of angiographic restenosis. Symptomatic restenosis may be particularly unreliable in this patient group owing to either progression of native coronary and vein graft disease or ungraftable vessels. As with native vessel angioplasty, angiographic follow-up is essential to document the true restenosis rate in these patients. No previous study performed systematic repeat angiography after angioplasty of IMA grafts. In 3 studies, recatheterization was performed in patients with progressive symptoms or an abnormal stress test.[8,10,11] Shimshak et al[8] performed repeat coronary arteriography in only 8 of 24 patients (33%) at a mean interval of 6.4 months; despite incomplete angiographic follow-up, restenosis was infrequent, occurring in only 1 of 8 IMA grafts (13%) restudied. In our series, 12 of 13 patients (92%) eligible for long-term follow-up underwent repeat coronary arteriography, and only 1 (8%) had restenosis.

Compared with the reported restenosis rates of 38 to 53% for saphenous vein graft angioplasty,[14-16] IMA graft angioplasty appears to have a significantly better long-term outcome. Part of this discrepancy may be related to lesion location. In our experience, 93% of the IMA lesions involved the distal anastomosis, and restenosis occurred in only 1 of these cases. In saphenous vein grafts, Dorros et al[15] reported an 80% restenosis rate at the proximal anastomotic site and only a 22% rate at the distal anastomotic site. Douglas et al[16] found similar saphenous vein graft restenosis rates. Thus, it appears that lesions involving the distal anastomosis, whether in saphenous vein or IMA grafts, are less prone to restenosis. The explanation for this is unclear; however, it may be related to injury during mobilization of the graft, faulty anastomotic technique, or differing tissue plasticity and healing characteristics at anastomoses compared with at other sites.[17]

Because of increased mortality and morbidity with reoperation, percutaneous revascularization of IMA stenoses appears to be a viable alternative. IMA graft angioplasty is a safe and effective alternative, with an excellent early outcome and a low incidence of late restenosis.

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Diagnostic Significance of Deep T-Wave Inversion Induced by Exercise Testing in Patients with Suspected Coronary Artery Disease

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In the diagnosis of coronary artery disease (CAD), no uniform criteria has been established for T-wave changes during exercise testing,[1-3] although deep T-wave inversion (similar to coronary T wave) often occurs during this test in patients with severe CAD.[2] The purpose of this study was to evaluate the prevalence and diagnostic implications of deep T-wave inversion that appears during exercise testing.

Seven hundred and thirteen consecutive patients (527 men and 186 women, aged 14 to 84 years, mean 59) who were suspected of having CAD underwent both exercise testing and cardiac catheterization. Three hundred and seventy-eight patients (53%) had previous myocardial infarction. Two hundred and sixty-nine patients had 1-vessel, 120 had 2-vessel, 107 had 3-vessel and 42 had left main CAD; the remaining 175 had insignificant coronary artery narrowings.

Treadmill exercise testing was performed with the patient off cardioactive medications, using a modified Bruce protocol.[4] Chest pain, ST depression and submaximal heart rate (85% of age-predicted maximal heart rate)[5] were regarded as indications for stopping exercise. Heart rate, blood pressure, 12-lead electrocardiography and symptoms at rest, during exercise and for at least the

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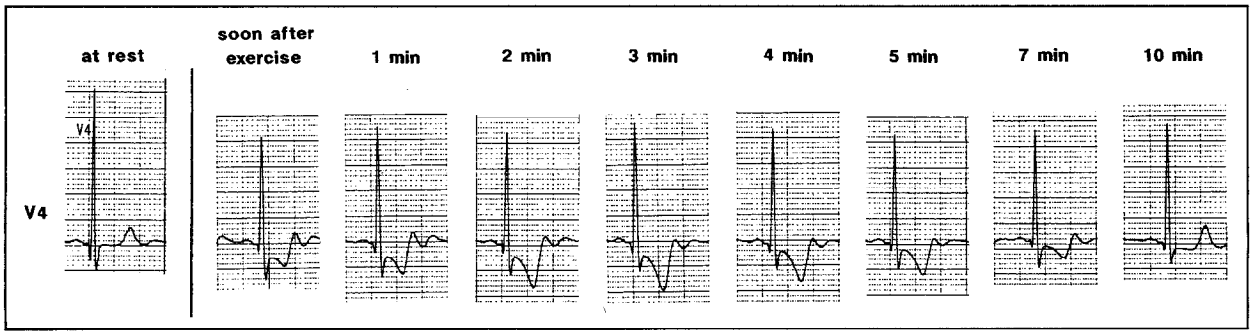

FIGURE 1. An example of deep T-wave inversion in a patient with 3-vessel coronary artery disease.

