Relationships of the Systolic Blood Pressure Response During Exercise With Insulin Resistance, Obesity, and Endurance Fitness in Men With Type 2 Diabetes Mellitus

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The purpose of the present study was to investigate the relationships among the resting systolic (SBP) and diastolic blood pressure (DBP) or SBP response during exercise with insulin resistance evaluated by a homeostasis model (HOMA-IR), abdominal fat accumulation (visceral fat area [VFA], subcutaneous fat area [SFA]) by computed tomography (CT), and an estimation of the maximal oxygen uptake ($\dot{V}O_2$max) in 63 Japanese middle-aged male patients with type 2 diabetes mellitus (type 2 DM). Body mass index (BMI) and waist-to-hip ratio (WHR) in type 2 DM subjects were significantly higher than in age-matched healthy male control subjects (n = 135) with normal glucose tolerance. Resting SBP (127.7 ± 16.2 mm Hg *v* 119.4 ± 13.0 mm Hg) and DBP (82.2 ± 11.9mmHg *v* 76.8 ± 9.4 mm Hg) levels, and the percentage of hypertension (20.6% *v* 1.5%) in type 2 DM subjects were significantly higher than in the control subjects ($P < .05$). According to a multiple regression analysis for resting blood pressure in type 2 DM, VFA was found to be an independent predictor of SBP, while $\dot{V}O_2$max and HOMA-IR were independent predictors of DBP. In the controls, however, HOMA-IR was not found to be a significantly independent predictor for either resting SBP or resting DBP. Measurement of the SBP response during graded exercise using a ramp test was performed by an electrical braked cycle ergometer in 54 patients with type 2 DM only. The SBP was measured at 15-second intervals during exercise. The exercise intensity at the double product breaking point (DPBP), which strongly correlated with the exercise intensity at the lactate threshold, was used as an index for the SBP response to standardized exercise intensity. The SBP corresponding to exercise intensity at DPBP (SBP@DPBP) was evaluated as an index of the SBP response to standardized exercise intensity. The change in SBP (ΔSBP = SBP@DPBP − resting SBP) was significantly and positively associated with log area under the curve for glucose (log AUCPG) during a 75-g oral glucose tolerance test (OGTT). In addition, ΔSBP significantly and negatively correlated with the log area under the curve for insulin (log AUCIRI) and log AUCIRI/log AUCPG. Based on these results, insulin resistance was suggested to be independently associated with the resting DBP and SBP response to standardized exercise intensity in type 2 DM patients.

IT HAS BEEN postulated that insulin resistance or hyperinsulinemia might be an etiologic cause of hypertension.[1,2] Obese patients, especially those with visceral fat obesity, and patients with type 2 diabetes mellitus (type 2 DM) frequently demonstrate hypertension.[3] In animal studies, spontaneously hypertensive rats have been reported to have more insulin resistance and/or hyperinsulinemia.[4] However, a few reports have suggested that such insulin action as an etiologic cause of hypertension may be independent of factors such as obesity and glucose intolerance. For example, Modan et al[5] demonstrated significantly higher glucose and insulin responses to a 75-g oral glucose tolerance test (OGTT) in obese hypertensives compared with obese normotensives. In addition, DeFronzo and Ferrannini[6] reported that insulin sensitivity, as evaluated by a hyperinsulinemic eugycemic clamp, in essential hypertension patients was significantly lower than in normotensive controls after matching for age and sex, and independent of obesity and glucose intolerance.

Several cross-sectional studies observed a good correlation between physical activity or endurance fitness (ie, maximal oxygen uptake [$\dot{V}O_2$max]) and resting blood pressure in healthy men and women.[7] In addition, several prospective epidemiologic studies in normotensive subjects have demonstrated that an exaggerated blood pressure response to a given and relative exercise intensity[8-11] and a lower quintile of the $\dot{V}O_2$max or endurance capacity[12] are good predictors for developing hypertension. Aerobic exercise is recommended to be a useful antihypertensive treatment for hypertensive patients with and without obesity,[13] and aerobic exercise training results in a reduction of the blood pressure response to a given and relative exercise intensity.[14] The resting blood pressure level in hypertensive patients has also been shown to be significantly reduced by exercise therapy, independent of weight loss.[15]

However, there have been few reports concerning the contribution of insulin resistance or hyperinsulinemia on blood pressure at rest and during exercise in type 2 DM subjects, who have insulin resistance as a pathophysiologic condition. Based on the aforementioned evidence, we investigated the relationships between resting blood pressure or blood pressure response during exercise to insulin resistance, obesity indices, and endurance fitness in Japanese male patients with type 2 DM who had not yet been treated with any intervention therapy for diabetes mellitus.

