The Journal of International Medical Research
2010; 38: 782 – 791

Resistance Exercise Did Not Alter Intramuscular Adipose Tissue but Reduced Retinol-binding Protein-4 Concentration in Individuals with Type 2 Diabetes Mellitus

YH Ku[1], KA Han[1], H Ahn[3], H Kwon[3], BK Koo[4], HC Kim[2] and KW Min[1]

[1]Department of Internal Medicine, and [2]Department of Radiology, Eulji University School of Medicine, Daejeon, Republic of Korea; [3]Diabetes Centre, Eulji Hospital, Seoul, Republic of Korea; [4]Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea

Lipid accumulation in muscle is associated with diminished insulin sensitivity. It was hypothesized that resistance exercise decreases muscular adipose tissue and reduces the level of retinol-binding protein-4 (RBP4), which is linked to adipose tissue and insulin sensitivity in diabetics. Forty-four women with type 2 diabetes were randomly assigned to three groups for a period of 12 weeks: control (asked to maintain a sedentary lifestyle); resistance exercise (elastic band exercise at moderate intensity five times per week); and aerobic exercise (walking for 60 min at moderate intensity five times per week). Subcutaneous (SCAT), subfascial (SFAT) and intramuscular (IMAT) adipose tissues at mid-thigh level were assessed using computed tomography, and RBP4 level and insulin sensitivity (fractional disappearance rate of insulin, k_{ITT}) were assessed before and after intervention. Changes in SCAT, SFAT, IMAT, RBP4 and k_{ITT} were similar among the three groups. Within-group analysis revealed that body mass index and waist circumference decreased significantly in both exercise groups, but RBP4 decreased significantly only with resistance exercise. Resistance exercise did not alter muscular adipose tissue or improve insulin sensitivity.

KEY WORDS: Diabetes mellitus type 2; Insulin resistance; Resistance training; Retinol-binding proteins; Adipose tissue

Introduction

Evidence has shown that an excess supply of fatty acids, beyond that required for energy needs, is a cause of insulin resistance in muscle.[1,2] Intramyocellular triglyceride accumulation is a marker of an excessive supply of fatty acid to muscle and studies have demonstrated an association between intramyocellular triglyceride accumulation and insulin resistance.[3 – 5] In addition,

circulating adipokines, such as retinol-binding protein-4 (RBP4), leptin and adiponectin, are emerging as important links between obesity, insulin resistance and type 2 diabetes mellitus.[6 – 9]

A universally accepted component of the non-pharmacological treatment of type 2 diabetes mellitus is exercise.[10 – 12] In particular, resistance training studies have revealed positive relationships between resistance exercise and glycaemic control.[13,14] Although the precise mechanisms underlying the positive effects of resistance training remain to be clarified, one process may be through the down-regulation of pro-inflammatory factors. Acute phase reactants, cytokines and adipokines have recently been implicated in the pathogenesis of type 2 diabetes mellitus.[15] Limited research has been conducted to examine the effects of resistance training on these pro-inflammatory factors, which may present an opportunity for improved management of type 2 diabetes mellitus.

It is reasonable to hypothesize that resistance exercise decreases muscular adipose tissue, and that it may also have favourable effects on RBP4 which is linked to adipose tissue accumulation in muscle and insulin sensitivity in individuals with diabetes. In the present study, the effect of resistance and aerobic training on regional adipose tissues, levels of adipokines – especially RBP4 – and insulin resistance was investigated in overweight Korean women with type 2 diabetes mellitus.

Patients and methods

PATIENTS

Overweight Korean women (body mass index [BMI] > 23 kg/m^2) with type 2 diabetes who were attending the Diabetes Centre at Eulji Hospital, Seoul, Republic of Korea, were enrolled sequentially into the study between August and October 2008. All patients had taken > 1 g/day metformin for > 3 months previously and were on a stable antidiabetes regimen (sulphonylurea and metformin). Patients receiving lipid-lowering medications, insulin or thiazolidinediones were excluded. Individuals with diabetic vascular complications, life-threatening diseases, orthopaedic problems, or liver and renal impairment were also excluded. During the intervention period, all participants were asked to maintain a standard calorific intake (ideal body weight [in kg] × 30 kcal/kg [kcal] per day), and they were monitored by self-report once every 2 weeks. The patients were randomly assigned to undertake resistance exercise, aerobic exercise or no exercise (control group).

