rameters and physical fitness remains unknown.

Thus, here we have investigated the effects of a low-intensity and low-volume exercise program suitable for the elderly on lipid and glucose metabolism in this population. Where exercise resulted in metabolic improvements, we also investigated the association between these metabolic improvements and the exercise-related physical improvements in body composition and aerobic fitness.

Methods

Subjects

A total of 75 older adults (26 males, aged 68±6 years; and 49 females, aged 65±6 years) volunteered to participate in the exercise program through public advertisement. Individuals were excluded if they had 1) cardiovascular disease, renal failure or other serious illnesses; 2) orthopedic problems likely to interfere with exercise participation; 3) resting blood pressure >159/99 mmHg; or 4) plasma total cholesterol >300 mg/dL, and triglyceride concentration >500 mg/dL. Individuals on medication, including antihyperlipidemic or antihypertensive drugs, were included if there was no change in the dose throughout the intervention period. Subjects gave their written consent to participate in the study, which had received the approval of the Ethics Committee of University of Tsukuba.

Measurement of body composition

Body composition was evaluated by BMI and abdominal fat area. BMI was calculated as the weight/(height)^2(kg/m^2). Abdominal fat area was determined by computed tomography (CT) scan (Aquilion16, Toshiba, Tokyo, Japan) according to the procedure of Tokunaga et al (16), in which the total fat area (TFA) and visceral fat area (VFA) were measured at the level of the umbilicus.

Measurement of aerobic capacity

Aerobic fitness was assessed as peak oxygen uptake (VO$_2$ peak). The subjects sat quietly on a cycle ergometer (75 XLII, Combi Co, Tokyo, Japan) for 3 min and then warmed up at a rate of 0.5 Kp over 4 min. They then pedaled at the higher rate of 0.5 Kp/min. The air expired was analyzed breath-by-breath by using an automatic expired gas analyzer (AE280, MINATO, Osaka, Japan). The VO$_2$ peak tests fulfilled at least one of the following three criteria: 1) systolic blood pressure >250 mmHg; 2) heart rate within 10 beats/min of the maximal heart rate predicted for age; 3) volitional fatigue. Ventilatory threshold (VT) was determined by the V-slope method (12), using computer regression analysis of the plot of carbon dioxide production versus oxygen consumption.

Blood sampling

Blood was drawn in the morning after an overnight fast. Total cholesterol (TC), HDL-C, TG, fasting immunoactive insulin (IRI), fasting plasma glucose (FPG) and glycosylated hemoglobin (HbA$_1$c) were determined. Plasma glucose was measured by the glucose oxidase method. HbA$_1$c was measured by Latex agglutination. Serum TC, TG and HDL-C were determined by enzymatic methods. Low density lipoprotein cholesterol (LDL-C) was calculated by the Friedewald formula (13). However, LDL-C was not calculated if the TG level was >300 mg/dL. Serum insulin was determined by enzyme immunoassay (EIA). Insulin resistance was evaluated by HOMA-IR [FPG (mg/dL)×IRI (µLU/mL)/405], according to the method developed by Matthews et al (14).

Measurement of blood pressure (BP)

BP was not measured for practical reasons, namely, minimizing the variation across measurements calls for five or more BP measurements to be taken in at least two settings (15) and the reproducibility of within-day BP measurements is known to be poor (16).

Diet evaluation

Dietary intake was estimated on the basis of consecutive three-day (including one weekday) food diaries at the beginning and the end of the program. Each participant was instructed on how to record detailed descriptions of all foods consumed. Total dietary energy and lipid intake were calculated with the PC software 'Food Frequency Questionnaire Based on Food Groups' Ver. 2.3 (Kenpaku Co., Tokyo).

Exercise training program

A 12-week supervised training program was designed to improve the aerobic capacity and strength of large muscle groups (back, abdomen, lower and upper bodies). Two different training elements were employed in the program: low-intensity aerobic training three times a week, and resistance training with body weight alone (no external load) twice a week. Aerobic training was carried out for 30 min at 80% VT (corresponding to 50.2±8.6% of VO$_2$ peak) on the basis of an initial maximal graded exercise tolerance test. The resistance exercises selected were seated knee extension, hip extension in the standing position, knee flexion while holding onto a wall, calf raise, bent-knee sit up, back extension in the prone position, and bent knee push up (with knees on the floor). The subjects performed three sets of 10 repetitions.

