Differentiation Between Patients With Takotsubo Cardiomyopathy and Those With Anterior Acute Myocardial Infarction

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Background  There has not been a comparison of the electrocardiographic (ECG) finding of ST-segment elevation in the precordial leads in patients with takotsubo cardiomyopathy (TC) and those with anterior acute myocardial infarction (AMI), with regard to the location of the culprit lesion.

Methods and Results  The present study evaluated 18 patients with TC, and 85 with anterior AMI who were divided into 3 groups: group A had the culprit lesion proximal to both the first septal branch (S1) and the first diagonal branch (D1), group B had the culprit lesion proximal to either S1 or D1, and group C had the culprit lesion distal to both S1 and D1. In patients with TC, reciprocal ST-segment depression in the inferior leads was observed less frequently than in patients in groups A (p<0.0001) and B (p=0.0002), and abnormal Q waves and ST-segment elevation in the inferior leads were observed more frequently than in group A (p=0.0007, p=0.0057, respectively). The ECG findings in TC did not differ from those in group C.

Conclusion  Electrocadiographic findings may differentiate TC from AMI with a proximal lesion of left anterior descending coronary artery, but not those with distal lesions. (Circ J 2005; 69: 89–94)

Key Words: Anterior myocardial infarction; Electrocardiogram; Takotsubo cardiomyopathy; Transient left ventricular apical ballooning

The cardiac syndrome known as ‘takotsubo cardiomyopathy’ (TC) or ‘transient left ventricular apical ballooning’ is characterized by (1) acute onset and reversible left ventricular (LV) apical wall motion abnormalities (ballooning) with chest symptoms, (2) ST-segment elevation and T-wave inversion on the electrocardiogram (ECG), (3) minimal myocardial enzymatic release, and (4) no significant stenosis on coronary angiography (CAG).1–7 Because these characteristics mimic acute myocardial infarction (AMI), it is difficult to differentiate TC from AMI, especially in the acute phase, until coronary artery stenosis and occlusion are ruled out. Consequently, CAG is frequently needed to select the appropriate emergency therapeutic strategy.

ST-segment elevation in the precordial leads is often found in patients with TC, which may then be diagnosed as AMI with a lesion of the left anterior descending (LAD) coronary artery. ECG findings that might distinguish TC from anterior AMI have been reported,3,8 but the ECG findings in anterior AMI may be affected by the site of the culprit lesion5–15 and there have not been any comparative studies of TC and anterior AMI with regard to the site of the culprit lesion and thus we made that the aim of our study.

Methods

Patients and Clinical Evaluations  Consecutive patients who underwent CAG from January 1998 to April 2003 because of ST-segment elevation in the precordial leads were studied retrospectively. Takotsubo cardiomyopathy was defined as follows: (1) ST-segment elevation >0.2 mV in at least 2 adjacent precordial leads on ECG; (2) reversible balloon-like LV wall motion abnormality; (3) normal coronary arteries confirmed by CAG (luminal narrowing <50% in all 3 coronary arteries); (4) no history of myocardial infarction (MI) or known cardiomyopathies; and, (5) no complications of subarachnoid hemorrhage or pheochromocytoma crisis. Balloon-like LV wall motion abnormality was defined as akinesis or dyskinesis from the mid portion to the apical area and hyperkinesis of the basal area on left ventriculography (LVG) performed in the 30-degree right anterior oblique projection. The balloon-like LV wall motion abnormality was defined as akinesis or dyskinesis from the mid portion to the apical area and hyperkinesis of the basal area on left ventriculography (LVG) performed in the 30-degree right anterior oblique projection.
other stenosis >50% on CAG; (4) no previous MI. Patients with AMI who did not achieve successful reperfusion were excluded as were patients with atrial fibrillation or intraventricular conduction abnormalities. According to these criteria, 18 patients with TC and 85 patients with anterior AMI were enrolled.

