Epicardial Activation and Repolarization Patterns in Patients With Right Ventricular Hypertrophy*

Peng-Sheng Chen, MD; Kenneth M. Moser, MD; Walter P. Dembitsky, MD; William R. Auger, MD; Pat O. Daily, MD; Constance M. Calisi, RN; Stuart W. Jamieson, MD; and Gregory K. Feld, MD

To map global epicardial repolarization patterns and test the “SI” model of T wave generation, the patterns of epicardial activation and repolarization in patients with chronic pulmonary thromboembolism and right ventricular hypertrophy were studied by computerized mapping techniques and monophasic action potential (MAP) recordings. The ventricular activation patterns were characterized by delayed right ventricular activation and the absence of normal early epicardial ventricular breakthrough in some cases. The repolarization patterns were characterized by nonuniform distribution of T wave morphologies. The T waves were predominantly positive over the left ventricular epicardium and negative or biphasic over the right ventricular epicardium. The activation-recovery (A–R) intervals were measured from the local activation to the maximal dV/dt of the upstroke of the T waves (Wyatt method). The difference between the A–R intervals and the MAP from onset of activation to 90% repolarization (MAP90) varies according to T wave morphology and could be as high as 96 msec with positive T waves, despite significant correlations (r = 0.56–0.90) between MAP90 and A–R intervals for each morphology. Better overall correlations were found if the minimal dV/dt on the downslope of the positive T waves was chosen to estimate the time of local repolarization (alternative method). Using this method, the mean A–R intervals were the same over the right and left ventricles. Cardiopulmonary bypass significantly prolonged the action potential duration equally at all parts of the epicardium. We conclude that in patients with right ventricular hypertrophy, the time of local repolarization can best be estimated by our alternative method; the right ventricle completes activation and repolarization later than the left ventricle, and the distribution of T wave morphologies is nonuniform, with predominantly positive T waves observed over the left ventricle and negative or biphasic T waves observed over the right ventricle. These findings are compatible with the SI model of the generation of T waves. (Circulation 1991;83:104–118)

*All editorial decisions for this article, including selection of reviewers and the final decision, were made by a guest editor. This procedure applies to all manuscripts with authors from the University of California San Diego or UCSD Medical Center.

From the Divisions of Cardiology (P.S.C., C.M.C., G.K.F.) and Pulmonary and Critical Care Medicine (K.M.M., W.R.A), Department of Medicine, and the Division of Cardiothoracic Surgery (W.P.D., P.O.D., S.W.J.), Department of Surgery, University of California San Diego Medical Center and Veterans Affairs Med-ical Center, San Diego, Calif.

Supported by Clinician-Scientist Award 88-414 from the American Heart Association, a Merit Review from the Department of Veterans Affairs, and a grant from the Whitaker Foundation to P.S.C.

Address for correspondence: Peng-Sheng Chen, MD, H811A, Division of Cardiology, Department of Medicine, UCSD Medical Center, 225 Dickinson Street, San Diego, CA 92103.

Received March 1, 1990; revision accepted August 14, 1990.
dial ST-T wave morphology can be predicted by spatial analysis of intracellular potentials. Because the intracellular potential distribution is determined by the excitation sequence, the model predicts that ST-T wave polarities will be positive at the earliest site of epicardial activation and repolarization and negative at the latest site of epicardial activation and repolarization. This model can be tested in patients by correlating the time sequence of epicardial activation and repolarization with epicardial ST-T wave morphologies. The University of California San Diego Medical Center has a unique population of patients with pulmonary hypertension and right ventricular hypertrophy due to chronic, thromboembolic obstruction of the major pulmonary arteries who have been referred for pulmonary thromboendarterectomy.4,5 Most of these patients have electrocardiographic evidence of right ventricular hypertrophy, with characteristic QRS and ST-T wave changes.6,7 Because pulmonary thromboendarterectomy is an open-chest procedure requiring cardiopulmonary bypass, the epicardial activation and repolarization patterns can be readily determined in these patients. Therefore, we recorded the epicardial monophasic action potentials (MAP) from multiple left and right ventricular sites and compared them with 56 unipolar epicardial electrograms before and after the initiation of cardiopulmonary bypass to determine whether the Wyatt method can be applied to humans and whether the distribution of epicardial ST-T wave morphologies can be predicted by the excitation and repolarization sequence, as predicted by the SI model.

Methods

The protocol of the study was reviewed and approved by the Human Subjects Committee of the University of California San Diego. All patients had documented chronic pulmonary thromboembolism and pulmonary hypertension. The preoperative evaluation and surgical procedures were performed according to standard protocols described elsewhere.4,5 Included in the preoperative evaluation were right heart catheterization and pulmonary angiography for all patients. Left heart catheterization and coronary angiography were performed in patients who were more than 35 years old or who had risk factors for coronary artery disease. A written informed consent was obtained from each patient before surgery.

At the time of surgery, a balloon-tipped catheter was inserted via the right internal jugular vein and positioned in the pulmonary artery to continuously monitor pulmonary arterial pressure and cardiac output. Endotracheal intubation was then performed, and general anesthesia was achieved with the anesthetic agents fentanyl, pancuronium bromide (Pavulon), metocurine iodide (Metubine), and diazepam (Valium). The chest was opened, and the heart was suspended in a pericardial cradle. Cannulation was then performed in preparation for total cardiopulmonary bypass.