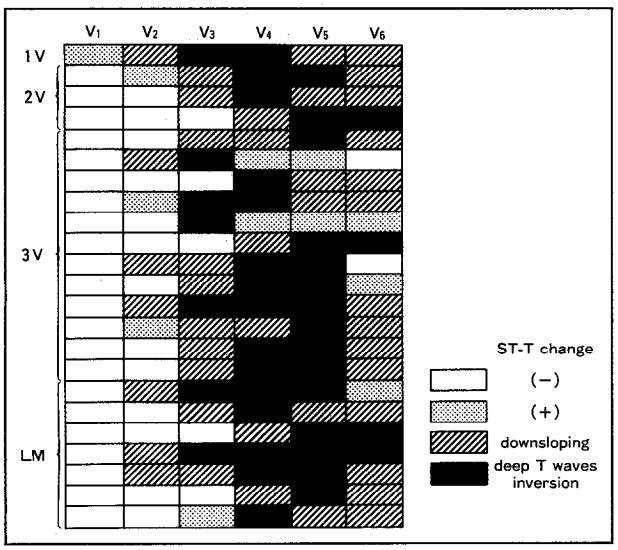

FIGURE 2. Sites of deep T-wave inversion in precordial leads. Deep T-wave inversion was not observed in limb leads. LM = left main coronary artery disease; 1V, 2V and 3V = 1-, 2- and 3-vessel coronary artery disease.

first 5 minutes after exercise were recorded. Electrocardiography soon after exercise was compared with that performed at rest for the magnitude of ST depression, which was measured at 80 ms after the J point. Furthermore, the depth of the inverted T wave that appeared after exercise was measured, with T-P segment as the baseline. An inverted T wave ≥8 mm was defined as deep T-wave inversion. A cutoff point of ≥8 mm was set between previously described negative T waves ≥5 mm[6] and ≥10 mm.[7]

Coronary angiography was performed in multiple oblique projections by the Judkins or Sones technique and was interpreted using the the criteria proposed by the American Heart Association.[6]

Results are expressed as mean ± 1 SD. Student's t *test was used to compare means of continuous variables, and contingency tables were analyzed using a chi-square test. Statistical computations were performed using the SPSS-PC+ computer program.*

Downsloping ST depression ≥1 mm was observed in 187 patients (26%), of whom 23 (3%) developed deep T-wave inversion ≥8 mm. Inverted T waves ≥5 and 10 mm were observed in 58 (8%) and 13 (2%) patients, respectively. After a marked ST depression of 2 to 8 mm, deep T-wave inversion appeared usually at 2 or 3 minutes in the recovery period and remained for 2 to 10 minutes. The depth of inverted T wave reached its maximum at 3 to 5 minutes (mean 11 ± 3 mm). A typical case is shown in Figure 1. Deep T-wave inversion was observed predominantly in leads V_4 and V_5, whereas it was not in V_1, V_2 or limb leads (Figure 2). In patients with downsloping ST depression, the duration of exercise was shorter, heart rate at peak exercise was slower and the magnitude of maximal ST depression was greater in those with than without deep T-wave inversion, whereas age, gender, previous myocardial infarction, heart rate and blood pressure at rest, and chest pain during the test were similar between the 2 groups (Table I). The duration of exercise and the magnitude of maximal ST depression in patients with inverted T waves ≥8 and <10 mm were similar to those with inverted T waves ≥5 and <8 mm, or ≥10 mm (3.8 ± 0.9 vs 3.7 ± 1.3 and 3.0 ± 1.3 minutes [p = not significant (NS)], respectively; and 3.4 ± 1.3 vs 3.4 ± 1.2 and 4.5 ± 1.7 mm [p = NS], respectively).

TABLE I Clinical Features and Findings of Exercise Testing in Patients with Significant Downsloping ST Depression

	Deep T-Wave Inversion (+) (n = 23)	Deep T-Wave Inversion (−) (n = 164)	p Value
Age (yr)	64 ± 8	62 ± 9	NS
Men/women	20 (87%)/3 (13%)	124 (76%)/40 (24%)	NS
Previous MI	13 (57)	76 (46)	NS
Duration of exercise (min)	3.3 ± 1.2	4.4 ± 1.8	0.001
Chest pain	13 (57%)	90 (55%)	NS
HR at rest (beats/min)	68 ± 10	71 ± 12	NS
HR at peak exercise (beats/min)	115 ± 22	128 ± 19	0.01
BP at rest (mm Hg)	144 ± 27	138 ± 20	NS
BP at peak exercise (mm Hg)	156 ± 30	167 ± 28	NS
HR × BP at peak exercise (× 1,000)	18 ± 5	21 ± 5	0.003
ST depression (mm)	4.0 ± 1.6	2.3 ± 1.1	<0.001

BP = blood pressure; HR = heart rate; MI = myocardial infarction; NS = not significant.