Statistical analysis

The results are expressed as the mean ± standard deviation (SD). Analysis of variance (ANOVA) was used to compare variables between males and females or among stratified groups. Duncan's multiple range test was used to identify the difference across stratified groups if the ANOVA was significant. Pearson's correlation coefficient (r) was used to assess the relationship between changes in physical and metabolic parameters. A P value of less than or equal to 0.05 was considered to be statistically significant. SPSS 13.0

Table 1. Physical and Metabolic Profiles before and after Training

variable	before	after	Mean Relative Changes (%)	Confidence Interval (%)
age (yr)	64 ± 6			
Body mass index (kg/m^2)	23.4 ± 2.4	22.9 ± 2.3	−1.9 ± 2.9^b	[−2.7, −1.1]
Total fat area (cm^2)	202 ± 75	187 ± 72	−1.0 ± 3.3	[−10.0, 8.0]
Visceral fat area (cm^2)	72 ± 45	63 ± 40	−1.8 ± 4.9	[−15.2, 11.7]
VO_2 peak (mL/kg/min)	22.5 ± 4.2	22.8 ± 3.6	2.7 ± 12.4	[−0.7, 6.1]
Triglycerides (mmol/L)	1.20 ± 0.66	1.12 ± 0.58	0.3 ± 33.1	[−8.7, 9.3]
HDL cholesterol (mmol/L)	1.55 ± 0.37	1.59 ± 0.37	3.2 ± 13.2	[−0.4, 6.8]
LDL cholesterol (mmol/L)	3.31 ± 0.70	3.12 ± 0.65	−4.1 ± 14.8^c	[8.2, −0.0]
Fasting plasma glucose (mmol/L)	5.81 ± 0.72	5.73 ± 0.78	−0.9 ± 7.2	[−2.9, 1.0]
Fasting plasma insulin (pmol/L)	58.0 ± 36.2	44.5 ± 36.3	−20.6 ± 31.5^b	[−29.2, −12.0]
HOMA-IR	2.2 ± 1.5	1.7 ± 1.4	−18.4 ± 34.7^b	[−27.7, −9.0]
HbA_1c (%)	5.2 ± 0.5	5.1 ± 0.5	−1.0 ± 4.0	[−2.1, 0.1]

Data were mean±SD. [a]Relative changes are post-training to pre-training values. $^b P < 0.01$, $^c P < 0.05$

J for Windows software (SPSS Institute, Chicago, IL) was used for the analysis.

Results

Effect of exercise on physical and metabolic profiles

Of the 75 participants enrolled in the trial, 56 (14 males and 42 females; mean age, 64±6 years) who attended more than 85% of the 12-week training program and provided all of the pre- and post-training data were included in the analysis. Dietary intake did not change significantly during the intervention (data not shown). The physical and metabolic characteristics of the subjects at the beginning and the end of the 12-week training program are shown in Table 1. There were no differences between the genders in the baseline values or in the responses to the 12-week exercise program, except that women had significantly higher LDL-C than men (3.46±0.60 mmol/L vs. 2.85±0.81 mmol/L; $P=0.02$). There were no significant changes in TFA, VFA, VO_2 peak, HDL-C, TG, FPG, or HbA_{1c}. The reduction in BMI was small but highly significant ($P<0.001$). A borderline-significant reduction was seen in LDL-C (-4%, $P=0.05$). By contrast, the relative changes in IRI and HOMA-IR were larger (-20% and -21%, respectively) than those in the other variables and were statistically significant ($P<0.001$ for both).

Relationship between physical and metabolic profiles

To investigate whether there was an association between the improvement in insulin resistance and physical changes, we tested for a correlation between the reduction in HOMA-IR and other physical changes. We found a borderline significant correlation between the reduction in HOMA-IR and the reduction in BMI ($r=0.26$, $P=0.06$). However, neither the improvement in VO_2 peak nor that in VFA was significantly related to the reduction in HOMA-IR ($r=-0.19$, $P=0.17$, and $r=0.06$, $P=0.65$, respectively).

To investigate in more detail the relationship between the reduction in HOMA-IR and the physical changes, we divided the data into tertiles on the basis of the baseline BMI and VO_2 peak values. The data stratified into tertiles by baseline BMI are shown in Table 2. The reduction in BMI was small but statistically significant in all groups. A paired t-test confirmed that there was a significant reduction in HOMA-IR in the Middle- and High-BMI groups ($P<0.01$ and $P=0.04$, respectively). In the High-BMI group, there was a significant correlation between the reduction in HOMA-IR and the reduction in BMI ($r=0.61$, $P=0.01$) (Fig. 1), and the association between the reduction in HOMA-IR and the reduction in VFA was borderline significant ($r=0.47$, $P=0.06$). In the Middle-BMI group, however, the reduction in HOMA-IR was independent of the reduction in BMI ($r=0.08$, $P=0.74$) (Fig. 1) or VFA ($r=0.07$, $P=0.79$).