Hypertension, hypercholesterolemia, diabetes mellitus, and smoking history were evaluated as conventional coronary risk factors. Hypertension was defined as systolic blood pressure >140 mmHg and/or a diastolic pressure >90 mmHg, or use of antihypertensive medication; hypercholesterolemia was defined as a serum total cholesterol concentration >220 mg/dl, or use of lipid-lowering medication; diabetes mellitus was defined as a fasting plasma glucose concentration >126 mg/dl, or use of hypoglycemic medications. Patients were assessed for the presence of heart failure, defined as pulmonary congestion on chest roentgenograms or pulmonary artery wedge pressure above 18 mmHg. Serum CK was measured every 3 h and the concentration at the time of ST-segment elevation in the precordial leads, as well as the maximum concentration, were determined.

Twelve-Lead ECG Analysis

All patients underwent 12-lead ECG before CAG and the findings were analyzed by separate cardiologists unaware of the clinical data. If the initial ECG was inadequate for analysis, a later record was used. Displacement of the ST-segment was measured at 80 ms after the J point. All ECGs were recorded at 10 mm for 1.0 mV. Significant ST-segment elevation was defined as an elevation from the preceding T-P line more than 2 mm in the precordial leads and 1 mm in the limb leads, and ST-segment depression was defined as a decrease of more than 1 mm from the preceding T-P line. Abnormal Q waves were considered significant when greater than 40 ms in duration or more than 25% of the height of the R wave for that lead. Displacement of the ST-segment was assessed in the inferior leads (leads II, III, and aVF), and lead V6. Reciprocal ST-segment depression in the inferior leads was defined as an ST-segment that was depressed in at least 1 inferior lead with no ST-segment elevation in the other inferior leads. ST-segment elevation in the inferior leads was defined as an ST-segment that was depressed at least in 1 inferior lead with no ST-segment depression in the other inferior leads.

Abnormal Q wave formation was assessed in the precordial leads (leads V2–6) and inferior leads. Q wave formation in the precordial leads was defined as abnormal Q wave formation in at least 1 precordial lead. Q wave formation in the inferior leads was defined as abnormal Q wave formation in at least 1 inferior lead.

We calculated the sum of the ST level from the preceding T-P line at 80 ms after the J point, added when the ST-segment was elevated, and subtracted when the ST-segment was depressed, in the inferior leads (ΣST inferior), leads V1–3 (ΣST V1–3), and V4–6 (ΣST V4–6). The ratio of ΣST V4–6 to ΣST V1–3 (ΣST V4–6/ΣST V1–3) was assessed.

Analysis of CAG

Multiple-view CAG images were reviewed by separate investigators unaware of the ECG findings. The grade of collateral filling in the LAD was evaluated in the patients with anterior AMI as described by Rentrop et al16 and good collateral filling was defined as grade 2 or 3. The presence of a wrapped LAD, defined as a long artery surrounding and supplying the inferior apex, was assessed in all patients. Patients with anterior AMI were divided into 3 groups: Group A had a culprit lesion proximal to both the first septal branch (S1) and the first diagonal branch (D1), Group B had a culprit lesion proximal to either the S1 or the D1, and Group C had a culprit lesion distal to both the S1 and the D113.

Statistical Analysis

Values are expressed as the mean (SD). Comparison of the data from the 4 groups was performed by one-way ANOVA followed by Bonferroni/Dunn analysis. Categorical data were compared using Fisher’s exact test. Logistic regression analysis was performed using StatView 5.0 (Abacus Concepts, Berkeley, CA, USA). A p-value <0.05 was considered statistically significant.

Results

Clinical Characteristics of TC

The age of patients with TC ranged from 60 to 86 years. Apparent trigger events were bronchial asthma attack, bronchoscopy, colonectomy, surgery for ileus, consciousness disturbance, peritonitis, and attending a funeral in 1 patient each, and pneumonia in 2 patients. One patient

