Diagnostic usefulness of the post-exercise systolic blood pressure response for the detection of coronary artery disease in patients with diabetes mellitus

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Diagnostic Usefulness of the Post-Exercise Systolic Blood Pressure Response for the Detection of Coronary Artery Disease in Patients With Diabetes Mellitus

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Patients with diabetes mellitus (DM) often have a positive result on exercise testing despite a normal coronary arteriogram, which indicates that exercise-induced ST depression is not always an accurate indicator of the presence of coronary artery disease (CAD) in such patients. The present study evaluated the usefulness of the post-exercise systolic blood pressure (SBP) response for the detection of CAD in 47 consecutive patients with DM. Significant stenotic lesions were detected by angiography in 25 patients; 18 of these had true positive (TP) exercise testing results, and 7 had false negative (FN) results. No significant stenotic lesions were detected in the remaining 22 patients and of these 10 had true negative (TN) exercise testing results, and 12 had false positive (FP) results. The SBP ratio (SBP after 3 min of recovery divided by the SBP at peak exercise) was significantly higher in patients with coronary stenoses than in those without. Analysis of the relative cumulative frequency revealed that a SBP ratio greater than 0.87 was associated with significant stenoses. The sensitivity, specificity, and accuracy of ST change combined with a SBP ratio greater than 0.87 for detecting stenoses in patients with DM were 68%, 82%, and 74%, respectively. These results suggest that calculating the SBP ratio, in combination with monitoring for ST depression, improves the accuracy of treadmill exercise testing for the detection of CAD in patients with DM. (*Jpn Circ J* 2000; **64:** 949–952)

Key Words: Coronary artery disease; Diabetes mellitus; Systolic blood pressure ratio; Treadmill exercise test

Diabetes mellitus (DM) is an independent risk factor for coronary artery disease (CAD). Exercise-induced electrocardiographic ST-segment changes are commonly used to detect CAD, but such changes can also occur in patients with DM without epicardial coronary artery stenoses. Myocardial ischemia in the setting of DM may result from pathophysiologic factors other than epicardial coronary stenoses.

A decrease in blood pressure (BP), during exercise testing can be a sign of severe CAD.[1,2] Furthermore, delayed recovery of systolic BP (SBP) after peak exercise can be seen in patients with CAD[3] and the SBP recovery ratio has been reported as useful for detecting CAD. We investigated the usefulness of the post-exercise SBP response for detecting CAD in patients with DM.

Methods

Study Population

We retrospectively reviewed the clinical records of consecutive patients with DM who underwent both treadmill exercise testing and coronary angiography between April 1986 and July 1999. From this patient group, those with previous myocardial infarction, valvular or congenital heart disease, left ventricular hypertrophy, orthostatic hypotension or hypertension were excluded. DM was diagnosed in accordance with the criteria of the WHO Study Group.[4] Left ventricular hypertrophy was diagnosed by (1) a Romhilt-Estes score ≥4 on ECG,[5] or (2) left ventricular wall thickness >12 mm on echocardiogram. The criterion of orthostatic hypotension was a standing BP 20 mmHg less than the sitting BP before treadmill testing. The diagnosis of hypertension was based on (1) a resting BP before treadmill test of >160/95 mmHg in an unmedicated state, (2) a history of elevated blood pressure >160/95 mmHg, or (3) a history of antihypertensive drug therapy. Consequently, 47 patients with DM (36 men and 11 women aged 19–74 years; mean age, 57 years) were enrolled. These patients underwent coronary angiography because of ST-T change on the treadmill test or 24-h Holter ECG or angina-like symptoms. Informed consent was obtained from all patients for participation in the study.

Exercise Testing

Symptom-limited maximal multistage treadmill exercise testing was performed according to either the Bruce or the modified Bruce protocol. BP was measured with an automated sphygmomanometer (STBP-780B, COLIN, Inc, Tokyo) before, during and after exercise at 1-min intervals. A 12-lead ECG was also obtained at 1-min intervals during the test. Horizontal or downsloping ST depression greater than 0.1 mV below the resting level measured 80 ms after the J point was defined as significant ST depression. The usual clinical cutoff point of 0.1 mV horizontal or downsloping

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differences for discrete data were compared by chi-square analysis. Differences between subgroups were analyzed by the one-factor ANOVA test combined with Scheffe's test after rank transformation. A p value less than 0.05 was considered statistically significant.

