Background—Postpacing precordial T-wave inversion (TWI), known as cardiac memory (CM), mimics ischemic precordial TWI, and there are no established ECG criteria that adequately distinguish between the two. On the basis of CM properties (postpacing sinus rhythm T vector approaching the direction of the paced QRS vector), we hypothesized that CM induced by right ventricular pacing would manifest a TWI pattern different from that of precordial ischemic TWI, thereby discriminating between the two.

Methods and Results—T-wave axis, polarity, and amplitude on a 12-lead ECG during sinus rhythm were compared between CM and ischemic patients. The CM group incorporated 13 patients who were paced in DDD mode with short atrioventricular delay for 1 week after elective pacemaker implantation. The ischemic group consisted of 47 patients with precordial TWI identified among 228 consecutive patients undergoing percutaneous coronary intervention for an acute coronary syndrome. The combination of (1) positive $T_{aVL}$, (2) positive or isoelectric $T_i$, and (3) maximal precordial TWI was 92% sensitive and 100% specific for CM, discriminating it from ischemic precordial TWI.

Conclusions—CM induced by right ventricular pacing results in a distinctive T-vector pattern that allows discrimination from ischemic precordial T-wave inversions regardless of the coronary artery involved. (Circulation. 2005;111:969-974.)

Key Words: electrocardiography • pacing • ischemia
Methods

Groups of Patients
The CM group consisted of 13 patients followed up prospectively after implantation of a permanent dual-chamber pacemaker who had sinus rhythm with 1:1 AV conduction at physiological heart rates at baseline. CM was induced by 1 week of DDD pacing with a short AV delay to ensure ventricular activation from the endocardial pacemaker electrode positioned in the right ventricular apex. At 1 week, a 12-lead ECG was recorded after the pacemaker was reprogrammed in AAI mode. This ECG was used for analysis.

The ischemic TWI (ISC) group of patients was retrospectively identified among the 228 consecutive patients who underwent PCI for a non–ST-elevation myocardial infarction (as identified by symptoms of ischemia and elevated cardiac markers, eg, troponin I, troponin T, or creatine kinase-MB [CK-MB] in the absence of ST elevations on the ECG) at the Beth Israel Deaconess Medical Center from January to November 2003 as noted in the cardiac catheterization laboratory database. Precordial TWI was defined as TWI ≥0.1 mV in 2 or more adjacent precordial leads (V1 to V6) on a 12-lead ECG recorded within 48 hours after admission. If TWI was present on >1 ECG, the earliest one was used for analysis. The ISC group was further divided into 3 subgroups (LAD, LCx, and RCA) according to the infarct-related artery. Patients with atrial fibrillation, left bundle-branch block, presence of a pacemaker, multivessel PCI, planned PCI for stable coronary disease, and frequent ventricular ectopy were excluded from the ISC group.

ECG Analysis
All ECGs were recorded on a Burdick Spacelabs Eclipse Plus ECG (Burdick Spacelabs) at a paper speed of 25 mm/s. The tracings were analyzed manually without magnification. T-wave amplitude was measured by ruler in each lead from T-wave peak/nadir to the baseline determined by T-P segment. In case of biphasic T waves, the most negative deflection was measured, and the T wave was classified as isoelectric (amplitude <0) if both positive and negative components were present with amplitude <0.05 mV (Figure 1). QT was measured manually over 3 consecutive RR intervals in lead II, and the results were averaged. The corrected QT interval (QTc) was calculated according to Bazett’s formula. Frontal-plane QRS and T-vector angles were independently determined. All ECGs were analyzed by a single investigator blinded to the patient group allocation.

Biochemical Data
For LAD ISC patients, the highest level of CK-MB during admission was used for analysis.

Angiographic Data
The culprit coronary artery lesion was determined by a high-volume interventional cardiologist at the time of PCI on the basis of a coronary artery occlusion or stenosis >80% by visual estimation corresponding to the clinical and ECG data. The location of the culprit lesion was determined from angiographic reports and confirmed by visual analysis of digital angiographic images.

