Effects of resistance exercise on lipolysis pathway in obese pre and postmenopausal women

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Research

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Abstract

Background and objectives: The purpose of study was to examine the effects of regular resistance exercise for 12 weeks on lipolysis pathway in pre- and post- menopausal women with obesity.

Methods: Twenty-three pre- and post- menopausal women with body fat percentages of 30% or more divided into pre- menopausal group (n=9) and post- menopausal group (n=14). All subjects participated in resistance exercise training for 12 weeks. Anthropometric and physical fitness tests were performed on all participants. Protein analyses were performed with subcutaneous fatty tissue extracted, and the samples were analyzed of relevant protein levels changes by using Western blotting. All serum samples were submitted for enzyme-linked immunosorbent assay measurements of adipocyte factors.

Results: After 12 weeks between pre- menopausal and post- menopausal groups adipose triglyceride lipase (ATGL), monoacylglycerol lipase (MGL) and perilipin (PLIN) protein levels were significantly lower in the post- menopausal group than in the pre- menopausal group. Hormone-sensitive lipase (HSL) protein levels were significantly higher in the post- menopausal group than in the pre- menopausal group. In addition, leptin concentration was significantly decreased after resistance exercise in the post-menopausal group. Adiponectin concentration was significantly increased after resistance exercise in the both groups.

Conclusions: This study indicates that regular resistance exercise to change of leptin and adiponectin might be release of reduction of % fat, and driving overall greater change ATGL, HSL, MGL and PLIN levels in subcutaneous fatty tissue in the obese post- menopausal group more than obese pre-menopausal group.

Introduction

Adipose tissue is recognized as an endocrine organ. A complex interplay between multiple endocrine mediators and the sympathetic nervous system has been shown to govern adipocyte metabolism. In the postprandial state, insulin promotes glucose and fatty acid uptake as well as lipogenesis and suppresses triglyceride lipolysis [1].

Excess body weight results from an imbalance between energy intake and energy expenditure [2], one way to maintain a correct body weight is to stimulate lipid catabolism through increased physical activity. Properly designed training simulates fat breakdown, that is, hydrolysis of triacylglycerol stored in adipose tissue, releasing free fatty acids into the circulation and causing oxidation in muscles and other tissues [3]. Some studies demonstrated that low-intensity endurance training leads to maximal lipid oxidation, but available evidence in this matter is inconclusive [4]. The post-exercise decrease in triacylglycerols content in adipose tissue is with no doubt a consequence of enhanced lipolysis. The process, initiated by adipose triglyceride lipase (ATGL), is then continued by hormone-sensitive lipase (HSL), upon phosphorylation thereof; eventually, the last free fat chain is hydrolyzed by monoacylglycerol lipase (MGL) [5]. Chronic exercise was shown to normalize the markers of this process, phosphorylated HSL and

ATGL, in mice that have been previously maintained on a high fat diet [5]. In addition, the lipolysis response to exercise is also reduced in elderly subjects, which can be attributed to a decrease in intracellular activation of fat breakdown in fat cells to some extent [6], and a recent study demonstrated that acute resistance exercise contributed to triacylglycerol lipase activity increased 16-fold at 10 min in the obese men's adipose tissue [7]. However, voluntary wheel running for 42 days contributed to a decrease in phosphorylated HSL level in rat [8].

Changes in the metabolism of adipose tissue can greatly contribute to changes in body fat distribution during menopause transition, and the menopause condition might be also affect adipose tissue lipolysis, which in turn can contribute to changes in body composition [9]. Previous study observed that higher lipolytic reactions and sensitivities in the abdomen and breast compared to premenopausal female femoral adipose cells, but no postmenopausal female [10]. However, resistance exercises have been effective in improving body composition for pre- and post- menopausal women [11], acute resistance exercise increases subcutaneous abdominal adipose tissue lipid decomposition and fatty oxidation in women [12].

Thus, physical exercise may stimulate lipolytic activity within adipose tissue. Furthermore, resistance exercise may contribute to more efficient reduction of adipose tissue mass and prevent accumulation thereof. However, there is a lack of research that directly analyzes adipose tissue in humans and long-term resistance exercise intervention.

The purpose of this study was to investigate the modulation of 12-weeks of regular resistance exercise on lipolysis pathway in obese pre and postmenopausal women. In addition, this study aims to provide basic data on the prevention of postmenopausal who may be exposed to obesity or metabolic syndrome. In this study, it was hypothesized that resistance exercise would be effective for lipolysis like endurance exercise in obese human, and regular resistance exercise would be independently associated with menopause.

Materials And Methods

Participations

Participants were arbitrary recruited from the general population of local communities. Among the 40 women participants enrolled in the study. To be eligible for inclusion, participants had to meet the following inclusion criteria: 1) postmenopausal (absence of a menstrual cycle for at least 1 year and follicle-stimulating hormone >30 IU/L) at least 40 (premenopausal) and 50 (postmenopausal) years of age on the date of the assessment; 2) at least body fat percentages of 30% or more on the date of the assessment; 3) not receiving hormone replacement treatment; and 4) not using drugs such as beta-blockers, and statins. To achieve a final sample of 23 women were divided into PRM (pre- menopausal group, n=9) and POM (post- menopausal group, n=14). The sample size of the participations was calculated by using ANOVA a large size of effect size of .90, a significance level of .05 and a power of .80 (G*power 3.2.1).

All volunteers underwent medical screening by medical specialist, including a health status interview and physical examination. Written informed consent was obtained from all subjects. The study was approved by Kangwon National University Institutional Review Board (KWNUIRB-2016-04-009-002), and conducted in agreement with the Declaration of Helsinki.

Table 1. Characteristic of the participations

Variable	Group	Mean ± SD (range)	*P*-value
Age (year)	PRM (n=9)	44.44±3.50 (41 - 47)	<0.0001
	POM (n=14)	60.50±6.12 (56 - 64)	
Height (cm)	PRM (n=9)	158.71±5.28 (154 – 167)	.190
	POM (n=14)	155.95±3.48 (151 – 164)	
Weight (kg)	PRM (n=9)	66.90±13.40 (48 – 83)	.313
	POM (n=14)	61.81±6.51 (50 – 72)	
Fat (%)	PRM (n=9)	36.98±7.41 (31 - 42)	.512
	POM (n=14)	35.04±5.59 (31 - 38)	

Mean±SD
PRM; premenopausal, POM; postmenopausal
P-value was analyzed by independent t-test

Body composition and physical fitness

All subjects underwent anthropometric measurements. A body compositions measured using a multi-frequency bioelectrical impedance analyzer with eight tactile electrodes (MF- BIA8) (Inbody 720 body compostion analyzer, Biospace, Seoul, Korea) at the Exercise Physiology Laboratory of Kangwon National University. Bioelectrical impedance analysis was performed after at least 8 h of fasting and voiding. This analyzer uses an alternating current of 250 mA at a multi-frequency of 1 kHz, 5 kHz, 50 kHz, 250 kHz, 500 kHz and 1,000 kHz. It measures segmental impedances at the right arm, left arm, right, leg, left leg and trunk for all frequencies. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Waist-to-hip ratio (WHR) was calculated as waist circumference divided by the rip circumference.

