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Research Paper

Effect of Home-based Aerobic Exercise on Leukocyte *TERT* Gene Expression Without Altering DNA Oxidative Damage in Postmenopausal Women

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ABSTRACT

Objectives: In middle-aged women, the postmenopausal period is associated with increased oxidative, inflammatory, and psychological stress. We intend to investigate the effect of home-based aerobic exercise (HAE) on serum levels of 8-hydroxy-2'-deoxyguanosine (*8-C*) and the expression of telomerase reverse transcriptase (*TERT*) in leukocytes of postmenopausal women.

Methods: A total of 20 sedentary postmenopausal women who had at least 12 months passed since their last menstruation participated in the study voluntarily. Their Mean±SD age, height, weight, and body mass index (BMI) were respectively 52.4±3.8 years, 161.4±3.7 cm, 74.4±6.8 kg, and 28.6±3.4 kg/m^2. They were randomly divided into two groups: Home-based aerobic exercise (HAE, n=10) and inactive control (CON, n=10). HAE group undertook 4 weeks of home-based aerobic exercise (4 d/wk, intensity: 70%-80% maximal heart rate) with online supervision. Participants' weight and fasting blood samples (12-h fasting state) were measured and taken before and 48 hours after the intervention. *TERT* expression in blood leukocytes and serum levels of *8-OHDG* were assessed by real-time PCR and ELISA methods, respectively. The collected data were analyzed using mixed (2×2) repeated measure ANOVA and independent samples t-test in SPSS software. A significance level of P<0.05 was considered for all tests.

Results: The findings showed that 4 weeks of HAE increased *TERT* expression significantly compared to the CON (ES=0.40, P<0.05). Although *8-OHDG* serum level in the HAE group increased following training compared to pre-training (P<0.05), no significant difference was observed between the CON and HAE groups (P>0.05). Also, the interaction effect on *8-OHDG* was not significant (ES=0.11, P>0.05). In addition, after 4 weeks of HAE, body weight and BMI significantly decreased in the training group compared to the control (P<0.05).

Discussion: According to these findings, HEA effectively reduces telomere erosion and improves weight control in postmenopausal women.

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Introduction

Menopause marks a pivotal stage in a woman's life when menstrual cycles end, and fertility declines due to decreased ovarian function and estrogen concentrations [1]. Menopause and its concomitant hormonal changes, especially the reduction of sex hormones, are associated with many problems, such as cardiovascular diseases, diabetes, osteoporosis, breast cancer, and mental health problems [1]. Decreased estrogen levels due to menopause increase oxidative stress, inflammation, and DNA impairment [2]. Another challenge reported during this stage is the decrease in telomere length, telomerase activity, and telomerase reverse transcriptase (*TERT*) gene expression [3]. These changes play an essential role in the unpleasant consequences of menopause [4]. Telomere, a complex of protective nucleoproteins (non-coding DNA) at the end of a eukaryotic chromosome, consists of repeated TTA sequences with a simple sequence rich in guanine nucleotide [3]. Changes in telomere length results from a delicate balance between repair and degradation [3]. Telomeres primarily protect the integrity of the genome, and their destruction contributes to age-related diseases [3, 4].

In the telomeric complex, the telomerase enzyme contains a degrading subunit known as telomerase reverse transcriptase, or *TERT* [4], an essential enzyme to add deoxyribonucleotides to the end of 3' DNA by telomerase, underlining its role in cell survival and genome stability [4]. Accordingly, telomere erosion results in increased oxidative stress, chronic inflammation, and hormonal changes due to aging [3-5]. Therefore, many studies have focused on changes in telomere length and telomerase activity at the level of blood cells, especially in leukocytes, as biomarkers of age-related diseases [4, 6].

