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Association Between Silent ST Segment Depression in Exercise Electrocardiography and Insulin Resistance in Obese Subjects

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Abstract

Objectives. This study was designed to clarify the association between ST segment depression in exercise electrocardiography (ECG) and insulin resistance in obese subjects.

Methods. A multistage graded submaximal exercise stress test on the bicycle ergometer was performed under CM_5-lead ECG monitoring in 114 obese subjects (39 men and 75 women, mean age 50.9 ± 12.2 years, mean body mass index 28.6 ± 3.1 kg/m^2).

Results. In 27 patients showing ST segment depression at the final exercise intensities (abnormal ST), insulin resistance index by homeostasis model assessment (HOMA-IR) was higher and insulin sensitivity index was lower than in the remaining 87 patients with normal ST segment level (normal ST). The abnormal ST group showed significantly higher plasma glucose and serum insulin levels during the oral glucose tolerance test (OGTT) than the normal ST group. The abnormal ST group showed a significantly higher prevalence of hypertension, impaired glucose tolerance and metabolic syndrome than the normal ST group. Multiple logistic regression analysis showed that insulin resistance as evaluated by fasting insulin, Σ insulin during OGTT, HOMA-IR, insulin sensitivity index, the levels of uric acid, fasting glucose, systolic blood pressure and maximal oxygen uptake were independently associated with ST segment depression.

Conclusions. These results suggest that insulin resistance may involve pathological ST depression during exercise, as well as previously reported factors such as hyperglycemia, hyperuricemia, hypertension and lower aerobic capacity.

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Key Words
■Exercise test ■Insulin ■Ischemia ■Obesity ■ST segment

INTRODUCTION

Insulin resistance or hyperinsulinemia might be an etiologic cause of obesity, hypertension, type 2 diabetes mellitus, hyperuricemia and arteriosclerosis.[1–3] The common association of obesity, hyper-

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tension, type 2 diabetes mellitus, hyperuricemia and arteriosclerosis is thought to be attributable to hyperinsulinemia and insulin resistance. Moreover, some studies indicating the involvement of visceral obesity in atherosclerois and its relationship with insulin resistance have been reported.[2–4] In addition, insulin resistance or hyperinsulinemia is correlated with the incidence of coronary heart disease [5–7] and stroke.[5, 8] Several studies[9–11] have demonstrated a relationship between abnormal ST-T in resting 12-lead electrocardiography (ECG) and insulin resistance or hyperinsulinemia. However, the relationship between ST segment depression in exercise ECG and insulin resistance or hyperinsulinemia is still unknown.

Our hypothesis is that insulin resistance or hyperinsulinemia may be a sensitive factor for predicting myocardial ischemia during exercise. This study was designed to clarify the relationship between ST segment depression in exercise ECG and insulin resistance or hyperinsulinemia as well as coronary risk factors in obese subjects.

SUBJECTS AND METHODS

Subjects

The subjects consisted of 114 obese subjects, 39 men and 75 women with mean age 50.9 ± 12.2 years and mean body mass index (BMI) 28.6 ± 3.1 kg/m^2, with coronary risk factors including hypertension, impaired glucose tolerance, hyperlipidemia, hyperuricemia and hyperinsulinemia. All patients were recruited to participate in our program of exercise therapy for risk factor intervention. Patients taking cardioactive drugs such as antihypertensive drugs, statin and hypoglycemia agents, patients with a history of angina pectoris or myocardial infarction, or patients with an abnormal resting 12-lead ECG were excluded from this study. There were no patients with left ventricular hypertrophy ($RV_5 + SV_1 \geq 3.5$ mV or $RV_5 \geq 2.6$ mV on resting ECG). The design and methods of this study were approved by the Ethics Committee of Saga University. Written informed consent was obtained from each patient after the study design and the potential risks of the study were explained.

