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QT Dispersion plus ST-Segment Depression: A New Predictor of Restenosis after Successful Percutaneous Transluminal Coronary Angioplasty

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Summary

Background: ST-segment depression during exercise testing is frequently observed in the absence of restenosis after percutaneous transluminal coronary angioplasty (PTCA).

Hypothesis: With the goal of improving the prediction of restenosis after PTCA, we evaluated the usefulness of ST-segment depression plus QT dispersion (QTd = QT max − QTmin) during treadmill stress test.

Methods and results: Fifty-six patients (37 men, 19 women, mean age 51 ± 14 years) were evaluated with treadmill exercise testing and coronary angiography 7 ± 5 months after PTCA. Treadmill test was positive in 30 patients and negative in 26 patients. At coronary angiography, restenosis was present in 16 patients with positive exercise electrocardiogram (ECG) and in 6 patients with negative exercise ECG. Fourteen patients with a positive stress test did not have restenosis. There was no difference in QTd values between groups at baseline ($p > 0.05$). Exercise QTd was 63 ± 9 ms in patients with positive exercise test, 54 ± 18 ms in patients with negative exercise test ($p = 0.003$), 71 ± 13 ms in patients with restenosis, and 53 ± 17 ms in patients without restenosis ($p = 0.001$). ST-segment depression during the stress test determined restenosis with a sensitivity of 80% and a specificity of 58%. Sensitivity and specificity of QTd of ≥60 ms for prediction of restenosis were 83 and 61%, respectively. When QTd of ≥60 ms was added to ST-segment depression as a condition for positive test, the sensitivity and specificity increased to 91 and 78%, respectively. QT dispersion plus ST-segment depression had higher sensitivity and specificity than either QTd or ST-segment depression alone ($p < 0.05$).

Conclusion: The addition of QTd to ST-segment depression during exercise test improves the diagnostic value and can be used as a noninvasive tool in the diagnosis of restenosis after PTCA.

Key words: percutaneous transluminal coronary angioplasty, restenosis, exercise stress test, QT dispersion

Introduction

After the first application of angioplasty,[1] percutaneous transluminal coronary angioplasty (PTCA) has been widely used for treatment of coronary artery disease (CAD) as alternative treatment to medical or coronary artery bypass surgery. Although PTCA has been a well-accepted treatment for CAD, restenosis after successful intervention is the major problem and the restenosis rate is 12 to 40% in a 6-month follow-up period.[2–5] Coronary angiography is the most accurate and reliable method for detecting restenosis, but it is costly, time consuming, and invasive. Therefore, coronary angiography is not recommended as a first choice method for the detection of restenosis. In many studies, the role of noninvasive methods such as thallium scintigraphy, radionuclide ventriculography, stress echocardiography, and exercise electrocardiographic (ECG) testing were evaluated.[6–11] Among these tests, exercise ECG testing is simpler and less expensive than the others, but its predictive value for detecting restenosis is not as high as expected. Therefore, many investigators have started to search for new ECG parameters in addition to standard ST-segment depression for more accurate detection of restenosis.[12–14] In one study, delta ST/delta heart rate (HR) indices were proposed as a more reliable and sensitive technique than ST-segment changes to confirm restenosis.[12]

QT interlead variability of QT interval, known as QT dispersion (QTd), is believed to reflect the regional variations in ventricular repolarization.[15–17] In many studies, QTd has been shown to increase during ischemia, and it increases the sensitivity and specificity of stress test.[17–19] Therefore QTd plus ST-segment depression may increase the predictive value of exercise stress testing for the diagnosis of restenosis.

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In this study, we evaluated the clinical usefulness of QTd plus ST-segment depression for the detection of restenosis after successful PTCA.

Methods

We studied 56 patients (19 women, 37 men, mean age 51 ± 14 years, range 38–68) who underwent successful PTCA for left anterior coronary artery stenosis. All patients underwent treadmill exercise test with Bruce protocol. All medications except aspirin were discontinued at least five half lives before the exercise testing. Treadmill exercise test was considered positive if there was ≥1 mm horizontal or downsloping ST-segment depression or upsloping ST depression ≥1.5 mm measured at 80 ms after the J point, compared with the resting value. All patients who had negative stress test achieved the maximal predicted (220−age) HR.