Results

Clinical Characteristics and Exercise Testing Variables (Tables 1–3)

Significant stenotic lesions were detected by coronary angiography in 25 of the 47 patients: 18 had true positive (TP) exercise stress testing results, and 7 had false negative (FN) results. No significant stenotic lesions were detected in the remaining 22 patients: 10 had true negative (TN) stress test results, and 12 had false positive (FP) results. Of the 25 patients with coronary stenoses, 12 had 1-vessel, 6 had 2-vessel, and 7 had 3-vessel disease. Two patients had left main coronary artery involvement. There were no significant differences between the groups with respect to gender distribution. Patients in the TN group were younger than those in the other groups. There were no significant differences in body mass index (BMI), hemoglobin (Hb) A1c or treatment between the groups nor were there significant differences in the SBP, the diastolic BP or heart rate at baseline between the groups. However the peak METs achieved was significantly lower in the TP group than in the TN group. There was no significant difference in recovery time of ST change between TP and FP groups. In the TN group, SBP increased immediately during and decreased immediately after exercise, returning to baseline in a linear fashion. In contrast, in the TP and FN groups, SBP either did not change or only increased slowly during exercise and either decreased slowly or did not change after exercise (Fig 1). There was no significant difference in the change in diastolic BP between the 4 groups.

Systolic Blood Pressure Ratio

The SBP ratio was significantly higher in the TP and FN groups than in the TN and FP groups (Fig 2). Significant CAD was present in 13 of the 14 patients (93%) with SBP ratios >0.9, whereas 13 of 13 patients (100%) with SBP ratios <0.8 had no evidence of CAD. Analysis of the relative cumulative frequency of the SBP ratio indicated that a SBP ratio of 0.87 was associated with the highest value for detecting CAD (Fig 3). The sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of a SBP ratio >0.87 combined with ST change for detecting CAD were 68%, 82%, 74%, 81%, and 69%, respectively (Table 3).

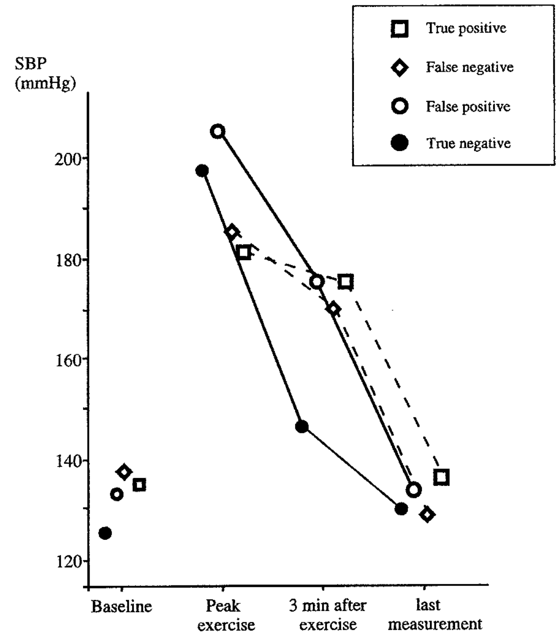

Fig 1. Systolic blood pressure (SBP) at baseline, at peak exercise, at 3 min during the recovery phase, and at the last measurement. Values are expressed as the mean.