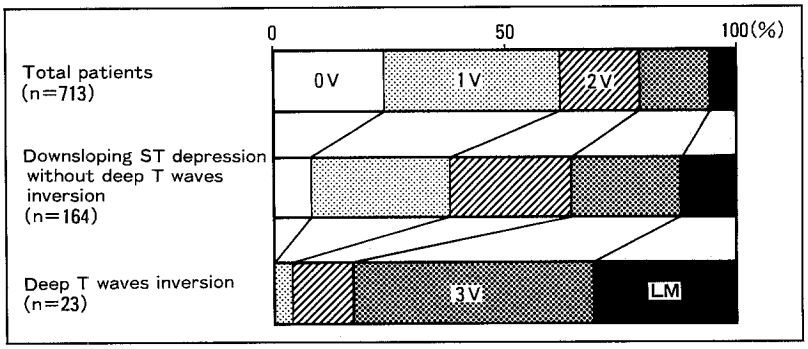

FIGURE 3. Extent of coronary artery disease in relation to type of ST-T changes. 0V = insignificant lesions; other abbreviations as in Figure 2.

The relation of the extent of CAD to the type of T-wave inversion is shown in Figure 3. Three-vessel or left main CAD was found in 21% of patients. Patients with deep T-wave inversion had a higher incidence of 3-vessel or left main CAD than those who had downsloping ST depression without deep T-wave inversion (83 vs 36%; p <0.0001); no significant coronary artery narrowing was observed in 8% of the latter group (Figure 3). When compared with patients who had deep T-wave inversion ≥8 and <10 mm, those with inverted T-waves ≥5 and <8 mm had a lower incidence of 3-vessel and left main CAD, whereas those with T-wave inversion ≥10 mm had a similar incidence (9 of 10 vs 14 of 35 and 10 of 13 [p = 0.005 and NS], respectively). When a cutoff point was determined as 5, 8 or 10 mm, inverted T waves ≥8 mm had the highest specificity and a positive predictive value in identifying 3-vessel or left main CAD (Table II). Of 23 patients with deep T-wave inversion, 13 had previous myocardial infarction (3 anterior, 9 inferior and 1 lateral). Most patients had 3-vessel or left main CAD with multiple severe narrowings in the 3 major coronary arteries or their branches. Three patients with 2-vessel CAD also had 99 or 100% narrowing in the right coronary artery and severe narrowings at the proximal portion of the left anterior descending or circumflex coronary artery. The remaining patient with 1-vessel CAD had ST elevation followed by deep T-wave inversion and was suspected of having vasospastic angina induced by exercise testing.[8]

The present study demonstrated that although the incidence of deep T-wave inversion induced by exercise testing was low, it had high sensitivity (99%) and positive predictive value (83%) in the identification of 3-vessel or left main CAD. Furthermore, patients had multiple severe narrowings in the major coronary arteries or their branches. The depth of inverted T waves was important, because only 40% of patients with inverted T waves ≥5 and <8 mm had 3-vessel or left main CAD. Thus, positive predictive value would decrease to 57% if a cutoff point of 5 mm was used as the criterion for deep T-wave inversion (Table II). Although downsloping ST depression was regarded as a marker for severe CAD,[1–3] the positive predictive value of this marker alone in identifying 3-vessel or left main CAD was approximately 40% (half that yielded by deep T-wave inversion). Moreover, 8% of patients with downsloping ST depression did not have significant CAD. The importance of downsloping ST depression together with early onset and prolonged duration was reported previously in detecting 3-vessel or left main CAD.[9–11] However 3-vessel and left main CAD are not uniform in the severity of the disease, because of the different severity and site of coronary artery narrowings, which influence the outcome of treatment.[12,13] Details of coronary artery findings were unclear in previous studies.[9–11] Our observation that almost all patients with deep T-wave inversion had multivessel CAD with multiple severe narrowings is particularly important in the clinical setting, because these patients are usually regarded as candidates for surgical treatment.

TABLE II Depths of Inverted T Waves in Detecting Three-Vessel or Left Main Coronary Artery Disease

Depths of Inverted T Waves	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)
≥10 mm	7	99	77
≥8 mm	13	99	83
≥5 mm	22	96	57

Positive predictive value = true positives/true + false positives; Sensitivity = number of true-positive detections/total number of positives in group tested; Specificity = number of true-negative detections/total number of negatives in group tested.

