia by bipolar stimulation. The basic drive and extrastimuli initiating polymorphic tachycardia had their earliest site of excitation at the cathode in all four patients. Among the 11 patients with evidence of anodal excitation during bipolar stimulation, repetitive ventricular responses were initiated by both unipolar and bipolar stimulation in seven patients, by unipolar stimulation only in one patient, and by bipolar stimulation only in one patient. Evidence of anodal excitation during either the basic drive or extrastimuli was present at the steps initiating repetitive ventricular responses during bipolar stimulation in six patients. Thus, the risk of initiation of either nonsustained polymorphic ventricular tachycardia or repetitive ventricular responses in patients with anodal excitation during bipolar stimulation was no greater than that during unipolar stimulation, despite the fact that anodal excitation was associated with a shorter ventricular refractory period.

Discussion
During bipolar ventricular stimulation excitation may begin in myocardium adjacent to the cathode, in
that adjacent to the anode, or simultaneously at both sites depending on the excitation threshold at each electrode, the stimulus strength used, and the coupling interval of the stimuli. During late diastole the cathodal threshold is lower than the anodal threshold. At short coupling intervals of premature stimuli the anodal threshold falls below the cathodal threshold due to an early diastolic “dip” in the anodal strength interval curve, which results in a shorter ventricular effective refractory period for anodal than for cathodal stimulation. During bipolar endocardial programmed ventricular stimulation these factors interact to produce varying combinations of predominantly cathodal, predominantly anodal, and simultaneous cathodal and anodal excitation during both the basic drive and premature stimuli. The resulting changing sequences of local ventricular activation, which may influence the local dispersion of refractoriness, and the shorter ventricular refractory period of anodal as compared with cathodal stimulation, may facilitate fractionation of the local excitatory wave front leading to reentrant arrhythmias. This is supported by the fact that the ventricular fibrillation threshold for bipolar stimulation is lower than that for unipolar cathodal stimulation in the canine heart. This has been suggested to account for the increased risk of ventricular fibrillation with bipolar as opposed to unipolar permanent pacemakers found by Preston in a retrospective study.

The potentially arrhythmogenic features of anodal stimulation may be especially relevant to the production of polymorphic ventricular tachycardia and repetitive ventricular responses, which can be initiated in patients without documented spontaneous arrhythmias in whom arrhythmias may be a nonspecific response to aggressive ventricular stimulation. These arrhythmias may be due to “random reentry” which occurs when a sufficiently premature stimulus encounters areas of conduction block, the substrate for reentry, in normal tissue.

We hypothesized that the use of unipolar cathodal stimulation, by removing the possibility of anodal excitation, may result in a lower incidence of nonspecific ventricular arrhythmias during programmed ventricular stimulation. However, despite the fact that changes in local ventricular activation sequences consistent with an anodal contribution to ventricular excitation were observed in 44% of our patients during bipolar stimulation, we were unable to demonstrate any increase in the incidence of initiation of repetitive ventricular responses or nonsustained polymorphic ventricular tachycardia with bipolar as opposed to unipolar stimulation. None of the patients in whom polymorphic ventricular tachycardia was initiated during bipolar stimulation had evidence of an anodal contribution to ventricular excitation from the initiating extrastimuli. These findings are in agreement with those of Pop.
et al.,14 who found no difference in the incidence of initiation of repetitive ventricular responses during unipolar cathodal, unipolar anodal, or bipolar stimulation during ventricular pacing at one cycle length with delivery of one and two extrastimuli.

Although we found no difference in the risk of initiation of ventricular arrhythmias with unipolar and bipolar stimulation for the entire group of patients, responses to unipolar and bipolar stimulation were not always concordant in individual patients. Two patients had reproducible nonsustained polymorphic ventricular tachycardia initiated only during unipolar stimulation (figure 2) and one patient had nonsustained polymorphic ventricular tachycardia initiated only with bipolar stimulation. Similarly, sustained monomorphic ventricular tachycardia was initiated only by unipolar stimulation in two patients and only by bipolar stimulation in one patient. It is likely that had the pacing protocol been continued and the number of stimuli and basic drive increased further, sustained tachycardia would have been initiated by the unsuccessful electrode configuration at a later step in the stimulation protocol, since sustained monomorphic ventricular tachycardia can be initiated by bipolar right ventricular stimulation in over 90% of patients with coronary artery disease and spontaneous episodes of sustained ventricular tachycardia.15 Thus, the use of unipolar as opposed to bipolar stimulation may influence the step in the pacing protocol at which a clinically documented tachycardia is initiated.

Clinical implications. The initiation of nonspecific arrhythmias that may occasionally produce syncope or deteriorate to ventricular fibrillation in the electrophysiology laboratory continues to be a risk in performing programmed ventricular stimulation. Our results demonstrate that this risk is unlikely to be reduced by the use of unipolar cathodal stimulation, despite the theoretically increased arrhythmogenic potential of the anodal excitation that can occur during bipolar pacing. Although no difference in inducibility of ventricular arrhythmias with unipolar as compared with bipolar stimulation was seen for the group, differences were seen in individual patients. Thus, for purposes of serial assessment with programmed stimulation in a given patient a consistent mode of stimulation, bipolar or unipolar, should be used.

References
9. Mera W, Han J, Yoon MS: Effects of unipolar cathodal and bipolar stimulation on vulnerability of ischemic ventricles to fibrillation. Am J Cardiol 35: 37, 1975

<table>
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<tr>
<th></th>
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<td>Patients with anodal excitation</td>
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<td>14</td>
</tr>
<tr>
<td>n</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Threshold (mA)</td>
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<td>0.61 ± 0.29</td>
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<tr>
<td>Slow BCL ERP</td>
<td>266 ± 17</td>
<td>266 ± 21</td>
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<td>Slow S ERP</td>
<td>209 ± 18</td>
<td>208 ± 18</td>
</tr>
<tr>
<td>Fast BCL ERP</td>
<td>203 ± 22</td>
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<td>Fast S ERP</td>
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<tr>
<td>ERP</td>
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<td>RVR</td>
<td>180 ± 12</td>
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</tr>
<tr>
<td>NSPVT</td>
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Abbreviations are as in table 2. All times are in msec.

*p < .05 patients with compared to those without anodal excitation.


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