Recording of diastolic slope with catheters during junctional rhythm in humans

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ABSTRACT Junctional diastolic slopes were recorded in 11 of 15 patients (73.3%) with junctional rhythm that occurred spontaneously, after intravenous administration of atropine (1 mg), or during carotid sinus massage. The diastolic slopes were recorded through a unipolar lead consisting of a terminal of an electrode catheter placed in the His bundle area paired with an indifferent terminal on the superior vena cava. The slope of these diastolic deflections averaged \(-0.18 \pm 0.06\) mV/sec (mean \pm SD). Overdrive atrial and ventricular stimulations were followed by slowing of the junctional rate and decrease in the diastolic slope. Strong negative correlations (r values from \(-0.71\) to \(-0.95\)) were found between the junctional cycle lengths and the diastolic slopes after atrial or ventricular pacing. Carotid sinus massage decreased the junctional rate and the junctional diastolic slope, whereas atropine increased the junctional rate and the junctional diastolic slope. Since prolongation of junctional cycle lengths after atrial pacing did not depend on frequency of impulse penetration into the His bundle, we postulate that the junctional pacemaker responsible for the junctional rhythm in some of our patients was in the N region of the AV node. Application of this recording method should help in the identification and characterization of automatic junctional pacemakers.


DIFFERENTIATION between automatic and reentrant arrhythmias is frequently done in the electrophysiologic laboratory by evaluating the response of the rhythm to electrical stimulation. For example, overdrive suppression is considered a hallmark of an automatic rhythm caused by phase 4 depolarization. On the other hand, differentiation between triggered rhythm, a form of automatic rhythm, and reentrant rhythm cannot be made with certainty because both rhythms can be initiated and terminated by electrical stimuli. Phase 4 depolarization, a marker of automatic activity, can be extracellularly recorded from the junctional area in dogs with junctional rhythm.1 In this article we describe application of this technique in patients with junctional rhythm.

Methods

Fifteen men with junctional rhythm were used for the study (table 1). Junctional rhythm in these patients was characterized as a rhythm with a P wave occurring within or immediately after the QRS complex and with a QRS configuration and HV interval identical to those during sinus rhythm or atrial pacing. The patients' ages averaged 66.7 ± 10.9 years (mean ± SD).

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Twelve patients had an underlying clinical diagnosis of sick sinus syndrome, two had junctional rhythm after treatment with digitalis and propranolol, and one had escape junctional rhythm associated with myocardial infarction of the inferior wall (table 1). Seven of the patients had a stable junctional rhythm during the study, five had a junctional rhythm after intravenous administration of 1 mg of atropine, and three had reproducible junctional rhythm during carotid sinus massage.

Electrophysiologic studies were performed with patients in the nonsedated, postabsorptive state after the nature of the procedure was explained and informed consent was obtained. Up to three quadripolar catheters were introduced percutaneously into the femoral veins and the brachial veins and positioned at the level of the tricuspid valve, in the superior vena cava, and either in the right atrium or at the right ventricular apex. Three electrocardiographic leads (leads I, II, and V1) were displayed and recorded simultaneously with intracardiac electrograms by means of a multichannel oscilloscope (Electronics for Medicine VR-12) at paper speeds of 50 to 100 mm/sec. Bipolar electrograms of the His bundle, right atrium, and right ventricle were recorded with filters set between 40 and 500 Hz. Junctional diastolic slope was recorded through a unipolar lead consisting of one terminal of the electrode catheter in the area of the tricuspid valve showing the largest His bundle deflection, paired with the indifferent superior vena caval electrode. Filters were set between 0.1 and 25 or 50 Hz. Reversed polarity and high amplification in the range of 0.1 mV/cm were used to record the unipolar junctional electrogram. The slope of the diastolic deflection, calculated as the tangent of the angle of the diastolic deflection and a horizontal line, was expressed as millivolts per second.

