Detection of Diastolic Potentials Around the Mitral Annulus of Structurally Normal Human Hearts

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Summary
To examine the electrophysiologic characteristics of the subvalvular mitral region, we retrospectively searched for the presence of subvalvular diastolic potentials (DP) in 91 patients (mean age, 46.9 ± 16.6 years) who underwent catheter ablation of left-sided accessory pathways (AP).

We detected low-amplitude (0.19 ± 0.09 mV) DP in 14 patients (15.4%), including 8 with overt preexcitation and 6 patients with concealed AP. The mean interval between ventricular electrogram and DP was 383 ± 46 ms (range, 306-475). DP were detected in 4 of 20 patients with antero-lateral, 3 of 38 with lateral, 4 of 12 with postero-lateral, 2 of 14 with posterior, and 3 of 10 patients with postero-septal AP. In 6 of 14 patients, DP were detected before ablation. In 4 of 8 patients with overt preexcitation, DP were consistently recorded after elimination of the delta wave, suggesting that they were not associated with AP conduction. In 6 of 11 patients, DP were observed during both sinus rhythm and ventricular pacing, suggesting that they were not artifacts.

The electrophysiologic characteristics of clinically relevant DP around the mitral annulus suggest that, in normal human hearts, an anatomical substrate may be present around the mitral annulus. (Int Heart J 2010; 51: 394-398)

Key words: Diastolic myocardial potential, Specialized conduction system, Purkinje fiber, Wolf-Parkinson-White syndrome, Human heart electrophysiology

Endocavitary surfaces in the left ventricle are not structurally simple due to the presence of some endocavitary structures such as the papillary muscle, the moderator bands, and false tendons,1,9 which are candidates of arrhythmogenic substrates.1,9 These structures may make it complex to clinically analyze electrophysiological phenomena occurring in the left ventricular cavity, because they might cause systolic or diastolic potentials.6-8 It is important to clarify the genesis of these delayed potentials, which may possibly lead to elucidating an unknown etiology of some ventricular tachyarrhythmias. In contrast, the submural ventricular area seems to be anatomically unique in the left ventricle, because it is away from any endocavitary structures,1,9 and is adjacent to the dead end of the Purkinje network.9,10 It is also the site of origin of unusual ventricular tachyarrhythmias.11-13 Thus, it is possible that this area may possess unique electrophysiologic properties. Detection of any delayed potentials in this area might provide new insight into the understanding of the genesis of these potentials. The present study examined the electrophysiologic characteristics of the subvalvular mitral annulus in structurally normal human hearts.

Methods
Study population: The mean age of the 91 patients (60 men) enrolled in this study was 46.9 ± 16.6 years. The 43 patients with overt and 48 with concealed Wolf-Parkinson-White (WPW) syndrome underwent radiofrequency (RF) catheter ablation of left-sided accessory pathways (AP) via the retrograde, transaortic approach. No patient had manifestations of structural heart disease by physical examination, chest roentgenogram, or transthoracic echocardiography.

Electrophysiologic studies and radiofrequency ablation: Electrophysiologic studies and catheter ablation were performed after the discontinuation of antiarrhythmic drug therapy and after the patients had provided informed consent. Diagnostic multi-electrode catheters were placed in the high right atrium, His-bundle region, right ventricular apex, and coronary sinus. Bipolar intracardiac electrograms and 12-lead surface electrocardiograms were recorded and stored on an EPLab/EP Amp™ (Quinton Electrophysiology Co., Seattle, WA) or EP Work Mate™ (EP MedSystems, Inc., West Berlin, NJ) recording system, after filtering of the signals between 30 and 400 Hz (EPLab/EP Amp), or 30 and 500 Hz (EP Work Mate). RF catheter ablation of the AP was performed using a 7F quadripolar electrode catheter, with a 4-mm deflectable tip elec-
trode, an embedded thermistor, and 2.5-2 mm interelectrode spacing (Biosense Webster Inc., Diamond Bar, CA). A site where the application of RF energy eliminated bidirectional AP conduction was classified as successful, and was further divided into anterior, antero-lateral, lateral, postero-lateral, posterior, and postero-septal by confining the position of the tip of the ablation catheter under fluoroscopy. Bidirectional AP conduction was eliminated in all patients by delivering a mean of 5.1 ± 5.7 RF applications (range, 1-22) at the subvalvular mitral annulus.