Blood sampling and anthropometric measurements

Blood samples were collected early in the morning by venipuncture from an antecubital vein after at least 12 hours' fasting. Next, the 75 g oral glucose tolerance test (OGTT) was performed to analyze plasma glucose and serum insulin concentration. Blood samples were taken at 30, 60, 90 and 120 min after the administration of an oral glucose load. High-density lipoprotein cholesterol was measured by the direct method, low-density lipoprotein cholesterol, triglyceride and plasma glucose by an enzymatic method, serum insulin level by the enzyme immunoassay method, hemoglobin A_{1c} by the high performance liquid chromatography method, and serum uric acid by the uricase peroxidase method, using the fasting blood samples.

The insulin resistance was assessed using fasting serum insulin, Σ insulin during OGTT and Matthews's homeostasis model assessment (HOMA-IR)[12] based on the following formula: fasting glucose (mg/dl) × fasting insulin (μU/ml) /405. The insulin sensitivity index was calculated using a method by Matsuda and DeFronzo[13] based on the following formula: 10,000/square root of (fasting glucose × fasting insulin) × (mean glucose × mean insulin during OGTT). Hypertension, impaired glucose tolerance, hyperlipidemia, hyperuricemia and hyperinsulinemia were defined as coronary risk factors, and the total number of risk factors was also calculated for each subjects. Metabolic syndrome was defined according to the metabolic syndrome diagnostic criteria in Japan.[14]

BMI was calculated as the ratio of body weight (kg) to height (m^2). The waist circumference was measured at the level of umbilicus. The percentage body fat, fat mass and lean body mass (LBM) was measured using the bioelectrical impedance method (HBF-302, OMRON).

Exercise stress test

Prior to starting the exercise therapy, a multistage graded submaximal exercise stress test on an electric bicycle ergometer was performed for each subject. The workload was increased by 5 or 10 W every 4 min, depending on their daily activity level. The CM_5-lead ECG (ML-1800, FUKUDA DENSHI) was recorded continuously during exercise. The ST segment was automatically measured at 0.04 sec from J point. More than 0.10 mV of horizontal or downslope ST segment depressions were considered to be significant. The following parameters were simultaneously measured at rest and at the last 1 min of each stage: the rate of perceived exhaustion, the blood pressure (FB-300, FUKUDA DENSHI), and the blood lactate concentration

(Lactate Pro, ARKRAY), and were plotted against the exercise intensities. The workload at the first breaking point of the blood lactate level was used to determine the lactate threshold (LT). When no clear LT could be obtained, the LT was determined by the method of Beaver *et al*.[15] The estimated maximal oxygen uptake ($\dot{V}O_2max$) was determined by the nomogram of Åstrand and Ryhming,[16] which was measured from heart rate at three different submaximal workloads. The end point of the exercise test (final exercise intensity) was determined on the basis of either achieving 4 mmol/*l* of blood lactate concentration or the criteria of the guidelines of the American College of Sports Medicine.[17]

Statistical analysis

The data are shown as the mean ± SD. Statistical analysis was performed using the StatView software package. The subjects were divided into two groups, which were defined as patients with and without 0.10 mV ST segment depression at the final exercise intensities (normal and abnormal ST groups). Inter-group comparisons were performed using the unpaired *t*-test for continuous variables and chi-square test for categorical variables. Serial changes in plasma glucose and serum insulin levels during OGTT were assessed using repeated measures analysis of variance for intra- and inter-group comparisons. Stepwise multiple logistic regression analysis was performed to determine the association between the ST segment depression at the final exercise intensities and the coronary risk factors. A

Table 1 Comparison of patient characteristics between the normal and abnormal ST groups

