Occurrence of Transient U-Wave Inversion During Vasospastic Anginal Attack Is Not Related to the Direction of Concurrent ST-Segment Shift*

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**Study objectives:** We sought to assess the incidence of transient U-wave inversion during vasospasm of the left anterior descending coronary artery (LAD) with ST-segment depression as opposed to that with ST-segment elevation.

**Design:** Retrospective study.

**Setting:** Cardiology division of acute-care hospitals.

**Patients:** We studied 49 patients with vasospastic angina whose vasospasm was induced in the LAD, not in the left circumflex coronary artery, by intracoronary injection of acetylcholine.

**Measurements and results:** The ECG traces obtained during acetylcholine-induced vasospasm of the LAD were examined. Based on the direction of ST-segment shift, the patients were categorized into two groups: the ST-segment elevation group (n = 27) and the depression group (n = 22). There were no differences in age, gender, or cardiovascular risk factors between the two groups. The distribution of the spastic site in the LAD was also similar. A total reduction in luminal diameter during a provoked attack was more often observed in the ST-segment elevation group than in the ST-segment depression group (37% vs 9%, p = 0.02). Collateral circulation to the LAD was found in only one patient in each group. There were no differences between the two groups in heart rate, systolic BP, and double product of heart rate and systolic BP during the attack. The incidence of acetylcholine-induced anginal attack with U-wave inversion in the ST-segment depression group was nearly as high as that in the ST-segment elevation group (77% vs 78%, p > 0.99).

**Conclusions:** The development of transient U-wave inversion during vasospasm of the LAD induced by intracoronary injection of acetylcholine does not depend on the magnitude of myocardial ischemia as judged by the direction of ST-segment shift.

**Key words:** acetylcholine; left anterior descending coronary artery; ST-segment shift; U-wave inversion; vasospastic angina

**Abbreviations:** LAD = left anterior descending coronary artery; mV = millivolt; TIMI = Thrombolysis in Myocardial Infarction

Exercise-induced U-wave inversion in patients with significant narrowing of the left anterior descending coronary artery (LAD) indicates a severe degree of myocardial ischemia in the territory perfused by the LAD.1 This transient U-wave inversion is not very sensitive for the detection of LAD disease and only develops during treadmill exercise testing in 20 to 30% of patients with LAD disease.1,2 During exercise, ST-segment depression, rather than elevation, is found. However, a new negative U wave often appears during spasm of the LAD in patients with variant angina,3–5 which is clinically characterized by recurrent episodes of chest pain caused by coronary vasospasm associated with reversible ST-segment elevation. Even during exercise, myocardial ischemia followed by ST-segment elevation often produces transient U-wave inversion.1 The severity of myocardial ischemia with ST-segment elevation is generally worse than that with ST-segment depression.6,7 Thus, it is expected that the incidence of new
negative U waves during exercise and during a variant anginal attack depends on the severity of myocardial ischemia as judged by the direction of ST-segment shift.

Patients with vasospastic angina in whom ST-segment elevation during the attack has not been confirmed are labeled as patients with nonvariant angina. These patients have ST-segment depression during an episode of coronary vasospasm. To date, there are no estimates of the incidence of transient U-wave inversion during a vasospastic anginal attack associated with ST-segment depression. Accordingly, the aim of this study was to assess the incidence of transient U-wave inversion during vasospasm of the LAD with ST-segment depression as opposed to that with ST-segment elevation.