**Electrogram analysis:** The intracardiac electrograms were quantitatively analyzed post hoc. We first searched for the presence of diastolic potentials (DP) following the ventricular electrogram recorded from the distal poles of the ablation catheter, during sinus rhythm, immediately before each RF application in all patients. To confirm that the DP reflected the activation of cardiac tissue and were not artifacts, we verified that a) the signals were recorded under stable conditions and b) the intervals between DP and ventricular electrograms and the signal amplitude were both constant. Second, although ventricular electrograms ≤ 0.1 mV have been accepted by others,21 we only retained signals > 0.1 mV in amplitude. Third, to verify that the DP were not artifacts attributable to the characteristics of the recording system, we searched for their presence on the intracardiac recordings stored on 2 different recording systems made by different manufacturers, and detected DP in 11 of 53 patients using the EPLab/EP Amp™ system, and in 3 of 38 patients using the EP Work Mate™ system. Furthermore, as reported in the results, DP were not systematically present immediately before all RF applications delivered to an individual patient, also suggesting that they were not caused by a faulty recording system. Finally, to further confirm that the DP were biologic signals, we examined whether ventricular burst stimulation, performed before the application of RF energy, reproduced DP similar to those recorded during sinus rhythm. The importance of the reproducibility of potentials during pacing to verify that they reflect the activation of cardiac tissue has been emphasized in a previous study.27 These combined observations confirmed the presence of potentials associated with the activation of myocardial tissue around the mitral annulus.

When a DP was detected at a site of successful ablation, we also examined whether it was visible immediately after the elimination of AP conduction, to confirm an association between AP conduction and DP. The recordings were analyzed a) during sinus rhythm, b) during ventricular pacing, and c) immediately after elimination of AP conduction, including measurements of the maximum LP amplitude and of the interval between onset of DP and onset of the ventricular electrogram, using electronic calipers. Since DP were detected at either successful or unsuccessful ablation sites in individual patients, and since the sites of unsuccessful ablation where DP were detected were anatomically close to sites of successful ablation, the anatomical locations where DP were detected were classified as sites of successful ablation.

**Data analysis:** Continuous variables are expressed as the mean ± SD. Statistical significance was examined by Student’s paired t-test for comparisons between two variables. A P < 0.05 was considered statistically significant.

**Results**

**Detection of the diastolic potentials during sinus rhythm:** DP (Figure 1) were detected during sinus rhythm in 14 of the 91 (15.4%) patients (Table). The prevalence of DP among patients with manifest (8 of 43 patients) versus concealed (6 of 48 patients) AP was similar. The mean amplitude of the DP was 0.19 ± 0.09 mV (range, 0.1-0.38 mV). The mean interval between onset of ventricular electrogram and diastolic potentials was 383 ± 46 ms (range, 306-475 ms). The potentials were detected all around the mitral annulus (Figure 2). The mean number of RF energy applications delivered before the detection of a

**Table.** Study Measurements

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age</th>
<th>Sex</th>
<th>AP location</th>
<th>Delta wave</th>
<th>Sinus rhythm</th>
<th>Ventricular pacing</th>
<th>After ablation</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>QRS-LP (ms)</td>
<td>Amp (mV)</td>
<td>QRS-LP (ms)</td>
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<tr>
<td>1</td>
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<td>F</td>
<td>LT</td>
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<tr>
<td>2</td>
<td>40</td>
<td>M</td>
<td>PO</td>
<td>+</td>
<td>375</td>
<td>0.10</td>
<td>400</td>
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<tr>
<td>3</td>
<td>22</td>
<td>M</td>
<td>PL</td>
<td>+</td>
<td>475</td>
<td>0.11</td>
<td>413</td>
</tr>
<tr>
<td>4</td>
<td>17</td>
<td>M</td>
<td>PL</td>
<td>-</td>
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<td>0.14</td>
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</tr>
<tr>
<td>5</td>
<td>46</td>
<td>M</td>
<td>AL</td>
<td>-</td>
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<td>0.14</td>
<td>376</td>
</tr>
<tr>
<td>6</td>
<td>43</td>
<td>M</td>
<td>PL</td>
<td>-</td>
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<tr>
<td>7</td>
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<td>M</td>
<td>AL</td>
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<tr>
<td>8</td>
<td>15</td>
<td>M</td>
<td>PS</td>
<td>+</td>
<td>440</td>
<td>0.17</td>
<td>360</td>
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<tr>
<td>9</td>
<td>35</td>
<td>M</td>
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<td>-</td>
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<tr>
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<td>48</td>
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<tr>
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<tr>
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<td>F</td>
<td>PS</td>
<td>-</td>
<td>395</td>
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</tbody>
</table>

**Mean ± SD** 38.8 ± 12.6 - - 383 ± 46 0.19 ± 0.09 367 ± 34 16 ± 0.08 373 ± 29 18 ± 0.08

+ indicates present; - absent; AL, antero-lateral; Amp, maximum amplitude of late potential; AP, accessory pathway; LA, lateral; NA, not analyzed; ND, not detected; PL, postero-lateral; PO, posterior; PS, postero-septal; and QRS-LP, interval between onset of ventricular electrogram and onset of late potential.
DP was 1.9 ± 3.1 (range, 0-17). DP were detected before the 1st application in 6 patients, the 2nd in 6, the 3rd in 1, and the 17th application in 1 patient.