	Normal ST group (n=87)	Abnormal ST group (n=27)	p value
Men/women	28/59	11/16	NS
Age (yr)	49.2±12.9	51.4±12.1	NS
Smoking habit (no/yes)	67/20	21/6	NS
HDL-C (mg/d*l*)	55.6±11.9	53.3±14.4	NS
LDL-C (mg/d*l*)	133.4±34.6	140.4±30.1	NS
Triglyceride (mg/d*l*)	108.6±49.2	164.7±166.5	<0.01
HbA_{1c} (%)	5.2±0.5	5.3±0.6	NS
Fasting glucose (mg/d*l*)	93.9±11.9	103.0±15.1	<0.01
Fasting insulin (U/m*l*)	8.4±4.9	12.6±4.2	<0.01
HOMA-IR	1.99±1.25	3.12±1.17	<0.01
Insulin sensitivity index	6.12±3.16	3.51±1.53	<0.01
Uric acid (mg/d*l*)	5.3±1.3	6.1±1.6	<0.05
BMI (kg/m^2)	28.6±3.4	28.5±2.7	NS
Percent body fat (%)	34.0±9.1	33.8±9.3	NS
Waist circumference (cm)	89.8±10.9	92.3±11.0	NS
Resting SBP (mmHg)	121.2±16.6	131.0±20.0	<0.05
Resting DBP (mmHg)	79.4±10.4	83.7±12.3	0.07
Resting ST segment (mV)	0.003±0.028	−0.006±0.038	NS
$\dot{V}O_2max$/LBM (m*l*/min/kg)	43.1±6.2	39.1±3.7	<0.01
LT/body weight (W/kg)	0.79±0.85	0.60±0.20	0.06
Number of risk factors	2.6±1.3	3.5±1.4	<0.05

Continuous values are mean±SD.
Hypertension, impaired glucose tolerance, hyperlipidemia, hyperuricemia and hyperinsulinemia were defined as risk factors for coronary heart disease, and the total number of risk factors was also calculated for each subject.
HDL-C=high-density lipoprotein cholesterol; LDL-C=low-density lipoprotein cholesterol; HbA_{c1}=hemoglobin A_{1c}; HOMA-IR=insulin resistance by homeostasis model assessment; BMI=body mass index; SBP=systolic blood pressure; DBP=diastolic blood pressure; $\dot{V}O_2max$=maximum oxygen uptake; LBM=lean body mass; LT=lactate threshold.