Physical fitness tests were performed with a circulation measuring device using O2run's Hellmass system 3 (grip strength, sit-ups, sit and reach test, standing long jump, and side step). All measurements were entered into an electronic card and transmitted to the computer. To measure grip strength, subjects stood with both feet at shoulder width and maintained an angle of 15 degrees so that the torso and the arm did not touch each other. They held the handle of the dynamometer with second joints of their fingers and pulled the handle while keeping their arms from shaking. For sit-ups, subjects laid on a mat and bent their knees about 140 degrees. Their feet were flat on the floor. Then the upper body was raised until elbows touched knees. The number of repetitions made in 60 secs was recorded. For sit and reach test, subjects were asked to bend their upper body while fixing the two legs in plate. For standing long jump, all subjects started with their feet in place and jumped as far as possible with the two feet landing together. For side

step, parallel lines were drawn at a distance of 120cm on the floor and subjects stood on both feet, one foot on the left side and the other foot on the right side, from the center line.

Subcutaneous fatty tissue extracted and Western blot

All study participants agreed to an abdominal biopsy.

Plastic surgeon extracts the abdominal fat 30g twice before and after exercise program by Hirsch et al. [13]. At first time, right side abdominal fat was extracted. At second time, left side abdominal fat was extracted after exercise program. The participant lied on the operation bed and plastic surgeon clean the abdomen of applicant with betadine. Plastic surgeon anesthetize the incisional window (1cm length) for liposuction machine tip with 2% lidocaine. The incisional window was made by no 15 blade and tumescent solution (500cc saline, 2% lidocaine 5cc and 0.1cc epinephrine were mixed) was infiltrated to the around of incisional window. Plastic surgeon extracts the abdominal fat (30cc) with liposuction machine by Hirsch and Gallian [14]. The fat was centrifuged during 3 minutes and pure fat cell could be separated. The pure abdominal fat was stored at –18 degrees immediately. The incisional window was sutured with 4-0 nylon and covered the waterproof bandage. The suture materials were removed at 7 postoperative days.

To extract protein from the subcutaneous fatty tissue, the tissues were lysed in 200 ul radioimmunoprecipitation assay (RIPA) buffer. The tissue was homogenized and centrifuged for 30 min at 14,000 rpm. The protein concentration of the supernatant was measured using the BCA protein assay kit (Pierce, Rockford, IL, USA). Samples of equal protein content were resolved by SDS-polyacrylaminde gel electrophoresis on a 10 or 12 % gel, and transferred to a membrane. The membrane was blocked with 5% skim milk in phosphate-buffered saline (PBS), and subsequently incubated at 4°C overnight with primary antibodies (1:1,000 dilution) against perilipin (PLIN) (sc-240627), ATGL (adipose triglyceride lipase, sc-67355), MGL (monoglyceride lipase, sc-72277), and HSL (hormone-sensitive lipase, sc-25843) (all from Santa Cruz Biotechnology Inc., Santa Cruz, CA, USA). The signal was developed with an ECL solution (Amersham Pharmacia Biotech Inc., Piscataway, NJ, USA) and visualized with the Image Quant TM LAS-4000 system (GE Healthcare, Uppsala, Sweden).

Blood collection and analysis

Fasting venous blood samples were collected from all participants at baseline, 6-weeks, and 12-weeks. Fasting was maintained for at least 8 h, and blood samples were collected on the following day. Enough sleep and the radical movement as much as possible to refrain. All samples were taken at 0830 AM from an antecubital vein. Serum samples were obtained after centrifugation and stored at -80°C. Serum levels of leptin and adiponectin were measured using enzyme-linked immunosorbent assay Dueset kits (R&D systems, Minneapolis, MN, USA) according to the manufacturer's instructions, as described previously.

Exercise intervention

Resistance exercise programs were used following experiments performed by Gurudut and Rajan with slight [15], modifications to fit the purpose of our experiment. The goal of the resistance exercise intervention was to moderate intensity exercise 60 min per day, 3 days per week for 12 weeks. At the beginning of each session, there was a 10 min of warm-up. It was followed by 40 min of the main part of the exercise with specific content and 10 min of cool-down. Warm-up exercises included 5 minutes of stretching, and 5 minutes of power walking at 50% intensity of the maximal heart rate reserve. Among resistance exercises, moderate intensity exercise was defined as circuit exercise at 55~65% intensity of 1 RM with burn 230~260kcal, 12 repetitions, and 3 sets. The rest period between each category was 30 seconds. The rest period between sets was 1 minute in total resistance exercise time of 60 min. Participants performed the same five lower and upper body resistance exercise (upper body resistance exercise: chest press, let pull down, biceps curl, triceps extension, and crunch; lower body resistance exercises: squat, lunge, knee extension, and calf raises). All exercise groups were given a polar (heart rate monitor; M400, Kempele, Finland), a portable exercise intensity setting device, for 60 minutes. Measurement of 1RM was calculated using formula of Brzycki: 1RM = Lifted weight (lb) / (1.0278 - repetitions×0.0278). All exercises were performed by re-measuring 1RM every two weeks [16].

In addition, dietitians and exercise physiologists met regularly with a clinical health psychologist experienced in lifestyle behavior change to discuss participant progress and refine behavior modification goals (pain during exercise, side effects due to weight loss, and encouragement to participate in exercise) according to each participant's needs. Nutritional education, self-management exercise, and behavior change techniques were provided. Furthermore, telephone consultations were scheduled biweekly for monitoring and motivation.

Table 2. Resistance exercise program

Exercise	Type	Time (min)	Total exercise volume
Resistance Exercise	Warm-up	10	3 times per week
	1. Squat	40	3 sets
	2. Chest press		55~65% RM
	3. Lunge		burn 230~260 kcal
	4. Let pull down		
	5. Knee extension		
	6. Biceps curl		
	7. Knee flexion		
	8. Triceps Extension		
	9. Calf raises		
	10. Crunch		
	Cool-down	10	

Results

Change of body composition after exercise

The change of body composition according to each group is shown in Table 3. Results from two-way factor ANOVA showed that no significant group × time interaction. Weight (main effect of time, $p<0.01$), BMI (main effect of time, $p<0.0001$), % fat (main effect of time, $p<0.0001$), WHR (main effect of time, $p<0.0001$), and SBP (main effect of time, $p<0.01$) were significantly decreased than baseline values after 12 weeks.