MATERIALS AND METHODS

Subjects

Age-matched Japanese male patients with type 2 DM (n = 63; 49.3 ± 8.6 years) and control subjects with normal glucose tolerance (n = 135; 48.4 ± 5.4 years) were selected for this study. Type 2 DM was classified based on the criteria of the Japan Diabetes Society

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(1999) and was defined as a fasting glucose level ≥ 126 mg/dL and/or 2-hour glucose level ≥ 200 mg/dL. None of the patients had been taking any medication or receiving any intervention therapy such as exercise or diet before participating in the present study. No subject had a history of microalbuminuria. The duration of diabetes mellitus was relatively short, ranging from 2 months to 2 years. The control subjects were apparently healthy male employees working at a food company located in southwestern Japan. Among this group, any subjects taking medications that might affect their lipid and glucose metabolism or resting blood pressure, as well as subjects with a fasting blood glucose greater than 120 mg/dL, were excluded.[16] All experiments and procedures were approved by the Ethics Committee in the Institute of Health Science, Kyushu University. We obtained informed consent from all participants.

Obesity Indices

The anthropometric parameters of shoeless subjects wearing light clothing in an upright position were measured by the same researcher. Body mass index (BMI) was calculated as weight (in kilograms) divided by height (in meters) squared. Skinfold thickness was measured by Harpenden caliper to calculate the percentage of body fat (%Fat) using the formula described by Brozek and Henschel[17] after estimating body density according to Nagamine and Suzuki.[18] The waist-to-hip ratio (WHR) was used as an index of abdominal fat distribution. Waist circumference was measured at the narrowest point between the rib cage and the iliac crest, and hip circumference was measured at the level of the greater trochanter. In addition to these obesity indices, abdominal fat accumulation at the level of umblicus was measured by computed tomography (CT) scan, and visceral fat area (VFA) and subcutaneous fat area (SFA) were calculated in the type 2 DM patients only. Ordinary CT parameters were used, specifically 120 kV and 200 mA, and a slice thickness of 5 mm, scanning time of 2 seconds, and field of view of 400 mm. Briefly, a region of interest of the subcutaneous fat layer was defined by tracing its contour on each scan, and the attenuation range of the CT numbers (in Hounsfiled units) for fat tissue was calculated. A histogram for fat tissue was computed based on the mean attenuation ± 2 SD. Total and intraperitoneal tissue with attenuation within the mean ± 2 SD were considered to be the total fat area and VFA. The SFA was calculated by subtracting the VFA from the total fat area.

Estimated Maximal Oxygen Uptake

To evaluate the level of endurance fitness, $\dot{V}O_2$max was calculated by an indirect method using a cycle ergometer.[19]

