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ORIGINAL ARTICLE

Exercise training–induced changes in metabolic syndrome parameters, carotid wall thickness, and thyroid function in middle-aged women with subclinical hypothyroidism

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Abstract

This study analyzed the differences in effects of a 12-week combination of exercise training program with resistance training and aerobic exercises on the risk factors of metabolic syndrome, carotid wall thickness, and thyroid function, between subclinical hypothyroidism patients and obese groups, in middle-aged women. Subjects consisted of either 20 middle-aged women in the subclinical hypothyroidism (SCH) group or 20 obese (body mass indices [BMI], ≥ 25 kg/m^2) women without hypothyroidism in the obese (OB) group. The body composition, blood lipid factors, hormones associated with thyroid functions, blood pressure (BP), and carotid intima-media thickness were measured, while physical fitness was ascertained. In the SCH group, waist circumference (WC) and high-density lipoprotein cholesterol values were outside the normal ranges, while WC and systolic BP (SBP) were outside the normal ranges in the OB group. Following the 12-week training program, significantly positive changes occurred in body fat percentage, sit and reach test results, and SBP ($p < 0.05$) in the SCH group, while in the OB group, significantly positive changes in BMI, WC, sit and reach test results, SBP, and diastolic BP (DBP, $p < 0.05$) were observed. In addition, both groups showed significant decreases in intima-media thickness of the right carotid bifurcation ($p < 0.05$). However, in the two groups, the 12-week exercise training program did not have similar significant impact on the hormones related to thyroid functions and blood lipids. Therefore, further research on exercise training that can effectively induce changes in the hormones associated with thyroid functions in patients with subclinical hypothyroidism is necessary.

Keywords Subclinical hypothyroidism · Obesity · Exercise training · Middle-aged women

Introduction

Hypothyroidism results in negative impairment of metabolic functions accompanied by atherosclerosis and increased insulin resistance. It increases the prevalence of obesity and cardiovascular diseases [32] and the risk factors of metabolic syndrome [64]. In subclinical hypothyroidism (recently a more prevalent condition), thyroid hormones such as free triiodothyronine (T3), total thyroxine (T4), and free thyroxine (FT4) are within normal ranges, while thyroid-stimulating hormone (TSH) levels increase significantly. Subclinical hypothyroidism can increase plasma cholesterol levels, blood pressure (BP) [17, 21], adult bone maintenance [4], and the common carotid artery intima-media thickness (IMT) [28, 45]. Subclinical hypothyroidism is associated with multiple factors of metabolic syndrome. Subclinical hypothyroidism is inseparably linked with obesity; it is a major risk factor of obesity (which in turn increases its prevalence) [31] and insulin resistance [26]. However, blood lipids may remain within normal limits despite subclinical hypothyroidism [1]. Furthermore, when subclinical hypothyroidism is not accompanied with factors such as older age or obesity, the negative effects of lipid factors are not suitable as clinical diagnostic markers [69]. Moreover, men with subclinical hypothyroidism

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exhibit negative effects of lipid factors, whereas in women, these factors maintained within the normal ranges [10].

The challenges in the clinical treatment of subclinical hypothyroidism and the effectiveness of such treatment have been pointed out. In subclinical hypothyroidism, exercise training seems to be the most effective method on the risk factors for metabolic syndrome with minimizing the side effects of other treatments of these conditions [52]. Therefore, exercise has been suggested as an effective method of treatment for subclinical hypothyroidism and related metabolic syndrome. The importance of treating obesity, one of the comprehensive risk factors of metabolic syndrome during the treatment process, has been raised [63]. Since subclinical hypothyroidism is inseparably associated with energy metabolism, long-term exercise training has important effects on the activation of energy metabolism and may be proposed as an effective method of treatment [36]. Exercise training accelerates the release of thyroid hormones [20] to promote catabolism within cells, increase metabolism, and influence the activation of protein anabolism [40]. However, change in thyroid hormone levels following long-term exercise training is observed to be a consistent increase or no decrease. In an experiment on human subjects, Tremblay et al. [55] reported reduced T3 and T4 levels in the exercise group. On the other hand, Baylor and Hackney [5] reported reduced T4 and TSH levels and increased T3 levels following exercise training. In addition, Evason et al. [19] reported decreased T4 levels following exercise training and increased TSH. Despite the importance of the association of thyroid hormones with energy metabolism, the effect of long-term exercise training has not been clearly examined with very few attempts made [38]. Especially, Almas et al. [2] reported that subclinical hypothyroidism patients showed slower heart rate kinetics in the transition from rest to exercise during performing a constant-load exercise. It needs more study for exact exercise prescription with subclinical hypothyroidism patients.

Therefore, it is necessary to determine the differences in the therapeutic effects of exercise training and complex effect of the risk factors of metabolic syndrome including obesity between patients with subclinical hypothyroidism and obese patients. These two groups share similar risk factors of metabolic syndrome. The overall goal was to explore effective methods of treatment for subclinical hypothyroidism. To understand the negative effects of subclinical hypothyroidism on energy metabolism and to review the positive effect and feasibility of exercise training as an effective method of treatment for subclinical hypothyroidism, this study examined the therapeutic effect of resistance and aerobic exercise training program combination in patients with subclinical hypothyroidism and obese patients.