Post-hoc analysis using Bonferroni correction with a paired t-test indicated in the PRM group that significantly decreased 12-weeks than 6-weeks and baseline in weight, % fat, BMI, WHR, SBP and DBP. Weight, BMI, % fat and WHR were greater at 12-weeks than 6-weeks and baseline in the POM group.

Table 3. Change of body composition

variable		0week	6weeks	12weeks	F-value (*p*-value)
Weight (kg)	PRM	66.90±13.40	66.47±12.83	64.46±11.73[a, c]	G: 1.513 (.232) T: 10.692 (.001) G×T: 2.463 (.097)
	POM	61.81±6.51	60.98±6.14[b]	60.65±5.68[a]	
BMI (kg/m^2)	PRM	26.36±4.29	26.33±4.40	25.46±3.74[c]	G: 0.392 (.538) T: 10.606 (<0.0001) G×T: 2.624 (.084)
	POM	25.49±2.69	25.10±2.56[b]	24.96±2.44[a]	
Muscle (kg)	PRM	22.72±4.10	23.16±4.03	23.26±4.22	G: 0.884 (.358) T: 2.144 (.130) G×T: 0.438 (.619)
	POM	21.68±1.95	22.10±2.06	21.86±1.87	
Fat (%)	PRM	36.98±7.41	35.48±7.08[b]	33.57±6.49[a]	G: 0.407 (.530) T: 10.719 (<0.0001) G×T: 1.958 (.155)
	POM	35.04±5.59	32.87±6.03[b]	33.20±5.37[a]	
WHR	PRM	0.93±0.06	0.92±0.06[b]	0.90±0.05[a, c]	G: 3.133 (.091) T: 14.601 (<0.0001) G×T: 1.855 (.168)
	POM	0.90±0.04	0.87±0.04[b]	0.88±0.03[a]	
SBP (mmHg)	PRM	132.44±17.56	126.44±13.28	115.78±12.16[a, c]	G: 3.565 (.073) T: 8.754 (.001) G×T: 1.270 (.291)
	POM	139.00±15.63	135.79±14.85	131.43±16.49	
DBP (mmHg)	PRM	81.00±6.86	82.67±7.45	76.22±7.64[a, c]	G: 2.585 (.123) T: 3.609 (.071) G×T: 1.667 (.206)
	POM	83.07±7.74	87.93±9.40	83.50±8.34	

Mean±SD,
PRM; premenopausal, POM; postmenopausal, BMI; body mass index, WHR; waist-to-hip ratio, SBP; systolic blood pressure, DBP; diastolic blood pressure, G; Group, T; Time, G×T; Group×Time
post-hoc: a: 0week vs. 12weeks; b: 0week vs. 6weeks; c: 6weeks vs. 12weeks

Change of physical fitness after exercise

The change in physical fitness according to each group is shown in Table 4. Results from two-way factor ANOVA showed that no significant group × time interaction. Grip strength (main effect of time, p<0.0001), sit and reach test (main effect of time, p<0.0001), sit-up (main effect of time, p<0.0001), standing long jump (main effect of time, p<0.05), and side step test (main effect of time, p<0.0001) were significantly increased than baseline values after 12 weeks.

Post-hoc analysis using Bonferroni correction with a paired t-test indicated in the PRM group that significantly increased 12weeks than 6weeks and baseline in grip strength, sit and reach, sit-up, and side step test. Left grip strength, sit and reach, sit-up, standing long jump, and side step test were greater at 12-weeks than 6-weeks and baseline in the POM group.

Table 4. Change of physical fitness

variable		0week	6weeks	12weeks	F-value (*p*-value)
GS (kg)	PRM	22.09±5.70	23.34±5.30	25.6±5.64[a, c]	G: 0.021 (.887) T: 10.532 (<0.0001) G×T: 0.912 (.410)
	POM	22.47±4.88	23.19±6.18	24.39±5.56[a]	
SRT (kg)	PRM	13.40±6.58	17.21±5.05[b]	17.92±4.92[a]	G: 2.027 (.169) T: 21.764 (<0.0001) G×T: 2.061 (.140)
	POM	18.54±7.40	20.29±6.82[b]	21.13±6.54[a, c]	
Sit-up (fre/60sec)	PRM	19.33±12.09	22.00±12.93	26.44±12.04[a, c]	G: 4.194 (.053) T: 27.445 (<0.0001) G×T: 1.444 (.247)
	POM	10.50±8.61	14.14±9.81[b]	15.79±9.92[a]	
SLJ (cm)	PRM	139.00±24.68	142.44±24.11	143.22±24.60	G: 9.404 (.006) T: 3.313 (.046) G×T: 0.442 (.646)
	POM	108.79±23.51	117.07±16.89[b]	116.36±20.88	
SST (fre/30sec)	PRM	30.00±4.87	33.55±5.29[b]	35.22±5.74[a]	G: 0.584 (.453) T: 28.394 (<0.0001) G×T: 0.196 (.823)
	POM	29.07±3.95	32.43±2.98[b]	33.50±3.30[a]	

Mean±SD,
PRM; premenopausal, POM; postmenopausal, GS; grip strength, SRT; sit and reach test, SLJ; standing long jump, SST; side step test, G; Group, T; Time, G×T; Group×Time
post-hoc: a: 0week vs. 12weeks; b: 0week vs. 6weeks; c: 6weeks vs. 12weeks

Change of adipokines after exercise

The change in adipokines according to each group is shown in Table 5. Results from two-way factor ANOVA showed that no significant group × time interaction. Leptin (main effect of time, $p<0.01$) was significantly decreased than baseline values after 12 weeks. Adiponectin (main effect of time, $p<0.0001$) was significantly increased than baseline values after 12 weeks.

Post-hoc analysis using Bonferroni correction with a paired t-test indicated in the POM group that significantly decreased 12weeks than 6weeks and baseline in leptin concentration. Adiponectin concentration was greater at 12-weeks than 6-weeks and baseline in the both groups.