It has also been suggested that leukocyte telomere length affects female reproductive function and ability. One study found that for every kilobase (kb) increase in leukocyte telomere length, the average age at normal menopause increased by 10.2 months [6]. However, oxidative DNA damage is also considered as crucial as telomere length in the pathology of age-related diseases. Oxidative stress at the DNA base level damages the genetic structure of cells and affects telomere length dynamics and cellular aging [5]. According to epidemiological studies on white blood cells, exposure to high levels of reactive oxygen species (ROS) is associated with shorter telomere lengths [5]. In addition, by exposing cells to oxidative agents, higher amounts of 8-oxoguanine (8-oxoG), a marker of oxidative damage to guanine bases in nucleotides, are produced in telomeres than in other genomic components [5]. This marker can impair telomere renewal and exacerbate telomere shortening. Thus, many researchers investigate other strategies, such as exercise training and lifestyle modification to counteract these mechanisms.

Evidence suggests that exercise and physical activity are effective non-pharmacological strategies for reducing oxidative stress, inflammation, and adverse outcomes of menopause [7]. Therefore, exercise and physical activity are interesting topics because they reduce the negative consequences of increased oxidative stress in postmenopausal women. A study found that 16 weeks of strenuous training increased 8-hydroxy-2-dioxyguanosine (*8-OHDG*), a marker of oxidative DNA damage, while moderate-intensity training significantly reduced *8-OHDG* [8]. Regarding the effects of exercise on the telomere of female leukocytes, a recent study indicates that 8 weeks of combined exercise can reduce telomere erosion of leukocytes [9]. However, 12 weeks of aerobic exercise did not affect leukocyte telomere [10]. Based on these findings, the positive effects of exercise training on oxidative damage and telomere length are somewhat obvious; however, none of these studies have addressed DNA oxidative damage markers and leukocyte *TERT* gene expression in response to home-based aerobics exercise.

Generally, long-term adherence to exercise is often challenging. In this regard, home-based exercise programs offer an alternative with an advantage that helps postmenopausal women spend more time with their families and reduce costs compared to supervised exercise in gym centers [11]. Home-based exercise eliminates barriers such as transportation, dressing up for the gym, and time constraints for exercise (due to matching work hours with gym hours).

Considering the benefits of aerobic exercise, this study investigated the effect of a 4-week home-based aerobic exercise on DNA oxidative damage reduction and *TERT* gene expression in postmenopausal women.

Materials and Methods

This research was a quasi-experimental study. A total of 20 sedentary middle-aged postmenopausal women who had 12 months passed since their last menstrual period participated in the study. Their Mean±SD age, height, weight, and body mass index (BMI) were 52.4±3.8 years, 161.4±3.7 cm, 74.4±6.8 kg, and 28.6±3.4 kg/m^2, respectively. The inclusion criteria comprised menopausal women without a history of hysterectomy, chemo-

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therapy, hormone therapy, and nutritional supplements. Also, they should not have participated in regular exercise during the past year. The exclusion criteria included those with infectious diseases (such as cold), musculoskeletal injuries, and absenteeism from training sessions or tests during the implementation of the intervention. At first, the research process and interventions were explained to the participants. After their agreement, they signed their consent form. Then, the participants were randomly divided into two groups: Home-based aerobic exercise (HAE, n=10) and control (CON, n=10). Before implementing the HAE protocol, the participants were introduced to rhythmic movements and exercises and recording heart rate (with Polar H10 Heart Rate Monitor Chest Strap) during three sessions.

Sample size calculation

The number of participants was determined based on the study by Hejazi et al. [12], who reported that aerobic training significantly improves *8-OHDG* compared to the control group (Cohen's d=1.25). Considering the confidence interval of 95% and the analysis power of 0.80, it was found that at least 18 participants (n=9 for each group) are needed for this study using G*Power software, version 3.1. To ensure a sufficient sample size, 20 participants were selected for this study.