To evaluate the effects of overdrive suppression on the junctional rhythm and the diastolic slope, electrical stimuli of twice diastolic threshold and 2 msec width were delivered through the right atrial or right ventricular catheter electrode with a con-
TABLE 1
Clinical and electrophysiologic characteristics of the patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Clinical diagnosis</th>
<th>Mode of induction of junctional rhythm</th>
<th>Junctional cycle lengths (msec)</th>
<th>Diastolic slope (mV/sec)</th>
</tr>
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<td>1</td>
<td>63</td>
<td>Sick sinus syndrome</td>
<td>CSM</td>
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<td>2</td>
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<tr>
<td>3</td>
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<td>907</td>
<td>Not recorded</td>
</tr>
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<td>4</td>
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<td>Atropine (iv)</td>
<td>838</td>
<td>0.15</td>
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<td>5</td>
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<td>Atropine (iv)</td>
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<tr>
<td>6</td>
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<td>Spontaneous</td>
<td>1086</td>
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</tr>
<tr>
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<td>Atropine (iv)</td>
<td>1017</td>
<td>Not recorded</td>
</tr>
<tr>
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<td>CSM</td>
<td>1164</td>
<td>0.17</td>
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<td>14</td>
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<td>1126</td>
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<tr>
<td>15</td>
<td>66</td>
<td>Sick sinus syndrome</td>
<td>Spontaneous</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CSM = carotid sinus massage; MI = myocardial infarction.

*Average of 10 consecutive beats.

The overdrive suppression was performed in all patients who had a stable junctional rhythm, either spontaneously or after intravenous administration of atropine. In patients who developed junctional rhythm after intravenous atropine injection, continuous recording of the electrocardiograms and intracardiac electrograms was also made until sinus rhythm reappeared. Similarly, continuous recording was made before, during, and after carotid sinus massage that produced junctional rhythm.

**Statistical analysis.** Linear regression analysis was used to determine the correlation between diastolic slopes and postpacing cycle lengths or cycle lengths at various times after injection of atropine. The data are presented as mean ± SD.

**Results**

Negative-going diastolic slopes (upward-going because of reversed polarity) were recorded in 11 of the 15 patients. In the other four patients no stable baseline recording could be obtained. This was probably related to the inability to achieve a stable position of the electrode catheter in the region of the tricuspid valve. The cycle length of the junctional rhythm in those patients ranged from 838 to 1314 msec (mean 1035 ± 167) and the diastolic slope ranged from 0.10 to 0.31 mV/sec (mean 0.18 ± 0.06). Cycle lengths of the junctional rhythm, the average of 10 consecutive beats in each patient, and the corresponding junctional diastolic slopes are listed in table 1. The range for the cycle lengths in those 10 consecutive beats was less than 50 msec and the range for junctional diastolic slopes was less than 0.04 mV/sec.

**Effects of atrial and ventricular pacing on junctional cycle length and diastolic slope.** Atrial and ventricular pacing produced overdrive suppression in all patients and a decrease in the slope of the diastolic deflection. Figure 1, which shows records obtained from patient 5 in table 1, provides an example of overdrive suppression and decrease in junctional slope after atrial stimulation. Figure 1, A, shows a stable junctional rhythm with cycle lengths (HH intervals) of 820 to 860 msec that was recorded after the patient had been given 1 mg of atropine intravenously. During this rhythm His bundle deflection preceded both atrial and ventricular electrograms with an HV interval of 50 msec. A negative-going diastolic slope (arrow) of 0.08 to 0.12 mV/sec preceded the His bundle deflection. Figure 1, B, shows that atrial pacing at a cycle length of 600 msec for 30 sec was followed by prolongation of the junctional (HH) cycle length to 1440 msec and markedly reduced diastolic slope to 0.005 mV/sec. The junctional cycle lengths and diastolic slopes returned to control levels after 2 beats. In all seven patients studied with atrial pacing the overdrive suppression did not depend on the frequency of atrial impulses that penetrated into the His bundle. An example of this phenomenon is also shown in figure 1, B. Atrial impulses at a cycle length of 600 msec were conducted with 2:1 block to the His bundle. Thus the His bundle was penetrated by the electrical impulses at a cycle length of 1200 msec, longer than the control junctional cycle length of 820 to 860 msec measured from a record obtained immediately before atrial pacing (figure 1, A). The fact that the junctional cycle length prolonged after pacing despite the underdrive of the His bundle suggests that the junctional pacemaker is located cranial to the His bundle.
Underdrive of such a pacemaker in the His bundle would have resulted in no prolongation of the junctional cycle length. Furthermore, if the junctional pacemaker were located in the His bundle, impulse penetration at a cycle length of 1200 msec (longer than control pacemaker cycle length) should have resulted in a pacemaker escape rhythm during pacing. The exact location of the pacemaker will be discussed.

Similarly, ventricular pacing also resulted in overdrive suppression and decrease in the diastolic slope. Figure 2, which shows a record obtained from patient 4 in table 1, provides this example. Ventricular pacing for 30 sec at a cycle length of 750 msec resulted in 1:1 VA conduction and was followed by a prolongation of the ventricular cycle length from 830 to 860 msec during control to 960 msec immediately after pacing. The prolongation of the cycle length was associated with a decrease of the diastolic slope from an average of 0.15 to 0.05 mV/sec. The junctional cycle length and diastolic slope returned to control levels after the prolonged cycle length.