Table 5. Change of adipokines

variable		0week	6weeks	12weeks	F-value (*p*-value)
Leptin (pg/ml)	PRM	386.2±103.9	347.7±116.1	293.6±155.1	G: 0.519 (.479) T: 7.022 (.002) G×T: 0.247 (.782)
	POM	368.1±73.9	304.0±87.7[b]	281.7±91.7[a]	
Adiponectin (pg/ml)	PRM	59.04±4.78	62.99±5.88[b]	66.38±5.51[a, c]	G: 0.117 (.736) T: 53.389 (<0.0001) G×T: 1.710 (.193)
	POM	58.98±3.06	62.60±4.75[b]	68.80±6.04[a, c]	

Mean±SD,
PRM; premenopausal, POM; postmenopausal, G; Group, T; Time, G×T; Group×Time
post-hoc: a: 0week vs. 12weeks; b: 0week vs. 6weeks; c: 6weeks vs. 12weeks

ATGL, HSL, MGL and PLIN levels in subcutaneous fatty tissue

As shown in Figure. 1, ATGL levels in subcutaneous fatty tissue two groups at baseline and post 12weeks. Within-group analysis showed that the ATGL protein levels was significantly decreased in the post- menopausal group after 12 weeks relative to the baseline values (-37.15%, *P*<.05), but no significant changes was observed in the pre- menopausal group. After 12 weeks between pre- menopausal and post- menopausal groups, ATGL protein levels was 42.51% significantly lower in the post- menopausal group than in the pre- menopausal group.

As shown in Figure. 2, HSL levels in subcutaneous fatty tissue two groups at baseline and post 12weeks. After 12 weeks between pre- menopausal and post- menopausal groups, HSL protein levels was 79.27% significantly higher in the post- menopausal group than in the pre- menopausal group. However, no significant difference in the within-group.

As shown in Figure. 3, MGL levels in subcutaneous fatty tissue two groups at baseline and post 12weeks. Within-group analysis showed that the MGL protein levels was significantly decreased in the post- menopausal group after 12 weeks relative to the baseline values (-56.34%, *P*<.001), but no significant changes was observed in the pre- menopausal group. After 12 weeks between pre- menopausal and post- menopausal groups, MGL protein levels was 43.21% significantly lower in the post- menopausal group than in the pre- menopausal group.

As shown in Figure. 4, PLIN levels in subcutaneous fatty tissue two groups at baseline and post 12weeks. After 12 weeks between pre- menopausal and post- menopausal groups, PLIN protein levels was 27.50% significantly lower in the post- menopausal group than in the pre- menopausal group. However, no significant difference in the within-group.

Discussion

In this study, investigate the modulation of regular resistance exercise on the lipolysis pathway in pre- and post- menopausal women. The main finding of this study after 12 weeks between pre- menopausal and post- menopausal groups ATGL, MGL, and PLIN protein levels were lower by 42.51%, 43.21%, and 27.50%, HSL protein levels were higher by 79.27% in the post- menopausal group than in the pre- menopausal group. In addition, leptin concentration was significantly decreased after resistance exercise both groups, and adiponectin concentration was significantly increased after resistance exercise both groups. In physical fitness, grip strength, sit and reach, sit-up and standing long-jump were significantly increased after exercise both groups.

The postmenopausal women have higher intramuscular fat and subcutaneous adipose tissue compared to men and premenopausal women, in the activity of key enzymes involved in free fatty acid (FFA) metabolism between pre- and post- menopausal women [17, 18]. The relationship of FFA release to the amount of body fat that originating from the release of adipose tissue triglyceride fatty acid represents virtually the only route by which these fat stores can be transported through oxidation to non-adipose tissue for net loss [19]. Triacylglycerol and diacylglycerol are degraded by the lipases ATGL and HSL, and fasting lipolysis, expressed per unit fat mass in obese patients may be reduced [20]. Diacylglycerol is converted to monoacylglycerol and a second fatty acid by the action of HSL, after which MGL hydrolyzes monoacylglycero to producing glycerol and the last fatty acid [21]. Besides protein perilipin (PLIN) which is thought to modulate the accession of HSL to the surface of the fat droplet [22], that plays a major role in lipogenesis by regulating the function of lipases [23]. In this study, changes lipolysis related lipase such as ATGL, HSL, MGL, and PLIN were observed after 12 weeks of resistance exercise in pre- and post-menopausal obese women. As the results that ATGL and MGL levels were 37.15% and 56.34% significantly decreased after 12 weeks of resistance exercise in post- menopausal group. Cyclic adenosine monophosphate (cAMP) produced by adenylate cyclase activates protein kinase A (PKA) and PKA phosphorylates and activates two or more substrates: HSL and PLIN [24]. HSL and PLIN phosphorylation leads to the translocation of HSL from the cytosol to the surface of the lipid droplet and insulin can activate protein phosphatases resulting in the subsequent dephosphorylation of HSL at which time, ATGL instead of phosphate and translation [24]. Estrogen and estrogen receptor alpha are known to repress intra-abdominal adipose formation [25]. Wend et al. reported that lipid droplet size (relative area per lipid droplet) and the number of lipid droplets per cell were measured in estrogen receptor alpha knockout (ERαKO) with postmenopausal model mice, as ATGL levels and lipid droplets in ERαKO cells significantly decreased compared to wild model mice [26]. It is mean that ERαKO mice develop more adipose tissue in the perirenal, periovarian, and mesenteric/omental regions than wild-type model mice [27]. Walhin et al. reported that HSL was downgraded to positive energy balance period and HSL was raised to negative energy balance period [28]. However, other studies have shown that activation of lipolysis occurred through increase levels of ATGL, HSL, and MGL and glycerol release [29]. The activities of ATGL, HSL, and MGL were significantly higher in the diet and exercise mice group than the high-fat diet mice group [30]. In this study results, ATGL and MGL levels were significantly decreased after 12 weeks of resistance exercise. HSL and PLIN levels tended to decrease after 12 weeks of resistance exercise in post-menopausal group more than pre- menopausal group which similar to Wend et al. and Walhin et al [26,

27]. After 12 weeks of resistance exercise, total adipose tissue may be reduced due to a significant decrease in body weight and body % fat. In addition, a greater decrease in lipolysis factors in post-menopausal group seems to have a greater effect on resistance exercise than in the pre- menopausal group.

Moreover, 12weeks were significantly reduced than 6 weeks and the baseline of leptin concentration and adiponectin concentration was higher at 12 weeks than 6 weeks, and the baseline in post- menopausal group than pre- menopausal group, and these results supported lipolysis at ATGL, HSL, MGL and PLIN levels in the study.