Statistical Analysis
Continuous variables are expressed as mean±SEM and compared by ANOVA with Bonferroni correction. Categorical data were compared with χ² test and Fisher’s exact test, as appropriate. These analyses were performed with SPSS 11.5 (SPSS Inc). Angular variables were compared with Watson-Williams F test (Oriana 2.0, KCS Inc). Probability values less than 0.05 were considered statistically significant.

Approval for the study was obtained in accordance with the requirements of the Institutional Review Board of the Beth Israel Deaconess Medical Center. All patients undergoing pacemaker implantation signed informed consent for the study.

Results

ISC Patient Selection
A total of 228 patients underwent PCI for a non–ST-elevation myocardial infarction. Fifty patients were excluded (9 with atrial fibrillation, 18 with left bundle-branch block, 12 with ventricular paced rhythm, 3 with multivessel PCI, and 1 with frequent ventricular ectopy). Forty-seven (26%) of the remaining 178 patients had preordial TWI and made up the ISC group.

Precordial TWI was present significantly more often in patients with LAD lesions (47%) than in those with LCx (21%) and RCA lesions (11%; P<0.05). TWI was observed in 57% cases of proximal LAD disease and 44% of mid-LAD/distal LAD lesions (P<0.05 vs other LAD locations). (See Table 1.)

Baseline ISC and CM group characteristics are presented in Table 2. Age, gender distribution, prevalence of prior MI,

<table>
<thead>
<tr>
<th>Vessel Involved</th>
<th>TWI, n (%)</th>
<th>No TWI</th>
<th>Excluded</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD</td>
<td>28 (47)†</td>
<td>31</td>
<td>20</td>
<td>79</td>
</tr>
<tr>
<td>Proximal</td>
<td>16 (57)</td>
<td>12</td>
<td>7</td>
<td>35</td>
</tr>
<tr>
<td>Mid, diagonal</td>
<td>12 (44)</td>
<td>15</td>
<td>10</td>
<td>37</td>
</tr>
<tr>
<td>Distal</td>
<td>0‡</td>
<td>4</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>LCx</td>
<td>12 (21)†</td>
<td>44†</td>
<td>17</td>
<td>73</td>
</tr>
<tr>
<td>RCA</td>
<td>7 (11)</td>
<td>56</td>
<td>13</td>
<td>76</td>
</tr>
<tr>
<td>Total</td>
<td>47 (26)</td>
<td>131</td>
<td>50</td>
<td>228</td>
</tr>
</tbody>
</table>

Percentages represent the fraction of nonexcluded tracings with TWI.
*P<0.05 vs LCx and RCA groups.
†Includes 5 patients with isolated TWI in I and aVL.
‡P<0.05 vs other LAD locations.

Available 19/47 13/13*

Prior history of MI, n (%) 12 (26%) 3 (23%)

History of CABG, n (%) 8 (17) 2 (15)

Prior ECG

Available 19/47 13/13*

Precordial TWI 4/19 0/13

Right bundle-branch block 1/19 3/13

Q waves 4/19 2/13

*P<0.05.
and CABG did not differ between groups. Nineteen patients in the ISC group (40%) and all patients in the CM group had prior ECGs available. Within that subset of patients, the prevalence of baseline ECG abnormalities (Q waves, right bundle-branch block, TWI) was similar between groups.