All patients underwent control angiography 7 ± 5 months after PTCA for the detection of possible restenosis no later than 1 week following the treadmill exercise test. Restenosis detected on the angiogram was defined according to National Heart, Lung, and Blood Institute definitions as (1) loss of at least 50% of the gain achieved by angioplasty, and/or (2) stenosis at follow-up <20% wider than before angioplasty, and/or (3) increase in stenosis diameter of at least 30% at follow-up compared with the initial result.[5]

The following exclusion criteria were applied: ST-segment depression at rest, hypertension, previous myocardial infarction (MI), angina pectoris, bundle-branch block, cardiomyopathy, ventricular hypertrophy, valvular heart disease, preexcitation syndrome, mitral valve prolapse syndrome, and appearance of a new critical lesion far from the dilated site or another vessel lesion. Patients who showed angina, hypotension, ST elevation, or ventricular arrhythmia during the stress test were not included in this study, because these symptoms and signs were considered to be reliable markers of ischemia. Thus, our purpose was to assess the diagnostic ability of QTd plus ST-segment depression for detection of restenosis after single-vessel coronary angioplasty.

For QT-interval measurements, standard paper-based 12-lead ECGs were recorded (all 12 leads simultaneously, PPG Hellige Cardiotest EK53R) at 50 mm/s paper speed at baseline and during the stress test. The QT interval was measured in as many limb leads and precordial leads as possible (minimum of 8 and mean of 9.8 leads) in the 12-lead ECG (from the onset of the Q wave to the end of the T wave) at baseline and then 1 min after the start of the recovery period after the exercise test. If U waves were present, the QT interval was measured to the nadir of the curve between the T and U waves. Four consecutive cycles in each of the 12 leads were measured. All ECG measurements were made by two experienced cardiologists who were blinded to the time it was obtained. From the four cycles, mean maximum and minimum QT were calculated. QT-interval dispersion was defined as the difference between the maximal and minimal QT interval measurements occurring in any of the 12 leads on ECG. Blinded inter- and intraobserver reproducibility of QT measurement was evaluated, and comparison revealed a Spearman correlation coefficient of 0.88 and 0.90, respectively.

In this study we did not calculate corrected QTd because it has been shown that a rate correction of parameters of dispersion of repolarization is probably unnecessary and may even distort the values and the predictive value of QTd.[20–22]

Statistical Analysis

For statistical analysis, *t*-test, chi-square, and Mann-Whitney U tests were used. Correlation analysis was performed by using Spearmen rank correlation test. All data were presented as mean ± standard deviation. A p value of <0.05 was considered significant.

Results

Of 56 patients (22 men, 8 women, mean age 52), 30 had positive exercise stress test, and 26 patients (15 men, 11 women, mean age 50) had a negative exercise stress test. There was no difference in age and gender between patients with positive and a negative stress test (p > 0.05). At coronary angiography, restenosis was present in 16 patients with positive stress test and in 6 patients with negative stress test. Fourteen patients with positive stress test did not have restenosis. There was no difference in QTd values between patient groups at baseline (52 ± 18 ms, 51 ± 22 ms, 50 ± 19 ms, and 53 ± 23 ms, respectively, p > 0.05). QT-dispersion values were higher in patients with positive stress test than in patients with a negative stress test (63 ± 9 ms vs. 54 ± 18 ms, p = 0.003, Table I, Fig. 1) and in patients with than in those without restenosis (71 ± 13 ms vs. 53 ± 17 ms, p = 0.001, Table I, Fig. 1). ST-segment depression during stress test determined restenosis with a sensitivity of 80% and a specificity of 58%. Sensitivity and specificity of QTd ≥ 60 ms for detection of restenosis were 83 and 61%, respectively. When QTd of ≥60 ms was added to ST-segment depression as a condition for positive test, the sensitivity and specificity increased to 91 and 78%, respectively. The sensitiv-

TABLE I Mean heart rates (beats/min) and QT dispersion values (ms) during exercise test

	No. of patients	Heart rate	p Value	QT dispersion	p Value
Positive stress test	30	102 ± 21	0.41	63 ± 9	0.003
Negative stress test	26	104 ± 18		54 ± 14	
Patients without restenosis	34	103 ± 16	0.22	53 ± 17	0.001
Patients with restenosis	22	105 ± 19		71 ± 13	

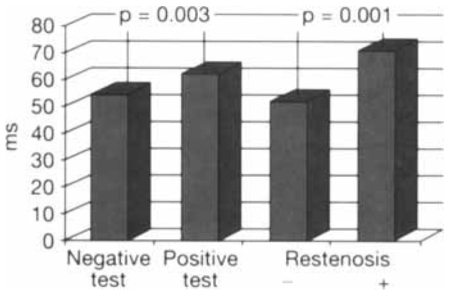

FIG. 1 Mean QT dispersion values (ms).

ity and specificity of QTd were not significantly different from ST-segment depression ($p > 0.05$). However QTd plus ST-segment depression had significantly higher sensitivity and specificity than that of either QTd or ST-segment depression alone ($p < 0.05$).