Adipose tissue releases several polypeptides from adipocyte, as well as free fatty acids, which are products of lipolysis, which are also known as adipocytokines, leptin, and adiponectin [31]. In humans, plasma adiponectin concentrations decrease with increasing obesity, and plasma leptin concentrations are highly correlated with BMI [32]. Adiponectin is an adipocyte-derived hormone that sensitizes insulin and improves energy metabolism of tissues [33]. In this regard, adiponectin is relatively unique as adipokine because it is expressed at highest levels in lean and healthy individuals [34]. Several studies reported about impacts of resistance exercise on women. Park et al. showed that significant differences in leptin and adiponectin levels in pre- and post- menopausal women after 12 weeks of resistance exercise [35]. Dieli-Conwright et al. showed that leptin, adiponectin, and body mass index were significantly improved after 16 weeks of aerobic and resistance exercise in overweight or obese survivors of breast cancer [36]. Rosety-Rodriguez et al. reported that leptin level was significantly decreased after the completion of the resistance circuit training [37]. Above previous studies, regular resistance exercise improved leptin and adiponectin levels in both groups with reduced body fat percentage. The concentration control idealization of adipokin (leptin and adiponectin), lipolysis lipase (ATGL, HSL, MGL) and PLIN in adipose tissues that cause inflammation by cholesterol has contributed to the increase in fat decomposition and the increase in cyclic nonesterified fatty acids [38]. In this study, regular resistance exercise might be reducing leptin, body weight, % fat, and increase adiponectin levels. This reason why reduced total adipose tissue supported by decreased ATGL, HSL, MGL, and PLIN levels in subcutaneous fatty tissue after 12 weeks' resistance exercise.

Resistance exercise is well-known improve body composition in obese adults [39]. In additional, resistance exercise increasing fat free mass and decreasing body weight in pre- and post- menopausal with obesity [40, 41]. In this study observed that body weight, body mass index, % fat, waist-to-hip ratio were significantly decreased after 12-weeks than 6-weeks resistance exercise in both groups. Although, did not significantly in muscle mass but tended to increased. Even though, significantly improvement of grip strength, sit and reach, sit-up, and side step test after 12-weeks than 6-weeks resistance exercise in both groups. Weight gain and obesity largely drives the increased prevalence of metabolic syndrome in pre- and post- menopausal women [42]. Because of the associated sequelae of coronary heart disease, cardiovascular disease, diabetes, and mortality, life style management should be of paramount importance in obese women.

Finally, in this study meaningful to directly analyzes adipose tissue in humans, however the present study has some limitations. The sample size was small, which limits our ability to determine the significance of the results. Therefore, additional studies with larger sample sizes and control group are required to determine the effectiveness of regular resistance exercise on lipolysis. Another limitation is that to determine whether there is a gender and age difference in lipolysis factors. Also, we did not control for confounding factors such as food energy intake and habitual activity. Lipolysis reaction and lipid storage for food energy intake and habitual activity are key factors in determining body fat stores, confounding factors should be considered in future studies.

Conclusion

In conclusion, this study indicates that regular resistance exercise to change of lipolysis factors (ATGL, HSL, MGL and PLIN) of subcutaneous fatty tissue, and adipokines (leptin and adiponectin) of serum in the post- menopausal group more than pre- menopausal group. Moreover, improvement of body composition and physical fitness in obese pre- and post- menopausal women. The positive change leptin and adiponectin might be might be release of reduction of % fat, and driving overall greater change ATGL, HSL, MGL and PLIN levels in subcutaneous fatty tissue in the obese post- menopausal group more than obese pre- menopausal group.

Abbreviation

ATGL: adipose triglyceride lipase; BMI: body mass index; DBP: diastolic blood pressure; FFA: free fatty acid; HSL: hormone-sensitive lipase; MGL: monoacylglycerol lipase; PLIN: perilipin; POM: post-menopausal; PRM: pre- menopausal; RM: repetition maximum; SBP: systolic blood pressure; WHR: waist-to-hip ratio

Declarations

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Authors' contributions

Kyu-Min Park, Seung-Taek Lim, and Sunghwun Kang contributed to conception and design of the study.

Kyu-Min Park, Seung-Taek Lim, and Kun-Young Sung implemented the measurements and training sessions. Kun-Young Sung analysed the participant data. All authors interpreted and discussed the results. All authors drafted parts of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The study was approved by Kangwon National University Institutional Review Board, and conducted in agreement with the Declaration of Helsinki. In advance of their participation, all of the participants were fully informed about the purpose and experimental procedures of the study. All of the participants completed consent forms. The participants were informed that all data collected would be processed anonymously.

Consent for publication

All participants provided consent for publishing their data anonymously.

Competing interests

All authors declare that they have no competing interest

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References

1. Samuel VT, Shulman GI. Mechanisms for insulin resistance: common threads and missing links. Cell. 2012;148:852-71. https://doi.org/10.1016/j.cell.2012.02.017
2. Jakicic JM, Otto AD. Physical activity considerations for the treatment and prevention of obesity. Am J Clin Nutr. 2005;82:226S-9S. https://doi.org/10.1093/ajcn/82.1.226S
3. Mika A, Macaluso F, Barone R, Felice VD, Sledzinski T. Effect of Exercise on Fatty Acid Metabolism and Adipokine Secretion in Adipose Tissue. Front Physiol. 2019;10:26. http://doi:10.3389/fphys.2019.00026.
4. Romain AJ, Carayol M, Desplan M, Fedou C, Ninot G, Mercier J, Avignon A, Brun JF. Physical activity targeted at maximal lipid oxidation: a meta-analysis. J Nutr Metab. 2012;2012:285395.