TABLE 3. ECG Data

<table>
<thead>
<tr>
<th>Group</th>
<th>LAD (n=28)</th>
<th>LCx (n=12)</th>
<th>RCA (n=7)</th>
<th>CM (n=13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR, min⁻¹</td>
<td>69.4±2.1</td>
<td>74.2±3.1</td>
<td>66.9±3.6</td>
<td>71.7±3.7</td>
</tr>
<tr>
<td>QT, ms</td>
<td>440±10</td>
<td>415±11</td>
<td>438±10</td>
<td>417±10</td>
</tr>
<tr>
<td>QTC, ms</td>
<td>415±14</td>
<td>377±16</td>
<td>418±15</td>
<td>371±11</td>
</tr>
<tr>
<td>No. of precordial leads with TWI</td>
<td>4.0±0.3</td>
<td>3.25±0.5*</td>
<td>2.9±0.3*</td>
<td>4.8±0.3*</td>
</tr>
<tr>
<td>Maximal precordial TWI, mV</td>
<td>-0.45±0.06</td>
<td>-0.21±0.10*</td>
<td>-0.26±0.11*</td>
<td>-0.53±0.06</td>
</tr>
<tr>
<td>QRS frontal axis, degrees</td>
<td>20±7</td>
<td>6±11</td>
<td>6±46</td>
<td>18±12</td>
</tr>
<tr>
<td>T-wave frontal axis, degrees</td>
<td>128±10*</td>
<td>146±15*</td>
<td>-98±30</td>
<td>-70±5</td>
</tr>
</tbody>
</table>

*P<0.05 compared with CM group.

Values are n (%).

TABLE 4. Lead Distribution of TWI in ISC and CM Groups

<table>
<thead>
<tr>
<th>Lead</th>
<th>ISC</th>
<th>LAD (n=28)</th>
<th>LCx (n=12)</th>
<th>RCA (n=7)</th>
<th>CM (n=13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>20 (71)*</td>
<td>11 (91)*</td>
<td>4 (57)*</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>8 (29)*</td>
<td>5 (42)*</td>
<td>6 (86)</td>
<td>13 (100)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>3 (11)*</td>
<td>2 (17)*</td>
<td>4 (57)*</td>
<td>13 (100)</td>
<td></td>
</tr>
<tr>
<td>aVR</td>
<td>10 (36)*</td>
<td>0</td>
<td>1 (14)</td>
<td>1 (8)</td>
<td></td>
</tr>
<tr>
<td>aVL</td>
<td>23 (82)*</td>
<td>11 (92)*</td>
<td>2 (29)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>aVF</td>
<td>6 (21)*</td>
<td>4 (33)*</td>
<td>5 (71)</td>
<td>13 (100)</td>
<td></td>
</tr>
<tr>
<td>(I+aVL)†</td>
<td>0*</td>
<td>0*</td>
<td>3 (43)*</td>
<td>13 (100)</td>
<td></td>
</tr>
<tr>
<td>(I+aVL)† and maximal precordial TWI&gt;TWIL</td>
<td>...</td>
<td>...</td>
<td>0‡</td>
<td>12 (92)</td>
<td></td>
</tr>
</tbody>
</table>

Values are n (%).

*<P<0.05 compared with CM group.

†(I+aVL) indicates positive T wave in lead aVL, positive or isoelectric T wave in lead I.

‡P<0.05 for all ISC patients compared with CM patients.

Shvilkin et al T-Wave Inversion 971

and CABG did not differ between groups. Nineteen patients in the ISC group (40%) and all patients in the CM group had prior ECGs available. Within that subset of patients, the prevalence of baseline ECG abnormalities (Q waves, right bundle-branch block, TWI) was similar between groups (P>0.1). None of the CM patients had symptoms suggestive of ischemia during the study. Within the last 2 years, 5 CM patients had negative stress test with imaging, and 6 underwent cardiac catheterization that demonstrated the absence of obstructive coronary disease in 3 patients, stable single-vessel occlusion with collaterals in 1, and stable revascularized 3-vessel disease in 2. The remaining 2 patients had both a normal ECG and echocardiogram before pacemaker implantation. In 1 patient, the procedure was compli-
The majority of LAD and LCx patients had negative T waves in leads I and aVL. Only 3 LAD/LCx patients had positive T waves in lead I, and 1 patient had a positive T wave in lead aVL, but none had positive T waves in both leads. In vectorcardiographic terms, this translated into a left-to-right frontal-plane direction of the T vector, significantly different from that of CM group (Table 3; Figure 3). Limb-lead TWI pattern in the RCA group was consistent with a T vector directed away from the area of ischemia, with a progressive increase in the frequency of lateral precordial lead involvement from LAD to LCx to RCA culprit vessels (Table 4).

