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The Correlation between Insulin Resistance and the Visceral Fat to Skeletal Muscle Ratio in Middle-aged Women

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Central obesity with visceral fat accumulation and the amount of skeletal muscle mass may influence insulin sensitivity via its capacity for glucose load uptake. We investigated the relationships among the following metabolic variables: ratio of fat area to skeletal muscle area (VMR), percent ideal body weight, body mass index, waist-to-hip circumference (WHR) and visceral fat to subcutaneous fat ratio (VSR) in 114 nondiabetic middle-aged women. Anthropometric parameters, lipid profiles and sex hormone- binding globulin were measured. Visceral and subcutaneous fat areas at the umbilical level and the skeletal muscle area at the mid-thigh level were measured and computed. 75-gram OGTT tests were performed, along with measuring plasma glucose, insulin and free fatty acid levels, according to which area under the curve of glucose (Glu-AUC), insulin (Ins-AUC), free fatty acid (FFA-AUC) and glucose/insulin ratio (GIR=Glu-AUC/Ins-AUC), were calculated. 1) Triglyceride was more correlated with VSR than VMR. 2) The independent anthropometric parameters for each metabolic variable were In conclusion, VMR for Ins-AUC, WHR for Glu-AUC and total cholesterol, and VSR for triglyceride. 3) For subjects with higher VMR, age, Ins-AUC and triglyceride were significantly higher. 4) Subjects with higher VMR were older and showed higher Ins-AUC and lower GIR than the subjects with lower VMR. In conclusion, VMR is an anthropometric parameter that reflects insulin resistance concerning glucose metabolism, and VSR is thought to be a good parameter that that reflects the serum lipid levels. Further prospective studies are necessary to reevaluate the visceral fat vs. skeletal muscle relationship.

Key Words: Insulin resistance, visceral fat, skeletal muscle, visceral fat to skeletal muscle ratio, visceral fat to subcutaneous fat ratio

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INTRODUCTION

Metabolic syndrome is a major cardiovascular risk factor syndrome that mainly results from insulin resistance, and this condition clinically manifests as obesity, glucose intolerance, hypertension, dyslipidemia and atherosclerosis.[1-3] In addition, obesity is frequently associated with chronic metabolic disorders, such as diabetes mellitus, atherosclerosis, and dyslipidemia, and the obesity itself is one of the main causes of insulin resistance. However, no clear mechanism about how obesity causes insulin resistance has yet been proposed.[4] Meanwhile, it is widely known that the different distribution of body fat, rather than degree of obesity according to the percent of ideal body weight (PIBW), is more closely related with metabolic diseases such as DM, hypertension, dyslipidemia, atherosclerosis, and ischemic heart disease.[5-11]

In 1950s, Vague et al.[12] divided obesity into the android type and gynecoid type, and they found that the android type of obesity is more related to diabetes, atherosclerosis and gout than is the gynecoid type of obesity. In the 1980s, Kissebach et al.[13] found that the WHR is correlated with obesity-related metabolic complications. Further, Tarui et al.[14-17] classified obesity into visceral and subcutaneous types by using a CT-scan cross-sectional picture of the umbilical region, and when the VSR exceeded 0.4, then this visceral type

obesity presented with significantly higher risks of coronary artery disease, such as increased blood pressure, plasma glucose level, triglyceride (TG) and total cholesterol (TC) levels.[16,18]

It is known that visceral fat accumulation increases the free fatty acid concentration in the portal vein, which results in decreased insulin sensitivity,[19,20] and also, an increased insulin-disposal rate by the liver.[21] In addition, an increased free fatty acid concentration in the portal vein promotes the synthesis and excretion of glucose and triglyceride in the liver[22-25] and decreases glucose utilization in skeletal muscle, which ultimately reduces insulin resistance.[20,26] Meanwhile, subcutaneous fat in peripheral tissues such as the femoral area has relatively less effect on the metabolism of glucose and lipid than visceral fat because of the resistance to lipolysis offered by adrenalin. This resistance to lipolysis by adrenalin is related to the increased activity of α-adrenalin receptors and the decreased activity of β-adrenalin receptors.[27,28]

Therefore, the excessive accumulation of visceral fat is considered to cause insulin resistance, and it results in the development of metabolic disorders such as diabetes mellitus. However, in patients with diabetes mellitus, other complicated factors should be considered. One of these complicating factors is that 35-40% of body weight in humans consists of skeletal muscle, which is a major site of glucose disposal at high insulin concentrations or after an oral glucose load.[29-31] Therefore, the bulk of skeletal muscle mass could influence insulin sensitivity via its glucose uptake capacity.[32]

The ratio of visceral fat area at the umbi1ical level over the skeletal muscle area at midthigh level, as measured by CT scan, could represent an important anthropometric parameter for determining insulin resistance.