MATERIALS AND METHODS

Patient Population

A total of 82 consecutive patients with vasospastic angina who underwent coronary angiography, including provocative testing for coronary vasospasm with acetylcholine, at our hospitals between April 1998 and March 2001 were screened for enrollment in this study. During this period, nine patients with vasospastic angina were not considered for enrollment. Five patients had high disease activity and did not undergo the acetylcholine tests during coronary angiography because antianginal agents were not withdrawn because of frequent anginal attacks. The other four patients, who had spontaneous anginal attacks at the time of coronary angiography performed after discontinuation of antianginal agents, ultimately did not undergo the acetylcholine tests. Exclusion criteria included the presence of spasms in the LAD induced by intracoronary injection of acetylcholine, and ECGs showing sinus rhythm and no conduction disturbance that could interfere with interpretation of ST-segment deviation. Exclusion criteria included > 50% stenosis of the luminal diameter in the major epicardial coronary arteries, prior myocardial infarction, left ventricular ejection fraction at rest < 50%, significant other heart disease, and treatment with digitalis or antiarrhythmic agents. Patients with inducible coronary vasospasm in both the LAD and left circumflex coronary arteries were not included in this study. Eligible patients provided written informed consent.

Baseline characteristics were collected as described previously. In brief, body mass index, cardiovascular risk factors, and left ventricular mass were assessed. The risk factors used for statistical analysis in this study were smoking habit, hypertension, hypercholesterolemia, and diabetes mellitus. The left ventricular mass was estimated with two-dimensionally targeted M-mode echocardiography.

Coronary Angiographic Study

Coronary angiography was performed in the fasting state after premedication with pentazocine (15 mg IM). All antianginal medications, except sublingual nitroglycerin, were withheld for at least 24 h before the test. After local anesthesia, sheaths were inserted into either the femoral or brachial artery and vein, and a bolus of heparin (3,000 IU) was administered. Selective control coronary angiograms were obtained in one to two projections for the right coronary artery and in two to four projections for the left coronary artery. If neither atherosclerotic disease with > 50% reduction of luminal diameter or spontaneous vasospasm in the large epicardial coronary arteries was observed on baseline angiography, provocative testing for coronary vasospasm using acetylcholine was performed in a manner similar to a protocol described elsewhere. First, to prevent bradycardia from developing during intracoronary injection of acetylcholine, a bipolar pacing catheter was inserted into the right ventricle and connected to a temporary pacemaker set at a rate of 40 beats/min. Acetylcholine was administered in gradually increasing doses into the left coronary artery (20, 50, and 100 µg) and subsequently into the right coronary artery (20 µg and 50 µg). Each dose was given over 15 s, and doses were administered at approximately 3-min intervals. Coronary arteriograms were obtained either 1 min after each injection of acetylcholine or when chest pain or ECG change suggestive of myocardial ischemia occurred. The injection of acetylcholine was discontinued when coronary vasospasm was induced or when a maximal dose of acetylcholine was administered. Coronary vasospasm was determined to have occurred when severe vasoconstriction with grade 0 to 2 flow in the epicardial coronary arteries, according to the classification of the Thrombolysis in Myocardial Infarction (TIMI) trial, was revealed angiographically after intracoronary injection of acetylcholine, and was accompanied by chest pain typical of the patient’s usual complaint or ischemic changes on the ECG. If coronary vasospasm developed, repetitive shots of contrast media were given at 15- to 20-s intervals until the vasospasm disappeared. When unbearable chest pain (70 to 80% of the maximum that patients had experienced), severe hypotension (a systemic systolic BP drop of approximately 30 mm Hg), ventricular arrhythmia requiring therapy, or prolonged angina (≥ 3 min) occurred during provoked vasospastic anginal attack, isosorbide dinitrate was injected into the affected vessel immediately to resolve the vasospasm, and injections were repeated until the vasospasm was completely reversed. If isosorbide dinitrate was administered into the left coronary artery, injection of acetylcholine into the right coronary artery was initiated 10 min after the final dose of isosorbide dinitrate. If isosorbide dinitrate was not required, acetylcholine was injected into the right coronary artery immediately after the vasospasm of the left coronary artery resolved spontaneously. Ultimately, coronary arteriograms were obtained again after the acetylcholine tests were finished, and 2 to 3 mg of isosorbide dinitrate was injected into each coronary artery. The systemic BP measured through the catheters using the fluid-filled method, and a standard 12-lead ECG were continuously monitored and recorded on a multichannel recorder.