The ISC group selection criteria served 2 purposes. First, the small number of patients in our study (especially those with prior inferior-wall MI) allowed differentiation from CM. Bearing in mind these vector concepts, we devised a simple rule for discriminating CM from ISC regardless of the coronary artery involved.

**CM Versus RCA**

Four of 7 RCA patients conformed to the pattern of LAD/LCx TWI. The remaining 3 RCA patients with positive T wave in lead I and aVL had maximal precordial TWI > TWI<sub>II</sub> in contrast to all but 1 CM patient. Therefore, the combination of (1) positive T<sub>aVL</sub>, (2) positive or isoelectric T<sub>I</sub>, and (3) maximal precordial TWI > TWI<sub>II</sub> was 92% sensitive and 100% specific for CM, discriminating it from ISC regardless of the coronary artery involved.

**Discussion**

We describe an approach to differentiate preischemic ischemic TWI from postpacing TWI on the basis of the unique characteristics of the postpacing T-wave vector. The latter is characterized by the left-superior frontal direction, with the magnitude of preischemic TWI exceeding that in the inferior leads. We demonstrated that in most cases (LAD, LCx, and the majority of RCA culprit lesions), ischemic preischemic TWI is characterized by a rightward frontal-plane T-wave axis. In a small number of patients with inferolateral ischemia with a left T-wave axis, the inferior/preischemic TWI ratio still allowed differentiation from CM. Bearing in mind these vector concepts, we devised a simple rule for discriminating CM and ISC preischemic TWI using standard 12-lead ECG criteria.

The small number of patients in our study (especially those with preischemic TWI due to RCA lesions) and the retrospective nature of the analysis make it necessary to confirm these findings in a larger validation cohort. Nevertheless, our data provide the proof of concept for using T vector direction in differential diagnosis of preischemic TWI.

The ISC group selection criteria served 2 purposes. First, biochemical evidence of myocardial necrosis supported the ischemic nature of the TWI in this group. Second, the presence

**Extent of Myocardial Necrosis**

CK-MB levels were available in 27 of 28 LAD patients. Ten patients had CK-MB within the normal range (<10 ng/mL), and 17 (61%) had CK-MB elevation ranging from 13 to 366 ng/mL (median 46 ng/mL, upper limit of normal 10 ng/mL). The magnitude of preischemic TWI in patients with normal CK-MB was significantly greater than in those with elevated enzyme levels (P<0.01).
of a critical stenosis amenable to PCI minimized the potential ambiguity in culprit lesion identification in cases without total coronary occlusion. At the same time, this could create a bias toward larger ischemic area in the ISC group in the present study, and it is plausible that more localized ischemia could produce different TWI patterns.

We found, however, no precordial TWI among 4 patients with distal LAD lesions and presumably smaller areas of ischemia (Table 1). LCx lesions were less likely to produce precordial TWI, and the magnitude and number of leads affected were significantly less than seen with LAD lesions. Nevertheless, LCx ischemia produced a rightward T-wave axis shift similar to that seen with LAD involvement. In fact, among LCx lesions screened for precordial TWI, 5 patients had isolated TWI in I and aVL, demonstrating rightward T-axis direction even without precordial involvement. Therefore, it appears that anterolateral ischemia severe enough to produce precordial TWI results in a rightward frontal-plane T axis.

There were very few patients with RCA culprit lesions with precordial TWI in the present study. Although the ratio of inferior/precordial TWI allowed differentiation of inferolateral ischemic TWI and CM, a larger prospective patient sample is required to confirm this observation.