Therefore, we investigated the relationships between metabolic variables, i.e., the ratio of visceral fat area vs. skeletal muscle area (VMR), the percent ideal body weight (PIBW), the body mass index (BMI), the waist-to-hip circumference ratio (WHR) and the visceral fat to subcutaneous fat ratio (VSR), in healthy nondiabetic middle-aged women.

MATERIALS AND METHODS

Subjects

The subjects were 114 females aged 49.7 ± 5.3 (range 40 - 60) years who were overweight and obese when they visited the Division of Endocrinology, Severance Hospital, Yonsei University, for health-checkup purposes. The study protocol adopted was approved by the Yonsei University College of Medicine ethical committee, and an informed consent was obtained from all patients.

Their mean body weight was 63.2 ± 7.3 kg and their mean BMI was 26.1 ± 2.5 kg/m^2. Ten subjects had an impaired glucose tolerance pattern on the 75-g oral glucose tolerance test (OGTT) according to WHO criteria, but the other subjects had no metabolic or endocrinologic disorders.[33]

Methods

Measurement of anthropometric parameters

Height and weight were measured with the subjects unclothed and without shoes. BMI was calculated as weight (in kilograms) divided by the height (in meters) squared. Waist circumference was measured with a soft tape, midway between lowest rib and iliac crest, with the subject in a standing position. Hip circumference was measured over the widest part of the gluteal region, and the waist-to-hip ratio (WHR) was calculated accordingly.

Body composition was determined using a bioelectric impedance meter (Bioimpedance method, Inbody 2.0, Biospace, Seoul, Korea), and the results were expressed as the percent fat mass.

Measurement of biochemical profiles

Blood was drawn after an overnight fast to measure TC, TG, HDL-cholesterol (HDL-C) and sex hormone binding globulin (SHBG) levels. A blood sample was drawn from all subjects after fasting for more than 10 hours. Plasma glucose was measured using the glucose oxidase technique on an autoanalyzer (Beckman, Fullerton, CA, USA). HbA1C was analyzed using high performance liquid chromatography (HPLC) (Variant II, Bio-Rad, Hercules, CA, USA); the normal range was 4.0-6.0%. Insulin and C-peptide

levels (fasting, postprandial) were measured by radioimmunoassay (IRMA kit, Dainabot, Japan, and RIA kit, Daiichi, Japan, respectively). None of the subjects had received any lipid- lowering drug for 1 month prior to the trial, and no subject had taken any lipid lowering drugs within 1 month of the trial.

Plasma lipoprotein measurements were obtained from single fasting fresh plasma samples using the microplate method (Behring ELISA processor II plus, Marburg, Germany). Total cholesterol and triglyceride concentrations were measured using an autochemical analyzer (Hitachi 747, Nakashi, Japan) and an enzymatic method (Roche Diagnostics, Basel, Switzerland). HDL cholesterol was assayed using a selective inhibition test (Daichii, Tokyo, Japan), and LDL cholesterol was calculated according to the Friedewald formula. Serum FFA concentrations were determined by colorimetry. PAI-1 was measured by enzyme immunoassay (Biopool TintEllze kit, Ventura, CA, USA). Fibrinogen was measured in citrated plasma using a modification of the clot-rate assay and a Pacific Hemostasis Assay Set (Humlersville, North Calorina, USA). The technique used was based on the original method of Clauss.[29]

The 75 gram oral glucose tolerance test (OGTT)

Blood was taken from all subjects after fasting for more than 10 hours. The 75-g OGTT was performed, and blood samples were collected at 0, 30, 60 and 120 min to determine glucose, free fatty acid (FFA) and insulin levels. The area under the glucose (Glu-AUC), insulin (Ins-AUC), free fatty acid (FFA-AUC) and glucose/insulin ratio (GIR= Glu-AUC/Ins-AUC) curves were calculated. Plasma glucose was measured by using the glucose oxidase technique on an autoanalyzer (Beckman, Fullerton, CA, USA). Insulin was measured by radioimmunoassay (IRMA kit, Eiken Chemical Co., Tokyo, Japan).