The data categorized into tertiles by baseline VO_2 peak are shown in Table 3. Exercise training led to a significant improvement in VO_2 peak in the Middle- and Low-VO_2 peak groups ($P=0.02$ and $P=0.02$, respectively), but there was no significant improvement across all three groups (see Table 1) or in the High-VO_2 peak group.

ANOVA did not reveal a difference in the reduction in HOMA-IR among the three groups ($P=0.69$). In the Middle-VO_2 peak group, we did not find a significant relationship between the reduction in HOMA-IR and the improvement in VO_2 peak, as in the overall analysis. In the Low-VO_2 peak group, however, the reduction in HOMA-IR was related to the improvement in VO_2 peak (Fig. 2).

Discussion

Previous reports have noted that exercise training may improve insulin resistance and lipid metabolism in elderly subjects (17-21). However, it is doubtful whether the exercise training programs studied are feasible for most elderly people. Thus, here we implemented a low-intensity (~50% VO_2 peak) and low-volume (90 min/wk in aerobic training) exercise training program that, to our knowledge, has not previously been studied.

Table 2. Mean Values of the Subjects Stratified into Tertiles of BMI

BMI tertile	Low		Middle		High		Significance (at baseline)^c
	pre	post	pre	post	pre	post	
No. of participants (women)	19 (15)		19 (13)		18 (14)		
Age (yrs)	66±6		63±6		63±6		NS
BMI (kg/m^2)	20.9±1.1	20.7±1.2^a	23.4±0.7	22.7±0.9	26.0±1.3^a	25.5±1.6	L< M< H
TFA (cm^2)	146±42	134±50	193±51	181±53	268±75	246±65	L< M< H
VFA (cm^2)	37±21	34±19	70±32	63±34	106±47	88±44	L< M< H
VO_2 peak	24.2±4.5	23.1±3.5	22.1±2.4	23.9±3.4	21.2±4.9	21.2±3.5	L> H
TG (mmol/L)	0.91±1.42	0.83±0.33	1.22±0.78	1.11±0.71	1.48±0.42	1.42±0.50	L< H
HDL-C (mmol/L)	1.75±0.34	1.81±0.28	1.52±0.42	1.58±0.43	1.36±0.22	1.37±0.24	L> M, H
LDL-C (mmol/L)	3.30±0.60	3.05±0.52^a	3.44±0.66	3.22±0.61	3.18±0.84^a	3.09±0.82	NS
FPG (mmol/L)	5.81±0.86	5.83±1.12	5.75±0.76	5.63±0.65	5.83±1.12	5.75±0.76	NS
IRI (pmol/L)	45.0±36.6	41.7±53.8	53.7±28.1	34.5±17.1	76.3±38.6	58.8±23.1	L< H
HOMA-IR	1.8±0.6	1.6±2.1	2.0±1.1	1.3±0.7	2.9±1.5	2.1±0.9	L< H
HbA_1c (%)	5.3±0.7	5.3±0.8	5.2±0.4	5.1±0.3	5.3±0.8	5.2±0.4	NS

Data were mean±SD ^{a} Significant difference (P<0.01) between pre- and post-training value by the paired t test.

^{b} Significant difference (P<0.05) between pre- and post-training value by the paired t test.

^{c} Analysis of variance (ANOVA) and Duncan's multiple range test was performed to investigate the difference in initial values among tertiles. NS, not significant.

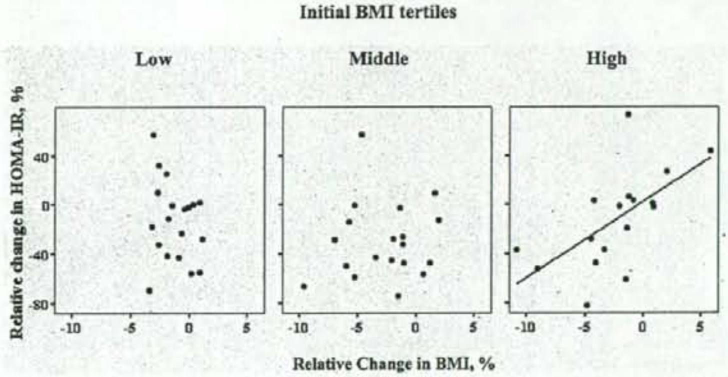

Figure 1. Relationships between relative change in HOMA-IR and relative change in BMI in three groups stratified on the basis of baseline BMI (Low, Middle, High). Low: y=-18.84+ -5.12x, r= -0.24 (P=0.33), Middle: y=-27.31+0.81x, r=0.08, (P=0.74), High: y=2.25+6.16x, r=0.61 (P=0.01).