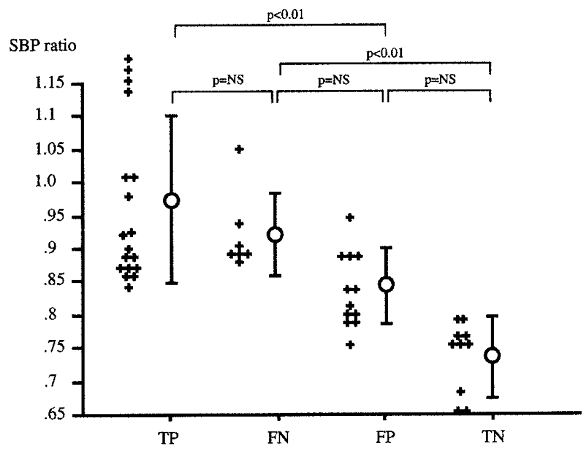

Fig 2. Systolic blood pressure (SBP) ratios based on the result of treadmill exercise testing. TP, true positive (n=18); FP, false positive (n=12); FN, false negative (n=7); TN, true negative (n=10). Values are expressed as the mean ± SD.

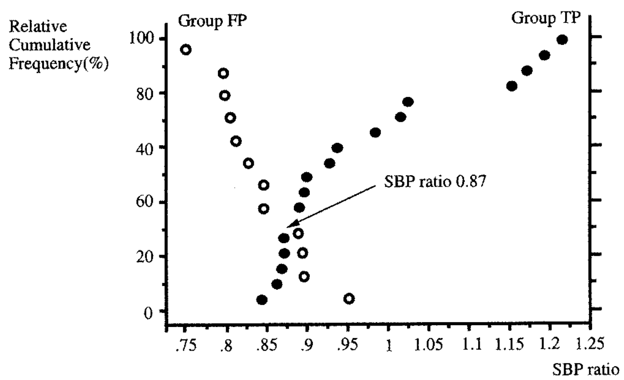

Fig 3. Relative cumulative frequency of the systolic blood pressure (SBP) ratio, for the highest to lowest value in the false positive (FP) group and for the lowest to highest value in the true positive (TP) group. The optimal cutoff point for detecting coronary artery disease was 0.87.

Table 1 Clinical Characteristics

	TP (n=18)	FN (n=7)	TN (n=10)	FP (n=12)
Age (years)	61±9	57±11	47±12*	59±11
Sex (M/F)	14/4	6/1	6/4	10/2
BMI (kg/m²)	23.1±3.4	22.4±3.0	22.4±3.0	22.8±3.5
Duration of DM (months)	20±42	36±47	22±20	38±30
HbA1c (%)	6.9±1.1	6.4±0.9	7.2±3.9	6.2±2.1
Treatment				
Insulin	1	0	1	4
SU	6	2	3	3
Diet	11	5	6	5
No. of stenotic vessels				
1	8	4	0	0
2	4	2	0	0
3	6	1	0	0
LVEF (%)	66±15	59±16	69±8	68±8
τ (ms)	44±8	43±8	46±11	47±7

*TP, true positive; FN, false negative; TN, true negative; FP, false positive; BMI, body mass index; DM, diabetes mellitus; LVEF, left ventricular ejection fraction. *p<0.05 vs FP, p<0.05 vs TP.*

Table 2 Exercise Testing Variables

	TP (n=18)	FN (n=7)	TN (n=10)	FP (n=12)
Peak METs	7.0±2.8*	8.1±3.2	10.8±3.7	8.8±2.2
PRP (×10²)	235±71	251±88	306±86	282±53
Max ST (mm)	1.9±1.0	0	0	1.7±0.5
Recovery time (min)	8.0±4.5	0	0	9.0±3.4
SBP (mmHg)	135±22	138±31	128±21	134±21
DBP (mmHg)	76±9	85±23	82±18	81±15
HR (beats/min)	82±19	80±23	84±15	69±10

*TP, true positive; FN, false negative; TN, true negative; FP, false positive; PRP, pressure rate product; Max ST, maximum ST depression during exercise; SBP, systolic blood pressure at baseline; DBP, diastolic blood pressure at baseline; HR, heart rate at baseline. *p<0.05 vs TN.*

Table 3 Exercise Testing in Patients With Diabetes Mellitus

	Angiographic coronary stenosis		Sensitivity	Specificity	PPV	NPV	Accuracy
	+	−					
Treadmill ST change							
+	18 TP	12 FP					
−	7 FN	10 TN					
Predictive value			72%	45%	60%	59%	49%
Treadmill ST change + SBP ratio >0.87							
+	22 TP	12 FP					
−	3 FN	10 TN					
Predictive value			68%	82%	81%	69%	74%

TP, true positive; FP, false positive; FN, false negative; TN, true negative; PPV, positive predictive value; NPV, negative predictive value.