Measurement of body composition

Body fat distribution and muscle area were determined by CT (CT Max II; General Electric Co., USA) according to the procedure of Tokunaga et al.,[14] and this involved measuring the cross-sectional area, the subcutaneous and visceral fat area (Hounsfield number, -150 to -50) at the level of umbilicus, and the subcutaneous fat area and muscle area (Hounsfield number, -49 to 100) at the midportion between the greater trochanter and upper portion of the patella. VSR and VMR were calculated by dividing the visceral fat area by the abdominal subcutaneous fat area and thigh mscle area, respectively.[34]

Statistical analysis

Data were expressed as means ± S.E.M. Correlation between subjects and each anthropometric variable was tested using Pearson's correlation, and multiple regression analysis was performed using a stepwise procedure.

Subjects were classified into four groups by the point of VSR 0.4 and VMR 0.6. Comparison between groups was carried out using student's unpaired t-test or one way Analysis of Variance (ANOVA). $P<0.05$ was considered significant.

All statistical analyses were performed using SAS (version 6.12) and SPSS (version 10.0) statistical programs.

RESULTS

Clinical and biochemical characteristics of the subjects

The mean values of WHR, VSR and VMR for all 114 subjects were 0.93 ± 0.05 (0.79-10.7), 0.40 ± 0.17 (0.15-0.95) and 0.61 ± 0.27 (0.17-1.40), respectively. Mean fasting levels of glucose, insulin, FFA, TC, HDL-C, TG, and SHBG were 5.1 ± 1.0 mmol/l, 68 ± 86 pmol/l, 623 ± 201 mmol/l, 5.41 ± 1.03 mmol/l, 1.19 ± 0.25 mmol/l, 1.65 ± 0.87 mmol/l, and 80 ± 37 nmol/l, respectively (Table 1).

Correlations among the metabolic variables and the anthropometric parameters

According to Pearson's correlation coefficient among the metabolic variables, the TG level was more significantly correlated with VSR than the VMR (r=0.3349, $p<0.001$ vs. r=2589, $p=0.006$, Table 2), but Ins-AUC, GIR and SHBG levels were more significantly correlated with the VMR than VSR

Table 1. Clinical and Serologic Characteristics of the 114 Non-diabetic Middle-aged Women

	Mean ± SD	Range		Mean ± SD	Range
Age (years)	49.7 ± 5.3	40 - 60	Fasting glucose (mmol/L)	5.1 ± 1.0	3.2 - 8.6
Weight (kg)	63.2 ± 7.3	46.0 - 86.0	Fasting insulin (pmol/L)	68 ± 86	18 - 711
PIBW (%)	127 ± 12	110 - 175	Fasting FFA (mmol/L)	623 ± 201	206 - 1083
BMI (kg/m2)	26.1 ± 2.5	21.6 - 36.0	Total cholesterol (mmol/L)	5.41 ± 1.03	3.50 - 8.99
WHR	0.93 ± 0.05	0.79 - 1.07	HDL-cholesterol (mmol/L)	1.19 ± 0.25	0.68 - 2.24
VSR	0.40 ± 0.17	0.15 - 0.95	Triglyceride (mmol/L)	1.65 ± 0.87	0.42 - 5.47
VMR	0.61 ± 0.27	0.17 - 1.40	SHBG (nmol/L)	80 ± 37	30 - 168

VSR, visceral fat vs. subcutaneous fat area ratio; VMR, visceral fat vs. skeletal muscle area ratio; FFA, free fatty acid; SHBG, sex hormone-binding globulin.

Table 2. Pearson's Correlation Coefficients between Anthropometric Parameters and Metabolic Variables in 114 Middle-aged Women

	Glu-AUG	Ins-AUC	GIR	FFA-AUC	SHBG	TC	HDL-C	TG
PIBW	.1437	.3556	-.2504*	.1133	-.3575†	.0771	-.0307	.0533
BMI	.1404	.3569	-.2736†	.0702	-.3531†	.0713	-.0343	.0897
WHR	.2885*	.1966	-.0788	.0743	-.2126	.3696‡	-.1879	.2898†
VSR	.1810	.3124†	-.2840†	.1254	-.3050*	.1811	-.1692	.3349
VMR	.0835	.4487‡	-.4836‡	.0751	-.4281‡	.0290	.1360	.2589

GIR, glucose/insulin ratio=Glu-AUC/Ins-AUC × 100; SHBG, sex hormone-binding globulin; TC, total cholesterol; HDL-C, HDL-cholesterol.
*$p<0.05$, $^{\dagger}p<0.01$, $^{\ddagger}p<0.001$.