Blood Pressure Measurement at Rest and During Exercise

The resting systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured indirectly using a mercury sphygmomanometer placed on the right arm of the seated participant after at least 30 minutes of rest in both the type 2 DM and the control groups. The SBP response to a linear-graded exercise test using a ramp test was measured by an electrical braked cycle ergometer (Examiner Type 400, Lode Co, Groningen, Netherlands) in the type 2 DM group only (n = 54). The work rate was initially set a 0 W and then was increased every 1 minute by 15 W, while cycling at 60 rpm. The test was stopped when the subject reached a relative perceived exertion score of 15 (hard). Inspired and expired gases were analyzed by a computerized on-line breath-by-breath system (System RM-300i, Minato Medical Science, Osaka, Japan). Oxygen uptake ($\dot{V}O_2$) was automatically and continuously measured every 30 seconds using a mass spectrometer (WSMR-1400, Westron, Chiba, Japan) for O_2 and CO_2 fractions. Inspiratory and expiratory flow rates were measured by a hot-wire flowmeter. SBP and heart rate (HR) were measured using a modified automated blood pressure and HR monitor (CM-4001, Kyokko Bussan, Tokyo, Japan) during exercise. The cuff-pressure decreased to 0 mm Hg immediately after determining the SBP and began to increase at 5-second intervals. The double product, which is defined as an indirect indicator of the myocardial oxygen demand, was calculated almost every 15 seconds from the SBP and the HR corresponding to the time when the SBP was measured. These measurements were done automatically and the data were displayed on the monitor during exercise using a personal computer (NEC PC9801, Tokyo, Japan). The exercise intensity at the double product breaking point (DPBP), which was strongly correlated with the exercise intensity at the lactate threshold,[20] was used as an index for the SBP response to standardized exercise intensity. Tanaka et al[20] reported that the test-retest mean difference in DPBP with CM-4001 was not statistically significant, and that the correlation coefficient between 2 tests was 0.95 ($P < .05$). The SBP corresponding to the exercise intensity at BPDP (SBP@DPBP) was evaluated. The change in SBP (ΔSBP) was calculated as SBP@DPBP − resting SBP. The test was continued until DPBP was detected by 2 researchers. This exercise test was not performed on the control subjects.

Oral Glucose Tolerance Test

Blood samples were drawn from an antecubital vein after a 12-hour fast to determine the fasting plasma glucose (FPG) and fasting insulin (FIRI). Thereafter, a 75-g OGTT was conducted in type 2 DM patients only and analyzed for plasma glucose and insulin. Blood samples were taken at 0, 30, 60, 90, and 120 minutes. Plasma glucose and insulin were measured by an enzymatic method and by radioimmunoassay using an IRI Kit (Pharmacia, Uppsala, Sweden), respectively. The plasma glucose area under the curve (AUCPG) and insulin area under the curve (AUCIRI) were calculated by the trapezoidal rule using absolute values. Insulin resistance (HOMA-IR) was evaluated using a homeostasis model (HOMA)[21] based on the following formula: FIRI(μU/mL) × FPG (mmol/mL)/22.5. A significant correlation has been reported between HOMA-IR and insulin sensitivity evaluated by hyperinsulinemic euglycemic glucose clamp in Japanese patients with type 2 DM with fasting blood glucose levels ranging from 80 to 170 mg/dL.[22] These results have also been reproduced by another group of Japanese researchers using similar samples of Japanese patients with type 2 DM.[23,24]

Statistical Analysis

Results were expressed as the mean ± SD. Linear correlation and stepwise multiple regression analyses were used for statistical analysis using the StatView software package. Because FIRI, AUCPG, and AUCIRI were not normally distributed, log-transformed values were used. After log transformation, FIRI, AUCPG, and AUCIRI were normally distributed. A probability value of less than .05 was considered to indicate statistical significance.

RESULTS

Table 1 shows the physical characteristics in both groups. Both the BMI and WHR were significantly higher in the type 2 DM group than in the control group. Resting SBP (127.7 ± 16.2 mm Hg *v* 119.4 ± 13.0 mm Hg) and DBP (82.2 ± 11.9 mm Hg *v* 76.8 ±9.4 mm Hg) were significantly higher in the type 2 DM group than in the control group. The percentages of hypertension evaluated by World Health Organization (WHO) criteria in the type 2 DM and control groups were 20.6% (n = 13) and 1.5% (n = 2), respectively ($P < .05$). No difference between the groups was observed in $\dot{V}O_2$max.