The study protocol was reviewed and approved by The Institutional Review Board of Eulji Hospital, Seoul, Republic of Korea, and written informed consent to participate in the study was obtained from all patients.

EXERCISE TRAINING

Subjects in the resistance and aerobic exercise groups took part in a 12-week programme of exercise, according to the protocol, under individual supervision. Participants in the resistance exercise group performed elastic band exercise at about 40 – 50% of maximal exercise capacity five times per week – three times as part of a group in the hospital gymnasium and twice at home. Elastic band exercise comprised three sets of 15 – 20 repetitions, with 10 different motions that included biceps curl, triceps extension, upright row, shoulder chest press, trunk side-bending, seated row, leg press, hip flexion, leg flexion and leg extension. The aerobic training group exercised by walking for 60 min at moderate intensity (3.6 – 5.2 metabolic equivalents [METs – a multiple of

resting oxygen consumption where 1 MET equals a person's oxygen uptake at rest, i.e. approximately 3.5 ml oxygen/kg body weight per min]) five times per week. The control group had experience of diabetes education, including benefits of diet and exercise, but did not receive any additional education during this study; they were asked to maintain their sedentary lifestyle. All participants received information about how to monitor their diet and exercise. Daily activities of all the participants were monitored with a Lifecorder® (Suzuken Co., Nagoya, Japan) and dietary intake was self-reported, using a 3-day diet diary.

LABORATORY AND CLINICAL MEASUREMENTS

On the first and last testing days, each participant's height and weight were measured. Body composition, including fat mass, fat-free mass, muscle mass and regional fat content, were assessed using dual-energy X-ray absorptiometry (DXA; Lunar Prodigy®, GE Healthcare Biosciences, Piscataway, NJ, USA) and all scans were analysed by one investigator (H.K.). The amount of regional adipose tissue – subcutaneous (ASAT) and visceral adipose tissue (AVAT) in the abdomen, and subcutaneous (SCAT), subfascial (SFAT) and intramuscular adipose tissue (IMAT) at mid-thigh level – was measured using computed tomography. In addition, muscle strength was tested by measuring one repetitive maximum (1RM) for the upper and lower extremities using a chest and leg press, respectively (Keiser®, Fresno, CA, USA), before and after the 12-week exercise programme. Muscle power of the upper extremities was measured in the deltoid, triceps and pectoralis muscles and, for the lower extremities, it was measured in the gluteal group, hamstring and quadriceps muscles. To measure 1RM, all patients performed a 5-min warm-up of mild stretching. After resting for 1 min, patients then performed three sets at 10% of maximal capacity, separated by 1-min rest intervals. Finally, patients performed three sets of repetitions at 90% of estimated maximal intensity.

Venous blood samples were drawn after 12 h of fasting at weeks 0 and 12. Samples were centrifuged and serum was removed and frozen at −70 °C for later analysis. Fasting plasma glucose level, glycosylated haemoglobin (HbA_{1c}), fasting C-peptide, lipid profiles, plasma levels of RBP4, leptin and adiponectin, and insulin sensitivity (insulin tolerance test: fractional disappearance rate of insulin [k_{ITT}]) were measured before and after the 12-week exercise programme.

STATISTICAL ANALYSIS

It was calculated that a sample size of 45 persons (15 per group) was needed to have 80% power to detect a moderate (SD ± 0.65) difference for each of the four comparisons tested simultaneously, with an overall value of $P = 0.05$. All data were analysed using the SPSS® statistical package, version 12.0 (SPSS Inc., Chicago, IL, USA) for Windows®. Variables that were not normally distributed were logarithmically transformed before statistical analysis. The results are presented as means ± SD. Analysis of variance was used to evaluate the changes across groups, *post hoc* test (the least significant difference test) was used for pair-wise comparisons, and univariate analysis was used to assess the correlation of the changes in parameters. A P value < 0.05 was considered to be statistically significant.

Results

The study included 44 overweight women

with type 2 diabetes who were assigned randomly to the resistance exercise group (n = 13), the aerobic exercise group (n = 15) or the control group (n = 16). They ranged in age from 38 to 68 years and their baseline characteristics are shown in Table 1. No significant differences were observed in any variable between the three groups at baseline with the exception of k_{ITT}, which was higher in the aerobic exercise group than in the resistance exercise or control groups (P = 0.011 across-group comparison).