HAE protocol

The protocol of the HAE included 4 weeks (4 d/wk) of home-based aerobic exercise with online supervision (Google Meet) by a trainer. Before implementing the HAE protocol, the participants were familiarized with rhythmic functional movements and exercises in three sessions. Each HAE session consisted of 3 parts: 10 minutes of warm-up (including 5 minutes of jogging, 2 minutes of dynamic stretching, and 3 minutes of aerobic movements with an intensity of 50%-55% of the maximum heart rate), the main body of the exercise (Table 1), and 5 minutes of cooling down (including static stretching exercises). The main body of the exercise consisted of 8 stations of functional aerobic movements (work interval) separated by active rest intervals (recovery interval: Walking). In the first and second weeks, the intensity of the main exercises was 70%-75%, and in the third and fourth weeks, the intensity was 75%-80% of the maximum heart rate (moderate to high intensity) [13]. The configuration of movements included moving the foot in right and left as well as up and down directions, rotating in place, walking while performing lunches, side steps, squats, stretching both legs in diagonal directions, running in place, and modified jumping jacks [14]. Heart rate was monitored using a Polar H10 chest strap. The maximum heart rate of each person was calculated based on the Equation 1:

1. 208–(0.7 x age) [15].

The perceived effort was also recorded using a 20-point Borg scale immediately after each training session [16].

Blood sampling and isolation of leukocytes

Fasting blood samples (following 12 hours of fasting) were taken from the participants 48 hours before the first training session and 48 hours after the last training session. The collected blood samples (10 mL from brachial veins) were poured into tubes without anticoagulant to separate serum and tubes containing anticoagulant to isolate peripheral blood mononuclear cells (leukocytes). Peripheral blood mononuclear cells were isolated using Ficoll and concentration gradient. After diluting with PBS (1:1 ratio), the blood samples were slowly added to the Ficoll solution. After centrifugation (3000 rpm for 15 min), the layer of mononuclear cells between the Ficoll layer and the plasma was slowly collected by a pipette. Then, after washing with PBS, it was kept at -80°C.

TERT and *8-OHDG* measurement

To measure the expression of *TERT*, the total RNA was first extracted using a Trizol solution (Kiagene Fanavar, Iran). The extracted RNA was dissolved in 50 µL of DEPC (diethylpyrocarbonate) water and kept at -80°C. Cyclic DNA synthesis was performed according to the instructions in the cDNA synthesis kit (Thermos Scientific, USA). The prepared cDNA was then stored at -20°C. The primers were designed by Allele ID software, version 7.8 to evaluate gene expression using real-time PCR, and the Gapdh (Glyceraldehyde 3-phosphate dehydrogenase) gene was used as the internal control (Table 2). Then, a mixture of PCR components, including the SYBR Green Master mix (Amplicon, Denmark), was prepared. After mixing and spinning, it was distributed inside the microtubes for the device, and 2 µL of cDNA sample was added to each vial. Afterward, the program of the real-time PCR device was adjusted. After completing the device activity and observing the graphs and the amount of fluorescence propagation, the amount of change in the expression of the desired gene compared to Gapdh (as a housekeeping gene) was measured by calculating ΔΔCt. Finally, the relative expression of the gene was calculated using the $2^{-\Delta\Delta Ct}$ formula.

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An ELISA kit (Zellbio, Germany, CAT No: ZX-55100-96) with a 50.9 pg/mL sensitivity was used to measure *8-OHDG* serum level. All measurement processes were performed according to the instructions of the kit guideline.

Data analysis

SPSS software, version 22 was used for the statistical analysis. The obtained data were analyzed by repeated measures mixed (time×group) ANOVA and Bonferroni post hoc test. In addition, the differences between the post-test and the pre-test results for weight and body mass index were calculated (gain score) and analyzed by the independent t-test. The significance level was considered at P<0.05.