![Figure 1. Schematic of electrode location. Shown is an apical polar projection of ventricles, with apex in center. Electodes at 12 o'clock position were positioned over left anterior descending coronary artery and serve as a landmark to separate left and right ventricles. Electodes at 1–3 o'clock positions were always over left ventricle. Electodes at 6–11 o'clock positions were always over right ventricle. Electrodes in hatched region were positioned over posterior septal area, apex, or overlying left anterior descending coronary artery and were not designated as recording from either right or left ventricle.](http://circ.ahajournals.org/doi/figure/105)
tical comparisons between the left and the right ventricular action potential durations, we designated the 12 electrodes in columns at the 1–3 o’clock positions as left ventricular and the 24 electrodes at the 6–11 o’clock positions as right ventricular. The eight electrodes in the apex, four electrodes at the 12 o’clock location, and eight electrodes at the 4 and the 5 o’clock positions were not designated as either right or left ventricular because it was not always certain whether they were overlaying the right ventricular or left ventricular epicardium.

For surface electrocardiographic leads, the low-pass filter was 100 Hz, and the high-pass filter was 0.05 Hz. The MAP recordings were made with an Ag/AgCl electrode catheter manufactured by Webster Laboratories, Baldwin Park, Calif. The electrode at the tip of the catheter was gently pushed against the epicardial surface; an indifferent electrode was connected to the chest wall as the ground. Both were connected to the Electronics for Medicine VR-16 recorder and filtered at 0.05–5,000 Hz to record the MAP. Before initiation of the cardiopulmonary bypass, unipolar electrograms were obtained from 56 epicardial sites during the sinus rhythm. The MAP was then recorded sequentially from eight epicardial sites. Each site was adjacent to an epicardial button electrode on the anterior wall of the right or left ventricle. Warm cardiopulmonary bypass was then initiated, and the 56 epicardial unipolar electrograms and the MAP were again recorded at the same epicardial sites during the sinus rhythm immediately after the onset and 1–6 minutes into the cardiopulmonary bypass. The total duration of the study was approximately 10 minutes. At the end of the study, the electrode sock was removed, and the surgical procedure continued as planned.

### Data Analysis

The MAP from onset of activation to 90% repolarization (MAP90) duration was measured as the time in milliseconds (Figure 2).9,10 The MAP90 was then used to estimate the activation potential duration. The unipolar electrograms recorded by the sock electrode array were displayed on the monitor of the mapping system. The T waves were classified into four different morphologies: positive, negative, bi-phasic,11 and those resembling the MAP (Figure 3). The time of the minimal negative slope of the QRS complex (dV/dtmin) of each channel was taken as the time of the local activation, and the time of the maximal positive slope of the T wave (dV/dtmax) was taken as the time of the local repolarization.1,2 For notched positive T waves, the dV/dtmax was taken on the upslope of the second peak. For the MAP-like T waves, the time to 90% repolarization was taken as the time of local repolarization. Although the software of the mapping system can automatically select the maximal slopes of the QRS and T waves, extensive manual editing was necessary because the algorithm of the mapping system does not differentiate between maximal positive and negative dV/dt. Manual editing was used so that only the dV/dtmin was selected for the QRS complex, and the dV/dtmax was selected for the T waves. To study the patterns of activation, isochronal activation maps were generated to determine the sequence of epicardial activation and whether the cardiopulmonary bypass alters the patterns of ventricular activation. The total epicardial activation time, which is the difference between the latest and the earliest epicardial activation times, was calculated for each isochronal map. Analysis of variance12 was used to compare the total
epicardial activation time before, immediately after, and 1–5 minutes after the initiation of the cardiopulmonary bypass. To determine whether the activation–recovery (A–R) intervals could be used as an alternative estimate of the local action potential duration, comparisons were made between the A–R intervals and the MAP90 at eight epicardial sites by paired t tests, correlation coefficient determination, and linear regression analysis using the multivariate general linear model to determine the standard error of estimates. The comparisons were also made between A–R intervals and MAP90 for each T wave morphology. Analysis of variance was used to compare the three sets of A–R intervals obtained before and after the initiation of the cardiopulmonary bypass to determine the effects of ventricular unloading on the action potential duration. Pearson’s $\chi^2$ test was used to test the distribution of T wave morphologies at different ventricular sites. Probability values equal to or less than 0.05 were considered significant.

**Part 2**

Three patients participated in part 2. The purpose of this part of the study was to compare the MAP90 obtained using unipolar techniques with that obtained using bipolar techniques. For unipolar recordings, the Ag/AgCl electrode was paired with an indifferent electrode on the chest wall as the reference electrode, as described in part 1. For bipolar recordings, the distal electrode of a standard 6F quadripolar electrode catheter (USCI, Billerica, Mass.) was held in contact with the epicardium 1–2 mm away from the Ag/AgCl electrode. Simultaneous surface electrocardiogram, unipolar MAP, and bipolar MAP recordings were made on the Electronics for Medicine VR-16 recorder. Multiple epicardial points were sampled for each patient. The total duration of the study was approximately 10 minutes or less.

**Data Analysis**

Simultaneously recorded MAP90 values obtained by the unipolar and bipolar methods were compared by paired t test and correlation coefficient.