The maximal reduction in the diameter of the LAD was determined by quantitative coronary analysis with coronary angiograms obtained after the injection of isosorbide dinitrate. The angiographic catheter was used for calibration. The presence of collateral circulation was also assessed both in the control state and during the acetylcholine test. During intracoronary injection of acetylcholine, however, angiographic examination of the noninjected coronary artery was not performed. The proximal and distal LAD were defined as the LAD proximal to and including the origin of the first major septal perforator branch and that immediately distal to the origin of the first major septal perforator branch, respectively, according to the criterion of the American Heart Association committee report.12

Estimation of ECG Changes

The degree of ST-segment depression was measured 0.08 s after the J-point with the PQ-segment as the isoelectric line. When an ECG obtained before the acetylcholine tests was
normal, a horizontal or downsloping ST-segment depression of ≥ 0.05 millivolts (mV) was considered significant. When the trace recorded before the acetylcholine tests showed ST-segment depression, a further increase of ≥ 0.05 mV in ST-segment depression was considered significant. The degree of ST-segment elevation was determined at the J-point. Positive ST-segment elevation was defined as an additional increase of ≥ 0.05 mV in at least two contiguous leads, compared with the baseline trace. U-wave polarity and amplitude were determined before and during the acetylcholine test, with the PQ-segment as the isoelectric line. If a resting ECG showed a positive U wave, transient U-wave inversion was defined as present when there was a discrete negative deflection of ≥ 0.05 mV within the TP-segment. If a resting ECG showed a negative U wave, transient U-wave inversion was considered to be present when there was an increase in negativity of the wave of ≥ 0.05 mV. All ECGs from each patient were interpreted by two independent investigators who were blinded to the study. When there was a disagreement in the interpretation of the ECG findings, a third observer evaluated the tracings in question and the judgment of the majority prevailed.

Patients were classified into two groups based on the direction of ST-segment shift, either ST-segment elevation or depression, during vasospasm of the LAD induced by intracoronary injection of ST-segment shift, either ST-segment elevation or depression, in which the latter was due to reciprocal change of the former, were classified in the ST-segment elevation group.

**Statistical Analysis**

Data are expressed as the mean ± SD or as frequencies unless otherwise specified. All continuous variables were compared using unpaired Student t tests, whereas categorical variables were compared using χ² tests. For expected cell sizes with less than five observations, Fisher exact probability tests were used. Statistical significance was defined as p < 0.05.

**Results**

**Baseline Characteristics**

Fifty-five patients were enrolled in this study. However, four patients and two patients who had no significant ST-segment shift and had transient atrial fibrillation, respectively, during the LAD spasm were excluded from the study, although five of the six patients had transient U-wave inversion. Thus, 49 patients formed the study group. Of these 49 patients, 27 patients (ST-segment elevation group) had ST-segment elevation during LAD spasm (19 men and 8 women; mean age, 62 ± 9 years; age range, 44 to 75 years), and the remaining 22 patients (ST-segment depression group) had ST-segment depression during the attack (13 men and 9 women; mean age, 60 ± 9 years; age range, 46 to 75 years). Of the 27 patients in the ST-segment elevation group, 24 patients had chest pains typical of vasospastic angina pectoris, and 1 patient had atypical chest pains. The remaining two patients did not have chest pain. In the ST-segment depression group, 20 patients had chest pains typical of vasospastic angina, 1 patient had atypical angina, and the remaining patients had no angina. Chest pain was considered to be typical of vasospastic angina when it had characteristics of angina pectoris in its quality, location, and duration, and mainly developed from midnight to early morning. In eight patients in the ST-segment elevation group and five patients in the ST-segment depression group, ECGs that showed significant ST-segment deviation were obtained during spontaneous anginal attacks. For patients without angina in both groups, the indication for coronary angiography was a positive exercise stress test result. That is, during multistage submaximal treadmill exercise testing of asymptomatic individuals, patients whose resting ECG showed abnormalities in the ST-segment or T wave had ST-segment depression of ≥ 0.1 mV below the baseline, and patients whose resting ECG was normal had horizontal or downsloping ST-segment depression of ≥ 0.1 mV, measured 0.08 s after the J-point using the PQ-segment as the isoelectric line. No patients had ST-segment elevation during exercise stress testing. As shown in Table 1, age and gender were similar. There were no differences in body mass index, left