Changes in all variables after 12 weeks compared with baseline are listed in Table 2. In the two exercise groups, anthropometric variables were significantly different from

TABLE 1:
Baseline characteristics of 44 women with type 2 diabetes mellitus before taking part in a 12-week programme of no exercise (control), resistance exercise or aerobic exercise

	Group			
Characteristic	**Control (n = 16)**	**Resistance exercise (n = 13)**	**Aerobic exercise (n = 15)**	**Statistical significance[a]**
Age (years)	57.8 ± 8.1	55.7 ± 6.2	55.7 ± 7.0	NS
Diabetes duration (years)	5.8 ± 6.1	5.7 ± 4.8	6.6 ± 5.3	NS
Weight (kg)	67.6 ± 7.5	66.1 ± 4.4	66.3 ± 6.0	NS
Waist circumference (cm)	90 ± 12	90 ± 5	89 ± 5	NS
BMI (kg/m^2)	27.4 ± 2.8	27.1 ± 2.3	27.1 ± 2.4	NS
ASAT (g)	24 686 ± 5617	24 402 ± 7903	23 896 ± 6035	NS
AVAT (g)	17 530 ± 4747	15 658 ± 4754	15 890 ± 4593	NS
SFAT (g)	2248 ± 760	2205 ± 849	2014 ± 488	NS
SCAT (g)	7371 ± 2620	6697 ± 2674	7187 ± 2960	NS
IMAT (g)	564 ± 222	412 ± 260	509 ± 178	NS
Systolic blood pressure (mmHg)	125 ± 19	133 ± 19	122 ± 18	NS
Diastolic blood pressure (mmHg)	80 ± 12	86 ± 11	73 ± 20	NS
1RM of UE (kg)	17.5 ± 6.4	16.5 ± 4.3	17.3 ± 2.8	NS
1RM of LE (kg)	86.8 ± 33.1	86.9 ± 24.8	88.5 ± 23.3	NS
FPG (mg/dl)	125 ± 20	113 ± 12	127 ± 19	NS
HbA_{1c} (%)	7.3 ± 0.7	7.3 ± 0.9	7.7 ± 1.0	NS
C-peptide (ng/ml)	1.7 ± 0.6	1.9 ± 0.8	1.5 ± 0.4	NS
Total cholesterol (mg/dl)	156 ± 38	156 ± 25	157 ± 38	NS
Triglyceride (mg/dl)	174 ± 153	185 ± 113	126 ± 73	NS
HDL cholesterol (mg/dl)	41 ± 15	43 ± 8	46 ± 10	NS
LDL cholesterol (mg/dl)	95 ± 33	89 ± 26	98 ± 36	NS
RBP4 (μg/ml)	95.0 ± 20.5	98.5 ± 28.8	87.0 ± 25.4	NS
Adiponectin (μg/ml)	4.83 ± 1.99	4.98 ± 2.52	3.86 ± 2.00	NS
Leptin (ng/ml)	11.6 ± 5.8	8.8 ± 4.0	9.86 ± 3.06	NS
k_{ITT} (%/min)	1.98 ± 0.78	1.76 ± 1.00	2.81 ± 1.02	P = 0.011

Data are presented as mean ± SD.
[a]Across-group comparisons by analysis of variance.
BMI, body mass index; ASAT, subcutaneous adipose tissue in abdomen; AVAT, visceral adipose tissue in abdomen; SFAT, subfascial adipose tissue at mid-thigh level; SCAT, subcutaneous adipose tissue at mid-thigh level; IMAT, intramuscular adipose tissue at mid-thigh level; 1RM, one repetitive maximum; UE, upper extremity; LE, lower extremity; FPG, fasting plasma glucose; HbA_{1c}, glycosylated haemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; RBP4, retinol-binding protein-4; k_{ITT}, fractional disappearance rate of insulin.