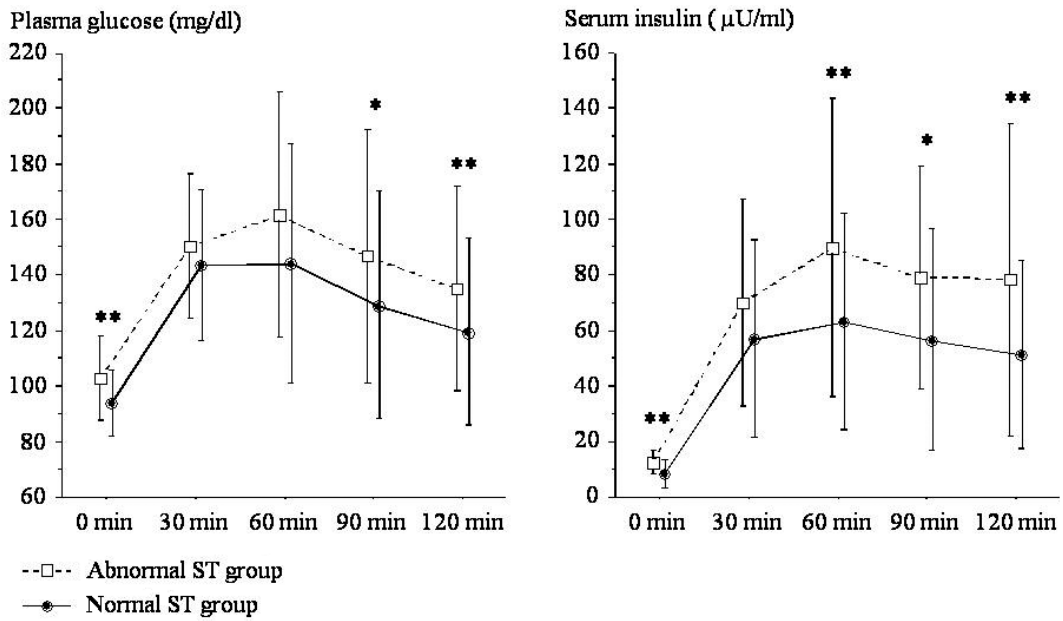

Fig. 1 Plasma glucose (*left*) and serum insulin (*right*) responses during the 75g oral glucose tolerance test in 87 patients with normal ST segment (normal ST group) and 27 patients with exercise-induced ST segment depression (abnormal ST group)
The results are shown as the mean ± SD. $^{*}p < 0.05$, $^{**}p < 0.01$.

probability value of less than 0.05 was considered to be statistically significant.

RESULTS

ST segment depression at the final exercise intensities was observed in 27/114 patients (23.7%). However, ST segment depression was observed in none of these 27 patients before the exercise reached LT level. There were no significant differences in sex, age and smoking habit between normal and abnormal ST groups. The maximum heart rate increase at the final exercise intensities was 72.6 ± 6.1% (maximum heart rate was calculated by 220−age), which showed no significant differences between the normal and abnormal ST groups (72.4 ± 6.3% vs 73.4 ± 5.3%). The blood lactate concentration at the final exercise intensities were 3.6 ± 0.6 mmol/*l*, which showed no significant differences between normal and abnormal ST groups (3.6 ± 0.6 vs 3.7 ± 0.8 mmol/*l*).

Table 1 shows comparisons of patient characteristics between normal and abnormal ST groups. Serum triglyceride ($p < 0.01$), fasting glucose ($p < 0.01$), fasting insulin ($p < 0.01$), HOMA-IR ($p < 0.01$), uric acid ($p < 0.05$), resting systolic blood pressure [SBP ($p < 0.05$)] and number of the risk factors ($p < 0.05$) were significantly higher and insulin sensitivity index ($p < 0.01$) and VO_2 max/LBM ($p < 0.01$) were significantly lower in the abnormal ST group than in the normal ST group. The plasma glucose levels at 90 ($p < 0.05$) and 120 min ($p < 0.01$) after oral glucose load and Σ glucose during OGTT ($p < 0.05$) were significantly higher in the abnormal ST group than in the normal ST group. The serum insulin levels at 60 ($p < 0.01$), 90 ($p < 0.05$) and 120 min ($p < 0.01$) after oral glucose load and Σ insulin during OGTT ($p < 0.01$) were also significantly higher in the abnormal ST group than in the normal ST group (**Fig. 1**). The abnormal ST group showed a significantly higher prevalence of hypertension, impaired glucose tolerance and metabolic syndrome than the normal ST group (**Fig. 2**).

For the stepwise multiple logistic regression models, first we included age, sex, smoking habit, triglyceride, fasting glucose, fasting insulin, uric acid, SBP and $\dot{V}O_2$max/LBM as variables (Model 1), then fasting glucose [odds ratio (OR): 1.050, 95% confidence interval (CI): 1.001−1.101, $p < 0.05$], fasting insulin (OR: 1.123, 95% CI: 1.009−1.250, $p < 0.05$), uric acid (OR: 1.915, 95% CI: 1.153−3.181, $p < 0.05$) and SBP (OR: 1.041, 95% CI: 1.001−1.082, $p < 0.05$) were positively and significantly associated with ST segment depres-