**Results**

**Part 1**

**Patient characteristics.** Table 1 gives patient characteristics. Seven patients were included in part 1 of the study. All patients had pulmonary hypertension, and a majority of them had a decreased cardiac index. All patients except patient 3 had a coronary angiogram performed and showed no evidence of significant coronary artery disease. Patient 4 developed severe hypotension after the sock electrode array was applied to the epicardium; thus, she was immediately put on cardiopulmonary bypass, and data from before the bypass were not obtained. Patient 5 developed atrial fibrillation at the initiation of the bypass and then converted to sinus rhythm. The data ob-
tained during atrial fibrillation could not be analyzed. Thus, in patients 4 and 5, only two sets of data were available for analysis. In the other five patients, three sets of data were available. Thus, a total of 19 sets of epicardial electrograms were available for analysis.

**Epicardial Depolarization Patterns**

Five patients (1, 3, 4, 5, and 6) had electrocardiographic evidence of right ventricular hypertrophy. Patient 2 had a normal electrocardiogram, and patient 7 had only nonspecific ST-T changes (Table 1). In these two patients, the earliest epicardial breakthrough was located at the right ventricular anterior wall (Figure 4). An area of early breakthrough was also found near the posterior apex. The location of the latest activation was at the basal area of the right ventricle. These early and late sites were similar to those reported for normal human hearts.17

In the five patients who had evidence of right ventricular hypertrophy on electrocardiography, 13 sets of epicardial activation maps before and during cardiopulmonary bypass were obtained. There were two types of activation patterns. The first type consisted of seven maps and was characterized by early epicardial breakthrough at both the right and left ventricles (Figure 5). Right ventricular epicardial breakthrough occurred 33–42 msec (36±3 msec) after the onset of the surface QRS complex, which was more than 10 msec later than that reported for the normal timing of right ventricular breakthrough.17 Despite an early breakthrough site, most of the right ventricle was still activated late. Using the onset of the surface QRS complex as time zero, the latest right ventricular epicardial activation occurred at 75±10 msec, significantly later than that of the left ventricular epicardium (64±10 msec; p<0.02). The second type of activation pattern consisted of six maps and was characterized by the absence of a discrete area of early right ventricular breakthrough (Figure 6). Left ventricular breakthrough occurred 22±10 msec after the onset of surface QRS. The activation started and completed earlier in the left ventricle. The latest right ventricular epicardial activation occurred at 79±20 msec, significantly later than that of the left ventricle (46±10 msec; p<0.001).

Cardiopulmonary bypass had little effect on the depolarization patterns, except in one patient who lost the right ventricular breakthrough at the later analysis time on bypass and thus converted from the first to the second type of depolarization pattern. The overall total epicardial activation time for all patients was 49±11 msec before bypass, 46±11 msec immediately after the initiation of bypass, and 48±14 msec later (86–329 seconds) into bypass (p=NS).

**Epicardial Repolarization Patterns**

* T wave morphology distribution. Figure 7 shows the actual epicardial T waves recorded for the same beat as that shown in Figure 5. There was an uneven distribution of the T wave morphologies, with positive T waves seen primarily over the left ventricle and the right ventricular anterior wall, which corresponds to the two areas of earliest depolarization shown in Figure 5. Negative or biphasic T waves were recorded in other parts of the ventricles. Table 2 shows the number of electrodes that recorded each T wave morphology at different locations of the epicardium for all patients. The most often observed T wave morphology was positive (44.1%), followed by biphasic (27.3%), negative (23.7%), and MAP-like (4.8%). The most often observed T wave morphology at the left ventricular site was positive. In contrast, electrodes over the right ventricular epicardium recorded predominantly negative or biphasic T waves. The small number of T waves that resembled the MAP were recorded in multiple locations.

**Correlation between A–R intervals and MAP**

Among a total of 112 possible MAP recordings (16
points per patient for seven patients), 16 were not available. In patient 4, data before bypass were not obtained due to severe hypotension resulting from application of the epicardial sock electrodes. In patient 6, MAP electrodes were misconnected and resulted in the loss of part of the data before the error was discovered. Thus, a total of 86 sites were analyzed. Of the 86 sites, 35 were on the left ventricle, and 51 were on the right ventricle. The discrepancy in the numbers occurred because patients 6 and 7 had right ventricular hypertrophy that was so severe that the right ventricle occupied all of the anterior surface of the heart. Recording the MAP at left ventricular sites was not possible without lifting the heart and compromising the hemodynamic status in these patients. Thus, the MAP recordings were obtained from right ventricular sites only in these patients. The upstroke of the MAP waveforms was interrupted in 65% of patients by a notch that represents the time of local activation (Figure 2A). In the other 35%, the upstroke was not interrupted by a notch, and local activation was defined as the onset of rapid upstroke (Figure 2B). Among the 86 sites in which MAP was recorded, 73 also had analyzable T waves recorded by the mapping system. The correlations between the MAP\_90 and the A–R intervals at these 73 sites were significant for all four T wave morphologies (Figure 8). However, despite the good correlation, the absolute values of the A–R intervals significantly differed from the MAP\_90 (Table 3A). This was most marked if the T waves were positive, where an up-to-96-msec underestimation of the