<table>
<thead>
<tr>
<th>Table 1 Clinical Characteristics</th>
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<tr>
<td>Takotsubo cardiomyopathy (n=18)</td>
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<tr>
<td><strong>Age (years)</strong></td>
</tr>
<tr>
<td><strong>Men</strong></td>
</tr>
<tr>
<td><strong>Chest pain</strong></td>
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<tr>
<td><strong>Risk factors</strong></td>
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<tr>
<td>Smoking</td>
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<tr>
<td>Hypertension</td>
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<tr>
<td>Diabetes mellitus</td>
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<td>Hypercholesterolemia</td>
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<tr>
<td><strong>Time from the onset to ECG recording (h)</strong></td>
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<td>Creatine kinase during ECG recording (IU/L)</td>
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<td>Peak creatine kinase (IU/L)</td>
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<td>Heart failure</td>
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<td>Wrapped LAD</td>
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<tr>
<td><strong>Anterior AMI</strong></td>
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<tr>
<td><strong>Group A (n=21)</strong></td>
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<td><strong>Group B (n=46)</strong></td>
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<td><strong>Group C (n=18)</strong></td>
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AMI, acute myocardial infarction; ECG, electrocardiogram; LAD, left anterior descending coronary artery.

*p<0.05 vs takotsubo cardiomyopathy, **p<0.01 vs takotsubo cardiomyopathy, ***p<0.0001 vs takotsubo cardiomyopathy.
ECG Findings of Takotsubo Cardiomyopathy

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suffered cardiogenic shock requiring intraaortic balloon pumping. One patient died from ovarian cancer, but the other patients were discharged from the hospitals.

Clinical Characteristics of Anterior AMI

No apparent trigger events as in TC were detected in patients with anterior AMI: 7, 9, and 3 patients were classified as Killip class 3 or class 4 in AMI groups A, B, and C, respectively; 8, 29, and 7 patients had experienced anginal chest pain before the MI; and good collateral filling was observed in 6, 6, and 1 patients, respectively.

Comparison of Clinical Characteristics

The clinical characteristics are summarized in Table 1. The patients with TC were older than those in AMI group A (p<0.0001), B (p<0.0001), and C (p=0.03), and there was a higher proportion of females (p<0.0001, p<0.0001 and p=0.007 for A, B and C, respectively). The frequency of presenting with chest pain was significantly lower in patients with TC than in patients in AMI group A (p=0.002), and group B (p=0.0013), but was not in group C. The frequency of smoking was lower in patients with TC than in patients in AMI group A (p=0.008) and group B (p=0.01), but did not differ from patients in group C. The frequency of hypercholesterolemia was lower in patients with TC than in patients in AMI group A (p=0.008) and B (p=0.01), but did not differ from patients in group B or C. The maximum CK concentration was significantly lower in patients with TC than in patients in AMI group A (p<0.0001) and B (p<0.0001), but not in group C.

### Table 2 Comparison of Electrocardiographic Findings

<table>
<thead>
<tr>
<th></th>
<th>Takotsubo cardiomyopathy (n=18)</th>
<th>Anterior AMI Group A (n=21)</th>
<th>Group B (n=46)</th>
<th>Group C (n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal Q wave</td>
<td>10 (56%)</td>
<td>15 (71%)</td>
<td>30 (65%)</td>
<td>8 (44%)</td>
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<tr>
<td>in the precordial leads</td>
<td></td>
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<tr>
<td>Abnormal Q wave</td>
<td>8 (44%)</td>
<td>0 (0%) **</td>
<td>7 (15%) *</td>
<td>6 (33%)</td>
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<tr>
<td>in the inferior leads</td>
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<tr>
<td>ST $^\uparrow$</td>
<td>6 (33%)</td>
<td>0 (0%) **</td>
<td>5 (11%)</td>
<td>1 (6%)</td>
</tr>
<tr>
<td>in inferior leads</td>
<td></td>
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<td></td>
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<tr>
<td>Reciprocal ST $\downarrow$ in the inferior leads</td>
<td>2 (11%)</td>
<td>17 (81%) ***</td>
<td>30 (65%) **</td>
<td>5 (28%)</td>
</tr>
<tr>
<td>ST $^\uparrow$ in lead V6</td>
<td>7 (39%)</td>
<td>2 (10%)</td>
<td>10 (22%)</td>
<td>3 (17%)</td>
</tr>
<tr>
<td>ST $\downarrow$ in lead V6</td>
<td>0 (0%)</td>
<td>12 (57%) ***</td>
<td>6 (13%)</td>
<td>1 (6%)</td>
</tr>
</tbody>
</table>

AMI, acute myocardial infarction; ST $^\uparrow$, ST segment elevation; ST $\downarrow$, ST segment depression.
*p<0.05 vs takotsubo cardiomyopathy, **p<0.01 vs takotsubo cardiomyopathy, ***p<0.0001 vs takotsubo cardiomyopathy.