Figure 3 shows plots correlating various junctional cycle lengths as a result of overdrive suppression by atrial pacing and the accompanying diastolic slopes obtained from patient 9 in table 1. A strong negative correlation \( r = -0.91 \) was found between the junctional cycle lengths and the diastolic slopes. Similar findings were observed in all seven patients who underwent atrial pacing \( r \) values ranged from \(-0.76\) to \(-0.95\) and in all three patients who underwent ventricular pacing \( r \) values ranged from \(-0.71\) to \(-0.91\).

Effects of carotid sinus massage and atropine on junctional cycle length and diastolic slope. Carotid sinus massage during stable junctional rhythm, which was per-
formed in five patients, produced slowing of the junctional rate and decrease in the junctional diastolic slope. In contrast, 1 mg of atropine administered intravenously increased the junctional rate and the junctional diastolic slope. In figure 4, A, obtained from patient 1, carotid sinus massage applied to the right carotid artery produced a prolongation of the sinus cycle and appearance of a junctional escape rhythm. The junctional cycle length (HH interval) was long (1310 msec) immediately after the sinus rhythm as a result of both overdrive suppression of the junctional pacemaker by the preceding sinus beats and the effect of carotid sinus massage. A diastolic slope of 0.09 mV/sec accompanied the long junctional cycle length. After this long junctional escape interval, the junctional cycle length shortened to 1260 msec and the diastolic slope increased to 0.15 to 0.16 mV/sec. After a few beats, sinus rhythm gradually ensued. Carotid sinus massage in five patients with junctional rhythm prolonged the junctional cycle length by 40 to 120 msec and decreased the junctional diastolic slope by 0.06 to 0.10 mV/sec.

Figure 5 shows gradual slowing of the junctional rhythm and decrease in the diastolic slope in patient 4, in whom junctional rhythm was induced by atropine. Immediately after the injection (figure 5, A) junctional rhythm with a cycle length of 830 msec appeared. Diastolic slopes of 0.17 to 0.18 mV/sec preceded each His bundle deflection. Twenty minutes after the injection (fig. 5, B), when the effect of atropine had partially dissipated, the junctional cycle lengths were longer, ranging from 960 to 1030 msec. The diastolic slopes were also decreased to 0.03 mV/sec. As the junctional rhythm slowed further, sinus rhythm ensued. In four patients strong negative correlations (r values = .69 to -.89) were observed when the junctional cycle lengths and diastolic slopes at various times after injection of atropine were plotted.

Discussion

The method used in this study represents extension of the method used in dogs.1 The basic difference of this method compared with the commonly used recording method of His bundle activity is the use of unipolar
lead, low-pass filters, high gains, and reversed polarity. This method, initially used on the canine and human sinus nodes, allows recognition of slow deflections that originate from phase 4 depolarization and slow upstroke slope of the sinus nodal cells. Its application in recording of ectopic pacemakers has shown that the method can be used to record phase 4 depolarization in the other parts of the heart. In this study we have demonstrated that (1) with electrode catheters it is possible to record diastolic slope from the junctional area in patients with junctional rhythm, and (2) the response of the diastolic slope to interventions like atrial and ventricular pacing, vagal stimulation by carotid sinus massage, and administration of atropine are identical to the expected responses of phase 4 depolarization to those interventions. These results, together with our previous results on recordings of diastolic slopes from the sinus node, ectopic atrial pacemakers, the AV junction, and the ventricles suggest that the diastolic slope recorded from the AV junction indeed reflects phase 4 activity of the junction.

As we discussed in our previous study, the ability to record His bundle activity and diastolic slope from the same electrode should not be interpreted as evidence that the junctional pacemaker is in the His bundle region. Recording of His bundle activity does not require direct contact of the electrode with the His bundle. In fact, with sufficiently high amplification, His bundle activity can be recorded from the body surface. In addition, the size of the catheter electrode, the specificity of extracellular recording for identification of structures, and the complex anatomy of the AV junction make it impossible to perform mapping to localize the site of the pacemaker in our patients. In a previous study we postulated that the location of the pacemaker in dogs with junctional rhythm induced by sinus nodal ablation is in the N region of the AV node. We arrived at this conclusion by analyzing the effects of verapamil on the junctional rhythm and the diastolic slope and by analyzing the pattern of retrograde conduction from the junctional pacemaker. The suppressive effect of verapamil on the canine junctional automaticity, the diastolic slope, and retrograde conduction suggest that the location of the pacemaker is the N region of the AV node, the verapamil-sensitive region.