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>ST-Segment Elevation Group (n = 27)</th>
<th>ST-Segment Depression Group (n = 22)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>62 ± 9</td>
<td>60 ± 9</td>
<td>0.48</td>
</tr>
<tr>
<td>Male gender</td>
<td>19 (70)</td>
<td>13 (59)</td>
<td>0.41</td>
</tr>
<tr>
<td>Body mass index</td>
<td>23.6 ± 3.0</td>
<td>23.2 ± 2.8</td>
<td>0.63</td>
</tr>
<tr>
<td>Hypertension</td>
<td>9 (33)</td>
<td>6 (27)</td>
<td>0.65</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>6 (22)</td>
<td>7 (32)</td>
<td>0.45</td>
</tr>
<tr>
<td>Current smoking</td>
<td>16 (59)</td>
<td>12 (55)</td>
<td>0.74</td>
</tr>
<tr>
<td>Diabetes</td>
<td>7 (26)</td>
<td>3 (14)</td>
<td>0.48</td>
</tr>
<tr>
<td>Left ventricular mass index, g/m²</td>
<td>98.0 ± 18.5</td>
<td>90.4 ± 15.5</td>
<td>0.22</td>
</tr>
</tbody>
</table>

*Values are expressed as mean ± SD or No. (%) of patients.

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ventricular mass index, or risk factors for coronary artery disease between the two groups.

**Angiographic Characteristics and U-Wave Inversion During LAD Spasm**

As shown in Table 2, the dose of acetylcholine that induced LAD spasm was similar between the two groups. In 12 patients (44%) in the ST-segment elevation group and 8 patients (36%) in the ST-segment depression group, the spasm occurred in the proximal LAD. This difference was not significant. The incidence of TIMI grade 0/1 occlusion during vasospastic anginal attacks was higher in the ST-segment elevation group than in the ST-segment depression group (*p* = 0.02). There were no differences between the two groups in heart rate, systemic systolic BP, and double product of heart rate and systolic BP during attacks induced by intracoronary injection of acetylcholine. The incidence of acetylcholine-induced anginal attacks with U-wave inversion in the ST-segment depression group (77%; 17 of 22 attacks) was nearly as high as that in the ST-segment elevation group (78%; 21 of 27 attacks; *p* > 0.99).

Collateral circulation to the LAD was only found in one patient in each group on baseline angiography. No patients had any collateral vessels from a proximal site to a distal site in the LAD or from the left circumflex coronary artery to the LAD during the acetylcholine test. No serious complications after intracoronary injection of acetylcholine, such as myocardial infarction or ventricular fibrillation, were noted. However, injection of isosorbide dinitrate to resolve the provoked spasm because of severe chest pain, a marked drop in systemic systolic BP, nonsustained ventricular tachycardia, or prolonged angina were needed more often in the ST-segment elevation group than in the ST-segment depression group (*p* = 0.03). The remaining vasospastic anginal attacks spontaneously subsided within a few minutes without the administration of nitrates. The maximal luminal narrowing in the LAD measured after injection of isosorbide dinitrate was similar. In 15 patients (56%) in the ST-segment elevation group and in 10 patients (45%) in the ST-segment depression group, injection of acetylcholine induced spasm in the right coronary artery, and the difference was not significant. An example of the electrocardiograms obtained during acetylcholine-induced LAD spasm is shown in Figure 1.