Table 2 shows the simple correlation coefficients in the control and type 2 DM groups. In the type 2 DM group, the

Table 1. Physical Characteristics of the Control and Type 2 DM Groups

	Control (n = 135)	Type 2 DM (n = 63)
Age (yr)	48.4 ± 5.4	49.3 ± 8.6
BMI (kg/m^2)	23.0 ± 2.3	25.3 ± 3.9*
WHR	0.87 ± 0.05	0.95 ± 0.05*
%Fat (%)	19.0 ± 6.3	20.3 ± 5.7
SFA (cm^2)	—	137.2 ± 66.6
VFA (cm^2)	—	167.3 ± 61.0
$\dot{V}O_2$max (mL/kg/min)	34.5 ± 4.2	34.1 ± 4.9
SBP (mm Hg)	119.4 ± 13.0	127.7 ± 16.2*
DBP (mm Hg)	76.8 ± 9.4	82.2 ± 11.9*
Hypertension (%)	1.5% (n = 2)	20.6% (n = 13)*
FPG (mg/dL)	89.1 ± 7.6	156.4 ± 36.6*
FIRI (μU/mL)	4.9 ± 2.5	7.6 ± 6.2*
HOMA-IR†	1.1 ± 0.6	3.0 ± 2.8*
Insulinogenic index‡	—	0.13 ± 0.14
AUCPG(mg/dL/h)	—	748.7 ± 163.9
AUCIRI (μU/mL/h)	—	79.5 ± 57.3

Abbreviations: BMI, body mass index; WHR, waist-to-hip ratio; % Fat, percentage of body fat; SFA, subcutaneous fat area; VFA, visceral fat area; $\dot{V}O_2$max, maximal oxygen uptake; SBP, systolic blood pressure; DBP, diastolic blood pressure, FPG; fasting plasma glucose, FIRI; fasting insulin level, AUCPG; area under the curve for plasma glucose; AUCIRI, area under the curve for plasma insulin.

*$P < .05$.

†HOMA-IR = FIRI (μU/mL) × FPG (mmol)/22.5.

‡Insulinogenic index = (IRI at 30 min - FIRI)/(PG at 30 min - FPG).

resting SBP level was significantly and positively associated with BMI, VFA, and log FIRI, and negatively with $\dot{V}O_2$max. Resting DBP was significantly and positively associated with BMI, %fat, VFA, SFA, log FIRI, log AUCIRI, and HOMA-IR, and negatively with $\dot{V}O_2$max. In the control group, resting SBP was significantly and positively correlated with age, BMI, WHR, log FIRI, and HOMA-IR, and negatively with $\dot{V}O_2$max. Resting DBP was significantly and positively correlated with BMI and WHR, and negatively with $\dot{V}O_2$max.

Table 3 shows the results of stepwise multiple linear regression analyses with resting SBP and DBP as dependent variables. All regression models included the following factors as potential independent variables; BMI, %fat, VFA, SFA, $\dot{V}O_2$max, HOMA-IR, and AUCIRI in the type 2 DM group, and age, BMI, WHR, $\dot{V}O_2$max, and HOMA-IR in the control group. In addition to these independent variables, model A included FIRI and model B included HOMA-IR. In the type 2 DM group, VFA was a significant independent variable of resting SBP in both models. Resting DBP was independently associated with $\dot{V}O_2$max and HOMA-IR. In the control group, however, insulin resistance was not associated with resting DBP. Age and BMI were independent predictors of resting SBP, and BMI was an independent predictor of resting DBP.

Table 3. Results of Stepwise Multiple Regression Analysis for the Resting SBP and DBP as Dependent Variables in the Control and Type 2 DM Groups

Dependent Variables	Independent Variables	β†	R^2 for the Model
Control (n = 135)			
SBP	Age	0.22	0.08*
	BMI	0.22	
DBP	BMI	0.28	0.07*
Type 2 DM (n = 63)			
SBP	VFA	0.46	0.19*
DBP	$\dot{V}O_2$max	−0.41	0.31*
	HOMA-IR	0.27	

*$P < .05$.

*β: Regression coefficient. In the control group, the regression models included the following variables as potential independent variables : age, BMI, WHR, $\dot{V}O_2$max, and HOMA-IR. In type 2 DM group, the regression models included the following variables as potential independent variables: BMI, %fat, VFA, SFA, $\dot{V}O_2$max, HOMA-IR, and AUCIRI.

Table 4 lists some physical characteristics and physiologic parameters corresponding to the exercise intensity at DPBP in the type 2 DM group (n = 54). SBP corresponding to the exercise intensity at DPBP was 148.4 ± 22.8 mm Hg.