TABLE 2:
Changes in all variables in 44 women with type 2 diabetes mellitus after taking part in a 12-week programme of no exercise (control, *n* = 16), resistance exercise (*n* = 13) or aerobic exercise (*n* = 15)

Variable	Baseline	After training	Change	Statistical significance[a]
Weight (kg)				$P = 0.048$
Resistance	66.1 ± 4.4	65.0 ± 4.7[b]	–1.1 ± 1.3	
Aerobic	66.3 ± 6.0	64.4 ± 5.4[b]	–1.9 ± 1.2	
Control	67.6 ± 7.5	67.0 ± 7.4	–0.6 ± 1.7	
BMI (kg/m^2)				$P = 0.044$
Resistance	27.1 ± 2.3	26.7 ± 2.3[b]	–0.4 ± 0.5	
Aerobic	27.1 ± 2.4	26.3 ± 2.1[b]	–0.8 ± 0.5[d]	
Control	27.4 ± 2.8	27.1 ± 2.8	–0.3 ± 0.7	
Waist circumference (cm)				NS
Resistance	90 ± 5	88 ± 6[b]	–2 ± 3	
Aerobic	89 ± 5	86 ± 5[b]	–3 ± 3	
Control	90 ± 12	90 ± 6	0 ± 14	
ASAT (g)				$P = 0.015$
Resistance	24 402 ± 7903	22 732 ± 7264[b]	–1670 ± 1744[d]	
Aerobic	23 896 ± 6035	21 851 ± 5767[b]	–2045 ± 1243[c]	
Control	24 686 ± 5617	24 057 ± 5541[b]	–629 ± 1028	
AVAT (g)				NS
Resistance	15 658 ± 4754	14 678 ± 3456	–980 ± 2353	
Aerobic	15 890 ± 4593	15 038 ± 3369	–852 ± 2839	
Control	17 530 ± 4747	17 362 ± 4728	–168 ± 1801	
SFAT (g)				NS
Resistance	2205 ± 849	1885 ± 617	–320 ± 616[d]	
Aerobic	2014 ± 849	2016 ± 639	2 ± 687	
Control	2248 ± 760	2563 ± 760	315 ± 868	
SCAT (g)				NS
Resistance	6697 ± 2674	7660 ± 2760[b]	963 ± 1157[d]	
Aerobic	7187 ± 2960	7849 ± 2510[b]	662 ± 966	
Control	7371 ± 2620	7313 ± 2479	–58 ± 1316	
IMAT (g)				NS
Resistance	412 ± 160	416 ± 159	4 ± 199	
Aerobic	509 ± 178	478 ± 184	–31 ± 159	
Control	564 ± 222	532 ± 215	–32 ± 171	
1RM of UE (kg)				$P < 0.001$
Resistance	17 ± 4	19 ± 4[b]	2 ± 2[c,e]	
Aerobic	17 ± 3	15 ± 3[b]	–2 ± 3[e]	
Control	18 ± 6	16 ± 7[b]	–2 ± 2	
1RM of LE (kg)				$P = 0.004$
Resistance	87 ± 25	97 ± 15[b]	10 ± 16[c,e]	
Aerobic	89 ± 23	82 ± 25	–7 ± 13[e]	
Control	87 ± 33	75 ± 24[b]	–12 ± 21	
FPG (mg/dl)				NS
Resistance	113 ± 12	127 ± 39	14 ± 39	
Aerobic	127 ± 19	120 ± 20	–7 ± 22	
Control	125 ± 20	121 ± 24	–4 ± 22	

TABLE 2 (continued):
Changes in all variables in 44 women with type 2 diabetes mellitus after taking part in a 12-week programme of no exercise (control, *n* = 16), resistance exercise (*n* = 13) or aerobic exercise (*n* = 15)

Variable	Baseline	After training	Change	Statistical significance[a]
HbA_{1c} (%)				NS
Resistance	7.3 ± 0.9	7.0 ± 0.9	–0.3 ± 0.9	
Aerobic	7.7 ± 1.0	7.1 ± 0.8	–0.6 ± 1.2	
Control	7.3 ± 0.7	7.2 ± 0.9	–0.1 ± 0.6	
C-peptide (ng/ml)				NS
Resistance	1.9 ± 0.8	1.8 ± 0.7	–0.1 ± 0.7	
Aerobic	1.5 ± 0.4	1.3 ± 0.3[b]	–0.2 ± 0.4	
Control	1.7 ± 0.6	1.7 ± 0.7	0.0 ± 0.6	
RBP4 (µg/ml)				NS
Resistance	98.5 ± 28.8	82.1 ± 27.1[b]	–16.4 ± 18.1[d,e]	
Aerobic	87.0 ± 25.4	84.7 ± 15.3	–2.3 ± 16.9	
Control	95.0 ± 20.5	96.2 ± 28.7	1.2 ± 23.2	
Adiponectin (µg/ml)				NS
Resistance	4.98 ± 2.52	7.28 ± 3.72[b]	2.30 ± 2.09	
Aerobic	3.86 ± 2.00	6.76 ± 1.24[b]	2.90 ± 2.32	
Control	4.83 ± 1.99	6.82 ± 2.39[b]	1.99 ± 2.06	
Leptin (ng/ml)				$P = 0.011$
Resistance	8.75 ± 3.97	7.73 ± 4.05	–1.02 ± 2.89	
Aerobic	9.86 ± 3.06	6.13 ± 4.00[b]	–3.73 ± 3.10[c,e]	
Control	11.60 ± 5.83	11.50 ± 4.92	–0.10 ± 3.52	
k_{ITT} (%/min)				NS
Resistance	1.87 ± 0.97	2.13 ± 0.76	0.26 ± 1.16	
Aerobic	2.81 ± 1.02	2.50 ± 0.63	–0.31 ± 0.93	
Control	1.98 ± 0.78	2.12 ± 0.62	0.14 ± 0.71	