**DISCUSSION**

There have been no estimates of the incidence of transient U-wave inversion during vasospastic anginal attacks associated with ST-segment depression. In this study, we have demonstrated that the incidence of transient U-wave inversion during acetylcholine-induced vasospasm of the LAD with ST-segment depression is nearly equal to that with ST-segment elevation.

**Relationship Between Transient U-Wave Inversion During Vasospastic Angina and the Magnitude of Myocardial Ischemia**

A U-wave inversion during exercise testing or vasospastic angina is undoubtedly ischemia-related, although the mechanism by which myocardial ischemia produces the wave remains to be determined. However, angina pectoris with ST-segment elevation

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**Table 2—Comparison of Angiographic Data Between the Groups*  
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<table>
<thead>
<tr>
<th>Characteristics</th>
<th>ST-Segment Elevation Group (n = 27)</th>
<th>ST-Segment Depression Group (n = 22)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose of acetylcholine that induced the LAD spasm, μg</td>
<td>66 ± 34</td>
<td>73 ± 32</td>
<td>0.43</td>
</tr>
<tr>
<td>Spastic site</td>
<td></td>
<td></td>
<td>0.57</td>
</tr>
<tr>
<td>Proximal LAD</td>
<td>12 (44)</td>
<td>8 (36)</td>
<td></td>
</tr>
<tr>
<td>Distal LAD</td>
<td>15 (56)</td>
<td>14 (64)</td>
<td></td>
</tr>
<tr>
<td>Extent of luminal reduction during the LAD spasm</td>
<td></td>
<td></td>
<td>0.02</td>
</tr>
<tr>
<td>Total occlusive spasm</td>
<td>10 (37)</td>
<td>2 (9)</td>
<td></td>
</tr>
<tr>
<td>Subtotal occlusive spasm</td>
<td>17 (63)</td>
<td>20 (91)</td>
<td></td>
</tr>
<tr>
<td>Heart rate during the LAD spasm, beats/min</td>
<td>67 ± 11</td>
<td>68 ± 14</td>
<td>0.94</td>
</tr>
<tr>
<td>Systemic BP during the LAD spasm, mm Hg</td>
<td>122 ± 19</td>
<td>132 ± 21</td>
<td>0.36</td>
</tr>
<tr>
<td>Double product during the LAD spasm</td>
<td>8,200 ± 2,700</td>
<td>9,000 ± 3,500</td>
<td>0.27</td>
</tr>
<tr>
<td>New negative U waves</td>
<td>21 (78)</td>
<td>17 (77)</td>
<td>&gt; 0.99</td>
</tr>
<tr>
<td>Collateral circulation to the LAD</td>
<td>1 (4)</td>
<td>1 (5)</td>
<td>&gt; 0.99</td>
</tr>
<tr>
<td>Need for injection of nitrates to resolve the attack</td>
<td>17 (63)</td>
<td>7 (32)</td>
<td>0.03</td>
</tr>
<tr>
<td>Maximal luminal narrowing in the LAD after nitrates injection, %</td>
<td>7 ± 9</td>
<td>8 ± 10</td>
<td>0.87</td>
</tr>
<tr>
<td>Vasospasm induced in the right coronary artery</td>
<td>15 (56)</td>
<td>10 (45)</td>
<td>0.48</td>
</tr>
</tbody>
</table>

*Values are expressed as mean ± SD or No. (%) of patients.
usually represents transmural ischemia and is more severe than that with ST-segment depression, which represents subendocardial ischemia.6,7 Thus, it is expected that the development of a new negative U wave is related to the magnitude of myocardial ischemia, as reported by Jain et al.16 In fact, during exercise, myocardial ischemia with ST-segment elevation more often produces transient U-wave inversion, compared with that with ST-segment depression.1 We also expected that new negative U waves would occur more frequently during vasospastic angina with ST-segment elevation than with ST-segment depression. However, this study demonstrated that the incidence of anginal attack associated with U-wave inversion in the ST-segment depression group was nearly as high as that in the ST-segment elevation group.