Table 5 shows the ΔSBP to be significantly and positively associated with log AUCPG and negatively with log AUCIRI and log AUCIRI/AUCPG (Fig 1). On the other hand, age, obesity indices, $\dot{V}O_2$max, and resting SBP were not associated with ΔSBP.

DISCUSSION

We demonstrated a significant correlation between insulin resistance and resting DBP in the type 2 DM group only. In addition, ΔSBP was significantly and positively associated with log AUCPG as an index for glucose intolerance, while it was negatively associated with log AUCIRI and log AUCIRI/AUCPG as an indirect index for insulin sensitivity in the type 2 DM group.

Recently, several studies[25] reported the contribution of insulin resistance or hyperinsulinemia to be one of the etiologic

Table 2. Simple Correlation Coefficients in the Control and Type 2 DM Groups

	Age	BMI	%Fat	WHR	$\dot{V}O_2$max	Log FIRI†	HOMA-IR	VFA	SFA	Insulinogenic Index	Log AUCIRI
Control (n = 135)											
SBP	0.22*	0.22*	0.10	0.21*	−0.18*	0.18*	0.19*				
DBP	0.12	0.28*	0.17	0.22*	−0.20*	0.13	0.14				
Type 2 DM (n = 63)											
SBP	0.18	0.34*	0.24	0.12	−0.33*	0.28*	0.24	0.46*	0.22	0.10	0.22
DBP	−0.09	0.49*	0.41*	0.21	−0.51*	0.42*	0.44*	0.51*	0.40*	0.18	0.26*

*$P < .05$.

†Log-transformed for statistical testing.

Table 4. Physical Characteristics of the Type 2 DM Group (n = 54)

	Type 2 DM Group (n = 54)
Age (yr)	50.7 ± 10.6
Weight (kg)	70.5 ± 13.4
Height (cm)	166.8 ± 6.9
BMI (kg/m^2)	25.3 ± 4.2
WHR	0.9 ± 0.5
%Fat	19.7 ± 5.8
SFA (cm^2)	138.6 ± 70.7
VFA (cm^2)	167.8 ± 65.9
$\dot{V}O_2$max (mL/kg/min)	34.1 ± 5.2
SBD (mm Hg)	127.3 ± 16.6
DBP (mm Hg)	81.5 ± 11.9
$\dot{V}O_2$ at DPBP (mL/kg/min)	11.7 ± 3.3
SBP at DPPP (mm Hg)	148.4 ± 22.8
Hypertension (%)	18.9% (n = 10)
Δ SBP (mm Hg)	26.9 ± 18.0
FPG (mg/dL)	152.6 ± 36.8
FIRI (μU/ml)	7.8 ± 6.6
HOMA-IR	3.0 ± 2.9
Insulinogenic index	0.15 ± 0.17
AUCPG (mg/dL/h)	1122.2 ± 708.5
AUCIRI (μU/mL/h)	85.9 ± 62.8
AUCIRI/AUCPG	0.11 ± 0.12

Abbreviation: Δ SBP, changes from resting SBP to SBP at DPBP.

causes of resting hypertension. However, cause and effect between both variables is still unknown. There have been conflicting findings concerning the resting blood pressure and fasting insulin level or insulin sensitivity.[26-30] The fasting insulin level was more closely correlated with the resting DBP than with the resting SBP.[26,27] Other studies[28-30] did not show any correlation between the fasting insulin level and either resting SBP or resting DBP. We demonstrated that resting DBP in the type 2 DM group was significantly and negatively associated with $\dot{V}O_2$max, while it was positively associated with the index of insulin resistance.

The mechanism for the underlying link between resting DBP and insulin resistance or hyperinsulinemia has been proposed and partially demonstrated in several studies.[25] However, the mechanism mediating the vosodilator action of insulin remains obscure at present. There is evidence for and against both systematic and local mechanisms.[25] The systematic mechanism includes sympathetic neural vasodilation and a humoral vasodilator substance such as epinephrine and insulin in the absence of increased circulating epinephrine levels. The potential local mechanism included a β-adrenergic mechanism, endothelium-dependent relaxation, stimulation of the sodium/potassium pump with hyperpolarization of vascular muscle, increased calcium-adenosine triphosphatase (Ca-ATPase) activity, and metabolic vasodilation secondary to increased skeletal muscle oxygen consumption.[6,25] However, the evidence for both vasodilator mechanisms of insulin is conflicting.