**Figure 4.** Epicardial activation patterns in patient 2, who had pulmonary hypertension but no evidence of right ventricular hypertrophy by a two-dimensional echocardiogram. Panel A: Baseline 12-lead electrocardiogram. There were T wave changes in leads III and aVF but no evidence of right ventricular hypertrophy. Panel B: Polar projection of ventricles. Numbers represent locations of electrodes with satisfactory recordings and give times of activation for those locations timed from beginning of surface QRS complex. An arrow points to earliest activation site. • Electrode sites at which adequate recordings were not obtained. Isochronal lines are 20 msec apart. Earliest epicardial breakthrough was at right ventricular anterior wall; latest site of activation was at base of right ventricle.
FIGURE 5. Electrocardiogram and isochronal epicardial activation map of patient 5 showing early breakthrough sites (arrows) at both right and left ventricles. Panel A: Surface electrocardiogram with evidence of right ventricular hypertrophy. Panel B: Isochronal map before cardiopulmonary bypass. Although an independent early site was noted at right ventricle, the timing (35 msec) was late compared with that reported for normals. In addition, most of posterobasal right ventricular epicardium was activated later than that of the left ventricle. Isochronal lines are 20 msec apart.

MAP₉₀ was observed. Because of the nonuniform distribution of T wave morphologies, global repolarization patterns could not be determined with accuracy. Thus, isochronal repolarization maps could not be generated with this method. In an attempt to decrease the discrepancy between the A–R intervals of the positive T waves and the MAP₉₀, two alternative methods were tested.

One method used the peak of the positive T wave as the time of repolarization, and the other method used the minimal dV/dt on the downslope of the positive T wave. The results are summarized in Table 3. If the peak of the positive T waves was used as the time of local repolarization (Table 3), there still were significant differences between the MAP₉₀ and the A–R interval. However, if the minimal dV/dt on the downslope of the positive T waves was chosen as the time of local repolarization, no difference was found between the MAP₉₀ and the A–R interval, and the overall correlation was improved (Table 3). However, the SEE remains large (22 msec). Because neither method offers a perfect estimation of the MAP₉₀, we analyzed the time of repolarization both by the Wyatt method as described in “Methods” and by the alternative method that used the dV/dtᵣ on the downslope of positive T waves as the time of local repolarization. The results of both methods are presented.

Epicardial A–R intervals before and after initiation of cardiopulmonary bypass. Cardiopulmonary bypass had significant effects on epicardial repolarization. The action potential prolonged immediately after the initiation of the cardiopulmonary bypass. Figure 9 shows an example of the unipolar electrogram and the MAP recorded at the same site for patient 1. Progressive A–R interval prolongation was noted after the onset of the bypass. Although the action potential duration lengthened, the shape of the action potential was the same before and after the
initiation of the bypass. When all data were pooled, regardless of the location of the recording electrodes and the morphology of the T waves, the A–R intervals measured by the Wyatt methods were $260\pm 41$ msec ($n=261$) before the bypass, $292\pm 41$ msec ($n=327$) immediately after the initiation of the bypass, and $335\pm 38$ msec ($n=274$) later into the bypass ($p<0.001$). Similar results were noted using our revised method. The A–R intervals estimated with our revised method before, immediately after, and later into the cardiopulmonary bypass were $292\pm 33$, $315\pm 37$, and $359\pm 29$ msec, respectively. The differences were statistically significant ($p<0.001$) at each time after the bypass compared with before the bypass.

This analysis, however, was complicated by the potential effects of heart rate change before and after the bypass. To rectify this problem, we eliminated the data from patient 3 because the sinus cycle length increased from 840 to 1,145 msec after the bypass. All data from patients 4 and 5 were excluded because of incomplete data collection. For the remaining four patients, 50 analyzable MAP potentials were recorded. The MAP90 before the bypass averaged $310\pm 17$ msec, which is significantly ($p<0.001$) shorter than that after the bypass ($350\pm 22$ msec). Also, in these four patients, a total of 192 channels recorded analyzable T waves before, at onset, and later into the cardiopulmonary bypass. Among these channels, 69 (36%) had consistent T wave morphologies in all three consecutive recordings, which allowed analysis by Wyatt methods. Table 4 shows the A–R interval changes for each T wave morphology before and after the bypass. Significant prolongation of the epicardial repolarization time was observed for each T wave morphology 86–329 seconds after the initiation of the bypass.
Effects of Cardiopulmonary Bypass on Repolarization Patterns of Left and Right Ventricles

With the revised method of A–R interval estimation, which is less dependent on T wave morphology for accuracy, it is possible to compare the effects of cardiopulmonary bypass on the A–R intervals of the normal left ventricle with those on the overloaded or hypertrophied right ventricle. As shown in Table 5, mean A–R intervals of the left and right ventricles before the bypass were similar. After the bypass, there were significant increases of the A–R intervals over time at both ventricles. However, the increments of the A–R interval of the left ventricle (297–357 msec) and of the right ventricle (297–359 msec) were not significantly different. Thus, mean A–R intervals were nearly identical between the normal left ventricles and the hypertrophied or hypertensive right ventricles, and cardiopulmonary bypass exerted similar effects on both.

The effects of cardiopulmonary bypass on the distribution of T wave morphologies are shown in Table 6. The most apparent change appears to be an increase in the percentage of negative T waves at left ventricular sites and an increase in the percentage of positive T waves at right ventricular sites. However, the changes at right ventricular sites did not reach statistical significance (p=0.064). The overall distribution of T wave morphologies was not changed before and after the initiation of cardiopulmonary bypass; both were characterized by predominantly positive T waves over the left ventricle and negative or bipolar T waves over the right ventricle.