We also believe that in some of our patients the location of the junctional pacemaker is probably in the N region of the AV node. The reasons for such an argument are as follows: First, in the majority of our patients the underlying cause for the junctional rhythm is sick sinus syndrome. Conceivably a disease process affecting the automaticity of the sinus node, such as ablation of the sinus node in dogs, would result in an escape pacemaker rhythm arising from the N region of the AV node. Second, the retrograde atrial activation during the junctional rhythm in our patients had the same characteristics as that of the junctional rhythm in dogs; that is, the atrial activity occurred immediately after or within the ventricular activity (figures 1, 2, 4, and 5). This suggests that the location of the junctional pacemaker in the two species is probably identical, i.e., in the N region of the AV node. Third, the fact that overdrive suppression of the junctional rhythm by atrial pacing did not depend on impulse conduction in the His bundle (figure 1) suggests that the junctional pacemaker is located cranial to the His bundle. Previous studies in rabbits showed that such rapid atrial pacing most likely blocked in the N region of the AV node. Thus the pause after rapid atrial pacing and underdrive of the His bundle in figure 1 is most consistent with a pacemaker location in the N or AN region. However, the AN location (coronary sinus ostial location) is unlikely, since in a rhythm arising from such a pacemaker location a P wave precedes the QRS complex.

In two of our patients (patients 3 and 8) the use of digitalis and propranolol caused the junctional rhythm. Presumably suppression of sinus nodal automaticity by these drugs and/or enhancement of junctional automaticity by digitalis could induce junctional escape rhythm that might arise from automaticity in the N region of the AV node. A recent study showed that digitalis might decrease the electrotonic influence of the atria on the N region and, by doing so, unmask the automaticity of the fibers in the N region. Junctional
rhythm in patient 14, who had recent myocardial infarction of the inferior wall, was also an escape rhythm (average cycle length 1164 msec), presumably caused by ischemia and decreased automaticity of the sinus node. Such an escape rhythm might also arise from the N region for the reasons we discussed.

One may argue against the above postulation, since sick sinus syndrome, digitalis excess, and myocardial infarction of the inferior wall are frequently associated with an abnormal automaticity of the AV junction and possibly with abnormal automaticity of the N region. However, since retrograde atrial activation was similar in all of our patients, i.e., the atrial activation occurred within or immediately after the QRS complex, we believe that the location of the pacemaker responsible for the junctional rhythm is probably similar in all cases. Furthermore, the acceleration of the junctional rhythm after intravenous administration of atropine would speak for intact automaticity in the AV junction. The above arguments support the belief that the junctional rhythm in our patients originated in the N region. However, this is only a hypothesis and confirmatory studies with drugs that suppress automaticity in the N region such as verapamil need to be performed.

If the junctional rhythm indeed originated from the N region of the AV node, why were we not able to record an upstroke slope that represents the phase O of the N fibers of the AV node, similar to what we have recorded in the sinus node? The explanation is most likely similar to that offered in our previous article. The distance between the catheter electrode to the N region of the node might preclude such a recording. Otherwise, the interval from the AV node to the His bundle might be too short for complete recognition of the AV nodal upstroke slope. When we used a rapid paper speed (figure 4, B), we noticed a slow deflection preceding the rapid deflection of the bipolar His bundle electrogram. However, we believe that this slow deflection is an artifact related to the high amplification and low-pass filters. In fact, a trace of the slow deflection (figure 4, B, arrowhead) can also be seen in the bipolar His bundle electrogram. The effects of different filters in His bundle recording have been discussed previously.

In conclusion, in this study we have demonstrated that it is possible to record diastolic slopes that accu-
rately reflect phase 4 depolarization of the pacemaker in the junctional area in patients with junctional rhythm. As concluded in studies suggesting the possibility of the N region as the location of the pacemaker,\textsuperscript{1, 10, 14} we postulated that in some of our patients the rhythm arose from automaticity in the N region of the AV node. Clinical application of the technique may help to elucidate the nature of junctional rhythms.

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FIGURE 5. Dissipating effect of atropine (1 mg iv) on the junctional cycle lengths and the diastolic slopes. Abbreviations, symbols, and calibration are as in figure 2. A. Recordings obtained immediately after injection of atropine; B, recordings obtained 20 min after the injection. Note the prolongation of junctional cycle lengths and the decrease in junctional diastolic slope as the effect of atropine dissipated.
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