Aoyama et al[31] reported that hyperinsulinemia as evaluated by the insulin level 2 hours after a 75-g OGTT was one of the independent predictors of resting SBP in Japanese middle-aged men including normal healthy controls as well as subjects with impaired glucose tolerance or type 2 DM. In contrast, we found that the HOMA-IR was one of the independent predictors of resting DBP. On the other hand, resting SBP in the type 2 DM group was independently associated with VFA, but not with insulin resistance or hyperinsulinemia.

In this study, we demonstrated that resting DBP in the type 2 DM group was significantly and negatively associated with $\dot{V}O_2$max and positively with insulin resistance. In this context, Dengel et al[32] reported the independent and combined effects of weight loss and aerobic exercise on resting blood pressure and oral glucose tolerance in older men with obesity. They demonstrated that aerobic exercise and weight loss were affective nonpharmacologic therapies to lower blood pressure and alter glucose and insulin responses to an oral glucose challenge. In addition, they found that the best predictor of changes in SBP, DBP, and mean blood pressure after treatment is the change in fasting blood glucose. Several studies[7,13,15,33] have reported an improvement in insulin resistance or glucose intolerance, and in resting blood pressure after exercise therapy in healthy subjects and patients with hypertension and diabetes mellitus with and without obesity. However, few studies have reported a link between the changes in insulin resistance and resting blood pressure. Although our research design was a cross-sectional study, our findings suggested that insulin resistance and endurance fitness were good predictors of resting DBP in type 2 DM. Further study is needed to clarify the effect of insulin resistance on the improvement of resting blood pressure in type 2 DM.

In addition to the correlation between resting DBP and insulin resistance, a significant correlation was observed between ΔSBP and insulin resistance in type 2 DM. A few studies[34,35] were reported concerning the link between blood pressure response during exercise and some risk factors for atherosclerosis. Prud'homme et al[34] demonstrated for the first time in premenopausal obese women that the SBP response to exercise intensity at 55% of an individual's $\dot{V}O_2$max was independently associated with total cholesterol, low-density lipoprotein apoprotein B, and apoprotein B, but not with fasting insulin. Recently, Brett et al[35] demonstrated that changes in DBP during gentle exercise are strongly associated with total

Table 5. Simple Correlation Coefficients in Type 2 DM Group (n = 54)

	Age	BMI	%Fat	WHR	VFA	SFA	$\dot{V}O_2$max
Δ SBP	0.007	−0.205	−0.171	0.025	0.160	−0.232	0.271
	SBP	FPG	Log FIRI	HOMA-IR	Log AUCPG	Log AUCIRI	Log AUCIRI/AUCPG
Δ SBP	−0.147	0.157	−0.241	−0.193	0.303*	−0.296*	−0.380*

*$P < .05$

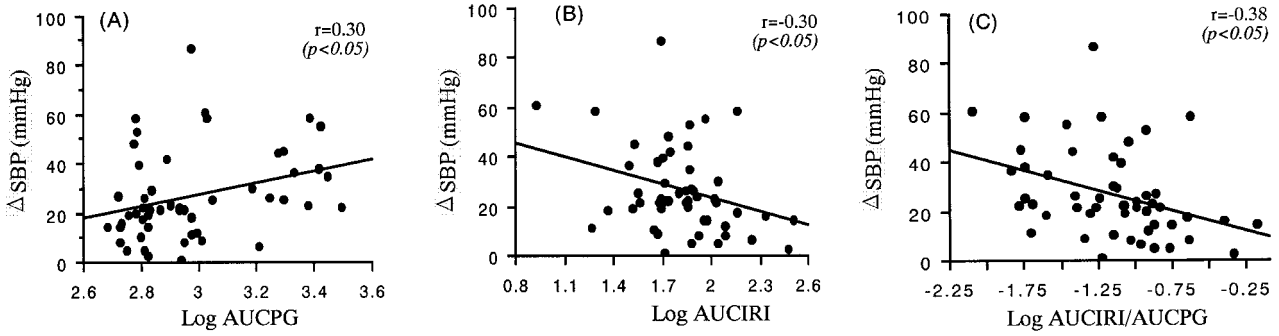

Fig 1. Relationship of SBP response to standardized exercise intensity (ΔSBP) with (A) log AUCPG, (B) log AUCIRI, and (C) log AURPG/AUCIRI.