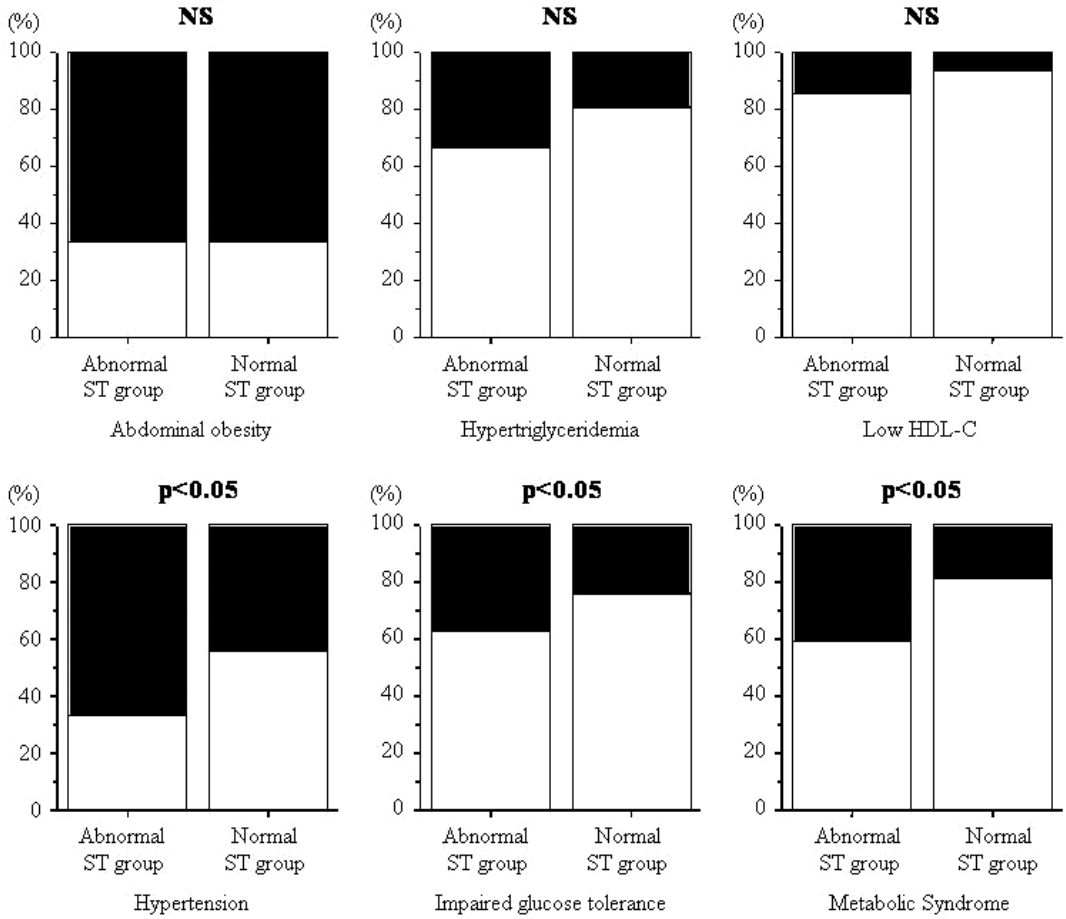

Fig. 2 Comparison of prevalence of coronary risk factors (■:abnormal, □:normal) between the normal and abnormal ST groups

Metabolic syndrome was defined according to the metabolic syndrome diagnostic criteria in Japan.[14] Abbreviation as in Table 1.