This exercise training did not result in an improvement in serum HDL-C or TG levels in the elderly. Several studies suggest that there is a dose-response relationship between exercise training volume and blood lipid changes in the general population (22). Our result indicates, however, that low-volume exercise training is not sufficient to alter lipid values in the elderly.

The American College of Sports Medicine (ACSM) has stated that exercise training at an intensity of less than about 50% maximal oxygen uptake (VO_2 max) is generally not sufficient for developing fitness in healthy adults (23). In the present study, the VO_2 peak did not significantly increase after training on average (Table 1) or in those individuals with an initially high VO_2 peak (Table 3), consistent with the statement by the ASCM. This finding suggests that low-intensity (i.e. 50% of maximal aerobic capacity or less) exercise training is also not necessarily effective in improving aerobic capacity in healthy elderly people. By contrast, a large reduction in mean IRI and HOMA-IR was seen after the exercise training program. This finding indicates that even a low level of exercise that fails to improve lipid values and/or aerobic fitness can improve insulin resistance in elderly subjects.

Several studies have indicated that an improvement in insulin resistance is associated with weight and/or fat loss but not with an exercise-induced improvement in aerobic capac-

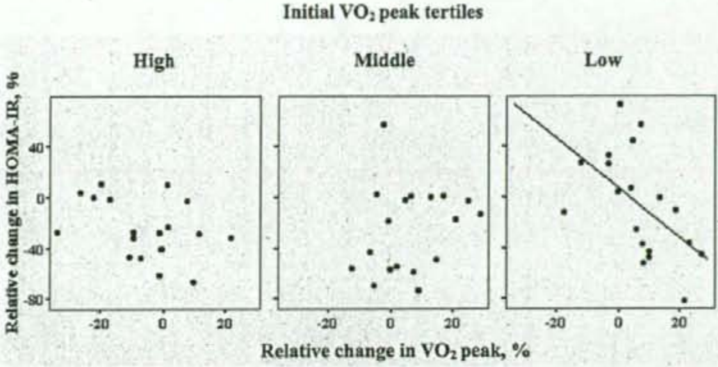

Figure 2. Relationships between relative change in HOMA-IR and relative change in VO_2 peak in three groups stratified on the basis of baseline aerobic fitness (Low, Middle, High-VO_2 peak). Low: y=7.01+1.97x, r=-0.54 (P=0.02), Middle: y=-29.30+0.63x, r=0.21 (P=0.40), High: y=-27.75+ -0.61x, r=-0.37 (P=0.13).

Table 3. Mean Values of the Subjects Stratified into Tertiles of VO_2 Peak

VO_2 peak tertile	Low pre	Low post	Middle pre	Middle post	High pre	High post	Significance (at baseline)[c]
No. of participants (female)	19 (13)		18 (14)		19 (15)		
age (yrs)	62±5		64±6		66±6		H< L
VO_2 peak (mL/kg/min)	27.0±3.2	25.1±2.5	22.2±0.8	23.7±2.6[b]	18.4±1.9	19.7±3.1[b]	H> M> L
BMI (kg/m^2)	22.8±2.1	22.3±2.0[a]	22.7±0.9	22.3±1.9[b]	24.7±2.7	24.2±2.6[b]	M, H< L
TFA (cm^2)	181±66	175±67	161±43	149±53	255±76	229±71	M< L
VFA (cm^2)	70±45	65±42	54±31	43±24	88±51	76±45	NS
TG (mmol/L)	1.18±0.82	1.06±0.69	1.06±0.58	0.91±0.41	1.36±0.54	1.36±0.54	NS
HDL-C (mmol/L)	1.58±0.41	1.63±0.43	1.60±0.39	1.68±0.36	1.48±0.32	1.47±0.29	NS
LDL-C (mmol/L)	3.26±0.71	3.09±0.65	3.26±0.83	2.97±0.68[a]	3.41±0.58	3.29±0.61	NS
FPG (mmol/L)	5.98±0.90	5.88±1.12	5.57±0.48	5.50±0.53	5.87±0.69	5.81±0.52	NS
IRI (pmol/L)	55.2±30.6	40.6±24.4[a]	53.3±33.8	42.7±54.6	65.1±43.4	49.9±23.4	NS
HOMA-IR	2.1±1.4	1.6±1.1[a]	1.9±1.3	1.5±2.0	2.5±1.7	1.9±0.9	NS
HbA_1c (%)	5.2±0.7	5.2±0.8	5.1±0.3	5.1±0.4	5.2±0.4	5.1±0.3	NS

[a] Significant difference (P<0.01) between pre- and post-training value by the paired t test.