https://doi.org/10.1155/2012/285395

5. Chen N, Cheng J, Zhou L, Lei T, Chen L, Shen Q, Qin L, Wan Z. Effects of treadmill running and rutin on lipolytic signaling pathways and TRPV4 protein expression in the adipose tissue of diet-induced obese mice. J Physiol Biochem. 2015;71:733-42. https://doi.org/10.1007/s13105-015-0437-5
6. Lönnqvist F, Nyberg B, Wahrenberg H, Arner P. Catecholamine-induced lipolysis in adipose tissue of the elderly. J Clin Invest. 1990;85:1614-21. https://doi:10.1172/JCI114612.
7. Chatzinikolaou A, Fatouros I, Petridou A, Jamurtas A, Avloniti A, Douroudos I, Mastorakos G, Lazaropoulou C, Papassotiriou I, Tournis S, Mitrakou A, Mougios V. Adipose tissue lipolysis is upregulated in lean and obese men during acute resistance exercise. Diabetes Care. 2008;31:1397-9. https://doi:10.2337/dc08-0072.
8. Holland AM, Kephart WC, Mumford PW, Mobley CB, Lowery RP, Shake JJ, Patel RK, Healy JC, McCullough DJ, Kluess HA, et al. Effects of a ketogenic diet on adipose tissue, liver, and serum biomarkers in sedentary rats and rats that exercised via resisted voluntary wheel running. Am J Physiol Regul Integr Comp Physiol. 2016;311:R337-51. https://doi.org/10.1152/ajpregu.00156.2016
9. Ferrara CM, Lynch NA, Nicklas BJ, Ryan AS, Berman DM. Differences in adipose tissue metabolism between postmenopausal and perimenopausal women. J Clin Endocrinol Metab. 2002;87:4166-70. https://doi:10.1210/jc.2001-012034.
10. Rebuffé-Scrive M, Eldh J, Hafström LO, Björntorp P. Metabolism of mammary, abdominal, and femoral adipocytes in women before and after menopause. Metabolism. 1986;35:792-7. https://doi:10.1016/0026-0495(86)90217-9.
11. Henríquez S, Monsalves-Alvarez M, Jimenez T, Barrera G, Hirsch S, de la Maza MP, Leiva L, Rodriguez JM, Silva C, Bunout D. Effects of Two Training Modalities on Body Fat and Insulin Resistance in Postmenopausal Women. J Strength Cond Res. 2017;31:2955-2964. https://doi:10.1519/JSC.0000000000002089.
12. Allman BR, Morrissey MC, Kim JS, Panton LB, Contreras RJ, Hickner RC, Ormsbee MJ. Fat metabolism and acute resistance exercise in trained women. J Appl Physiol (1985). 2019;126:739-745. https://doi:10.1152/japplphysiol.00752.2018. Epub 2019 Jan 3.
13. Hirsch J, Farquhar JW, Ahrens EH Jr, Peterson ML, Stoffel W. Studies of adipose tissue in man. A microtechnic for sampling and analysis. Am J Clin Nutr. 1960;8:499-511. http://doi:10.1093/ajcn/8.4.499.
14. Hirsch J, Gallian E. Methods for the determination of adipose cell size in man and animals. J Lipid Res. 1968;9:110-9.
15. Gurudut P, Rajan AP. Immediate effect of passive static stretching versus resistance exercises on postprandial blood sugar levels in type 2 diabetes mellitus: a randomized clinical trial. J Exerc Rehabil. 2017;13:581-7. https://doi.org/10.12965/jer.1735032.516
16. Brzycki M. Strength testing: predicting a one-rep max from a reps-to-fatigue. Journal of physical education, recreation & dance. 1993;64:88–90. https://doi.org/10.1080/07303084.1993.10606684

17. Kuk JL, Lee S, Heymsfield SB, Ross R. Waist circumference and abdominal adipose tissue distribution: influence of age and sex. Am J Clin Nutr 2005;81:1330-4. https://doi:10.1093/ajcn/81.6.1330.
18. Ortmeyer HK, Goldberg AP, Ryan AS. Exercise with weight loss improves adipose tissue and skeletal muscle markers of fatty acid metabolism in postmenopausal women. Obesity (Silver Spring). 2017;25:1246-53. https://doi.org/10.1002/oby.21877
19. Jensen MD, Haymond MW, Rizza RA, Cryer PE, Miles JM. Influence of body fat distribution on free fatty acid metabolism in obesity. J Clin Invest. 1989;83:1168-73. https://doi.org/10.1172/JCI113997
20. Stinkens R, Goossens GH, Jocken JW, Blaak EE. Targeting fatty acid metabolism to improve glucose metabolism. Obes Rev. 2015;16:715-57. https://doi.org/10.1111/obr.12298
21. Bolsoni-Lopes A, Alonso-Vale MI. Lipolysis and lipases in white adipose tissue - An update. Arch Endocrinol Metab. 2015;59:335-42. https://doi.org/10.1590/2359-3997000000067
22. Souza SC, de Vargas LM, Yamamoto MT, Lien P, Franciosa MD, Moss LG, Greenberg AS. Overexpression of perilipin A and B blocks the ability of tumor necrosis factor alpha to increase lipolysis in 3T3-L1 adipocytes. J Biol Chem. 1998;273:24665-9. https://doi.org/10.1074/jbc.273.38.24665
23. Zimmermann R, Lass A, Haemmerle G, Zechner R. Fate of fat: the role of adipose triglyceride lipase in lipolysis. Biochim Biophys Acta. 2009;1791:494-500. https://doi.org/10.1016/j.bbalip.2008.10.005
24. Jocken JWE, Blaak EE. Catecholamine-induced lipolysis in adipose tissue and skeletal muscle in obesity. Physiol Behav. 2008;94:219-30. https://doi:10.1016/j.physbeh.2008.01.002.
25. Santos RS, Frank AP, Fátima LA, Palmer BF, Öz OK, Clegg DJ. Activation of estrogen receptor alpha induces beiging of adipocytes. Mol Metab. 2018;18:51-9. https://doi.org/10.1016/j.molmet.2018.09.002
26. Wend K, Wend P, Drew BG, Hevener AL, Miranda-Carboni GA, Krum SA. ERα regulates lipid metabolism in bone through ATGL and perilipin. J Cell Biochem 2013;114:1306-14. https://doi.org/10.1002/jcb.24470
27. Ohlsson C, Hellberg N, Parini P, Vidal O, Bohlooly-Y M, Rudling M, Lindberg MK, Warner M, Angelin B, Gustafsson JA. Obesity and disturbed lipoprotein profile in estrogen receptor-alpha-deficient male mice. Biochem Biophys Res Commun. 2000;278:640-5. https://doi.org/10.1006/bbrc.2000.3827
28. Walhin JP, Dixon NC, Betts JA, Thompson D. The impact of exercise intensity on whole body and adipose tissue metabolism during energy restriction in sedentary overweight men and postmenopausal women. Physiol Rep. 2016;4:e13026. https://doi.org/10.14814/phy2.13026
29. Lo Furno D, Graziano AC, Avola R, Giuffrida R, Perciavalle V, Bonina F, Mannino G, Cardile V. A Citrus bergamia Extract Decreases Adipogenesis and Increases Lipolysis by Modulating PPAR Levels in Mesenchymal Stem Cells from Human Adipose Tissue. PPAR Res. 2016;2016:4563815. https://doi.org/10.1155/2016/4563815
30. Woo J, Kang S. Diet change and exercise enhance protein expression of CREB, CRTC 2 and lipolitic enzymes in adipocytes of obese mice. Lipids Health Dis. 2016;15:147. http://doi:10.1186/s12944-

016-0316-2.