During vasospastic angina or coronary angioplasty, U-wave inversion commonly precedes the occurrence of an ST-segment shift and lasts until after the ST-segment shift subsides, as shown in Figure 1.3,5,14 Interestingly, the maximal degree of U-wave negativity is not necessarily identical to the peak of myocardial ischemia as reflected by the degree of ST-segment elevation. Accordingly, the mechanism responsible for the genesis of U-wave inversion must be different from that of ST-segment shift. During vasospastic angina, moreover, attacks associated with U-wave inversion, but not ST-segment deviation, are not uncommon.5 Based on their experience with one patient in whom only U-wave inversion was present when coronary angiograms revealed LAD spasm without delayed distal filling, while both U-wave inversion and ST-segment depression were present when coronary angiograms showed further spastic narrowing of the LAD and delayed distal filling, Yamakado et al.17 speculated that myocardial ischemia associated with ST-segment depression is more severe than that associated only with U-wave inversion. Our observations in this study seem to support their speculation. We suggest that during vasospastic anginal attacks, the threshold of myocardial ischemia to produce transient U-wave inversion might be lower than that required to produce ST-segment deviation. However, ≥20% of all vasospastic anginal attacks of the LAD in both the ST-segment depression and ST-segment elevation groups did not have transient U-wave inversion. This false-negative rate may represent the relative insensitivity of the body surface ECG, in comparison with an electrogram with the recording leads proximate to the epicardial surface of the ischemic myocardium,18 such as intracoronary electrogram, at detecting myocardial ischemia.16 Also, our failure to observe a transient U-wave inversion may be related to its very small deflection. Furthermore, we cannot exclude the possibility that injection of isosorbide dinitrate needed to resolve the provoked spasm might have prevented the myocardial ischemia from becoming worse, resulting in underestimating the occurrence of new negative U waves.

Experimentally, U-wave inversion develops only when transmural ischemia is present.18 Thus, this study suggests that transmural ischemia caused by vasospastic angina pectoris is followed by ST-segment depression as well as ST-segment elevation. The persistence of ST-segment depression could result from a continuing gradient of ischemia, in which the subendocardial component is more severe than the epicardial one. Transmural ischemia in

![Figure 1](http://journal.publications.chestnet.org/pdftohtml.ashx?url=/data/journals/chest/21981/ on 06/21/2017)
response to sufficient epicardial coronary vasoconstriction in the ST-segment depression group might be as great as that in the ST-segment elevation group.

**Difference in the Appearance of U-Wave Inversion Between Exercise-Induced ST-Segment Depression and Vasospasm-Induced ST-Segment Depression**

During exercise testing, when ST-segment depression is generally found, transient U-wave inversion develops in only 20 to 30% of patients with significant atherosclerotic stenosis in the LAD,1,2,19 Even among patients with an exercise-induced ST-segment shift, the incidence of a new negative U wave only increases to 40%.1 In this study, however, the incidence of transient U-wave inversion during vasospasm of the LAD with ST-segment depression was 77%.