sion in exercise ECG. Next, we included Σ insulin during OGTT (Model 2), HOMA-IR (Model 3) and insulin sensitivity index (Model 4) in place of fasting insulin. In the model 2, fasting glucose (OR: 1.055, 95% CI: 1.005−1.108, $p < 0.05$), Σ insulin (OR: 1.013, 95% CI: 1.002−1.025, $p < 0.05$), uric acid (OR: 1877, 95% CI: 1.132−3.115, $p < 0.05$) and SBP (OR: 1.041, 95% CI: 1.001−1.082, $p < 0.05$) were positively and significantly associated with ST segment depression in exercise ECG. HOMA-IR (OR: 1.482, 95% CI: 1.048−2.219, $p < 0.05$) as well as uric acid (OR: 1.910, 95% CI: 1.157−3.154, $p < 0.05$) and SBP (OR: 1.041, 95% CI: 1.001−1.082, $p < 0.05$) in Model 3 and insulin sensitivity index (OR: 0.694, 95% CI: 0.497−0.968, $p < 0.05$), uric acid (OR: 1.857, 95% CI: 1.107−3.115, $p < 0.05$) and SBP (OR: 1.041, 95% CI: 1.001−1.084, $p < 0.05$) in Model 4 were positively associated with ST segment depression. In an additional model, after excluding for the indices of insulin resistance (Model 5), fasting glucose (OR: 1.045, 95% CI: 0.998−1.095, $p < 0.05$), uric acid (OR: 1.842, 95% CI: 1.131−3.001, $p < 0.05$), SBP (OR: 1.040, 95% CI: 1.001−1.080, $p < 0.05$) and $\dot{V}O_2$max/LBM (OR: 0.862, 95% CI: 0.758−0.980, $p < 0.05$) were positively and significantly associated with ST segment depression (**Table 2**). There were no significant associations regarding age, sex, smoking habit and ST segment depression at the final exercise intensities in all models.

DISCUSSION

This study was performed in a limited population of obese subjects with coronary risk factors who were recruited to participate in our exercise therapy program for intervention in their risk factors. Prior to exercise therapy, we performed the exercise stress test to evaluate myocardial ischemia. As a

Table 2 Association between exercise-induced ST segment depression and risk factors for coronary heart disease by stepwise multiple logistic regression analysis

	Model 1	Model 2	Model 3	Model 4	Model 5
Age	0.960 (0.916−1.006)	0.955 (0.912−1.003)	0.957 (0.914−1.002)	0.962 (0.918−1.009)	0.9579 (0.906−1.004)
Sex	0.379 (0.076−1.885)	0.412 (0.082−2.071)	0.373 (0.076−1.826)	0.404 (0.076−2.148)	0.358 (0.073−1.751)
Smoking habit	1.153 (0.258−5.148)	0.931 (0.210−4.119)	1.139 (0.260−4.994)	1.449 (0.301−6.975)	0.901 (0.220−3.682)
Triglyceride	1.005 (0.996−1.014)	1.005 (0.996−1.013)	1.005 (0.996−1.014)	1.004 (0.995−1.012)	1.006 (0.997−1.015)
Fasting glucose	1.050* (1.001−1.101)	1.055* (1.005−1.108)	1.036 (0.989−1.086)	1.037 (0.987−1.090)	1.045* (0.998−1.095)
Fasting insulin	1.123* (1.009−1.250)	—	—	—	—
Σ insulin	—	1.013* (1.002−1.025)	—	—	—
HOMA-IR	—	—	1.482* (1.048−2.219)	—	—
Insulin sensitivity index	—	—	—	0.694* (0.497−0.968)	—
Uric acid	1.915* (1.153−3.181)	1.877* (1.132−3.115)	1.910* (1.157−3.154)	1.857* (1.107−3.115)	1.842* (1.131−3.001)
SBP	1.041* (1.001−1.082)	1.041* (1.001−1.082)	1.041* (1.001−1.082)	1.041* (1.001−1.084)	1.040* (1.001−1.080)
$\dot{V}O_2$max/LBM	0.895 (0.784−1.022)	0.881 (0.768−1.011)	0.889 (0.779−1.013)	0.905 (0.789−1.034)	0.862* (0.758−0.980)
Number of risk factors	0.543 (0.274−1.075)	0.562 (0.286−1.105)	0.551 (0.279−1.088)	0.535 (0.270−1.060)	0.618 (0.323−1.184)

The results are shown as the odds ratio (95% confidence interval). *$p<0.05$.
Logistic regression used age, sex, smoking habit, triglyceride, fasting glucose, fasting insulin, uric acid, SBP, $\dot{V}O_2$max/LBM and number of the risk factors as continuous variables (Model 1). Other models used Σ insulin during the oral glucose tolerance test (Model 2), HOMA-IR (Model 3) and insulin sensitivity index (Model 4) instead of fasting insulin as a continuous variable. An additional model excluded the indices of insulin resistance, age, sex, smoking habit, triglyceride, fasting glucose, uric acid, SBP, $\dot{V}O_2$max/LBM and number of the risk factors as continuous variables (Model 5).
Abbreviations as in Table 1.