Discussion

The principal new finding of this study is that QTd plus ST-segment depression during stress test has increased sensitivity and specificity for the prediction of restenosis after PTCA.

Many studies have shown that, when exercise testing is performed in patients who have undergone PTCA for single coronary artery disease, exercise-induced ST-segment changes occur in a significant percentage of patients in the absence of documented restenosis.[12–14, 23–26]

The pathophysiologic significance of these false-positive tests is not clear, although many possible explanations such as fluid velocity and viscosity, length of stenosis on subcritical stenosis, inappropriate constriction of small coronary vessels, vasospasm, and coronary flow reserve have been proposed.[26–32] In addition to these studies, Beregi *et al.*[25] demonstrated that exercise-induced ST-segment depression on exercise testing in patients without restenosis after successful PTCA is strongly associated with the presence of left ventricular wall motion abnormalities.

To refrain from the effect of ventricular wall motion abnormalities on ST depression, we studied a very homogeneous group of patients with single coronary artery disease without previous MI. A study conducted by Hamasaki *et al.*[12] evaluated the value of exercise stress testing for detection of restenosis in a group of patients with single coronary artery disease without previous MI, and the authors found that sensitivity and specificity of positive exercise tests for prediction of restenosis were 83 and 65%, respectively.

We found that ST-segment depression had a sensitivity of 80% and a specificity of 58% for detection of restenosis, which is concordance with the findings of Hamasaki *et al.*[12] Recently, Michaelides *et al.*[26] have suggested that exercise-induced ST-segment depression is not a reliable marker of restenosis.

In addition to ST-segment depression, new ECG parameters have been evaluated to detect restenosis after PTCA. Hamasaki *et al.*[12] evaluated the usefulness of the delta ST/delta HR index derived from exercise ECG, with the goal of improving the prediction of restenosis after PTCA and found that delta ST/delta HR index had higher sensitivity and specificity than the standard ST-segment depression.

QT dispersion, which is a marker of ventricular repolarization, has recently been reported to be associated with myocardial ischemia, and it was found that it increases during ischemia.[17–19] Moreover, QTd plus ST-segment depression increases the sensitivity and specificity of the stress test for diagnosis of CAD.[17] We found that QTd plus ST-segment depression increases the sensitivity and specificity of the stress test for detection of restenosis after PTCA.

As far as we know, no other study in a global population has investigated the significance of QTd plus ST-segment depression compared with ST-segment depression alone for determination of restenosis.

Several limitations of our study should be noted. First, it has been well known that thallium-201 imaging and radionuclide angiography after symptom-limited exercise test are highly predictive of restenosis after coronary angioplasty.[27, 33] In this study, we did not perform myocardial perfusion imaging to correlate with the ECG data. Our study attempted to clarify the significance of QTd plus ST-segment depression during stress test for the detection of restenosis after PTCA. Second, the present study was undertaken as a part of a large restenosis determination trial, and all patients underwent control angiography to detect restenosis, although the indication of repeated intervention still needs to be clarified in asymptomatic patients with abnormal exercise ECG after PTCA. However, Pfisterer *et al.*[34] reported that angiographic severity of restenosis and incidence of recurrent ischemic events were similar in symptomatic and asymptomatic patients with abnormal exercise ECG; therefore, further studies are required in this area. Third, measurements of QTd are not standardized. Various investigators have different definitions for the end of the T wave, especially in the presence of a U wave and in situations of T- and P-wave fusion. In this study, we used the method suggested by Day *et al.*[16] and Barr *et al.*[35] Fourth, we could not measure the QT interval during peak exercise because we had difficulty in detecting the termination of the T wave clearly since ECG quality was not always good enough and noise level was too high. In addition to these problems, T and P wave were sometimes fused at a very fast HR so that the QT interval could not be measured during peak exercise test. Therefore, we had to measure QTd during the recovery period of stress test.

Conclusion

The present study suggests that the addition of QTd to ST-segment depression during stress test improves the diagnostic value and could be used as a noninvasive tool in the detection of restenosis. However, additional studies in this area are necessary to define the clinical applicability of QTd plus ST-segment depression for the detection of restenosis after PTCA.

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