ors et al assessed the orientation of the T-axis for cardiac risk stratification based on the theory of diagnostic vectorcardiography.1 The T-axis was a strong and independent predictor of fatal and non-fatal cardiac events in the population of the Rotterdam study. Furthermore, the prognostic value of an abnormal T-axis has been proved to be greater than other electrocardiogram (ECG) risk factors of T-wave inversion and ST depression. However, the physiologic meaning of an abnormal T-axis remains unclear.

Recently, T-wave morphology analysis (TMA) was hypothesized to quantify the irregularities of ventricular repolarization based on singular value decomposition of standard 12-lead ECGs.2 TMA analysis assesses both ventricular depolarization and repolarization independent of the accuracy of measuring the repolarization process, such as QT interval and QT dispersion. Thus, TMA makes important the relationship between the QRS and T-wave vectors, and the morphological varieties of the T-wave.

The total cosine R-to-T (TCRT) in the TMA descriptors is dependent on the spatial angle between depolarization and repolarization, in keeping with the concept of the ventricular gradient (VG). Zabel et al reported that the TCRT is the only descriptor of TMA that is a strong and independent predictor of adverse outcome in patients with myocardial infarction (MI).3 Both the T-axis and TCRT are derived from the computed analysis of a vectrocardiographic ECG reconstructed from the standard 12-lead ECG.1,2 A TCRT less than −0.888 is associated with increased 5-year cardiac mortality in a population with MI.4 Furthermore, a TCRT less than −0.888 occurs in the case of a vectorcardiographic ECG with an angle >150 degrees between the QRS loop and the T-wave loop. Thus, we propose a new indicator relating the axes of QRS and T-waves on the surface ECG. In this study, we evaluated its characteristics in patients with cardiomyopathy (CM) or MI, which often present with T-wave inversions and ST depression. The aim of this study was to assess the correlation between TCRT and the axes of QRS and T-wave on the surface ECG in patients with these conditions.

**Methods**

Subjects
Patients with CM or MI were recruited from Nippon Medical School Hospital (Tokyo, Japan) and Yashio Heart Hospital (Saitama, Japan) from February 2002 to February
2005. Informed consent was given by each patient before inclusion in the study. Patients with permanent pacemakers, atrial fibrillation, or frequent ectopic beats were excluded.

Patients were divided into 2 groups: patients with CM, including hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), or arrhythmogenic right ventricular cardiomyopathy (ARVC) (group CM, n=21, males =13), and patients with prior or acute MI (n=36, males =28). In the patients with acute MI, the ECG was recorded after the myocardial ischemia had been relieved by coronary intervention.

The diagnosis of HCM was based on echocardiographic demonstration of unexplained left ventricular hypertrophy. DCM was defined as markedly impaired left ventricular systolic function without epicardial atherosclerotic coronary artery disease as assessed by left ventriculography and coronary angiography. The diagnosis of ARVC was based on criteria proposed by the ESC-ISFC. MI was diagnosed by the presence of 2 of the following 3 criteria: (a) characteristic clinical history; (b) serial changes on the ECG suggesting infarction or injury; or (c) a transient increase in cardiac enzymes to more than 2-fold upper limit of the normal laboratory value. Acute MI was also defined as presenting within 1 month of onset of symptoms, and prior MI was defined as occurring more than 1 month from onset.

**ECG Recordings and Analysis**

In all patients, a digital 12-lead surface ECG sampled at 250 Hz was recorded 10 times using a MAC 5000 electrocardiographic system (GE Marquette Medical System, Milwaukee, WI, USA). All digital ECG files were sent to St George’s Hospital where they were analyzed automatically in a blinded manner. TMA descriptors [TCRT and T-wave morphology dispersion (TMD)] were calculated using a custom software package. Details of the physiologic background and the method of calculation of TMA have been previously published. Using singular value decomposition, which correspond to the X, Y, and Z lead of 3-dimensional (D) space. All repolarization descriptors were measured using the ECG vectors that constructed 3-D space. Then, we get QRS and T-wave vector loop in 3-D space, and TCRT was calculated from the cosine values between the QRS and T-wave vectors.

TCRT represents the difference between the orientation of the QRS loop and the T-wave loop, so, for example, negative values of TCRT correspond to large differences in the orientation of 2 loops. TMD represents the average angle between all possible reconstruction T-wave vector pairs. The left ventricular ejection fraction (LVEF) was estimated by transthoracic echocardiography.