Data are presented as mean ± SD.
[a]Across-group comparisons by analysis of variance.
[b]$P < 0.05$ versus baseline; [c]$P < 0.01$, [d]$P < 0.05$ versus the control group; [e]$P < 0.05$ versus the other exercise group.
BMI, body mass index; ASAT, subcutaneous adipose tissue in abdomen; AVAT, visceral adipose tissue in abdomen; SFAT, subfascial adipose tissue at mid-thigh level; SCAT, subcutaneous adipose tissue at mid-thigh level; IMAT, intramuscular adipose tissue at mid-thigh level; 1RM, one repetitive maximum; UE, upper extremity; LE, lower extremity; FPG, fasting plasma glucose; HbA_{1c}, glycosylated haemoglobin; RBP4, retinol-binding protein-4; k_{ITT}, fractional disappearance rate of insulin.

baseline. As expected, aerobic exercise training induced a greater body weight loss in comparison with the resistance exercise group and the control group; statistically significant difference between the three groups in terms of change from baseline (resistance exercise, –1.1 ± 1.3 kg; aerobic exercise, –1.9 ± 1.2 kg; control, –0.6 ± 1.7 kg; $P = 0.048$ across-group comparison).

After the 12-week training programme, overall fat mass of the whole body was reduced in both exercise groups, but the change was significantly greater in the aerobic exercise group versus the resistance exercise group (–5.4% versus –1.3%, respectively; $P = 0.038$; data not shown). The muscular mass of the upper and lower extremities in the resistance exercise group

increased from baseline (upper +5.3% and lower +1.3%, respectively), whereas that in the aerobic exercise group was unaltered (upper –0.3% and lower –0.1%, respectively); the difference between the aerobic and resistance exercise groups was statistically significant for the upper extremities (P = 0.001) but not for the lower extremities.

Decreases in BMI and ASAT were significantly different across the three groups (P = 0.044 and P = 0.015 respectively). Pair-wise multiple comparison revealed that the changes in BMI and ASAT in the aerobic exercise group were significantly greater than in the control group (P = 0.014 and P = 0.005, respectively), and ASAT in the resistance exercise group changed significantly more than in the control group (P = 0.044). The changes of SCAT, SFAT and IMAT were not statistically significantly different across the three groups, but SCAT and SFAT in the resistance exercise group changed significantly more than in the control group (P = 0.023 and P = 0.027, respectively, by pair-wise comparison). There was no statistically significant change in AVAT in the three groups (Table 2).

Resistance training was related to a greater increase in muscle strength compared with aerobic exercise. The resistance exercise group showed significant increases in 1RM for the upper and lower extremities (upper +11.8% and lower +11.5%; P = 0.040 and P = 0.006 versus baseline, respectively), whereas 1RM was reduced in the aerobic exercise group (upper –11.8%, lower –7.9%); the differences between the aerobic and resistance exercise groups were also statistically significant (upper, $P < 0.001$; lower, P = 0.006).