Part 2

Consistent with results reported by others, the morphology of the MAP recorded by the bipolar technique is characterized by a steeper upstroke and lower amplitude than the MAP recorded by the unipolar technique (Figure 10). However, MAP_{bal} recorded by the unipolar method (n=18, 383±180 msec) was not different from that recorded by the bipolar method (n=18, 387±180 msec, p=0.58). The two values were significantly correlated (r=0.87, p<0.001). Thus, despite differences in morphology, MAP_{bal} values measured by these two techniques were of the same duration.

Discussion

Patterns of Ventricular Activation in Right Ventricular Hypertrophy

The differentiation of right ventricular hypertrophy and right bundle branch block by means of surface electrocardiographic criteria is often difficult because both of these conditions are characterized by prominent R waves in lead V_1. In the development of criteria for the electrocardiographic diagnosis of right ventricular hypertrophy, one of the most frequently cited studies excluded all patients in whom the electrocardiogram showed an M-shaped QRS complex with a prominent R wave and a ventricular activation time exceeding 0.07 second in lead V_1. The authors, however, postulated that right ventricular hypertrophy and right bundle branch block could coexist. Compatible with reports by other investigators, our study showed that in patients with right ventricular hypertrophy, there was a delay or absence of right ventricular epicardial breakthrough, which may account for the abnormal rightward terminal QRS vector or the right bundle branch block QRS pattern in some patients. The surface electrocardiogram in some patients (e.g., patient 4) did not show an M-shaped QRS complex in lead V_1 (Figure 6A), yet early right ventricular epicardial breakthrough was absent, as demonstrated by the epicardial iso-

---

Table 2. T Wave Morphology and Recording Electrode Location

<table>
<thead>
<tr>
<th>T wave morphology</th>
<th>Positive</th>
<th>Biphasic</th>
<th>Negative</th>
<th>MAP-like</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricle</td>
<td>162 (81.8)</td>
<td>15 (7.6)</td>
<td>17 (8.6)</td>
<td>4 (2.0)</td>
<td>198 (100.0)</td>
</tr>
<tr>
<td>Right ventricle</td>
<td>84 (23.9)</td>
<td>118 (33.5)</td>
<td>134 (38.1)</td>
<td>16 (4.5)</td>
<td>352 (100.0)</td>
</tr>
<tr>
<td>Unclassified</td>
<td>137 (43.1)</td>
<td>104 (32.7)</td>
<td>55 (17.3)</td>
<td>22 (6.9)</td>
<td>318 (100.0)</td>
</tr>
<tr>
<td>Total</td>
<td>383 (44.1)</td>
<td>237 (27.3)</td>
<td>206 (23.7)</td>
<td>42 (4.8)</td>
<td>868 (100.0)</td>
</tr>
</tbody>
</table>

MAP, monophasic action potential.
*p<0.001 by Pearson’s x^2 test.
Values are absolute number of electrodes recording each morphology and, in parentheses, percentage of total.
chronal map. Based on these findings, it should be recognized that right bundle branch conduction delay or block may be present in right ventricular hypertrophy, regardless of surface electrocardiographic QRS morphology. Furthermore, acute reduction in ventricular pressures by cardiopulmonary bypass did not significantly alter depolarization patterns in the normal left ventricle or hypertrophied right ventricle.

**TABLE 3.** Comparison of MAP<sub>90</sub> With Activation-Recovery Interval

<table>
<thead>
<tr>
<th>T waveforms</th>
<th>n</th>
<th>MAP&lt;sub&gt;90&lt;/sub&gt; (msec)</th>
<th>A–R (msec)</th>
<th>p*</th>
<th>Correlation (r)</th>
<th>SEE (msec)</th>
<th>Maximal difference (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Wyatt method</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>18</td>
<td>323±36</td>
<td>267±42</td>
<td>&lt;0.001</td>
<td>0.85†</td>
<td>19</td>
<td>96</td>
</tr>
<tr>
<td>Biphasic</td>
<td>19</td>
<td>321±28</td>
<td>305±33</td>
<td>0.022</td>
<td>0.56‡</td>
<td>23</td>
<td>64</td>
</tr>
<tr>
<td>Negative</td>
<td>22</td>
<td>309±43</td>
<td>303±45</td>
<td>NS</td>
<td>0.88†</td>
<td>21</td>
<td>61</td>
</tr>
<tr>
<td>MAP-like</td>
<td>14</td>
<td>332±42</td>
<td>339±47</td>
<td>NS</td>
<td>0.90†</td>
<td>19</td>
<td>35</td>
</tr>
<tr>
<td>All</td>
<td>73</td>
<td>320±38</td>
<td>301±43</td>
<td>&lt;0.001</td>
<td>0.73†</td>
<td>26</td>
<td>. . .</td>
</tr>
<tr>
<td><strong>Peak of T waves as time of local repolarization for positive T waveforms</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>18</td>
<td>323±36</td>
<td>296±38</td>
<td>&lt;0.001</td>
<td>0.88†</td>
<td>17</td>
<td>65</td>
</tr>
<tr>
<td>All</td>
<td>73</td>
<td>320±38</td>
<td>309±43</td>
<td>&lt;0.001</td>
<td>0.81†</td>
<td>25</td>
<td>. . .</td>
</tr>
<tr>
<td><strong>Minimal dV/dt on downslope of T wave as time of local repolarization of positive T waveforms</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>18</td>
<td>323±36</td>
<td>322±41</td>
<td>NS</td>
<td>0.82†</td>
<td>21</td>
<td>47</td>
</tr>
<tr>
<td>All</td>
<td>73</td>
<td>320±38</td>
<td>315±43</td>
<td>NS</td>
<td>0.82†</td>
<td>22</td>
<td>. . .</td>
</tr>
</tbody>
</table>

MAP<sub>90</sub>, monophasic action potential from onset of activation to 90% repolarization; A–R, activation–recovery interval.