Methods

Subjects

Subjects were recruited by posting advertisements in hospitals specializing in thyroid diseases. Of middle-aged women with TSH levels within 5–10 mU/L in the last 6 months, 20 subjects who deemed capable of performing exercises by their physicians were assigned to the subclinical hypothyroidism (SCH) group. Twenty middle-aged obese women without hypothyroidism and with body mass index (BMI) of ≥ 25 kg/m^2 were assigned to the obese (OB) group. Table 1 shows the physical characteristics of the subjects. All subjects fasted for at least 10–12 h before participating in the experiment and had sufficient rest the night before the experiment day. The research protocol was approved by the Institutional Review Boards of Keimyung University College of Medicine and Keimyung University Dongsan Medical Center (approval number: 10-184-01.06).

Body composition and bone mineral density

The BMI was calculated using the following equation: body weight/height^2 (kg/m^2). The waist circumference (WC) was measured on midway point between the lowest ribs and the iliac crest in accordance with the definition of WC proposed by the World Health Organization (WHO) [66]. The hip circumference was measured around the widest portion of the buttocks and was used to calculate the waist-hip ratio (WHR). The body fat percentage (%fat) was calculated using Jackson et al. [29] and Siri's [49] equations after measuring the subcutaneous fat thickness at the triceps, suprailiac region, and femoral region with a skinfold caliper (Skyndex, USA). Bone mineral density (BMD) was evaluated at the femoral neck using DEXA (QDR-4500W, Hollogic Co. Waltham, USA).

Measurement of blood pressure and ultrasound carotid intima-media thickness

Blood pressure (BP) was measured with a mercury sphygmomanometer, while the intima-media thickness (IMT) was measured with a 7.5-MHz Linear probe (SONOS 2000, Hewlett-Packard, USA). IMT measurements were obtained from six locations: the left and right common carotid arteries, the carotid bifurcation, and the far walls of the internal carotid arteries.

Physical fitness measurement

Grip strength was measured using a dynamometer (TKK, Japan). Flexibility was measured by the sit and reach test. To measure cardiopulmonary function, the Balke treadmill protocol was used. During the treadmill test in which the subject

Table 1 Physical characteristics of subjects

Group	*N*	Age (year)	Height (cm)	Body weight (kg)	BMI (kg/m^2)
SCH	20	43.20 ± 9.55	159.49 ± 7.30	60.24 ± 8.86	23.76 ± 3.95
OB	20	47.40 ± 9.40	156.27 ± 6.13	67.35 ± 7.65	34.71 ± 6.23

Values are mean and standard deviation (SD); *BMI*, body mass index; *SCH*, subclinical hypothyroidism patients; *OB*, obese women

must reach an all-out state, an autobreath gas analyzer (Quiniton, USA) was used to measure the maximal oxygen uptake (VO_2max).

Blood parameters

After fasting for at least 12 h and fully rested, 10 mL of blood was collected from the antecubital veins of the subjects. Blood total cholesterol (TC), triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C) levels were measured by the enzyme method using Hitachi 747 autoanalyzer (Japan). Blood low-density lipoprotein cholesterol (LDL-C) levels were calculated using the Friedewald equation [22]. Blood glucose levels were measured by the hexokinase (HK) method (based on the enzyme method) using glucose measurement kit (GLU-HK, Asan Pharmaceuticals, South Korea). Blood levels of T3, T4, and FT4, which are hormones related to thyroid functions, were measured using Rodent T3 and T4 ELISA (enzyme-linked immunosorbent assay) test kit (Endocrine Technologies Inc., USA), and RIA-gnost FT4 ELISA test kit (CIS Bio International). Blood insulin levels were measured by a radioimmunoassay using insulin measurement reagents (Insulin IRMA, Biosource, Belgium). Blood dehydroepiandrosterone-sulfate (DHEA-s) levels were measured by Quantum Analyzer (COBRA 5010-II, USA) using coat-A-Count DHEA sulfate (Diagnostic Products CO., USA). The homeostasis model assessment (HOMA-IR) was used as a marker of insulin resistance. It was calculated using [fasting insulin level (μU/mL) × fasting glucose level (mmol/L)/22.5] [41].