ST-segment depression was adopted as the standard criterion. Upsloping ST depression was not considered abnormal. The exercise ECGs were evaluated in a blinded fashion by 2 or more observers. All medications were withheld at least 1 day before the study.

Coronary Angiography

Left heart catheterization was performed using standard techniques. Left ventriculography was performed in the right and left anterior oblique projections. The left ventricular ejection fraction was determined by the area–length method using an angiogram obtained in the 30° right anterior oblique view. The extent of CAD was determined by the number of diseased epicardial vessels with greater than 75% stenosis.

Data Analysis

To evaluate the post-exercise SBP response, the SBP ratio was calculated by dividing the SBP at peak exercise by the SBP 3 min after exercise. Cumulative frequency distributions were generated to determine the optimal cutoff value for detecting CAD. The sensitivity, specificity, accuracy, positive predictive value, and negative predictive value were calculated using standard formulae.

Statistical Analysis

Values are expressed as the mean ± 1 SD. Between-group

Discussion

DM is a known risk factor for the development of coronary atherosclerosis[6–8] and, moreover, myocardial ischemia caused by coronary atherosclerosis commonly occurs without symptoms in patients with DM.[9] As a result, significant multivessel atherosclerosis often is present before ischemic symptoms occur and treatment is instituted. Delayed recognition of CAD undoubtedly worsens the prognosis for these patients and therefore effective strategies for earlier detection of CAD could reduce morbidity and mortality. In addition, the detection of subclinical atherosclerosis and early clinical manifestation of CAD could lead to more effective primary prevention. However, patients with DM may have FP exercise stress tests and, in addition, many may have silent ischemia. Therefore, the diagnostic specificity of ST-segment depression is reduced. In the present study, we analyzed the SBP response during exercise testing, and found that combining ST depression and the SBP ratio increased the diagnostic accuracy of exercise stress testing in patients with DM. The diagnostic accuracy of treadmill exercise testing is also markedly decreased in patients with left ventricular hypertrophy and in female patients, and it has been reported that a postexercise SBP ratio of >0.8 is useful for detecting CAD.[3,10] In the present study, the recovery of SBP after exercise was delayed in TP patients compared with FP patients and we found that a SBP ratio >0.87 was useful for detecting CAD in patients with DM and exercise-induced ST segment depression.

The mechanism responsible for an abnormal SBP response might be the paradoxical increase in the stroke volume because of recovery following myocardial ischemia and an increase in systemic vascular resistance caused by enhanced sympathetic nervous activity.[11] Previous studies have described this paradoxical increase in stroke volume as overshoot[12] and Yoshio et al[13] reported that the VEST (continuous ventricular function monitor) could be used to assess overshoot phenomenon. They speculated that the mechanism responsible for the overshoot is a decrease in afterload. Tsuda et al hypothesized that enhanced peripheral vasomotor tone is one determinant of an abnormal post-exercise SBP response, and that increased catecholamine release might be important in its development.[14] Further investigations of these mechanisms are necessary.

In the present study, we used the 3-min SBP ratio to evaluate the postexercise SBP response, based on previous studies.[3,9,11] The standard ST-segment criterion has a positive predictive value of only 60% in patients with DM, but the combination of ST depression >0.1 mV and a SBP ratio >0.87 has a positive predictive value of 81%. Therefore, one need not necessarily proceed with coronary angiography in diabetic patients with a low SBP ratio simply because they had exercise-induced ST depression. We are sure that this index will be useful for the cardiac management of many diabetic patients.

Study Limitation

We analyzed a small number of patients. Further investigations are necessary to establish a multiple regression function for evaluating ischemic ST changes and SBP changes.

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