31. Staiger H, Tschritter O, Machann J, Thamer C, Fritsche A, Maerker E, Schick F, Häring HU, Stumvoll M. Relationship of serum adiponectin and leptin concentrations with body fat distribution in humans. Obes Res. 2003;11:368-72. https://doi.org/10.1038/oby.2003.48
32. Greenberg AS, Obin MS. Obesity and the role of adipose tissue in inflammation and metabolism. Am J Clin Nutr. 2006;83:461S-465S. https://doi:10.1093/ajcn/83.2.461S.
33. Qiao L, Kinney B, Schaack J, Shao J. Adiponectin inhibits lipolysis in mouse adipocytes. Diabetes. 2011;60:1519-27. https://doi.org/10.2337/db10-1017
34. Walsh K. Adipokines, myokines and cardiovascular disease. Circ J. 2009;73:13–8. https://doi.org/10.1253/circj.cj-08-0961
35. Park KM, Park SC, Kang S. Effects of resistance exercise on adipokine factors and body composition in pre- and postmenopausal women. J Exerc Rehabil. 2019;15:676-82. https://doi.org/10.12965/jer.1938368.184
36. Dieli-Conwright CM, Courneya KS, Demark-Wahnefried W, Sami N, Lee K, Buchanan TA, Spicer DV, Tripathy D, Bernstein L, Mortimer JE. Effects of Aerobic and Resistance Exercise on Metabolic Syndrome, Sarcopenic Obesity, and Circulating Biomarkers in Overweight or Obese Survivors of Breast Cancer: A Randomized Controlled Trial. J Clin Oncol. 2018;36:875-83. https://doi.org/10.1200/JCO.2017.75.7526
37. Rosety-Rodriguez M, Camacho A, Rosety I, Fornieles G, Rosety MA, Diaz AJ, Rosety M, Ordonez FJ. Resistance circuit training reduced inflammatory cytokines in a cohort of male adults with Down syndrome. Med Sci Monit. 2013;19:949-53. https://doi.org/10.12659/MSM.889362
38. Huang JP, Hsu SC, Meir YJ, Hsieh PS, Chang CC, Chen KH, Chen JK, Hung LM. Role of dysfunctional adipocytes in cholesterol-induced nonobese metabolic syndrome. J Mol Endocrinol. 2018;60:307-21. https://doi.org/10.1530/JME-17-0194
39. Villareal DT, Aguirre L, Gurney AB, Waters DL, Sinacore DR, Colombo E, Armamento-Villareal R, Qualls C. Aerobic or Resistance Exercise, or Both, in Dieting Obese Older Adults. N Engl J Med. 2017;376:1943-55. https://doi.org/10.1056/NEJMoa1616338
40. Cunha PM, Ribeiro AS, Tomeleri CM, Schoenfeld BJ, Silva AM, Souza MF, Nascimento MA, Sardinha LB, Cyrino ES. The effects of resistance training volume on osteosarcopenic obesity in older women. J Sports Sci. 2018;36:1564-71. https://doi.org/10.1080/02640414.2017.1403413
41. Ahn N, Kim HS, Kim K. Exercise training-induced changes in metabolic syndrome parameters, carotid wall thickness, and thyroid function in middle-aged women with subclinical hypothyroidism. Pflugers Arch. 2019;471:479-89. https://doi.org/10.1007/s00424-019-02254-7
42. Lobo RA. Metabolic syndrome after menopause and the role of hormones. Maturitas. 2008;60:10-8. https://doi.org/10.1016/j.maturitas.2008.02.008

Figures

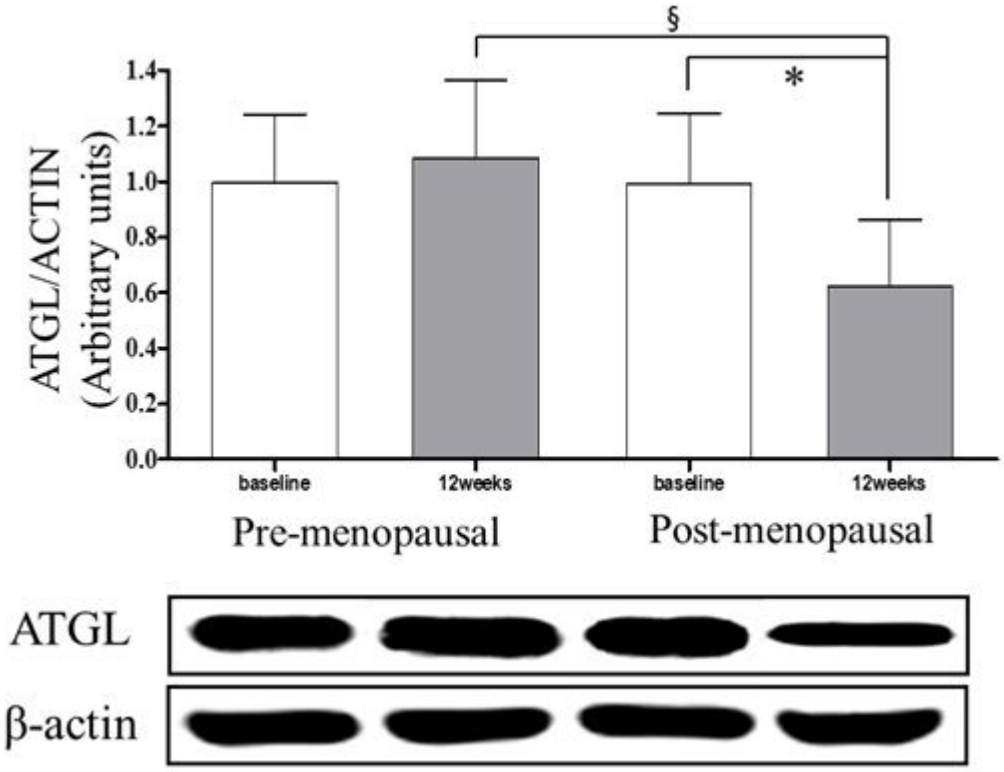

Figure 1

ATGL expression baseline and after exercise 12weeks in adipose tissue * $p < 0.05$, significantly different from baseline in the within group § $p < 0.05$, significantly different from 12weeks in the each groups