(r=0.4487, $p<0.001$ vs. r=0.3 124, $p=0.002$; r=-0.4386, $p<0.001$ vs. r=-0.2840, $p=0.004$; r=-0.4281, $p<0.001$ vs. r=-0.3050, $p=0.015$, respectively, Table 2). After the multiple linear regression analysis with adjustment for age and BMI, the independent anthropometric parameters of metabolic variables were VMR for Ins-AUC, GIR and SHBG, WHR for Glu-AUC and TC, and VSR for TG (Table 2).

After multiple linear regression analysis with adjustment for age and BMI, independent anthropometric parameters for each metabolic variable were; VMR for Ins-AUC, GIR and SHBG levels ($r^2=0.161$, $p<0.001$; $r^2=0.160$, $p<0.001$; $r^2=0.152$, $p=0.003$, respectively), WHR for Glu-AUC and total cholesterol levels ($r^2=0.073$, $p=0.004$; $r^2=0.127$, $p=0.003$, respectively), and VSR ($r^2=0.094$, $p=0.01$) for triglyceride level (Table 3).

Clinical and biochemical characteristics according to VSR or VMR

In subjects with a higher VMR (>0.6), age (53.0 ± 4.2 vs. 47.0 ± 4.6 years, $p<0.001$), the Ins-AUG (925 ± 403 vs. 600 ± 297 pmol/l × h, $p<0.001$), and TG (1.85 ± 1.00 vs. 1.49 ± 0.73 mmol/l, $p<0.05$) were significantly elevated (Table 4). The GIR (1.85 ± 0.78 vs. 2.74 ± 1.23, $p<0.001$) and SHBG (73.4 ± 34.6 vs. 97.5 ± 37.8 pmol/l, $p<0.05$) levels were lower than those subjects with a lower VMR (Table 4). Regardless of the magnitude of the VSR, those subjects with higher VMR (>0.6) were older and showed a higher Ins-AUC and lower GIR than the subjects with a lower VMR (Table 4).

By dividing subjects according to their visceral fat obesity and subcutaneous fat obesity (by a VSR of 0.4), and then comparing each group (that was divided by a VMR of 0.6), regardless of VSR level, the area under insulin curve was increased and GIR decreased more in the group with the higher VMR (Table 5).

To exclude confounding factors, we compared the metabolic variables for 72 subjects who were matched for age, BMI and WHR; nevertheless,

Table 3. Most Important Independent Anthropometric Parameter for Metabolic Variables after Multiple Linear Regression Analysis in 114 Middle-aged Women

Dependent variables	Glu-AUC	Ins-AUC	GIR	FFA-AUC	SHBG	TC	HDL-C	TG
independent variable	WHR	VMR	VMR	-	VMR	WHR	-	VSR
adjusted R square	.073	.161	.160	-	.152	.127	-	.094
beta	.288	.412	-.143	-	-.411	.370	-	.323
p value	0.004	<0.001	<0.001	-	0.003	<0.001	-	0.01

GIR, glucose/insulin ratio=Glu-AUC/Ins-AUC; SHBG, sex hormone-binding globulin; TC, total cholesterol; HDL-C, HDL-cholesterol; TG, Triglyceride.

Table 4. Comparisons of Anthropometric Parameters and Metabolic Variables According to the VSR and VMR in 114 Middle-aged Women