Fig 1. Representative 12-lead ECGs of patients with takotsubo cardiomyopathy (TC), acute myocardial infarction (AMI) group A, and AMI group C. All patients exhibited ST-segment elevation in the precordial leads. ST-segment depression in the inferior leads and lead V6 is apparent in AMI group A, but not in the TC and AMI group C patients.
Comparison of ECG Findings

The time from the onset of symptoms to ECG recording was 11.0±8.6h in patients with TC, 12.0±5.8h in AMI group A, 12.4±5.9h in AMI group B, and 11.8±5.7h in AMI group C. No significant difference was found between the groups.

A representative 12-lead ECG of a patient with TC and from one in AMI group A and group C are shown in Fig 1, and the comparison of the ECG findings is summarized in Table 2. In patients in AMI group A, the frequencies of ST-segment depression in lead V6 and reciprocal ST-segment depression in the inferior leads were significantly higher (both p<0.0001), and the frequencies of Q wave formation in the inferior leads, and ST-segment elevation in the inferior leads was significantly lower (p=0.0007, p=0.0057, respectively) than in patients with TC. In patients in AMI group B, the frequency of Q wave formation in the inferior leads was significantly lower (p=0.02) and the frequency of reciprocal ST-segment depression in the inferior leads was significantly higher (p=0.0002) than in the patients with TC. In contrast, no significant differences in ECG findings were found between patients with TC and AMI patients in group C.

A comparison of calculated ST level values is presented in both Table 3 and Fig 2. In AMI group A, \( \sum ST V_{1-3} \) was significantly higher (p=0.005), and \( \sum ST V_{4-6}/\sum ST V_{1-3} \) and \( \sum ST \) inferior significantly lower (p=0.001, p<0.0001, respectively) than in patients with TC. In AMI group B, \( \sum ST V_{1-3} \) was significantly higher (p=0.01) and \( \sum ST \) inferior significantly lower (p=0.0008) than in patients with TC. There were no significant differences in these values between patients with TC and patients in AMI group C.

Discussion

Comparison of Clinical Characteristics

In the present study, there were significant differences in age and gender between patients with TC and those with any type of AMI. Most of the patients with TC were elderly women as has been shown in previous reports. Although the precise reason is unknown, the pattern is clearly different from the established male predominant pattern seen in coronary artery disease.

The CK concentration during ECG recording might not be useful for distinguishing TC from AMI. The maximum CK concentration did not differ between patients with TC and those in AMI group C who had a smaller infarct area. Accordingly, the maximum CK concentration may not distinguish patients with TC from those with AMI and a distal lesion, but may be useful for distinguishing them...
from patients with proximal AMI.

Other than a predominance of females and older age, no clinical characteristics, including the conventional coronary risk factors, differed between patients with TC and those in AMI group C, suggesting that differentiation of TC from AMI with distal LAD lesions may be difficult based on clinical characteristics only.

**Comparison of ECG Findings**

The ST-segment changes every hour in both TC and AMI. In the present study, the main aim was to evaluate whether it is possible to differentiate patients with TC from those with an anterior AMI caused by a LAD lesion when there was ST-segment elevation in the precordial leads. Therefore, we analyzed ECGs recorded initially at the Division of Cardiology instead of those presenting with maximal ST-segment elevation and we believe our results give cardiologists important information that is useful when they see patients with ST-segment elevations on the ECG.