The exercise-induced sequential pattern of ST depression was reported by Chahine et al[14] to be a specific marker for multivessel CAD. Our results are consistent with that study. However, that study did not evaluate the depth of inverted T waves or its relation to ST depression. One may suspect that T-wave inversion may be just a facet of marked ST depression, because patients with inverted T waves had greater ST depression than did those without. However, the fact that deep T-wave inversion ≥8 mm had a significantly higher predictive value for 3-vessel or left main CAD than did T-wave inversion <8 mm despite a similar maximal ST depression suggests that this was not the case. The present study underscores the usefulness of this simple measurement of exercise-induced T-wave inversion. The magnitude of ST depression, as well as the depth of inverted T waves should be focused on in the analysis of standard exercise testing.

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Increase in Platelet Support of Thrombin Generation After Thrombolytic Therapy

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Thrombolytic therapy has been a major advance in the treatment of thrombotic diseases, particularly in patients with acute myocardial infarction. The multitude of effects of fibrinolytic agents on platelets has been reviewed by Coller.[1] Increasing evidence shows that platelet activation after thrombolytic therapy may have an important role in both preventing reperfusion and inducing reocclusion. Platelet activation in vivo has been assessed by elevated thromboxane A2 and serotonin, compounds released by platelets after activation.[2-5] The evidence for activation of coagulation includes increases in fibrinopeptide A, thrombin-antithrombin III complex and prothrombin fragment F1.2.[6-11] Unsuccessful reperfusion and early reocclusion is associated with increased fibrinopeptide A in patients with myocardial infarction.[6] The administration of thrombin or platelet inhibitors, or both, accelerates lysis of thrombi and prevents reocclusion in animal models.[4,11-13] It was shown that the in vitro treatment of platelet-rich plasma with fibrinolytic agents shortened the time to thrombin generation and that there was a parallel decrease in the clotting time.[14] In the present report, these observations were extended to patients treated with recombinant tissue-type plasminogen activator (rt-PA).

Patients (n = 10) with acute myocardial infarction were enrolled in the study after giving verbal informed consent. A 6 mg bolus of rt-PA was administered, followed by 54 mg in the first hour and 40 mg during the second hour for a total dose of 100 mg. Patients were administered a heparin bolus (5,000 IU) before the beginning of the rt-PA infusion, which was followed by a continuous infusion of 1,000 IU/hour. Patients routinely received intravenous nitroglycerin and aspirin. Blood samples were collected from patients before and 30 minutes after the beginning of infusion of rt-PA. Samples were also obtained from 4 patients 24 hours after the commencement of treatment.

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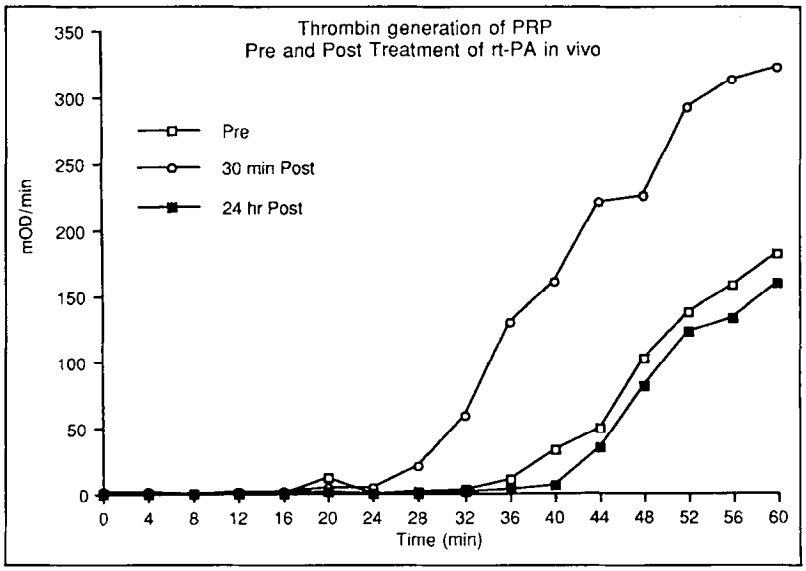

FIGURE 1. Thrombin generation in platelet-rich plasma (PRP) before, during and 24 hours after infusion of recombinant tissue-type plasminogen activator (rt-PA) in patient with acute myocardial infarction. Calcium chloride (25 mM) added to platelet-rich plasma (0.5 ml), and timing started.