Leptin levels decreased significantly by 37.8% (from 9.86 ± 3.06 to 6.13 ± 4.00 ng/ml, $P < 0.001$) and adiponectin increased significantly by 75.1% (from 3.86 ± 2.00 to 6.76 ± 1.24 ng/ml, $P < 0.001$) in the aerobic exercise group. In the resistance exercise group, leptin levels did not change significantly after the intervention although there was a significant increase in adiponectin of 46.2% (from 4.98 ± 2.52 to 7.28 ± 3.72 µg/ml, P = 0.002). The change in leptin, but not in adiponectin, was statistically significant across the three treatment groups (P = 0.011). The change in plasma RBP4 level was significantly greater in the resistance exercise group (–16.4 ± 18.1 µg/ml, –16.7%) compared with the changes in the control (1.2 ± 23.2 µg/ml, +1.3%; P = 0.033) and aerobic exercise groups (–2.3 ± 16.9 µg/ml, –2.7%; P = 0.046). The change in plasma RBP4 concentration was significantly positively correlated with that in SFAT (r = 0.664, P = 0.013) in the resistance exercise group (Fig. 1), but there was no statistically significant correlation in the aerobic exercise group (r = –0.405). The changes in k_{ITT} and HbA_{1c} showed no statistically significant differences between the groups.

Discussion

There has been increasing interest in the effects of resistance training on the control of type 2 diabetes mellitus. One study revealed that resistance exercise led to significant improvements in the amount of visceral and abdominal subcutaneous adipose tissue, which has been linked to metabolic syndrome.[16] In a meta-analysis, the importance of intramyocellular fat as a contributor to insulin resistance was reported.[5] It is not the total amount of fat but the fat that resides within skeletal muscle cells (intramyocellular fat) and intra-abdominal fat (visceral fat) that influence insulin resistance, through the systemic and local secretion of several adipokines.[5]

Based on these findings, the effects of

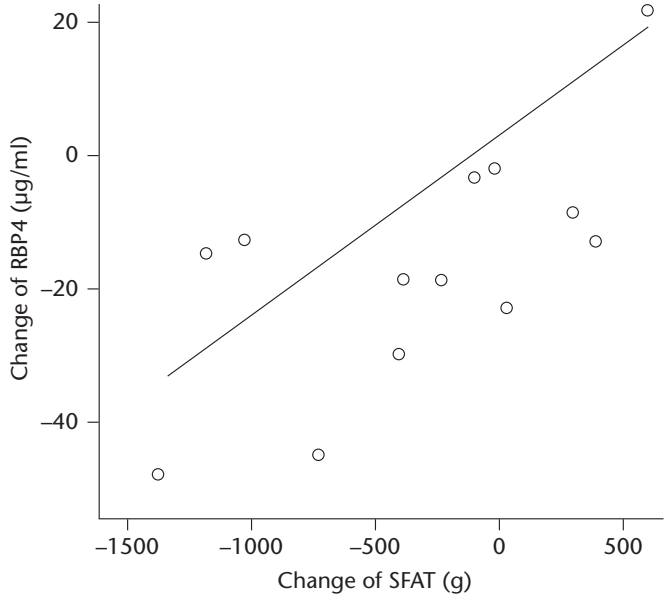

FIGURE 1: Correlation of the change in subfascial adipose tissue at mid-thigh level (SFAT) with the change in plasma retinol-binding protein-4 (RBP4) concentration during a 12-week programme of resistance exercise in 13 patients with diabetes mellitus type 2 ($r = 0.664$, $P = 0.013$)

different kinds of exercise on regional muscular adipose tissue were analysed in the present study. Perimuscular fat was divided into three categories – SCAT, SFAT and IMAT – and, using DXA, the effect of resistance training compared with aerobic training on each category was assessed. ASAT decreased significantly from baseline in each exercise group, and the decrease in ASAT across the three groups was also significant. No significant difference was observed across groups with respect to IMAT. Aerobic exercise was more effective in reducing adipose tissue than resistance exercise. Nonetheless, aerobic exercise was not always statistically superior to resistance exercise. For example, after 12 weeks of exercise training, maximal strength of both the lower and upper extremities increased significantly by 11.5% and 11.8%, respectively, only in the resistance group. In contrast, muscle strength did not increase in the aerobic exercise group. This result is consistent with previous studies in which resistance exercise was more effective in increasing muscle power than aerobic exercise.[17 – 21] To our knowledge, this is the first report to correlate the effects and type of exercise on categories of perimuscular adipose tissue.