Reproducibility of the diastolic potentials during ventricular pacing: In 6 of 8 patients (75%) who underwent ventricular pacing, among 14 in whom DP were detected during sinus rhythm, the potentials were reproducibly detected during ventricular pacing (Figure 3; Table). The mean interval between onset of ventricular electrogram and the DP during sinus rhythm (383 ± 46 ms) versus during ventricular pacing (346 ± 21 ms), and the maximum amplitude of the DP during sinus rhythm (0.19 ± 0.09 mV) versus during ventricular pacing (0.16 ± 0.08 mV), were similar.

Detection of the diastolic potentials after elimination of accessory pathway conduction: In 6 of 11 patients (54.5%) whose DP was detected during sinus rhythm just before the elimination
of AP conduction, including 8 patients with manifest and 3 with concealed AP, among 14 in whom DP were detected during sinus rhythm, the DP remained visible during sinus rhythm after elimination of AP conduction (Figure 4; Table). The mean interval between onset of ventricular electrogram and the DP immediately before (383 ± 46 ms) versus immediately after (367 ± 34 ms), and the mean maximum amplitude of the DP immediately before (0.19 ± 0.09 mV) versus immediately after (0.18 ± 0.08 mV) the elimination of AP conduction, were similar.

**Discussion**

The main observation made in the present study was the presence of previously unrecognized DP around the mitral annulus in 15% of patients without structural heart disease, who underwent catheter ablation of left-sided AP.

**Electrophysiologic characteristics of the diastolic potentials:** In infarcted hearts, fragmented intracardiac late potentials are often recorded in the systolic phase, following the QRS complex. These fragmented late potentials reflect the delayed activation of injured myocardium poorly coupled with surrounding healthy myocardium. In contrast, the DP recorded in the present study always appeared in mid-diastole, and were spiky and nonfragmented. The origin of these DP remains unclear, though it is probably different from that of scar-associated late potentials. Ouyang, et al and Kaneko, et al observed similar diastolic potentials, near the left posterior fascicle on the left interventricular septum, in patients with verapamil-sensitive idiopathic left ventricular tachycardia, and in patients with WPW syndrome and no structural heart disease, respectively. They suggested that these potentials are due to slow retrograde conduction over Purkinje-Purkinje or Purkinje-ventricular-Purkinje connections, caused by anterograde conduction block in the Purkinje network. If our DP were associated with specialized conduction properties, it is unlikely that the DP recorded in the present study were associated with these anatomical structures.

Miyachi, et al recorded slow potentials preceding the surface QRS complex in the subvalvular mitral region in patients with left-sided, concealed AP. They hypothesized that these potentials preceding the QRS were caused by concealed anterograde conduction across the AP since they disappeared during retroventricular (AV) reciprocating tachycardia and right ventricular pacing, and were eliminated by successful ablation. In contrast, the DP were consistently reproduced after elimination of the delta waves in most patients, suggesting that they were not associated with AP conduction.

While the so-called specialized cardiac tissues are the sinus node, AV conduction system, and Purkinje network, tissue with specialized conduction properties is also found within the AV annulus. Anderson, et al identified specialized tissue in the atrial margin of the mitral annulus fibrosus, at the junction of atrial and ventricular myocardium in 15% of 200 human hearts. The remnants of tissue were histologically and histochemically distinct from the surrounding atrial myocardium, and were always separated from, though contiguous with, the ventricular myocardium, however, without apparent AV myocardial bridges. These remnants were on the posterior aspect of the mitral orifice in the majority, and lateral or anterior in a minority of hearts. The prevalence and distribution of the remnants described by Anderson, et al are consistent with those of the DP found in the present study. We hypothesize that the DP detected around the mitral annulus reflect the activation of a segment of AV ring-specialized tissue, poorly coupled with the surrounding ventricular myocardium. However, another unknown type of myocardial tissue cannot be excluded by our observations.

**Clinical implications:** Our observations indicate that an arrhythmic substrate can be created at any point around the mitral annulus. Tada, et al and Kanagai, et al reported a distinct variety of idiopathic nonmonomorphic ventricular tachyarrhythmias originating from the mitral annulus. A low-amplitude presystolic potential was often found during ongoing tachycardia at the successful ablation site. The location and morphology of these prepotentials were similar to those of our DP. However, further studies are needed to determine whether these DP are at the source of ventricular tachyarrhythmias originating from the mitral annulus.

**Study limitations:** There are limitations to this retrospective study. First, since the DP were often detected immediately before unsuccessful RF delivery, their anatomical location might not precisely coincide with, though we believe that it was near, the successful ablation site. Second, ventricular extrastimulation was not performed to study the electrophysiological properties of these DP in detail. Third, we found the DP around the mitral annulus in a higher frequency (15.4%) than expected. However, the detection rate of these additional potentials might vary among institutes or the detection of the potentials might be previously underestimated, since intracardiac electrograms during diastolic phase are not commonly observed during catheter ablation of AP.

**Conclusions:** We recorded DP around the mitral annulus of structurally normal hearts, which may reflect the presence of a unique anatomical substrate.

**References**