Exercise training program

The exercise training program consisted of resistance and aerobic exercises and was conducted for 12 weeks. Before the training started, the VO_2max and maximum muscle strength (15RM) of each subject were measured to set the exercise intensity. The combined exercise program included warm-up exercises, which involved 10 min of exercise on a bicycle ergometer or treadmill to raise the body temperature, followed by 5 min of stretching. Resistance exercises were performed for 20 min using an elastic band. A red band was used in the early period of the training, and rated perceived exertion was checked over the course of the training to maintain the exercise intensity at 12–14 or 60–75% 15RM. The intensity of muscle strength exercises was determined relative to the maximum muscle strength of 15RM, and the exercises were performed in three sets each. The breaks in between each set lasted for 30 s to 1 min. For more detailed resistance exercises, the upper body exercises included chest press, incline chest press, lat pulldown, long poll, and shoulder press, while the lower body exercises included leg press, leg extension, leg curl, lunge, and leg raise. Aerobic exercise was performed on a bicycle ergometer or a treadmill at 40–60% of VO_2max for 30 min. After completing the exercises, the subjects stretched as a cool-down exercise to relax the muscles. All exercises were performed four times a week. The intensity of each exercise was evaluated once every 4 weeks and gradually increased based on the evaluation results. The basic descriptions of the exercise methods are shown in Table 2. Diet was not controlled during the training period.

Statistical analysis

The mean and standard deviation of each parameter were calculated using SPSS 18.0 Statistical Program. A two-way repeated ANOVA was performed to compare the values for each parameter between the SCH and OB groups at different time points. If significant interactions were found between the groups and time points, the Tukey post hoc test was performed. The level of statistical significance was set at 5%.

Results

Body composition

Changes in the body composition are shown in Fig. 1. The OB group showed significantly higher BMI than the SCH group before and after exercise training ($p < 0.05$). The OB group showed significantly higher %fat than the SCH group before and after exercise training ($p < 0.05$). Both groups showed significant decrease in %fat after exercise training ($p < 0.05$). The OB group showed significantly higher WHR than the SCH group before exercise training ($p < 0.05$). There was no significant difference in WHR before and after exercise

Table 2 Exercise program

Stage	Type	Intensity	Duration	Frequency
Warm-up	Stretching	–	15 min	4 times/week
Main	Resistance exercise	15RM	20 min	
	Aerobic exercise	40–60% VO_2max	30 min	
Cool-down	Stretching	–	15 min	

VO_2max, maximum oxygen uptake; *15RM*, 15 repetition maximum

training for both groups. Although BMD had no significant difference before and after exercise training, both groups showed the increase trend after exercise training.

Blood pressure

Changes in BP are shown in Fig. 2. Both groups showed a significant decrease in systolic BP (SBP) after exercise training ($p < 0.05$). Only the OB group showed a significant decrease in the diastolic BP (DBP) after exercise training ($p < 0.05$).

Blood lipid factor levels

Changes in blood lipid factor levels are shown in Table 3. LDL-C levels decreased significantly in both groups after exercise training. There were no significant differences in TC, TG, and HDL-C levels between the two groups and between the different time points.

Levels of thyroid hormones and hormones related to metabolism

Changes in the levels of hormones related to thyroid functions such as T3, T4, FT4, and DHEA-s are shown in Table 3. There were no significant differences in the levels of these hormones between the two groups and between the time points. DHEA-s level in SCH group showed a significant ($p < 0.05$) lower value than OB group. There were no significant differences in insulin, glucose, aspartate transaminase and alanine transaminase levels, and HOMA-IR between the groups and time points.

IMT

Changes in the coronary IMT are shown in Fig. 3. The OB group showed significantly higher IMT at the right common carotid artery (R-CCA), left common carotid artery (L-CCA), right bifurcation (R-Bifur), left bifurcation (L-Bifur), right