result, silent ST segment depression during exercise testing was observed in 27/114 patients (23.7%). The abnormal ST group showed higher fasting insulin level, Σ insulin during OGTT, HOMA-IR and lower insulin sensitivity index than the normal ST group. In addition, our multiple logistic regression analysis showed that these insulin resistance indices were more powerfully associated with ST segment depression, compared to other risk factors.

Several studies have reported an association between abnormal ST-T in the resting ECG and insulin resistance.[9−11] Marita *et al.*[9] and Sheu *et al.*[10] observed the insulin response during OGTT in hypertensive patients with abnormal ST-T to be higher than that in hypertensive patients without abnormal ST-T as well as that in normotensive subjects. Adachi *et al.*[11] also reported that the plasma insulin level was related to the incidence of ST-T abnormalities in resting ECG and that the blood pressure or other risk factors had little effect on the ST-T abnormalities. In a recent study, Gazzaruso *et al.*[18] showed an independent association of metabolic syndrome and insulin resistance with silent myocardial ischemia in patients with type 2 dia-

betes mellitus. We also observed that the abnormal ST group showed significantly higher prevalences of hypertension, impaired glucose tolerance and metabolic syndrome than the normal ST group, and our findings support the recent results from Gazzaruso *et al*. At present, the mechanisms regarding the association between exercise-induced ST segment depression and insulin resistance are not well known. Although none of our 27 patients with abnormal ST underwent coronary angiography, some of them might possibly have had occult atherosclerotic large coronary artery disease. On the other hand, abnormal glucose metabolism is considered to be associated with micro-vessel coronary artery disease,[19] which might cause ST abnormality in some patients. However, it is also possible that insulin resistance was correlated with a false-positive exercise ECG response for coronary heart disease that might in part be caused by cardiac metabolic abnormalities. In our study, final exercise intensity was above the LT in all patients. Insulin resistance or hyperinsulinemia induces an increase in plasma catecholamine concentration.[20,21] The plasma catecholamine concentration increased exponentially above the LT during the exercise test, and the plasma catecholamine threshold was significantly correlated to LT.[22] Insulin resistance or hyperinsulinemia promotes the release of plasma endothelin levels from vascular smooth muscle cells.[23] Plasma endothelin levels increase during exercise, due to an increased exercise intensity.[24] In addition, insulin is thought to promote the proliferation of cardiac myocytes.[25] Therefore, the association between ST segment depression in exercise ECG and insulin resistance might be caused by a sympathetic nervous system activity above the LT or cardiac hypertrophy.

In our data, not only the insulin resistance indices, but also other risk factors were related to exercise-induced ST segment depression. The ST segment depression was also correlated with fasting glucose, SBP, uric acid and $\dot{V}O_2$max/LBM after excluding for the indices of insulin resistance. Associations between ST segment depression and plasma glucose and blood pressure[9–11] level have been reported. Katzel *et al*.[26] observed that exercise-induced silent myocardial ischemia, and lower $\dot{V}O_2$max levels and sedentary lifestyle were independent predictors of cardiac events in healthy, sedentary, obese, middle-aged and older men. Our results might support the findings of these studies. There have been several reports indicating an association between ST segment depression and uric acid. Adachi *et al*.[11] reported that subjects with abnormal ST-T in resting ECG showed significantly higher levels of uric acid than subjects with normal ST-T. Uric acid might be an independent risk factor for cardiovascular disease.[27,28] The mechanism regarding the relationship between exercise-induced ST segment depression and uric acid might be related to the fact that increased sympathetic nervous system activity induces decreased uric acid excretion.[29] Increased risk factors for cardiovascular disease and decreased vasodilator action, *i.e*. decreased vascular nitric oxide production and nitric oxide activity,[30] are correlated with uric acid elevation. As a result, not only insulin resistance, but other factors such as hyperglycemia, hyperuricemia, hypertension and lower aerobic capacity may also be involved in the pathological ST depression during exercise.