*p value for paired t tests between MAP<sub>90</sub> and A–R intervals.

†p<0.001 for correlation.

‡p=0.012 for correlation.
FIGURE 9. Recordings of prolongation of activation-recovery (A–R) interval and monophasic action potential from onset of local activation to 90% repolarization (MAP$_{90}$) after initiation of cardiopulmonary bypass. Unipolar electrograms A, B, and C were recorded before, immediately, and 86 seconds after initiation of cardiopulmonary bypass, respectively. Panels D and E: MAP recorded before and after initiation of the cardiopulmonary bypass, respectively. T wave in panel A was notched; thus, $dV/dt_{\text{max}}$ was taken on the upslope of the second peak. There was a progressive prolongation of A–R intervals and MAP$_{90}$ after initiation of cardiopulmonary bypass. Heart rate did not change significantly after the bypass.

Use of Unipolar Electrograms to Estimate Local Repolarization Times in Right Ventricular Hypertrophy

There is a paucity of information regarding the patterns of repolarization in right ventricular hypertrophy, due in part to the technical difficulties inherent in the sequential recording of the MAP duration at multiple locations. These difficulties include the requirement for stable patterns of activation of each recorded beat and the long time required to map the entire epicardium. Computerized epicardial mapping techniques, which can determine the global epicardial patterns of activation by analyzing a single beat, obviate some of the difficulties involved in studying the patterns of activation. However, an accurate method for determining the instantaneous patterns of global repolarization using this technique has not been established. It is highly desirable to be able to determine instantaneous patterns of repolarization.

| Table 4. Effects of Cardiopulmonary Bypass on Activation–Recovery Intervals Estimated by Wyatt Method From Channels That Recorded Consistent T Wave Morphologies |
|-----------------|-----------------|-----------------|-----------------|
|                 | A–R intervals   | A–R intervals   | A–R intervals   |
|                 | before bypass   | immediately after bypass | 86–329 seconds after bypass |
|                 | (msec)          | (msec)          | (msec)          |
| Positive T waves | 252±30          | 258±23          | 303±30*         |
| Biphasic T waves | 297±38          | 302±30          | 362±27*         |
| Negative T waves | 280±21          | 294±17          | 353±20*         |
| MAP-like T waves† | 773±156        | 770±158         | 797±180‡        |

MAP, monophasic action potential; A–R interval, activation–recovery interval.

*Significantly longer than that before bypass and immediately after bypass.
†No channel recorded consistent MAP-like T waves.
‡No significant differences of cycle lengths between groups.
TABLE 5. Effects of Cardiopulmonary Bypass on Activation–Recovery Intervals Estimated by Revised Method

<table>
<thead>
<tr>
<th></th>
<th>Left ventricle</th>
<th>Right ventricle</th>
<th>n</th>
<th>A–R interval (msec)</th>
<th>n</th>
<th>A–R interval (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before bypass</td>
<td>46</td>
<td>297±27</td>
<td>73</td>
<td>297±31</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Immediately after bypass</td>
<td>46</td>
<td>319±31*</td>
<td>73</td>
<td>323±42*</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>86–329 seconds after bypass</td>
<td>46</td>
<td>357±33*</td>
<td>73</td>
<td>359±29*</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

A–R interval, activation–recovery interval.
*Significant differences (p <0.05) of A–R intervals between data obtained each time after bypass compared with before bypass and between times after bypass.

NS, no significant difference between right and left ventricles.
Data are from patients 1, 2, 6, and 7.

because such a determination may provide vital information regarding the generation of T waves on the surface electrocardiogram. In addition, because nonuniform dispersion of refractoriness is thought to be an important factor in ventricular vulnerability, the ability to determine instantaneous repolarization patterns may help elucidate the basic mechanisms of arrhythmogenesis. However, unlike the unipolar electrograms recorded during depolarization, the unipolar electrograms recorded during repolarization lack sharp intrinsic deflections. Exactly when local repolarization occurs during the T wave is not known. Experimental studies in dogs have demonstrated good correlations and small SEEIs between dV/dtmax and 90% repolarization in transmembrane action potential and between dV/dtmax and recovery of excitability measured by single premature stimuli. However, in neither of these studies did the authors comment on the correlation between the A–R intervals and the action potential duration of different T wave morphologies, nor did the authors report the distribution of T wave morphologies over the entire ventricular epicardium. Recently, a computer simulation study specifically addressed the limitations of using dV/dt to determine the time of local repolarization. It was shown that this method is most accurate under ideal conditions of uniform propagation in a long cable. The correlation may vary significantly, however, under nonideal situations, and the recovery times measured may be greatly affected by conditions during repolarization. Our results confirmed good correlation between the A–R intervals and the MAP90 but also indicated that the correlation differs among different morphologies of T waves. The biphase and positive T wave morphologies significantly underestimated the MAP90 in this group of patients. The results raised a question regarding the validity of using dV/dtmax as the time of local repolarization on unipolar electrograms in humans. This observation, however, is not unprecedented. Millar et al found that among all T wave morphologies, negative T waves gave A–R intervals that were on average closest to corresponding refractory periods. Based on the examples they gave, positive T waves appear to underestimate the refractory periods. Our data