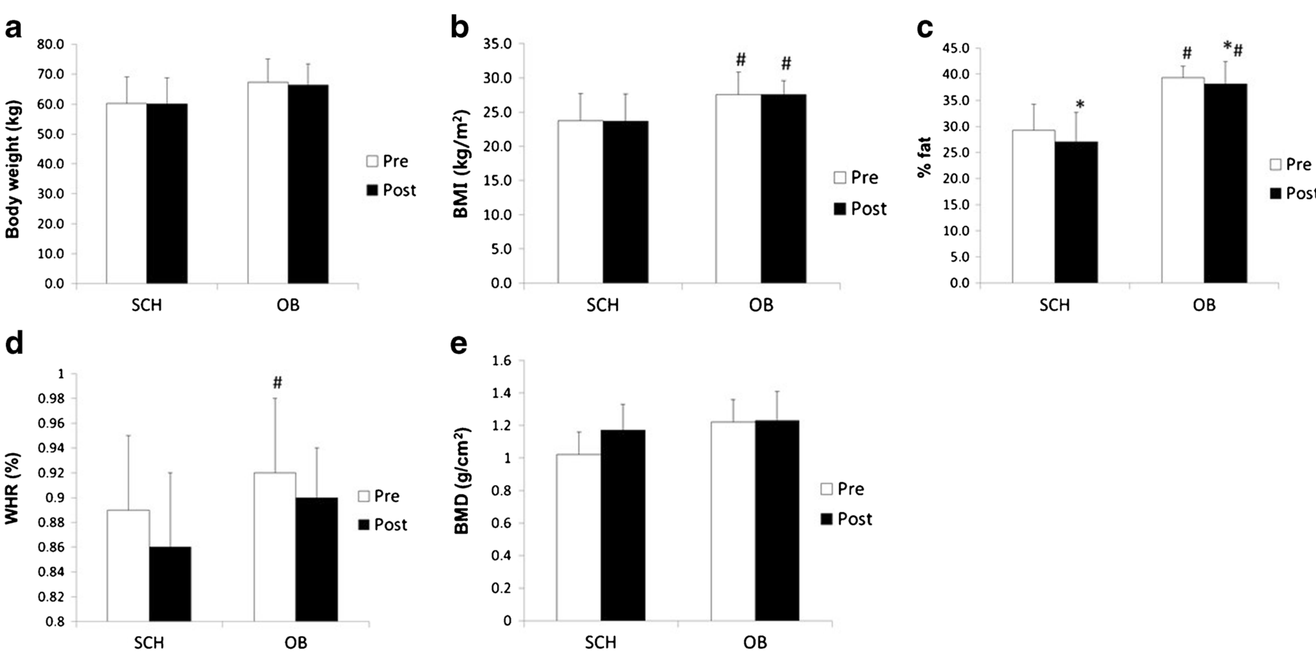

Fig. 1 Changes in body composition. **a** Body weight. **b** BMI. **c** %fat. **d** WHR. **e** BMD. BMI, body mass index; WC, waist circumference; WHR, waist-hip ratio; SCH, subclinical hypothyroidism; OB, obese women; %fat, body fat percentage; BMD, bone mineral density. $^{*}p < 0.05$ compared with the pre-test; $^{\#}p < 0.05$ compared with the SCH group

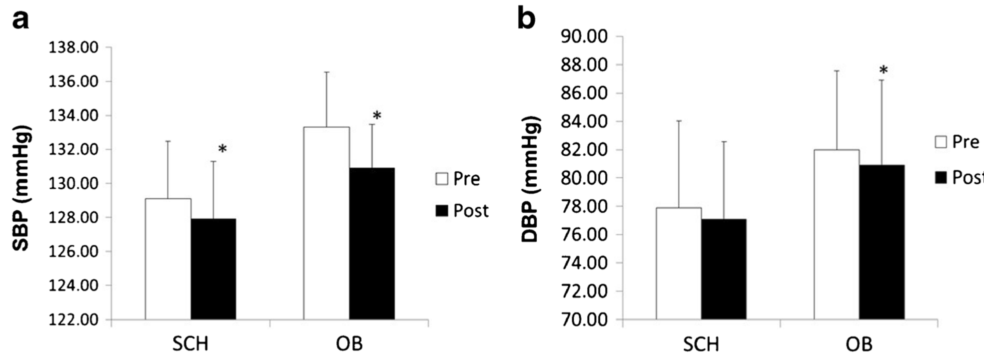

Fig. 2 Changes in systolic and diastolic blood pressure. **a** SBP. **b** DBP. SBP, systolic blood pressure; DBP, diastolic blood pressure; SCH, subclinical hypothyroidism; OB, obese women. *$p < 0.05$ compared with the pre-test

internal carotid artery (R-ICA), and left internal carotid artery (L-ICA) than the SCH group ($p < 0.05$). The IMT at the R-Bifur significantly decreased after exercise training in both groups ($p < 0.05$).

Physical fitness

Changes in physical fitness are shown in Fig. 4. Both OB and SCH groups showed significantly improved flexibility measured by the sit and reach test after exercise training ($p < 0.05$). However, there was no significant difference in the right and left grip strengths between the groups and between the time points. Both groups had a significant increase in the VO_2max after exercise training ($p < 0.05$); however, there was no significant difference in the VO_2max between the groups.

Discussion

In this study, a combined resistance and aerobic exercise training program was conducted among patients with subclinical hypothyroidism and obese patients, and the changes in the body composition, physical fitness, IMT, blood lipid factors, and factors associated with thyroid functions were measured.

Hypothyroidism negatively affects the risk factors of metabolic syndrome and is associated with obesity, hyperlipidemia, hyperglycemia, hypertension, and insulin resistance [18, 25]. Regarding the body composition results in this study, the SCH group was not classified as obese based on the BMI but had WHRs of ≥ 0.85, which is indicative of abdominal obesity, and could have had endocrine diseases due to hypothyroidism [18]. Hypothyroidism is accompanied by impaired lipid metabolism. It is characterized by increased TC and LDL-C levels.