Study limitation and clinical implication

There are several limitations in this study. First, our limited study population combined small numbers of subjects and middle-aged females predominanted. Second, our evaluation of ST segment depression was performed using only the CM_5-lead. Third, the presence of myocardial ischemia, left ventricular hypertrophy and mitral valve prolapse, abnormality in wall motion, wall thickness and valvular activity, which also affect exercise-induced ST segment depression, could not be determined in the 27 patients with ST segment depression. Modalities such as coronary angiography, nuclear myocardial perfusion imaging or echocardiography are needed. Finally, insulin sensitivity index was evaluated by a less sensitive method than the euglycemic hyperinsulinemic clamp and minimal model technique. However, Mark *et al*.[31] reported that silent ST segment depression during exercise alone could predict the long term prognosis. Therefore, our findings of the linkage between insulin resistance and exercise-induced ST segment depression may support the hypothesis that insulin resistance leads to future cardiovascular events.

There have been several studies[32] on the effect of exercise therapy for improving insulin resistance. However, whether exercise therapy improves the exercise-induced ST segment depression in association with the reduction in serum insulin levels remains unknown, so further research is required.

Since exercise-induced ST segment depression is a predictor of long term prognosis, evaluation should be recommended prior to exercise therapy in obese subjects with insulin resistance.

CONCLUSIONS

These results suggest that insulin resistance may involve the pathological ST depression during exercise, as well as with the previously reported factors such as hyperglycemia, hyperuricemia, hypertension and lower aerobic capacity.

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要　約

肥満者の運動負荷心電図ST下降とインスリン抵抗性との関係

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目　的: インスリン抵抗性は虚血性心疾患の独立した危険因子であり，安静時心電図ST低下の発症とも関与することが報告されている．しかし，運動負荷心電図ST下降とインスリン抵抗性との関係については明らかにされていない．本研究では肥満者を対象に運動負荷心電図ST下降とインスリン抵抗性との関係について検討した．

方　法: 冠危険因子を有する肥満者114例（男性39例，女性75例，平均年齢50.9±12.2歳，平均体格指数 28.6±3.1 kg/m^2）を対象に，自転車エルゴメーターを用いて4分ごとに5−10 W漸増する最大下多段階運動負荷試験を施行した．心電図はCM_5誘導により安静時より運動終了後まで連続して記録した．

結　果: 最大運動負荷時にST下降が認められた群（ST下降群）は，中性脂肪，インスリン抵抗性指数（HOMA-IR），血清尿酸値，収縮期血圧，空腹時ならびに糖負荷試験（OGTT）中の血糖，インスリンの各値がST下降のなかった群（正常 ST群）に比べて有意に高かった．また，ST下降群は，インスリン感受性指数，最大酸素摂取量（$\dot{V}O_2max$）が正常ST群に比べて有意に低かった．ロジスティック回帰分析を用い，年齢，性別，喫煙習慣，中性脂肪，血清尿酸値，収縮期血圧，$\dot{V}O_2max$，空腹時血糖，空腹時インスリンを連続変数としてST下降に対する相対危険度を検討したところ，空腹時インスリンはST下降と有意に相関し，HOMA-IR，Σインスリン，インスリン感受性指数を空腹時インスリンの代わりとした場合も同様に相関が認められた．また，インスリンの影響を除外してST下降に対する相対危険度を検討したところ，空腹時血糖，収縮期血圧，血清尿酸値，$\dot{V}O_2max$に有意な相関関係を認めた．

結　論: インスリン抵抗性はST下降の発症に関与し，運動負荷心電図ST下降の予測因子である可能性が示唆された．

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