TABLE 6. Effects of Cardiopulmonary Bypass on T Wave Distributions

<table>
<thead>
<tr>
<th></th>
<th>Positive</th>
<th>Biphasic</th>
<th>Negative</th>
<th>MAP-like</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Left ventricle</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before bypass</td>
<td>44 (89.8)</td>
<td>3 (6.1)</td>
<td>1 (2.0)</td>
<td>1 (2.0)</td>
<td>49 (100)</td>
</tr>
<tr>
<td>Immediately on bypass</td>
<td>50 (94.3)</td>
<td>3 (5.7)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>53 (100)</td>
</tr>
<tr>
<td>86–329 seconds after bypass</td>
<td>40 (75.5)</td>
<td>2 (3.8)</td>
<td>8 (15.1)</td>
<td>3 (5.7)</td>
<td>53 (100)</td>
</tr>
<tr>
<td>Total</td>
<td>134 (86.5)</td>
<td>8 (5.2)</td>
<td>9 (5.8)</td>
<td>4 (2.6)</td>
<td>155 (100)</td>
</tr>
<tr>
<td><strong>Right ventricle</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before bypass</td>
<td>13 (15.3)</td>
<td>35 (41.2)</td>
<td>34 (40.0)</td>
<td>3 (3.5)</td>
<td>85 (100)</td>
</tr>
<tr>
<td>Immediately on bypass</td>
<td>27 (29.3)</td>
<td>32 (34.8)</td>
<td>30 (32.6)</td>
<td>3 (3.3)</td>
<td>92 (100)</td>
</tr>
<tr>
<td>86–329 seconds after bypass</td>
<td>27 (30.7)</td>
<td>24 (27.3)</td>
<td>29 (33.0)</td>
<td>8 (9.1)</td>
<td>88 (100)</td>
</tr>
<tr>
<td>Total</td>
<td>67 (25.3)</td>
<td>91 (34.3)</td>
<td>93 (35.1)</td>
<td>14 (5.3)</td>
<td>265 (100)</td>
</tr>
</tbody>
</table>

MAP, monophasic action potential.
*p=0.009 by Pearson’s χ² test.
*p=0.064 by Pearson’s χ² test.
Data are from patients 1, 2, 3, 6, and 7.
Values are absolute number of electrodes recording each morphology and, in parentheses, percentage of total.
showed that this underestimation can be corrected by using the dV/dt\textsubscript{max} on the downslope of the positive T waves as the time of local repolarization, at least in this patient population. However, because of the large SEE\textsubscript{s}, the accuracy of either method in determining the time of repolarization at any specific epicardial site is limited.

**Local T Wave Morphologies and Patterns of Repolarization in Right Ventricular Hypertrophy**

An important finding in this study is that there was a nonuniform distribution of T wave morphologies, with positive T waves clustering over the left ventricular sites and negative and biphasic T waves clustering over the right ventricular sites. These findings are compatible with the results of previous animal studies\textsuperscript{3,11,23,24} and have significant implications for understanding the generation of T waves. According to studies performed with isolated papillary muscle, the morphologies of local T waves were determined by the spatial relation that exists between the wave of excitation and the recording electrode.\textsuperscript{11} The T wave polarity was positive when the recording electrode was near the origin of the activation, negative when it was opposite the origin of activation, and biphasic when the electrode was in the center of the muscle strip. This phenomenon was observed because in isolated papillary muscle, the repolarization sequence usually follows that of the depolarization sequence; thus, the cells near the origin of excitation are the earliest to begin repolarizing, and the cells near the end of excitation are the latest. The distribution of T wave potentials has also been studied extensively in the intact canine heart.\textsuperscript{3,23,24} These studies showed that in normal beats, the epicardial T wave polarity was primarily positive.\textsuperscript{23} However, an uneven distribution of epicardial T wave potentials was observed for ectopic beats.\textsuperscript{24} Transmural recordings showed that throughout the T wave in normal beats, there was a predominant transmural unidirectional gradient, with the inner wall being more negative than the outer wall, which suggests that the sequence of repolarization was from the epicardium to the endocardium. For ectopic beats, however, the ventricular repolarization potential distribution was predominantly influenced by gradients from one side of the heart to the other (i.e., the transventricular gradient),\textsuperscript{24} which is in contrast to the normal distributions that are predominantly influenced by transmural gradients.\textsuperscript{23} Thus, the normal pattern of T wave distribution was no longer observed. Further studies by the same group of investigators,\textsuperscript{3} using computer simulation and mapping of the repolarization potentials in the intact dog heart, showed that the potential distribution during ST-T wave can be predicted from the spatial intracellular potential distributions throughout the ventricles, which in turn are determined by the sequence of excitation. The authors named this model the "SI model" because it involves the spatial analysis of intracellular potentials. The SI

![Figure 10](http://circ.ahajournals.org/)

**FIGURE 10.** Monophasic action potential (MAP) recorded by bipolar and unipolar techniques. Panels A, B, and C are simultaneous electrocardiogram lead I, bipolar MAP and unipolar MAP, respectively. MAP recorded by the bipolar technique showed a rapid upstroke and a lower amplitude. Plateau of phase 2 was almost not present. In contrast, MAP recorded by the unipolar technique showed a slower upstroke with a notch. Phases 2 and 3 of the action potential were more clearly defined. Despite differences in shape and amplitude, the action potential duration is not significantly different.

model of T wave generation has not been tested in patients with right ventricular hypertrophy.