Table 3 Change of concentration of thyroid gland function–related hormones

Item	SCH ($n = 20$)		OB ($n = 20$)	
	Pre	Post	Pre	Post
TC (mg/dL)	176.90 ± 23.43	166.70 ± 32.40	178.60 ± 33.52	174.60 ± 38.71
TG (mg/dL)	93.70 ± 51.33	113.90 ± 99.87	121.30 ± 46.11	114.50 ± 44.80
HDL-C (mg/dL)	49.10 ± 12.43	47.60 ± 15.60	52.30 ± 6.58	51.50 ± 7.97
LDL-C (mg/dL)	113.30 ± 11.29	102.30 ± 20.65	112.30 ± 30.95	107.90 ± 34.58
T3 (ng/mL)	1.14 ± 0.12	1.12 ± 0.29	1.20 ± 0.21	1.18 ± 0.16
T4 (μg/dL)	7.97 ± 1.96	8.10 ± 2.08	8.01 ± 1.06	8.11 ± 1.13
Free T4 (ng/dL)	1.24 ± 0.42	1.22 ± 0.132	1.17 ± 0.10	1.18 ± 0.12
T3/T4 ratio	0.15 ± 0.03	0.14 ± 0.03	0.15 ± 0.03	0.15 ± 0.02
TSH (mU/L)	5.95 ± 1.87	5.47 ± 1.23	3.97 ± 1.96	3.87 ± 1.55
Insulin (uU/mL)	5.59 ± 5.62	6.54 ± 5.83	9.27 ± 4.11	8.55 ± 2.62
Glucose (mg/dL)	84.4 ± 15.89	89.70 ± 15.04	94.30 ± 7.44	97.60 ± 9.00
HOMA-IR	1.25 ± 1.38	1.52 ± 1.41	2.17 ± 0.97	2.06 ± 0.62
DHEA-s (μg/dL)	198.13 ± 109.65	158.71 ± 57.09	240.20±121.77*	226.70±100.81*
AST (U/L)	20.20 ± 6.54	19.10 ± 5.956	17.90 ± 6.17	19.10 ± 5.50
ALT (U/L)	12.70 ± 6.70	13.10 ± 4.74	11.80 ± 3.99	14.40 ± 5.23

*$p < 0.05$ compared to SCH group; *SCH*, subclinical hypothyroidism patients; *OB*, obese women; *TC*, total cholesterol; *TG*, triglyceride; *HDL-C*, high-density lipoprotein cholesterol; *LDL-C*, low-density lipoprotein cholesterol; *T3*, triiodothyronine; *T4*, thyroxine; *Free T4*, free thyroxine; *TSH*, thyroid-stimulating hormone; *HOMA-IR*, homeostatic model assessment for insulin resistance; *DHEA-s*, dehydroepiandrosterone sulphate; *AST*, aspartate transaminase; *ALT*, alanine transaminase

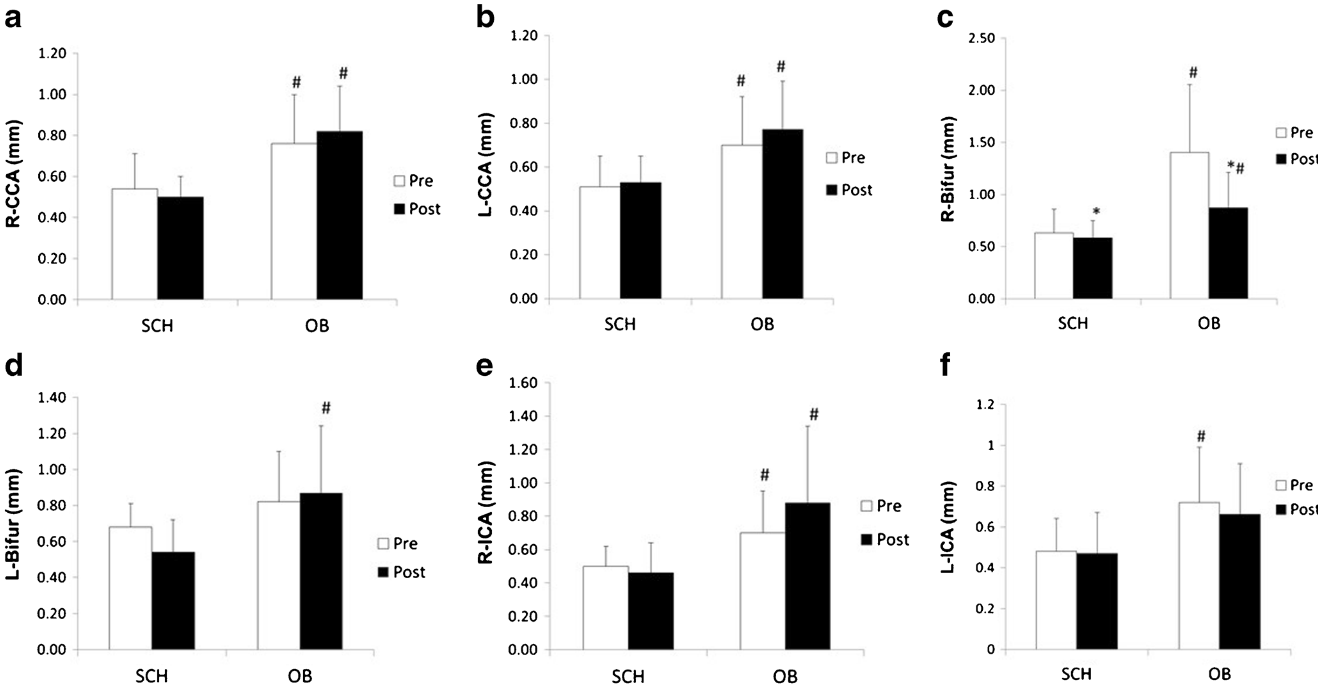

Fig. 3 Change in intima-media thickness of the carotid artery. SCH, subclinical hypothyroidism; OB, obese women. **a** R-CCA, right-common carotid artery; **b** L-CCA, left-common carotid artery; **c** R-Bifur, right-carotid bifurcation; **d** L-Bifur, left-carotid bifurcation; **e** R-ICA, right-internal carotid artery; **f** L-ICA, left-internal carotid artery. $^{*}p < 0.05$ compared with the pre-test; $^{\#}p < 0.05$ compared with the SCH group