	VSR		VMR	
	< 0.4	≥ 0.4	< 0.6	≥ 0.6
No	68	46	63	51
Age (years)	49.4 ± 5.8	50.1 ± 3.0	47.0 ± 4.6	53.0 ± 4.2§
PIBW (%)	129.1 ± 10.4	124.6 ± 10.2	126.6 ± 11.9	127.6 ± 12.7
BMI (kg/m^2)	26.4 ± 2.7	25.8 ± 2.0	26.1 ± 2.5	26.2 ± 2.4
WHR	0.94 ± 0.05	0.93 ± 0.05	0.94 ± 0.05	0.93 ± 0.04
Glu-AUC (mmol/L×hr)	14.1 ± 5.3	15.2 ± 3.3	14.5 ± 4.1	14.6 ± 2.9
Ins-AUC (pmol/L×hr)	637 ± 352	887 ± 379†	600 ± 297	925 ± 403§
FFA-AUC (mmol/L×hr)	561 ± 245	634 ± 260	597 ± 287	582 ± 202
GIR	2.60 ± 1.14	2.01 ± 1.07*	2.74 ± 1.23	1.85 ± 0.78§
SHBG (nmol/L)	90.4 ± 35.5	69.1 ± 35.7*	97.5 ± 37.8	73.4 ± 34.6‡
T-cholesterol (mmol/L)	5.24 ± 1.14	5.65 ± 0.78*	5.41 ± 1.04	5.40 ± 1.01
HDL-cholesterol (mmol/L)	1.22 ± 0.26	1.15 ± 0.24	1.17 ± 0.24	1.21 ± 0.28
Triglyceride (mmol/L)	1.49 ± 0.88	1.89 ± 0.81*	1.49 ± 0.73	1.85 ± 1.00‡

Values are means ± S.D.
GIR, glucose/insulin ratio=Glu-AUC/Ins-AUC × 100; SHBG, sex hormone-binding globulin.
*p<0.05, †p<0.01 compared to subjects with VSR < 0.4.
‡p<0.05, §p<0.001 compared to subjects with VMR < 0.6.

Ins-AUG was still significantly increased, and the GIR and SHBG levels significantly decreased in subjects with the higher VMR values (Table 6).

Comparisons of the clinical and biochemical characteristics of the groups before and after menopause

There were no remarkable differences in the anthropometric and metabolic variables of pre-menopausal and postmenopausal women, except for age (45.2 ± 3.1 vs. 52.5 ± 3.6 years, p< 0.001) and TG (1.27 ± 0.16 vs. 1.92 ± 0.27 mmol/l, p< 0.001) (data not shown).

DISCUSSION

Obesity associated with metabolic disorders is known to be caused by insulin resistance due to an increase of visceral fat accumulation in the omentum or mesenterium.[35-43] The metabolic affect of fat is significantly dependent on its distribution. That is, subcutaneous or visceral fat tissue of abdomen has a greater basic fat dissolution rate than subcutaneous fat tissue of the thigh.[44,45] In terms of fat dissolution by catecholamine, visceral fat has a greater rate than abdominal or thigh subcutaneous fat.[27] When obese patients are losing weight, visceral fat is the first

Table 5. Comparisons of Anthropometric Parameters and Metabolic Variables According to the VMR in both Subjects with Higher and Lower in 114 Middle-aged Women

	VSR < 0.4		VSR ≥ 0.4	
	VMR < 0.6	VMR ≥ 0.6	VMR < 0.6	VMR≥0.6
No	49	19	14	32
Age (years)	47.2 ± 4.8	55.1 ± 4.2‡	46.3 ± 4.2	51.7 ± 3.6‖
PIBW (%)	127.1 ± 12.8	33.9 ± 14.1	124.9 ± 8.5	123.9 ± 10.2
BMI (kg/m^2)	26.1 ± 2.7	27.1 ± 2.7	25.9 ± 1.8	25.7 ± 2.1
WHR	0.94 ± 0.05	0.92 ± 0.05	0.93 ± 0.06	0.93 ± 0.04
VSR	0.27 ± 0.07	0.32 ± 0.06†	0.54 ± 0.09	0.58 ± 0.14
VMR	0.38 ± 0.11	0.84 ± 0.19‡	0.46 ± 0.10	0.88 ± 0.18‖
Glu-AUC (mmol/L×hr)	14.1 ± 3.7	14.2 ± 2.9	16.0 ± 5.2	14.9 ± 2.0
Ins-AUC (pmol/L×hr)	586 ± 308	790 ± 435*	652 ± 265	997 ± 374§
FFA-AUC (mmol/L×hr)	560 ± 270	564 ± 154	733 ± 318	591 ± 225
GIR	2.76 ± 1.18	2.13 ± 0.90*	2.70 ± 1.45	1.70 ± 0.68§
SHBG (nmol/L)	105.1 ± 32.6	76.6 ± 33.2*	88.2 ± 42.2	71.5 ± 35.9
T-cholesterol (mmol/L)	5.31 ± 1.09	5.03 ± 1.25	5.74 ± 0.80	5.62 ± 0.78
HDL-cholesterol (mmol/L)	1.19 ± 0.24	1.30 ± 0.31	1.11 ± 0.23	1.16 ± 0.24
Triglyceride (mmol/L)	1.37 ± 0.64	1.82 ± 1.29	1.94 ± 0.87	1.96 ± 0.80