In the present study, we showed that in patients with right ventricular hypertrophy, depolarization of the right ventricle is delayed. In nearly half of the
cases, there were no right ventricular epicardial breakthrough points observed; hence, the excitation originated in the left ventricle, and the right ventricle was activated late. Because the action potential durations estimated by the A–R intervals at left and right ventricles were similar, the repolarization sequence must be the same as the depolarization sequence. According to the predictions of the SI model, the potential of the ST-T waves on the epicardium should be more positive on the left ventricular sites and negative or bipolar on the right ventricular sites. Our results are compatible with this analysis and thus suggest that the SI model can be used to explain the abnormal ST-T wave distribution in patients with right ventricular hypertrophy. Whether the SI model can also be applied to explain the ST-T wave changes in other pathological states, such as left ventricular hypertrophy, electrolyte abnormalities, and ischemia, is unknown.

Mechanoelectrical Feedback and Action Potential Duration in Right Ventricular Hypertrophy

Mechanoelectrical feedback is inferred when changes in mechanical stress or strain cause or precede changes in membrane potential. Various investigators have demonstrated that this feedback mechanism is present in isolated myocardial fibers, intact frog and canine ventricles, and humans during cardiac surgery or balloon valvuloplasty for congenital pulmonary stenosis. Cardiopulmonary bypass, which unloads the ventricles, was found to produce substantial and immediate prolongation of the MAP duration. In our study, we used cardiopulmonary bypass to perturb the action potential duration to test the correlation between the A–R intervals and the MAP. It is clear that cardiopulmonary bypass significantly prolonged the action potential duration estimated by both the A–R intervals and the MAP. Our data are compatible with the hypothesis that mechanoelectrical feedback can markedly alter the action potential duration in humans. However, other factors, such as alteration of the temperature and the chemical composition of the blood during the cardiopulmonary bypass, may also contribute to this phenomenon.

Methods Used to Record MAP

At least three different techniques have been used to record the MAP by different investigators. The unipolar technique records the MAP with one electrode that directly contacts the heart and uses a distant electrode as the reference. The rationale for using a distant reference electrode is to prevent the recording being affected by current generated by the “contracting muscle” nearby. This technique was validated by comparison with intracellular recordings. The second method is the catheter technique, which uses an electrode on the tip of the catheter to register the MAP and a proximal electrode located 3 mm from the tip for reference. The electrical signal is recorded with one electrode in contact with the heart and another electrode within the ventricular cavity or tissue bath. The catheter technique was also validated by comparisons with intracellular recordings. The shape and duration of the action potentials recorded by these two methods closely resembled the simultaneously recorded transmembrane potentials.

The third technique is the bipolar technique. This technique uses a specially engineered electrode array that contains two Ag/AgCl electrodes mounted closely together. One electrode directly contacts the heart, whereas the other electrode contacts the heart through a saline-soaked foam rubber wick or a ring electrode. The latter electrode, which is placed a few millimeters from the former electrode, serves as the reference. The hypothetical benefit of the bipolar recording technique is that by using two electrodes spaced near each other, the distant electrical effects may be cancelled. However, the reference electrode used in this technique is very close to the electrode used to register the MAP and therefore may not be a true indifferent electrode. Cowan et al reported that recording between the ring and a remote aortic electrode frequently revealed ST segment elevation, indicating that the ring overlay injured myocardium. The large ST segment elevation recorded by the ring electrode may thus cancel some of the electrical potentials, thereby altering the shape and diminishing the amplitude of the MAP. However, because the bipolar technique has not been validated by intracellular recordings, it is not known whether the alteration of shape and diminished amplitude of the MAP obtained by this technique also affect its accuracy for estimating the action potential duration.

Therefore, in this study, we chose to use the unipolar technique to record the MAP in part 1 because it is well validated. The reference electrode used in the unipolar technique is placed on the chest and thus cannot record the injury current and alter the shape or diminish the amplitude of the MAP. To compare the unipolar and bipolar recording techniques, we performed part 2 of the study and showed that the MAP values recorded by the unipolar and bipolar techniques were similar. Thus, the poor correlation between the MAP and the A–R interval measured by the Wyatt method and the better correlation by our alternative method are likely to be reproducible regardless of whether bipolar or unipolar techniques of recording MAP are used.

Acknowledgments

The authors wish to thank Dr. Hope Maki and Dr. Steven Schwartz for assisting in data collection during surgery.

References

1. Wyatt RF: Comparison of estimates of activation and recovery times from bipolar and unipolar electrogram to in vivo transmembrane action potential durations. Proceedings of IEEE/


5. Sosoklow M, Lyon TP: The ventricular complex in right ventricular hypertrophy as obtained by unipolar precordial and limb leads. Am Heart J 1968;38:273–294


Key Words: T waves • cardiopulmonary bypass • monophasic action potential • SI model
Epicardial activation and repolarization patterns in patients with right ventricular hypertrophy.

_Circulation._ 1991;83:104-118
doi: 10.1161/01.CIR.83.1.104

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1991 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/83/1/104

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org//subscriptions/