Evaluation of the ECG findings of patients with TC revealed that ST-segment elevation is most obvious in leads V3–6 in the acute phase, which mimics an anterior AMI! The absence of reciprocal changes, absence of abnormal Q waves, and ∑ST V4–6/∑ST V1–3 >1 have been reported as having high sensitivity and specificity for distinguishing TC from anterior AMI! However, it has been hypothesized that the ECG findings of anterior AMI depend on the site of the culprit lesion and the presence of a proximal LAD lesion8–13 and therefore, we divided the present patients with an anterior AMI into groups according to the site of the culprit lesion and compared their ECG findings with those from patients with TC.

Reciprocal ST-segment depression in the inferior leads is reported to strongly predict culprit LAD lesions proximal to both the S1 and the D1, whereas absence of that finding predicts distal culprit lesions in AMI.8–14 In the present study, patients with TC showed a lower frequency of reciprocal ST-segment depression in the inferior leads compared with patients in AMI groups A and B. However, this frequency did not differ between patients with TC and patients in AMI group C, which suggests that reciprocal ST-segment depression in the inferior leads may not be useful for TC from AMI with a culprit lesion in the distal LAD.

None of the present patients with TC exhibited ST-segment depression in lead V6, rather they had a higher frequency of ST-segment elevation in lead V6, although these differences were not statistically significant in comparison with patients in any AMI group. It has been reported that ST-segment depression in lead V5 is very specific for LAD lesions proximal to the S1, and that ST-segment depression in lead V6 is seen more often in proximal LAD disease.8,9 Basal anterior myocardial dysfunction in AMI, especially with a culprit lesion of the proximal LAD, might cause a higher frequency of ST depression in lead V6 than in TC, whereas the apical myocardial dysfunction of TC might cause ST-segment elevation in lead V6. These findings suggest that AMI rather than TC should be suspected in the patient who exhibits ST-segment depression in lead V6 in the acute phase.

The frequencies of ST-segment elevation and Q wave formation in the inferior leads were significantly higher in patients with TC than in patients in AMI groups A and B, but not patients in group C, and may reflect a difference in the presence of inferior wall dysfunction of the myocardial apex. The ST-segment in the inferior leads is elevated in some patients with anterior AMI and a smaller infarct and wrapped LAD10,14,15 and it might be difficult to distinguish TC from anterior AMI, particularly when the culprit lesion is in the distal LAD.

Basal anterior myocardial dysfunction may have been the reason for the higher levels of ∑ST V1–3 in patients from AMI groups A and B than in patients with TC. In AMI group A, a higher frequency of ST-segment depression in lead V6 might result in the reduction of ∑ST V4–6, and thus reduce ∑ST V4–6/∑ST V1–3 compared with patients with TC. The higher frequency of reciprocal ST-segment depression in the inferior leads might cause lower ∑ST inferior in patients from groups A and B compared with patients with TC.

As mentioned earlier, the absence of basal posterior myocardial dysfunction, which affects reciprocal ST-segment depression in the inferior leads and ST-segment depression in lead V6, and the presence of apical inferior myocardial dysfunction, which affects ST-segment elevation and Q wave formation in the inferior leads, might differ between patients with TC and patients with an anterior AMI with proximal LAD lesions. However, the absence of basal anterior myocardial dysfunction because of a distal LAD lesion and the presence of inferior wall dysfunction because of a wrapped LAD might make it difficult to distinguish patients with anterior AMI with distal LAD lesions from those with TC based on the ECG findings alone. Similarly, it might also be difficult to distinguish patients with AMI in the apical wall only, caused by other than a LAD lesion, from those with TC.

**Study Limitation**

There might be some discrepancies between the location of the culprit lesion and the extent of myocardial damage. We divided the AMI patients into groups on the basis of the location of the culprit lesion from CAG analysis and therefore the ECG findings might not exactly reflect the extent of the damaged myocardium. Second, because this was a retrospective study, we could not appropriately compare the time course of the ECG findings, only the ECG findings in the acute phase.

**Conclusion**

There is a predominance of older women among patients with TC compared with those with an anterior AMI. In the acute phase, it is possible to distinguish TC from an anterior AMI with a culprit lesion of the proximal LAD, but not AMI with a distal lesion, by the ECG findings.

**References**