Values are means ± S.D.
GIR, glucose/insulin ratio=Glu-AUC/Ins-AUC × 100; SHBG, sex hormone-binding globulin.
*$p<0.05$, †$p<0.01$, ‡$p<0.001$ compared to subjects with VSR < 0.4 and VMR < 0.6.
§$p<0.01$, ‖$p<0.001$ compared to subjects with VMR ≥ 0.4 and VMR < 0.6.

Table 6. Comparison of Anthropometric Parameters and Metabolic Variables According to the VSR and VMR after Adjustments for Age in 72 Middle-aged Women

	VMR	
	< 0.6	≥ 0.6
No	36	36
Age (years)	50.1 ± 2.6	50.9 ± 2.6
PIBW (%)	123.9 ± 10.4	125.9 ± 10.5
BMI (kg/m^2)	25.4 ± 2.7	25.9 ± 2.4
WHR	0.95 ± 0.04	0.93 ± 0.36
Glu-AUC (mmol/L×hr)	14.7 ± 3.9	14.6 ± 2.26
Ins-AUC (pmol/L×hr)	590 ± 792	956 ± 380†
FFA-AUC (mmol/L×hr)	601 ± 270	594 ± 197
GIR	2.77 ± 1.26	1.78 ± 0.81†
SHBG (nmol/L)	106 ± 37	68 ± 30*
T-cholesterol (mmol/L)	5.66 ± 1.10	5.45 ± 1.04
HDL-cholesterol (mmol/L)	1.14 ± 0.19	1.19 ± 0.28
Triglyceride (mmol/L)	1.65 ± 70	1.98 ± 1.08

Values are means ± S.D.
GIR, glucose/insulin ratio=Glu-AUC/Ins-AUC×100; SHBG, sex hormone-binding globulin.
*$p<0.01$, †$p<0.001$ compared to subjects with VMR < 0.6.

to decrease.[46]

Skeletal muscle accounts for about 35-40% of body weight, and it plays an important role in glucose metabolism.[47,48] On an oral glucose tolerance test, most of the glucose remaining after satisfying the requirements of brain is stored in the skeletal muscle,[30,31] 80-95% of glucose injected during a normal glucose clamp test is stored in skeletal muscle.[32,48] Also, considering that when insulin and glucose are intravenously injected together in the laboratory rat, 25% of the injected glucose is stored in skeletal muscle within one minute;[49] therefore, skeletal muscle has a great influence on the glucose metabolism. Up till now, in the research upon glucose metabolism in skeletal muscle, the problem was that a muscle biopsy was required, however, research on the glucose metabolism in muscles using 13C nuclear magnetic resonance (NMR) is making swift progress. Specifically, skeletal muscle is a tissue in which energy metabolism is actively under way in the basal state or after exercise, and more than 90% of glucose in the normal glucose clamp test is used in the muscle and most of it is stored as glycogen in the muscle.[50,51]

Although in diabetic patients the mobilization of glucose into muscle is half as fast as normal people, almost the same amount of glucose is used in the skeletal muscle.[50,51] Skeletal muscle and liver are the main places that use glucose during daily life.[52] Glucose moves into skeletal muscle much faster after exercise than in the basal state. After about 30 to 60 minutes of initial exercise, glucose is mobilized into the muscle regardless of insulin, and after that, glucose mobilization is done by insulin. Muscle cells after exercise become more sensitive to insulin than any other tissue,[53] and the mechanism involves the increased blood flow into the skeletal muscle and the enhanced expression of GLUT4.[48,54] Therefore, exercise therapy in diabetic patients is as important as diet management.

Given that visceral fat and skeletal muscle both have a great influence on the glucose metabolism, the ratio of visceral fat to skeletal muscle is thought to be a good index of insulin resistance. Previous studies have reported that the relative ratio of the thigh part to the abdominal obesity is a valid anthropometric parameter like the ratio of waist to hip circumference or the ratio of waist to thigh circumference, and it could reflect insulin resistance;[8,13,36] however, no study has ever reported upon such a correlation by directly measuring the amounts of visceral fat and skeletal muscle with the use of computer tomography.