One of the novel findings of this study was that the plasma RBP4 level was reduced more effectively in the resistance exercise group than in the aerobic exercise group. A few adipokines are related to the risk of developing insulin resistance, obesity, diabetes mellitus and cardiovascular disease, and there has been much interest in the effect of exercise training on adipokine levels. There have been reports that supervised exercise training reduces resistin levels[22] and that resting leptin responds positively to resistance training in persons with type 2 diabetes.[23]

Boudou *et al.*[24] reported that a supervised intensive training programme did not induce significant changes in adiponectin and leptin levels despite a tremendous decrease in abdominal fat and improvement in insulin sensitivity in sedentary middle-aged subjects with type 2 diabetes. In addition, Levinger *et al.*[25] reported that resistance training did not reduce inflammatory markers in individuals with a large number of metabolic risk factors. Thus, the association between exercise training and adipokines remains controversial. In particular, the effect of resistance exercise on plasma RBP4 concentrations still needs to be confirmed by further studies.

An association between regional fat and RBP4 level was identified in the present study, with RBP4 concentration being positively correlated with SFAT only in the resistance exercise group but not in the aerobic exercise group. To our knowledge, this is the first report of the correlation of plasma RBP4 concentration with regional fat in relation to the type of exercise.

It has been reported that resistance training is as effective as aerobic training in improving glucose control, glucose tolerance and the insulin response in both diabetic[13,14] and non-diabetic[26 – 28] participants. In the present study, however, no superiority was observed for resistance training in terms of glycaemic control or insulin sensitivity. For example, there was no significant difference in glycaemic control among groups after the 12 week training programme, although each group showed a slight, not statistically significant decrease in HbA_{1c} level. After completion of the study, the raw data were re-examined and it was found that, during the randomization process, patients with better insulin sensitivity based on k_{ITT} tended to be assigned to the aerobic exercise group, which may have biased the exercise effect. Furthermore, both exercise groups showed reasonable levels of glycaemic control at baseline as evidenced by the HbA_{1c} levels, which might have ameliorated the treatment effect.

In conclusion, the novel findings of the present study are that resistance exercise did not alter intramuscular adipose tissue but did reduce plasma RBP4 levels without improving insulin sensitivity.

Conflicts of interest

The authors had no conflict of interest to declare in relation to this article.

• Received for publication 19 November 2009 • Accepted subject to revision 10 December 2009
• Revised accepted 17 March 2010

References

1 Pan DA, Lillioja S, Kriketos AD, *et al*: Skeletal muscle triglyceride levels are inversely related to insulin action. *Diabetes* 1997; **46:** 983 – 988.
2 van Loon LJ, Koopman R, Manders R, *et al*: Intramyocellular lipid content in type 2 diabetes patients compared with overweight sedentary men and highly trained endurance athletes. *Am J Physiol Endocrinol Metab* 2004; **287:** E558 – E565.
3 Storlien LH, Jenkins AB, Chisholm DJ, *et al*: Influence of dietary fat composition on development of insulin resistance in rats. Relationship to muscle triglyceride and omega-3 fatty acids in muscle phospholipid. *Diabetes* 1991; **40:** 280 – 289.
4 Turcotte LP, Fisher JS: Skeletal muscle insulin resistance: roles of fatty acid metabolism and exercise. *Phys Ther* 2008; **88:** 1279 – 1296.
5 Rattarasarn C: Physiological and pathophysiological regulation of regional adipose tissue in the development of insulin resistance and type 2 diabetes. *Acta Physiol (Oxf)* 2006; **186:** 87 – 101.
6 Oberbach A, Tonjes A, Kloting N, *et al*: Effect of a 4 week physical training program on plasma concentrations of inflammatory markers in patients with abnormal glucose tolerance. *Eur J Endocrinol* 2006; **154:** 577 – 585.
7 Rasouli N, Kern PA: Adipocytokines and the