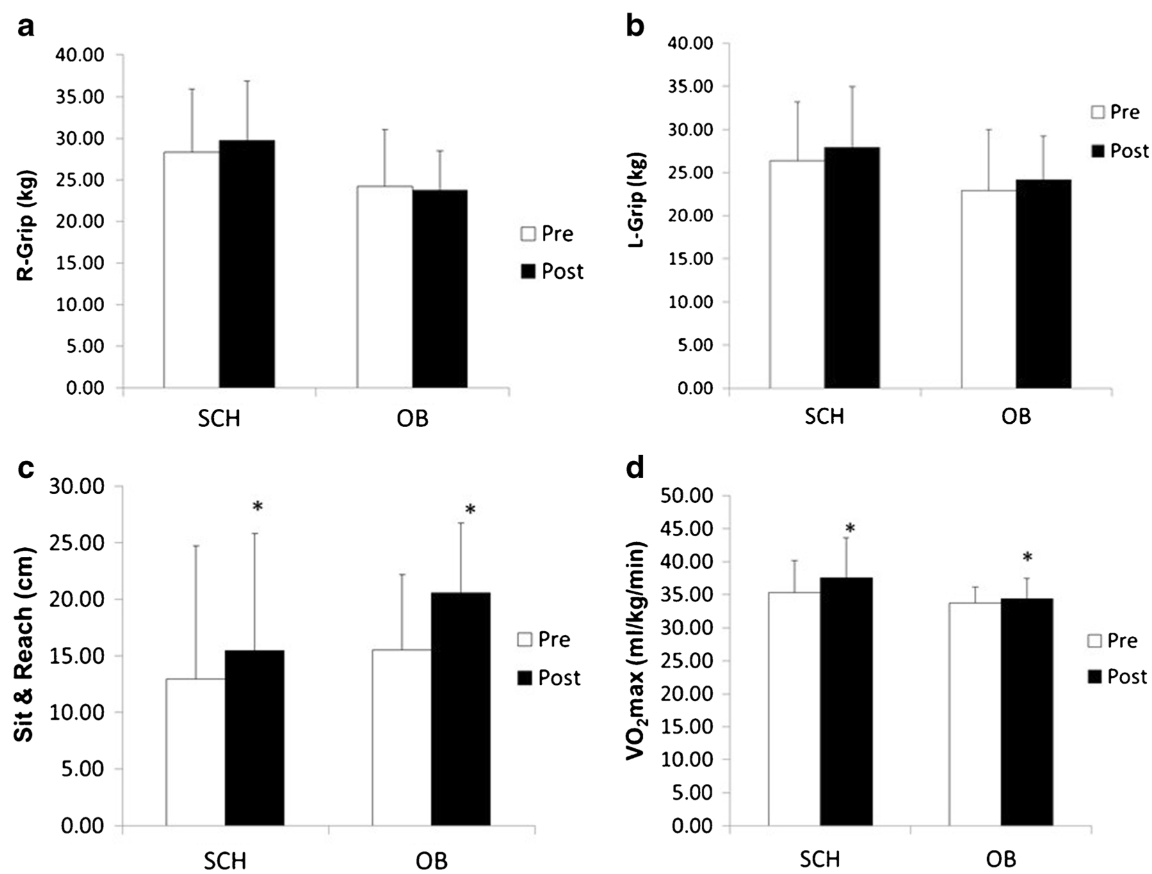

Fig. 4 Change in physical fitness. SCH, subclinical hypothyroidism; OB, obese women. **a** R-Grip, right grip strength; **b** L-Grip, left grip strength; **c** Sit and reach; **d** VO_2max, maximal oxygen uptake. $^{*}p < 0.05$ compared with the pre-test

Subclinical hypothyroidism may also be characterized by increased TC levels in addition to reduced HDL-C levels [15]. Although no evident patterns in the changes of TG have been observed in previous studies, changes in Lp(a), ApoB, and ApoA1 have been observed, and they tend to show no clear changes or increase in patients with subclinical hypothyroidism compared with normal subjects [54, 56, 70]. In patients with hypothyroidism, decreased activity of lipoprotein lipase leads to reduced blood TG levels, reduced activities of hepatic lipase and cholesteryl ester transfer proteins, and increased expression of ATP-binding cassette transporter A1, which then result in reduced blood levels of HDL-C. In this study, HDL-C levels were found to be decreased below 50 mg/dL in the SCH group. In addition, due to the reduced expression of LDL receptor in the liver, the LDL clearance in the blood decreases and blood LDL-C levels increase in patients with hypothyroidism [43]. However, both the SCH and OB groups did not show abnormal signs regarding lipid factors in this study; the effect of exercise training on these factors was also not evident. Therefore, this finding supports the notion that unless subclinical hypothyroidism is accompanied by old age (≥ 60 years) [30] or evident obesity [63], one cannot conclude that all abnormal lipid factor levels indicate negative results [69].