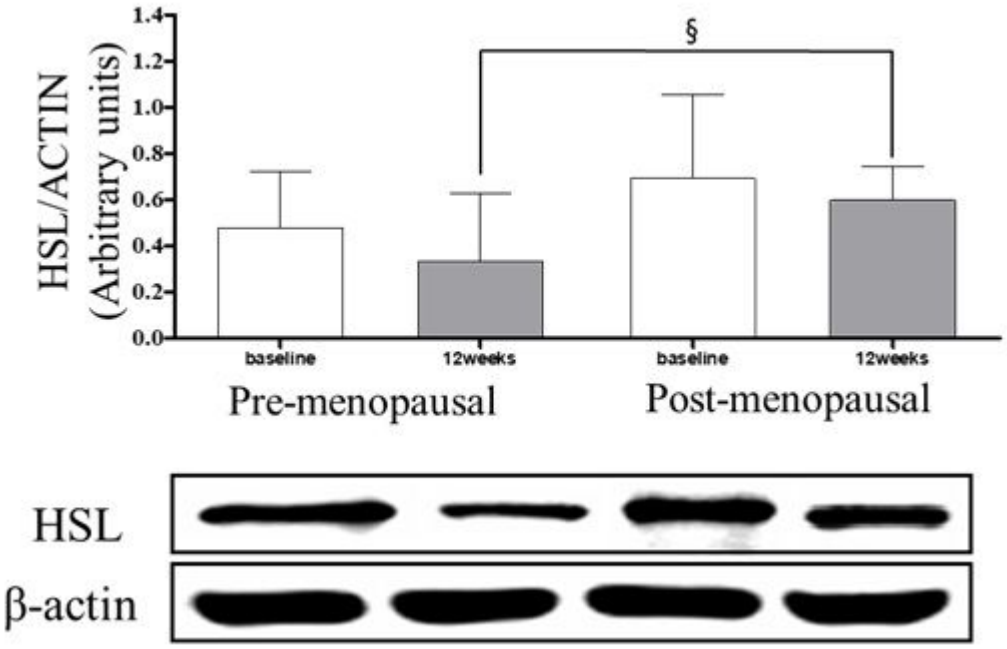

Figure 2

HSL expression baseline and after exercise 12weeks in adipose tissue § p < 0.05, significantly different from 12weeks in the each groups

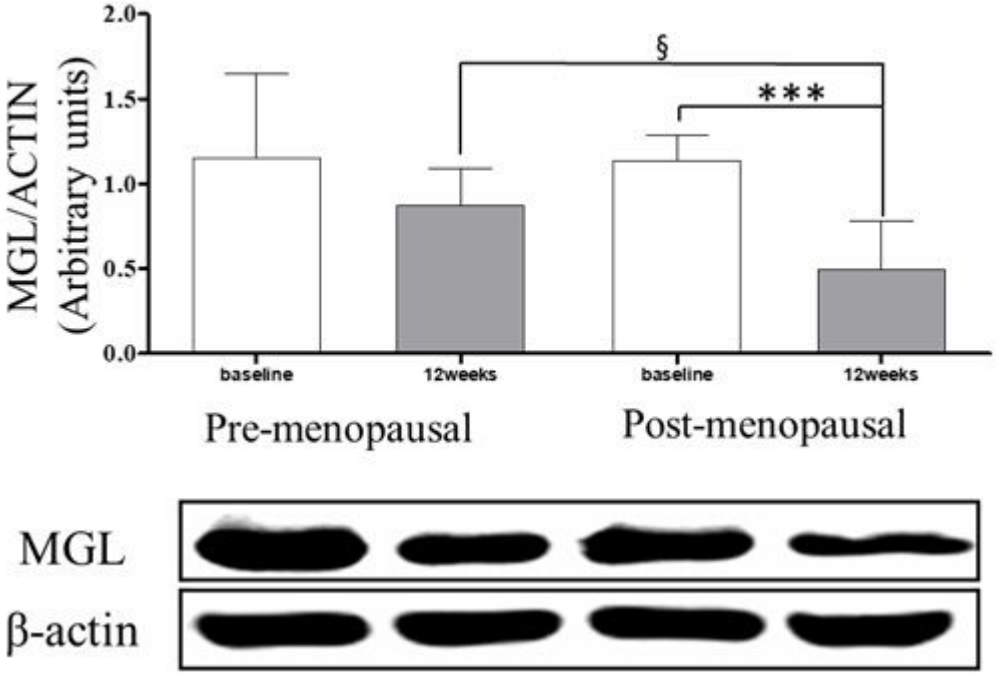

Figure 3

MGL expression baseline and after exercise 12weeks in adipose tissue *** p < 0.001, significantly different from baseline in the within group § p < 0.05, significantly different from 12weeks in the each groups

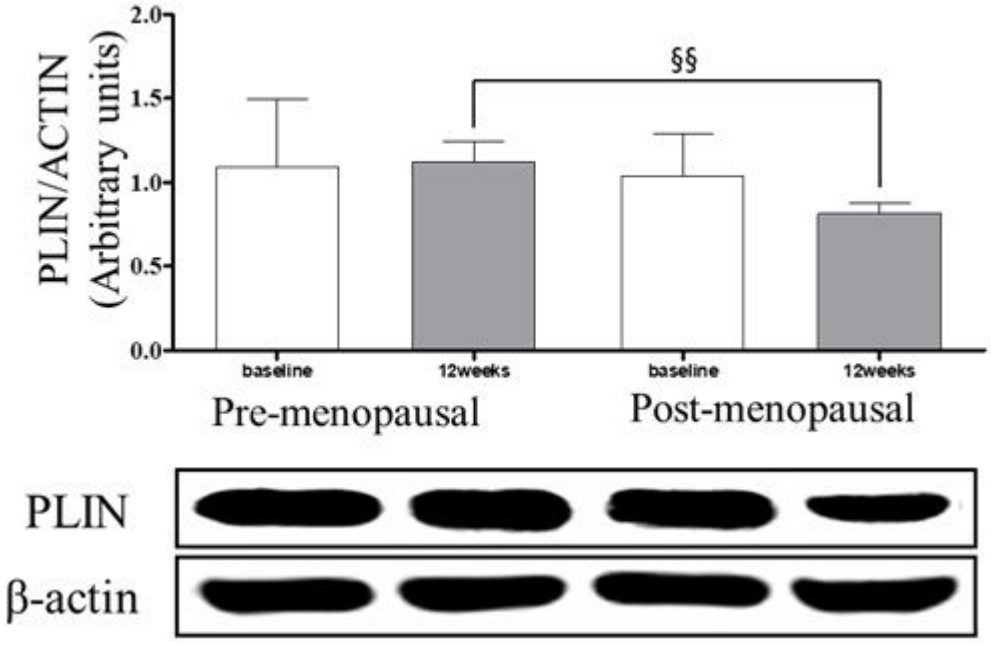

Figure 4

PLIN expression baseline and after exercise 12weeks in adipose tissue §§ $p < 0.01$, significantly different from 12weeks in the each groups