cholesterol and insulin resistance estimated by homeostasis model assessment in healthy active men. In addition, they reported that the type 2 DM group had a significantly greater DBP response to a given exercise intensity than the healthy controls. However, they did not use the standard exercise intensity for evaluating the blood pressure response during exercise.

Our results indicate the possibility of the increased exercise SBP in type 2 DM patients who have insulin resistance. The SBP response to standardized exercise intensity (ΔSBP) was significantly and positively associated with log AUCPG and negatively with log AUCIRI and log AUCIRI/AUCPG. This phenomenon suggested a significant association between insulin resistance and the blood pressure response to exercise. However, data concerning the contribution of insulin resistance to the blood pressure response to exercise are still limited.

The mechanism underlying the significant correlation between exercising SBP and insulin resistance is still unknown. As mentioned earlier, however, aerobic exercise training induced a reduction in the resting blood pressure and the blood pressure response to a given and relative exercise intensity.[13] Several prospective epidemiologic studies in normotensive subjects have demonstrated that an exaggerated blood pressure response to a given and relative exercise intensity[8-11] and a lower quintile of $\dot{V}O_2$max or endurance capacity[12] are good predictors for developing hypertension in the future. There are numerous reports[33] on the effect of exercise training for improving insulin resistance. However, there have been no studies on the relationship between an improvement in insulin resistance and the blood pressure response to exercise. Therefore, further research is needed to investigate the effect of exercise training on the relationship between the improvement in blood pressure upon exercise and the change in either insulin resistance or insulin action in patients with type 2 DM.

In summary, our findings suggest that insulin resistance was independently and significantly associated with the resting blood pressure and SBP response to standardized exercise intensity in type 2 DM patients.

REFERENCES

1. Reaven GM: Role of insulin resistance in human disease. Diabetes 37:1595-1607, 1988

2. Ferrannini P, Weidmann P: Insulin, insulin sensitivity and hypertension. J Hypertens 8:491-500, 1990

3. Matsuzawa Y, Shimomura I, Nakamura T, et al: Pathphysiology and pathogenesis of visceral fat obesity. Ann NY Acad Sci 676:270-278, 1993

4. Hulman S, Falker B, Freyvogal N: Insulin sensitivity in the conscious spontaneously hypertensive rat; euglycemic hyperinsulinemic clamp study. Metabolism 42:14-18, 1993

5. Modan M, Halkin H, Almog S, et al: Hyperinsulinemia; a link between hypertension, obesity and glucose tolerance. J Clin Invest 75:809-817, 1985

6. DeFronzo RA, Ferrannini E: Insulin resistance; a multiple syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and cardiovascular disease. Diabetes Care 14:174-194, 1991

7. Fagard RH: Habitual physical activity, training, and blood pressure in normo- and hypertension. Int J Sports Med 6:57-67, 1985

8. Dlin RA, Hanne N, Silverberg D, et al: Follow-up of normotensive men with exaggerated blood pressure response to exercise. Am Heart J 106:316-320, 1983

9. Benbassat J, Froom P: Blood pressure response to exercise as a predictor of hypertension. Arch Intern Med 146:2053-2055, 1986

10. Jacson AS, Squires WG, Grimes G, et al: Prediction of future resting hypertension from exercise blood pressure. J Card Rehab 3:263-268, 1983

11. Mundal R, Kjldsen SE, Sandvik L, et al: Exercise blood pressure predicts cardiovascular mortality in middle-aged men. Hypertension 24:56-62, 1994

12. Blair SN, Goodyear NN, Gibbons LW, et al: Physical fitness and incidence of hypertension in healthy normotensive men and women. JAMA 252:487-490, 1984