Thyroid hormones, secreted in adequate amounts, act on the thyroid hormone receptors in the smooth muscles and endothelial cells of blood vessels to increase the level of nitric oxide by the genomic and non-genomic mechanisms, thereby relaxing the smooth muscles and systemic vascular resistance [60]. The subsequent decrease in the mean arterial pressure is sensed by the juxtaglomerular apparatus, which then adequately activates renin production and secretion [37]. Thyroid hormones, which directly increase renin production [39], are also involved in the maintenance of BP within adequate ranges. Hypothyroidism usually induces an increase in the DBP and is considered an important risk factor of cardiovascular diseases as it excessively decreases systemic vascular resistance to increase the left ventricular contractility and blood volume [37]. Subclinical hypothyroidism may also increase the risk of vascular endothelial dysfunction, with reduced arterial compliance and increased diastolic pressure [14], and is likely to cause cardiovascular dysfunction [57]. However, both the SCH and OB groups showed normal DBP in this study, and the OB group showed a significant decrease in the DBP after 12 weeks of exercise training ($p < 0.05$). Both the OB group (SBP of ≥ 130 mmHg) and the SCH group (129.10 ± 3.38 mmHg) showed SBPs that were in the risk ranges for metabolic syndrome. However, both groups showed significant decreases in SBP and DBP after exercise training ($p < 0.05$). Therefore, exercise training was found to attenuate the negative effects of subclinical hypothyroidism and obesity on BP.

An increase in the vascular IMT is a change observed in the early stages of atherosclerotic plaques and may be used as an important marker to predict the onset and progression of atherosclerosis [51]. Hypothyroidism is directly associated with atherosclerosis and is known to increase IMT [28, 45]. In addition, subclinical thyroid dysfunction is reported as being highly associated with the incidence of carotid plaques [16, 59]. However, the OB group showed higher overall IMTs than the SCH group in this study ($p < 0.05$). Therefore, it appears that evident obesity is more likely to cause negative changes in vascular IMT than subclinical hypothyroidism. There has been a consistent controversy regarding the effect of subclinical hypothyroidism on plaques within blood vessels [11, 62]. Kim et al. [35] recently reported that subclinical hypothyroidism has almost no effect on plaque formation. In this present study, subclinical hypothyroidism did not cause significant changes in the IMT. Therefore, the direct effect of subclinical thyroid dysfunction on vascular plaque formation is still unclear and may involve a more complex process. Furthermore, although the SCH group showed reduced IMTs in the left common carotid artery, left and right bifurcations and left and right internal carotid arteries, after the 12 weeks of exercise training, showed no statistically significant changes. Therefore, the effect of exercise training on vascular IMT remains unclear, and further research is required.

Hypothyroidism significantly increases insulin resistance [47] and also causes increases in the levels of hormones that regulate glucose metabolism such as glucagon, epinephrine, cortisol, and growth hormones [50]. It reduces glycogen production [42] and intracellular activity of GLUT4 in the musculoskeletal system [46]. Subclinical hypothyroidism has also been reported to increase insulin resistance [33]. However, the OB group showed higher HOMA-IR than the SCH group, albeit not statistically significant, and therefore, no demonstrable effect of subclinical hypothyroidism on insulin resistance could be established. Sengupta et al. [48] reported that insulin resistance in patients with subclinical hypothyroidism is highly associated with blood lipid factors; therefore, it is necessary to consider the complex risk factors of metabolic syndrome during the clinical treatment. This is important because patients with mild subclinical hypothyroidism are likely to maintain insulin resistance within the normal ranges. In this study, the overall blood lipid factor levels were not very high, even when the subjects had subclinical hypothyroidism, and the SCH group showed lower HOMA-IR than the OB group. Thus, in patients with subclinical hypothyroidism, it appears that the complex interaction with lipid factors plays a huge role in insulin resistance; therefore, it must not be assumed that patients with subclinical hypothyroidism have high insulin resistance. Current recommendations for the treatment of insulin resistance include daily physical activity and exercise training [58], which were shown to reduce TSH in subclinical hypothyroidism. However, not all studies have shown the relationship between SHT and IR and the potential beneficial effect of exercise training on TSH in relation to markers of glucose tolerance and insulin sensitivity [68]. Wright et al. [67] reported health benefits of exercise training for the management of insulin resistance are not blunted by subclinical hypothyroidism. However, this study showed no significant effects of exercise training on the focus of insulin sensitivity in patients with subclinical hypothyroidism.