[b] Significant difference (P<0.05) between pre- and post-training value by the paired t test.

[c] Analysis of variance (ANOVA) and Duncan's multiple range test was performed to investigate the difference in initial values among tertiles. NS, not significant.

ity (2, 3, 5). However, the subjects in those studies were obese or overweight (BMI>25). It is not known whether weight and/or fat loss is an important indicator of an improvement in insulin resistance during exercise training in non-obese participants. Therefore, we categorized the participants into three groups based on their obesity level (i.e. BMI). As shown in Fig. 1, for the High-BMI group, the reduction in BMI was significantly associated with the reduction in HOMA-IR, in agreement with the results of previous studies. However, there was no relationship between the reduction in BMI and that in HOMA-IR in the Middle-BMI (non-obese) group. These results suggest that the improvement in insulin resistance after exercise training is independent of weight loss for non-obese elderly people. According to the results of the Japan Diabetes Complication Study Group, Japanese individuals with type 2 diabetes are less obese than their European counterparts (24). Therefore, it will be important to investigate whether exercise training can also improve insulin resistance independent of weight loss in individuals with type 2 diabetes.

By contrast, most studies (2, 5) have found no association between an improvement in insulin resistance and an improvement in aerobic capacity. However, those studies did not consider the effect of the initial fitness levels of the participants on this association and, in addition, the exercise intensity in those studies was higher than that in our study. Because differences in the initial aerobic capacities of the subjects affect the physical fitness response to the exercise training (particularly when the exercise intensity is low) (25), as indicated in the present study (see Table 3), it seems to be necessary to categorize the subjects on the basis of their initial fitness level in order to investigate the association between the improvement in insulin resistance and the improvement in aerobic capacity. Therefore, we categorized the participants into tertiles based on VO$_2$ peak.

In the overall study population, there was no significant correlation between the improvements in HOMA-IR and in VO$_2$ peak ($r=-0.19$, $P=0.17$), in support of previous studies. In the stratified analysis, by contrast, the improvement in HOMA-IR was associated with the improvement in VO$_2$ peak for the Low-VO$_2$ peak group. The present findings suggest that exercise training can be effective/important/indication, especially for elderly people with a low fitness level, because it improved insulin resistance in parallel with an increase in aerobic capacity.

The present study has the following strengths. First, the exercise level of the training program employed was low, and thus it would be suitable for most elderly people. Second, there was no dietary restriction. Some studies indicate that not only intentional but unintentional weight loss in elderly adults may lead to a decrease in total body mineral density (26), or the development of disease and an increase risk of mortality (27). The mean body weight loss during the intervention period was small (1.2 kg), and thus safe from a medical viewpoint.

Some limitations of the current study should be emphasized. First, the subjects recruited might be healthier than the general elderly population, who may possibly be more fragile and have barriers to exercise training. Second, we did not determine the effect of exercise training on BP. More than half the population over 60 years of age has hypertension (defined as systolic blood pressure of at least 140 mmHg and/or diastolic pressure of at least 90 mmHg) (28), and elevated BP leads to a number of cardiovascular complications (29). Although it is well known that exercise lowers resting blood pressure (30), there is little evidence that low-intensity, low-volume exercise training also has a BP-lowering effect. Further research is therefore needed to determine the effect on resting BP of a low-level exercise training program that is feasible for most elderly people. Third, no sedentary control group was included. Thus, we might not have adequately demonstrated the benefits of the exercise training program itself.

In conclusion, even low-intensity and low-volume exercise training, which would ordinarily be insufficient to improve aerobic fitness and lipid metabolism in healthy elderly subjects, was found to be effective in reducing insulin resistance in the elderly. In non-obese elderly subjects, exercise training can improve insulin resistance independent of weight loss; in obese subjects, by contrast, the improvement in insulin resistance and weight loss were found to be mutually associated. Furthermore, in elderly people with low aerobic fitness, insulin resistance was improved in relation to an exercise-induced improvement in their fitness level.

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