13. Arakawa K: Antihypertensive mechanism of exercise. J Hypertens 11:223-229.1993

14. Fagard RH: Physical fitness and blood pressure. J Hypertens 11:S47-S52, 1993 (suppl 5)

15. Aroll B, Beaglehole R: Does physical activity lower blood pressure; critical review of the clinical trials. J Clin Epidemiol 45:439-447, 1992

16. Shono N, Kumagai S, Higaki Y, et al: The relationships of testosterone, estradiol, dehydroepiandrosterone-sulfate and sex hormone-binding globulin to lipid and glucose metabolism in healthy men. J Atheroscler Thromb 3:45-51, 1996

17. Brozek J, Henschel A: Techniques for Measuring Body Composition. Washington, DC, National Academy of Science-National Research Council, 1961, p 300

18. Nagamine S, Suzuki S: Anthropometry and body composition of Japanese young men and women. Hum Biol 36:473-476, 1964

19. Astrand PO, Rhyming I: A nomogram for calculation of aerobic capacity (physical fitness) from pulse rate during submaximal work. J Appl Physiol 7:218-221, 1954

20. Tanaka H, Kiyonaga A, Terao Y, et al: Double product response is accelerated above the lactate threshold. Med Sci Sports Exerc 29: 503-508, 1997

21. Matthews DR, Hosker JP, Rudenski AS, et al: Homeostasis model assessment: Insulin resistance and β-cell function from fasting plasma glucose and insulin concentration in man. Diabetologia 28:412 419, 1985

22. Ono T, Shiga N, Tanabe Y, et al: The fasting-plasma glucose range in which insulin resistance measured by homeostasis model assessment correlates with euglycemic clamping. J Japan Diab Soc 42:1005-1011, 1999

23. Ikeda Y, Suehiro T, Nakamura T, et al: Clinical significance of the insulin resistance index as assessed by homeostasis model assessment. Endocrine J 48:81-86, 2001

24. Katsuki A, Sumida Y, Gabazza EC, et al: Homeostasis model assessment is a reliable indicator of insulin resistance during follow-up of patients with type 2 diabetes. Diabetes Care 24:362-365, 2001

25. Anderson E, Mark A: The vasodilator action of insulin: implications for the insulin hypothesis of hypertension. Hypertension 21: 136-141, 1993

26. Ferrannini E, Haffner SM, Stern MP, et al: High blood pressure and insulin resistance: Influence of ethnic background. Eur J Clin Invest 21:280-287, 1991

27. Every NR, Marshall JA, Byoko EJ, et al: Blood pressure, insulin and C-peptide level in San Lui Valley, Colorado. Diabetes Care 16: 1543-1550, 1993

28. Muller DC, Elahi D, Pratley RE, et al: An epidemiological test of the hyperinsulinemia-hypertension hypothesis. J Clin Endocrinol Metab 76:544-548, 1993

29. Mykkanen L, Haffner SM, Ronnemaa T, et al: Relationship of plasma insulin concentration and insulin sensitivity to blood pressure. J Hypertens 14:399-405, 1994

30. Isfan NW, Olaisted CS, Bristrian BR, et al: Insulin resistance and insulin secretion in the hypertension of obesity. Hypertension 19:385-392, 1992

31. Aoyama S., Saitoh S, Takagi S, et al: Epidemiological study on the relationship between hyperinsulinemia and cardiovascular risk factors—Tanno-Sobetsu study. J Japan Diab Soc 42:495-502, 1999

32. Dengel DR, Galecki AT, Hagberg JM, et al: The independent and combined effects of weight loss and aerobic exercise on resting blood and oral glucose tolerance in older men. Am J Hypertens 11: 1405-1412, 1998

33. Goodyear L, Kahn BB: Exercise, glucose transport, and insulin sensitivity. Ann Rev Med 49:235-261, 1998

34. Prud'homme D, Despres J-P, Lanadry J-F, et al: Systolic blood pressure during submaximal exercise: an important correlate of cardiovascular disease risk factors in normotensive obese women. Metabolism 43:18-23, 1994

35. Brett SE, Ritter JM, Choweinczyk PJ: Diastolic blood pressure changes during exercise positively correlate with serum cholesterol and insulin resistance. Circulation 101:611-615,2000