Degree of ischemia is another factor potentially affecting the expression of TWI. All ISC patients in the present study had positive biochemical markers of myocardial injury. Conceivably, a milder degree of ischemia could produce smaller T-wave changes. To address this issue, we compared patients with LAD culprit lesions with elevated versus normal CK-MB levels and found the latter to have significantly greater precordial TWI than those with elevated CK-MB. This finding is in accord with observations in patients with myocardial infarction who demonstrate an inverse relation to TWI magnitude, enzymatic estimate of myocardial infarction size, and functional recovery, which suggests that TWI indicates the presence of viable stunned myocardium. Therefore, it appears unlikely that milder ischemia would alter the T-wave pattern in ISC.

All CM patients in the present study had endocardial right ventricular apex lead implants. Other positions within the right ventricle can produce different pacing QRS vectors that result in different directions of memory T waves. Right ventricular electrodes can be implanted in the mid septum or right ventricular outflow tract. The QRS complex produced by pacing from these alternative sites can have variable morphology in leads I and aVL, resulting in a left axis with varying degrees of superior (closer to the right ventricular apex) or inferior (right ventricular outflow tract) angulation. Therefore, postpacing TWI will always assume a left axis, no matter where in the right ventricle the pacing lead is situated. With right ventricular outflow tract pacing, however, one would not see deep TWIs in inferior leads, which are considered typical for postpacing TWI. Additional studies are needed to characterize the TWI pattern after pacing from these alternative sites.

As demonstrated previously in animal studies, the early stages of CM development can be accompanied by T-vector rotation in the frontal plane before the T wave assumes the direction of the paced QRS complex. Therefore, shorter (or intermittent) pacing may result in an “intermediate” T-wave axis. Molecular mechanisms of CM include changes in ion channels such as $I_{Na}$, $I_{K}$, L-type Ca channel, and the angiotensin II system, which result in a change of the transmural repolarization gradient. Drugs that affect these systems, such as ACE inhibitors, calcium channel blockers, and quinidine, influence the development of CM and T-vector shape. It is unclear whether these drugs affect the clinical utility of T-wave patterns in distinguishing ischemic versus nonischemic TWIs.

Structural heart abnormalities and their ECG manifestations can alter the expression of CM. In the present study, patients with secondary TWI, such as preexisting left bundle-branch block or left ventricular hypertrophy with repolarization abnormalities, were excluded. Our preliminary observations suggest that CM does not change the abnormal T vector associated with these conditions. CM development might be altered in patients with postinfarction scar. Most molecular and cellular changes responsible for CM development are believed to occur in the proximity of the pacing electrode, and therefore a prior inferior-wall myocardial infarction could diminish CM development. Indeed, the only 2 CM patients in the present series with isoelectric rather than positive T waves in lead I had prior inferior-wall infarction. Another example of a structural confounder in the present series was a pericardial effusion blunting the postpacing precordial TWI.

At present, we have no data to predict the effect of the combination of ischemia and pacing on T-wave characteristics; therefore, extreme caution should be exercised in interpreting postpacing T-wave changes in patients with symptoms of ischemia. Three CM patients in the present series with known coronary artery disease had angiographically documented stable disease and were asymptomatic; therefore, we felt confident that their T-wave changes were attributed to CM rather than ischemia.

Conclusions

By applying vectorcardiographic principles to interpretation of a standard 12-lead ECG, we demonstrated that right ventricular apex pacing results in TWI with unique characteristics distinct from those induced by myocardial ischemia. A simple algorithm can be used to differentiate these 2 ECG patterns. The use of such vectorcardiographic information can significantly improve the differential diagnosis of precordial TWIs.

Acknowledgment

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T-Vector Direction Differentiates Postpacing From Ischemic T-Wave Inversion in Precordial Leads
Alexei Shvilkin, Kalon K.L. Ho, Michael R. Rosen and Mark E. Josephson

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