**Axis of the QRS Complex and the T-Wave on the Surface ECG**

We defined the new descriptor representing the opposite polarity between the QRS complex and T-wave on the surface 12-lead ECG as follows. The amplitudes of the Q, R, S, and T waves were measured on the ECG at a paper speed of 25 mm/s. The QRS and T amplitudes were defined as the difference between the height of a positive wave and the depth of a negative wave. In Fig 1, the QRS and T amplitudes were calculated as follows: QRS=a–c (or b), R=T=d–e (d > e). VG-positive was defined for each lead as a positive value for the QRS amplitude and a negative value for the T amplitude, or a negative value for the QRS amplitude and a positive value for the T amplitude. VG-index was defined as the total number of leads that are VG-positive. For each ECG, the VG-index and the number of leads with a negative T-wave were assessed by 1 observer.

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**Table 1 Clinical Characteristics of the Study Group**

<table>
<thead>
<tr>
<th></th>
<th>CM group (n=21)</th>
<th>MI group (n=36)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>55±17</td>
<td>65±13</td>
<td>0.046</td>
</tr>
<tr>
<td>Male (%)</td>
<td>13 (62)</td>
<td>28 (78)</td>
<td>NS</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>48±21</td>
<td>44±13</td>
<td>NS</td>
</tr>
<tr>
<td>ICD (%)</td>
<td>7 (33)</td>
<td>10 (27)</td>
<td>NS</td>
</tr>
<tr>
<td>CRBBB</td>
<td>5</td>
<td>3</td>
<td>NS</td>
</tr>
<tr>
<td>CLBBB</td>
<td>3</td>
<td>2</td>
<td>NS</td>
</tr>
<tr>
<td>IVD</td>
<td>0</td>
<td>2</td>
<td>NS</td>
</tr>
<tr>
<td>HCM</td>
<td>9</td>
<td>2</td>
<td>NS</td>
</tr>
<tr>
<td>DCM</td>
<td>10</td>
<td>2</td>
<td>NS</td>
</tr>
<tr>
<td>ARVC</td>
<td>2</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Prior MI</td>
<td>18</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Acute MI</td>
<td>16</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Ischemic cardiomyopathy</td>
<td>4 (19)</td>
<td>2 (6)</td>
<td>NS</td>
</tr>
<tr>
<td>NSVT (%)</td>
<td>8 (38)</td>
<td>13 (36)</td>
<td>NS</td>
</tr>
<tr>
<td>VT (%)</td>
<td>0 (0)</td>
<td>7 (19)</td>
<td>NS</td>
</tr>
<tr>
<td>Syncope (%)</td>
<td>1 (5)</td>
<td>1 (3)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

CM, cardiomyopathy; MI, myocardial infarction; LVEF, left ventricular ejection fraction; ICD, implanted cardioverter defibrillator; CRBBB, complete right bundle branch block; CLBBB, complete left bundle branch block; IVD, intraventricular conduction disturbance; HCM, hypertrophic cardiomyopathy; DCM, dilated cardiomyopathy; ARVC, arrhythmogenic right ventricular cardiomyopathy; NSVT, non-sustained ventricular tachycardia; VT, ventricular tachycardia; VF, ventricular fibrillation.

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Statistical Analysis

Clinical variables are presented as a percentage for categorical variables and mean value ± standard deviation for continuous variables. Statistical analysis was performed using Stat View J-5.0 (SAS Institute, Cary, NC, USA). The data were analyzed with Student’s t-test, Mann-Whitney, and chi-square for unpaired variables, as appropriate. The correlation between TCRT and the VG-index was analyzed by linear regression. A p-value <0.05 was considered statistically significant.

Results

Clinical Data

The mean age of group CM was significantly lower than that of group MI (55±17 vs 65±13 years, p<0.05). There were no differences between groups in LVEF, number of patients with implanted cardioverter defibrillator, and arrhythmic events. Ventricular fibrillation was, however, documented only in patients in group MI. The characteristics of the patients are summarized in Table 1.

TMA

CM vs MI The value for TCRT was significantly lower in group CM than in group MI (–0.50±0.51 vs –0.04±0.65, p<0.01, Fig 2). There was no difference in TMD between the 2 groups.

VG-Index The VG-index was significantly greater in group CM than in group MI (5.9±3.4 vs 4.2±2.4, p<0.05, Fig 3).

Negative T-Waves There were no differences between groups in the number of negative T-waves on the surface ECG. There was no relationship between the number of negative T-waves and the value of TCRT in any of the patients.

Correlation Between TCRT and VG-Index There was a significant correlation between TCRT and VG-index in all of the patients ($r^2=0.47$, Fig 4). There was also a significant correlation between TCRT and VG-index in group CM ($r^2=0.59$). There was a significant correlation between TCRT and VG-index in group MI ($r^2=0.39$). The patients with VG-index <3 nearly all had positive values of TCRT, whereas those with VG-index >6 had negative values of TCRT.