Changes in thyroid hormone levels due to long-term exercise training have not been seen as a consistent increase or decrease. Whereas T4 levels decreased due to exercise training, TSH [19] and T3 increased [5]. In addition, while the ratio of T4, FT4, and TSH increased to 90% of the maximal heart rate, the ratio of T3 and free triiodothyronine (FT3) decreased, showing that maximal aerobic exercise affects the level of circulating thyroid hormones [12]. Despite the importance of thyroid hormones associated with energy metabolism, very few studies have attempted to analyze the effect of long-term exercise training. In this study, the SCH group showed significantly increased levels of thyroid-stimulating hormones and normal T3, T4, and FT4 levels. No significant difference in these hormone levels was found following exercise training in both groups. In our previous study [36], blood T4 and T3 levels showed to have significantly increased after 12 weeks of exercise training, and it was thus believe that exercise training could improve thyroid functions. However, no such evidence is shown from the present study. Nonetheless, the slight increase in the level of T4, which has an important role in energy metabolism, observed in both groups following exercise training [34], suggests that exercise training can improve thyroid functions. Exercise training for patients with subclinical hypothyroidism is important as it can prevent reduced physical fitness and enhance self-esteem as well as prevent negative changes in the risk factors of metabolic syndrome [23]. Exercise training has been recommended as a good intervention for the conservation of musculoskeletal health [6]. Thyroid function is a very important marker for optimal maintenance of bone resorption, formation, and BMD [4]. In this study, the increase trend of BMD and T4 concentration after exercise training in SCH group could be suggested as a good intervention of exercise training to encounter the negative effects of subclinical hypothyroidism on focus of bone health.

The other study has shown a reduction in TSH following exercise training [68], and limited research suggests that SHT, versus a normal range, may blunt improvements in insulin sensitivity or thyroid function during exercise training [3]. These subjects with subclinical hypothyroidism have elevated TSH as results of greater fat mass and thyroid dysfunction, and SHT status did not influence the metabolic or physiological responses to exercise training such as changes in body composition and physical fitness. DHEA-s has been proposed to affect immune function and to be anti-aging [9]. Decrease of DHEA-s is associated with immune impairments and infection risk in elderly subjects [8]. Exercise training has been suggested as an intervention to improve immunity in elderly subjects, and DHEA-s has been found to be significantly increase in elderly subjects who regularly performed exercise training [27]. DHEA-s level in SCH group showed a significant ($p < 0.05$) lower value than OB group. Subclinical hypothyroidism would present with a more depression of DHEA-s than obesity. However, this study showed no significant increase of blood DHEA-s level after exercise training in both groups. Regular training seems to have little effect on basal DHEA-s values, probably because of its relative short half-life and insufficient workload [13].

Although the exercise training program did not directly or evidently improve the markers associated with thyroid functions, it is still important because it can improve cardiopulmonary functions and physical fitness. Although some patients with subclinical hypothyroidism do not have reduced physical fitness [44], they are still at risk of reduced physical fitness including reduced muscle strength [7]; therefore, they require active participation in exercise training during the treatment process. Although specific mechanism via which exercise training improves thyroid function is not fully elucidated yet, it could be accepted that health promotion is induced by exercise training. Therefore, we should try to study the more evident relation to the detailed contents of exercise training program for subclinical hypothyroidism. Exercise responses such as delayed heart rate kinetics during exercise [2] and the phenomenon in which the SBP decreases and DBP increases in patients with subclinical hypothyroidism compared with normal subjects during the same exercise intensity [53] must be thoroughly considered to increase the exercise effect. An earlier research found that patients with subclinical hypothyroidism showed lower scores in physical and psychological aspects, and the decreased quality of life negatively influences mood and enhances anxiety and depression rates [24]. In patients with subclinical hypothyroidism, improvement was found in relation to the disease symptoms after 12 weeks exercise training [61]. Therefore, exercise training could be apply as a strategy to improve health perception and lifestyle for patients with subclinical hypothyroidism. Although this study showed no significant responses of blood parameters related to direct positive effects, the entire trend of results of the physical fitness showed a positive effect of exercise training in patients with subclinical hypothyroidism. Therefore, exercise training has been able to improve quality of life in patients with subclinical hypothyroidism [65].

In summary, the SCH group showed WC and HDL-C outside of the normal ranges, while the OB group showed WC and SBP outside of the normal ranges. Following 12 weeks of exercise training, the SCH group showed significantly positive changes in %fat, SBP, and flexibility ($p < 0.05$), while the OB group showed significantly positive changes in the BMI, WC, SBP, DBP, and flexibility ($p < 0.05$). Both groups also showed positive changes in IMT at the right bifurcation (R-Bifur). However, the 12-week exercise training program did not similarly affect the levels of hormones related to thyroid functions and blood lipid factors in the patients to a similar extent. Therefore, further research on exercise training programs that can effectively change the levels of hormones related to thyroid functions in patients with subclinical hypothyroidism is necessary.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The research protocol was approved by the Institutional Review Boards of Keimyung University College of Medicine and Keimyung University Dongsan Medical Center (approval number: 10-184-01.06).

Informed consent Informed consent was obtained from all individual participants included in the study.

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