metabolic complications of obesity. *J Clin Endocrinol Metab* 2008; **93(11 suppl 1):** S64 – S73.
8 Yang Q, Graham TE, Mody N, *et al*: Serum retinol binding protein 4 contributes to insulin resistance in obesity and type 2 diabetes. *Nature* 2005; **436:** 356 – 362.
9 Corpeleijn E, Feskens EJ, Jansen EH, *et al*: Lifestyle intervention and adipokine levels in subjects at high risk for type 2 diabetes: the Study on Lifestyle intervention and Impaired glucose tolerance Maastricht (SLIM). *Diabetes Care* 2007; **30:** 3125 – 3127.
10 Kelley DE, Goodpaster BH: Effects of exercise on glucose homeostasis in Type 2 diabetes mellitus. *Med Sci Sports Exerc* 2001; **33(6 suppl):** S495 – S501; discussion S528 – S529.
11 Meltzer S, Leiter L, Daneman D, *et al*: 1998 clinical practice guidelines for the management of diabetes in Canada. Canadian Diabetes Association. *CMAJ* 1998; **159(suppl 8):** S1 – S29.
12 Ryan AS: Insulin resistance with aging: effects of diet and exercise. *Sports Med* 2000; **30:** 327 – 346.
13 Dunstan DW, Puddey IB, Beilin LJ, *et al*: Effects of a short-term circuit weight training program on glycaemic control in NIDDM. *Diabetes Res Clin Pract* 1998; **40:** 53 – 61.
14 Ishii T, Yamakita T, Sato T, *et al*: Resistance training improves insulin sensitivity in NIDDM subjects without altering maximal oxygen uptake. *Diabetes Care* 1998; **21:** 1353 – 1355.
15 Kadoglou NP, Iliadis F, Angelopoulou N, *et al*: The anti-inflammatory effects of exercise training in patients with type 2 diabetes mellitus. *Eur J Cardiovasc Prev Rehabil* 2007; **14:** 837 – 843.
16 Ibanez J, Izquierdo M, Arguelles I, *et al*: Twice-weekly progressive resistance training decreases abdominal fat and improves insulin sensitivity in older men with type 2 diabetes. *Diabetes Care* 2005; **28:** 662 – 667.
17 Hunter GR, McCarthy JP, Bamman MM: Effects of resistance training on older adults. *Sports Med* 2004; **34:** 329 – 348.
18 Ibanez J, Gorostiaga EM, Alonso AM, *et al*: Lower muscle strength gains in older men with type 2 diabetes after resistance training. *J Diabetes Complications* 2008; **22:** 112 – 118.
19 Häkkinen K, Pakarinen A, Kraemer WJ, *et al*: Basal concentrations and acute responses of serum hormones and strength development during heavy resistance training in middle-aged and elderly men and women. *J Gerontol A Biol Sci Med Sci* 2000; **55:** B95 – B105.
20 Kalapotharakos V, Smilios I, Parlavatzas A, *et al*: The effect of moderate resistance strength training and detraining on muscle strength and power in older men. *J Geriatr Phys Ther* 2007; **30:** 109 – 113.
21 Porter MM: Power training for older adults. *Appl Physiol Nutr Metab* 2006; **31:** 87 – 94.
22 Kadoglou NP, Perrea D, Iliadis F, *et al*: Exercise reduces resistin and inflammatory cytokines in patients with type 2 diabetes. *Diabetes Care* 2007; **30:** 719 – 721.
23 Kanaley JA, Fenicchia LM, Miller CS, *et al*: Resting leptin responses to acute and chronic resistance training in type 2 diabetic men and women. *Int J Obes Relat Metab Disord* 2001; **25:** 1474 – 1480.
24 Boudou P, Sobngwi E, Mauvais-Jarvis F, *et al*: Absence of exercise-induced variations in adiponectin levels despite decreased abdominal adiposity and improved insulin sensitivity in type 2 diabetic men. *Eur J Endocrinol* 2003; **149:** 421 – 424.
25 Levinger I, Goodman C, Peake J, *et al*: Inflammation, hepatic enzymes and resistance training in individuals with metabolic risk factors. *Diabet Med* 2009; **26:** 220 – 227.
26 Miller JP, Pratley RE, Goldberg AP, *et al*: Strength training increases insulin action in healthy 50- to 65-yr-old men. *J Appl Physiol* 1994; **77:** 1122 – 1127.
27 Ryan AS, Pratley RE, Elahi D, *et al*: Changes in plasma leptin and insulin action with resistive training in postmenopausal women. *Int J Obes Relat Metab Disord* 2000; **24:** 27 – 32.
28 Ryan AS, Hurlbut DE, Lott ME, *et al*: Insulin action after resistive training in insulin resistant older men and women. *J Am Geriatr Soc* 2001; **49:** 247 – 253.

Author's address for correspondence:
Dr Kyung-Wan Min
Department of Internal Medicine, Eulji University College of Medicine, 280-1 Hagye-Dong Nowon-Gu, Seoul 139-711, Republic of Korea.
E-mail: minyungwa@yahoo.co.kr