Discussion

The value for TCRT was significantly lower in group CM than in group MI, whereas there were no differences in TMD between the 2 groups. The VG-index was significantly greater in group CM than in group MI. Furthermore, there was a significant correlation between TCRT and the VG-index in all patients, but no relationship between
TCRT and negative T in any of the patients. Kors et al; Kardys et al; and de Torbal et al demonstrated the usefulness of the orientation of the T-axis for cardiac risk stratification, which is based on diagnostic vectorcardiography. Such an abnormal T-axis reflects repolarization abnormalities and its deviation can be attributed to ischemic changes such as T-wave inversion and ST-T changes. In addition, they reported that other ECG indicators, such as T-wave inversion and ST depression, have no prognostic value for cardiac risk stratification. Thus, Kardys et al and de Torbal et al elucidated that it is T-axis deviation in each lead in vectorcardiography, rather than the changes in T-wave morphology, that reflect repolarization abnormalities. In those studies, the electrical T-axis was assessed only in patients with coronary heart diseases, and it remains unclear whether the electrical T-axis is useful clinically for cardiac risk stratification for patients with CM.

Acar et al developed new ECG indicators of T-wave morphology, which were reported to characterize both depolarization and repolarization in order to detect repolarization abnormalities that contribute to arrhythmogenesis. TCRT in TMA is a strong and independent predictor of adverse outcome in post-MI patients. However, obtaining the value for TMA requires analyzing the surface digital ECG using special software. Thus, we proposed a new ECG descriptor, the VG-index, which does not require computed analysis. The VG-index consists of determining the orientations of the QRS and T-wave axes, which conforms with the concept of TCRT.

The genesis of T-wave inversions and ST-T changes differs between MI and CM, which caused the TCRT to be lower in patients from group CM than those from group MI, and the VG-index was greater in group CM than in group MI in this study. The clinical significance of negative T-wave after acute MI is controversial. T-wave morphology is generally changed during the time course of MI, the same as in takotsubo syndrome. In our study, the study group comprised patients with acute and prior MI, which meant each negative T-wave had the possibility of clinically different significance depending on the status of myocardial ischemia. Pierard et al evaluated persistent vs early or delayed T-wave normalization of negative T-wave after acute MI. Early normalization is associated with stunned myocardium, and delayed normalization is observed in patients with hibernating myocardium. The presence of persistent T-wave inversions after Q-wave MI has been shown to indicate transmural necrosis and loss of viable myocardium. Negative T-wave in MI reflects residual myocardial viability and ischemia. In contrast, giant negative T-waves are often present in patients with apical HCM. It has been suggested that a hyperdynamic left ventricle produces greater metabolic demands, which may produce T-wave abnormalities. Furthermore, the depth of negative T waves was reported not to be associated with the prognosis of patients with HCM. Our study also demonstrated no relationship between TCRT and negative T waves.

The concept of VG was first proposed in 1931, and originated from the observation that an altered ventricular activation sequence was associated with changes in the T-wave as well as the QRS complex of the ECGs from muscle strips. This classic VG concept was extended later to electrocardiographic mapping and, then several studies suggested that the body surface distribution of ORST deflection areas may have value for the recognition of cardiac conditions prone to develop arrhythmias. Recently, Batchvarov et al reported that VG and TCRT share the same physiologic background and could serve as an ECG index of vulnerability to arrhythmias. The decreased TCRT, which represents the increased vulnerability to arrhythmias, causes the angle between the QRS-loop and T-loop to be >150. If the QRS and T-wave vectors in many leads on the surface ECG have opposite polarity, the angle between them would increase greatly. So we defined a positive amplitude for the QRS-complex and a negative amplitude for the T-wave, or a negative amplitude for the QRS-complex and a positive amplitude for the T-wave, as VG-positive. We defined the VG-index as the number of leads that are VG-positive and this should correlate with the degree of TCRT. In our study, TCRT correlated with the VG-index. The value of the VG-index, especially >7, would indicate a very low value for the TCRT.

Acar et al compared the TCRT and TMD values of patients with HCM and of normal individuals, and demonstrated that abnormal values could differentiate patients with HCM from normal. We reported the possibility of assessing repolarization abnormalities in patients with CM and MI by TMA analysis. In patients with heart diseases other than MI, TMD would be superior to TCRT for differentiating normal and abnormal ventricular repolarization. However, in the present study TMD did not differentiate between CM and MI. It is possible that there are no differences in the morphology of T-waves between CM and MI. However, if one assesses the T-wave morphology based on its relationship with the QRS-complex, differences may be observed.

Study Limitations
The present study was not a prospective study, so we cannot determine whether TCRT and VG-index can predict arrhythmic events. If we evaluated those predictive values for the risk stratification, we would need to assess the TCRT and VG-index only in patients with prior MI. Although we conclude that the main reason for the difference in parameters between groups was the difference in the basic heart disease, we require further assessment of the arrhythmic substrate in each patient by other non-invasive methods, including ambulatory ECG, electrophysiological study, and signal averaged ECG.

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References