This study was undertaken to investigate the correlation between an index reflecting biochemical testing and insulin resistance, and the VSR and VMR in those middle aged women without any chronic metabolic disorder whose PIBWs were above 110%. Tarui et al.[15] reported that VSR is highly correlated with serum glucose, total cholesterol, and TG, and our study showed an association between total cholesterol and TG. Therefore, VSR is thought to be a good anthropometric parameter reflecting lipid disorder. However, when we examined the area under the insulin curve, the ratio of glucose to insulin reflected the insulin resistance associated with glucose metabolism, and SHBG and BMR were more closely correlated than the VSR. By performing multiple regression analysis that included body weight, PIBW, BMI, and WHR, VMR was identified as the most independent variable.

Insulin resistance is known to be increased when the VSR is higher because metabolically active visceral fat is easily dissolved, which leads to an increase in the serum lipid level, and glucose metabolism disorders are caused by increased gluconeogenesis in the liver, decreased insulin clearance, and similar metabolic imbalances. However, when considering the correlation with metabolic indices that reflected insulin resistance in the present study, VMR, which reflects hyperinsulinemia and insulin resistance, was found to have a more significant meaning than VSR. By dividing our subjects according to their visceral fat obesity and subcutaneous fat obesity (by a VSR of 0.4), and then comparing each group (that was divided by a VMR of 0.6), regardless of VSR level, the area under insulin curve was increased and GIR decreased more in the group with the higher VMR (>0.6). Upon close examination, it was found that ratio of skeletal muscle to visceral fat had a great impact on insulin resistance. Also, in subjects with lower visceral fat, whose VSR was lower than 0.4, those cases with lower skeletal muscle amounts showed

a decreased SHBG, which suggests an insulin resistance. In other words, we found that in spite of the higher visceral fat level, the higher amount of skeletal muscle was associated with lower insulin resistance and the lower amount of skeletal muscle was associated with higher insulin resistance, even for those subjects with lower visceral fat levels. When we compared the 72 age adjusted subjects divided by the standard VMR, differences in the area under insulin curve, GIR and SHBG, were found between the higher and lower VMR groups (Table 6). VMR increased according to age, but it is considered to be an anthropometric parameter reflecting insulin resistance regardless of age.

If SHBG decreases, whatever the cause may be (e.g. insulin resistance), the free androgen increases, and this hyperandrogenemia could lead to a vicious cycle causing insulin resistance. Therefore, SHBG is frequently used as an important index of insulin resistance in females. That is to say, SHBG is known to decrease in cases of increased WHR in both sexes,[55] for dyslipidemia,[56] and in cases of upper body part obesity in females.[57] In our study with female subjects, SHBG showed the closest correlation with VMR of all the various anthropometric parameters, and it functioned as the most important fact in the multiple regression analysis.

Around the time of menopause, women show a change of body fat distribution.[57,58] Before menopause, fat is accumulated in the buttocks and lower extremities by LPL (lipoprotein lipase) activation of the lower extremity fat tissue due to the presence of estrogen, but after menopause, this characteristic disappears due to the lack of estrogen, and the relatively increased testosterone level leads to visceral fat accumulation.

However in the male, with the decreased testosterone due to aging, visceral fat increases.[59] Sex hormone is known to operate differently depending upon gender, but there are many different views about this issue, and further studies are needed.[60-62]

Our study subjects were women aged between 40 and 60 years. Comparing the subjects around menopause and adjusting for PIBW, BMI, WHR and age, the VMR were found to be significantly increased in post-menopause women more than in pre-menopause women, but no metabolic index other than TG showed any difference (data not shown). These findings are a little different from those of previous studies, which reported that insulin resistance could be increased by the change of sex hormone level and fat distribution after menopause.

Such differences may be caused by dietary patterns, the amount of exercise, or female hormone replacement, and further studies are required to resolve these issues. From the above findings, we came to the conclusion that VMR is an anthropometric parameter, which reflects insulin resistance concerning glucose metabolism, and VSR is thought to be a good parameter reflecting serum lipid levels. Accordingly, in order to reduce insulin resistance, the VMR should be reduced, and specifically, visceral fat should be reduced and skeletal muscle should be increased. Especially in NIDDM patients with severe insulin resistance, we should place a heavy emphasis on non-drug therapies, like strict diet therapy and regular exercise.[63-65] The strengthening of skeletal muscle amount is thought to be as important as a weight reduction program based on simple visceral fat.

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