There are several reasons why exercise-induced ischemia with ST-segment depression produces a new negative U wave less frequently than vasospasm-induced ischemia with ST-segment depression. First, artifacts caused by muscle noise and baseline wandering are apt to be produced during exercise. A U-wave inversion, which is a tiny undulation, might easily fail to be detected. Second, during exercise testing, the heart rate increases and usually exceeds 100 beats/min during peak exercise and in the recovery period when myocardial ischemia develops. Shortening of the TP-segment secondary to a heart rate > 100 beats/min can blend with the U wave.1,20,21 Under such conditions, it becomes difficult to identify a U wave. However, the heart rate rarely exceeds 100 beats/min during acetylcholine-induced vasospastic anginal attacks. Thus, the detection of a new negative U wave might, in part, depend on the heart rate at which myocardial ischemia occurs. Third, ECG traces were continuously recorded in this study. In contrast, during exercise testing, traces are usually obtained at 1-min intervals.1,2 In some cases in this study, transient U-wave inversion disappeared in < 1 min as shown in Figure 1. If an ECG trace is continuously obtained during exercise testing, the incidence of new negative U waves might be higher than that reported. Fourth, in exercise testing studies, patients in whom the mean reduction in luminal diameter of the culprit lesion was approximately 90% were selected.1,2,22 In our study, only patients with vasospasm causing total or subtotal occlusion were selected. In patients with atherosclerotic coronary artery disease, not all exercises produce an ECG ST-segment shift reflecting physiologically significant coronary arterial lesions.23 Moreover, even angina with exercise-induced ST-segment depression would be associated with subendocardial, rather than transmural, ischemia, while vasospasm-induced ST-segment depression represents transmural ischemia as described elsewhere.

**Study Limitations**

This study has several limitations. First, the criteria for the magnitude of myocardial ischemia were not clearly defined in this study. The degree and direction of ST-segment shift are not necessarily precise measures of the magnitude of myocardial ischemia. Second, ECGs obtained during coronary vasospasm induced by intracoronary injection of acetylcholine were assessed in this study. Inducible vasospasm does not equal a spontaneous attack. Third, we did not include patients with inducible severe vasoconstriction of TIMI grade 3 flow leading to myocardial ischemia during the acetylcholine test. Myocardial ischemia induced by vasospasm of TIMI grade 3 flow produces ST-segment depression exclusively, and not elevation,7 if there is no coexistent microvascular spasm.24 The magnitude of myocardial ischemia secondary to vasospasm of TIMI grade 3 flow seems to be less severe than that of TIMI grade 0 to 2 flow.17 Thus, if patients with LAD spasm of TIMI grade 3 flow associated with myocardial ischemia were included in this study, different results might be seen. In addition, in this study, we did not assess the ECG taken during spasm of the right or left circumflex coronary artery. Myocardial ischemia in regions perfused by these arteries could produce transient negative U waves.3,5,16 Another limitation is in the acetylcholine test itself.25,26 The specificity and sensitivity of the test for detecting variant angina pectoris are 99% and 90%, respectively.27 Thus, some patients without vasospastic angina could be included in this study. For example, in patients with no or atypical chest pain, positive acetylcholine provocative test results might be considered as false-positive, although we think that most of these patients could have a silent ischemic episode of vasospastic angina, rather than have a false-positive acetylcholine response.28–30 Regarding provocative testing for coronary vasospasm, there are no perfect tests. Even the ergonovine maleate test, which is widely used to provoke coronary vasospasm, is neither 100% sensitive nor 100% specific.31,32

**Conclusions**

The incidence of transient U-wave inversion during acetylcholine-induced vasospasm of the LAD with ST-segment depression is nearly as high as that with ST-segment elevation. Although we did not include patients with vasospastic angina caused by inducible severe vasoconstriction of TIMI grade 3 flow, the development of transient U-wave inversion...
during LAD spasm induced by intracoronary injection of acetylcholine does not appear to be related to the magnitude of myocardial ischemia, as judged by the direction of ST-segment shift. This suggests that transient U-wave inversion could occur in the early phase of myocardial ischemia caused by coronary vasospasm, and that the threshold of myocardial ischemia necessary to produce transient U-wave inversion might be lower than that required to produce ST-segment deviation.

REFERENCES


2 Kodama K, Hamada M, Hiwada K. Transient leftward QRS axis shift during treadmill exercise testing or percutaneous transluminal coronary angioplasty is a highly specific marker of proximal left anterior descending coronary artery disease. Am J Cardiol 1997; 79:1530–1534


19 Chikamori T, Takata J, Furuno T, et al. Usefulness of U-wave analysis in detecting significant narrowing limited to a single coronary artery. Am J Cardiol 1995; 75:508–511