Results

The results showed that the main effect of time on the *8-OHDG* level was significant ($F_{(1, 18)}$=7.21, P<0.05). However, the interaction effect of time×group ($F_{(1, 18)}$=2.25, P=0.15) and the effect of group ($F_{(1, 18)}$=1.72, P=0.20) were not significant (Table 3). The post hoc test also showed that, unlike the CON (MD=0.004, P=0.41, 95% CI, 0.007%-0.016%), in the HAE, *8-OHDG* level increased significantly in the post-test compared to the pre-test (MD=0.016, P=0.009, 95% CI, 0.004%-0.027%) (Figure 1). The main effect of time ($F_{(1, 18)}$=7.15, P<0.05) and the interaction effect of time×group ($F_{(1, 18)}$=12.29, P<0.05) on *TERT* was significant (Table 3). Nevertheless, the group's main effect on *TERT* was not significant ($F_{(1, 18)}$=1.90, P=0.18). *TERT* expression increased significantly in the HAE group (MD=0.002, P=0.000, 95% CI, 0.001%-0.003%), while the CON group did not show significant changes (MD=0.0002, P=0.56, 95% CI, -0.001%-0.001%). Also, in the post-test, the *TERT* expression of the HAE group was significantly higher than that in the CON group (MD=0.002, P=0.006, 95% CI, 0.001%-0.003%) (Figure 1). There was no significant difference in the *TERT* levels for the pre-test (MD=0.001, P=0.24, 95% CI, 0.0001%-0.002%). In addition, the main effect of time ($F_{(1, 18)}$=6.91, P<0.05) and the interaction effect of time×group ($F_{(1, 18)}$=29.82, P<0.05) on body weight was significant (Table 3). However, the main effect of the group on body weight was not significant ($F_{(1, 18)}$=0.011, P=0.91). The post hoc test also showed that, unlike the CON group (MD=0.67, P=0.06, 95% CI, -0.033%-1.37%), in the HAE group, body weight decreased significantly in the post-test

Table 1. HAE protocol

Week	Frequency (d/wk)	Round Per Session	Duration	Intensity
1	4	2 (8 stations)	Work interval: 30 s Recovery interval: 30 s Rest between rounds: 2 min	70%-75% MHR
2	4	3 (8 stations)	Work interval: 30 s Recovery interval: 30 s Rest between rounds: 2 min	70%-75% MHR
3	4	4 (8 stations)	Work interval: 30 s Recovery interval: 30 s Rest between rounds: 2 min	75%-80% MHR
4	4	5 (8 stations)	Work interval: 30 s Recovery interval: 30 s Rest between rounds: 2 min	75%-80% MHR

MHR: Maximum heart rate.

Table 2. Sequence of primers designed for *TERT* and *GAPDH* genes

Gene (direction)	Primer Sequence
hGAP (F)	GCA GGG ATG ATG TTC TGG
hGAP (R)	CTT TGG TAT CGT GGA AGG AC
h-TERT (F)	CAGCTCCCATTTCATCAGCA
h-TERT (R)	TTCAGGATGGAGTAGCAGAGG

R: Reverse, F: Forward.

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Table 3. Mixed repeated measure ANOVA (2×2) results

Variables	Group	Pre-test	Post-test	Relative Change	Main Effects (Eta²)		
		Mean±SD	Mean±SD		Time	Group	Interaction
8-OHDG (pg/mL)	HAE	1.197±0.008	1.212±0.014*	1.68%	0.015 (0.29)	0.2 (0.09)	0.15 (0.11)
	CON	1.199±0.007	1.202±0.012	0.84%			
TERT (relative expression)	HAE	0.0023±0.0006	0.0044±0.001*#	91.3%	0.015 (0.28)	0.18 (0.095)	0.003 (0.48)
	CON	0.0029±0.0014	0.0027±0.001	-6.9%			
Weight (kg)	HAE	74.4±7.9	72.5±7.1*	-2.5%	0.017 (0.28)	0.91 (0.001)	0.000 (0.62)
	CON	74.2±5.8	75.1±5.9	1.21%			
BMI (kg/m²)	HAE	28.5±3.7	27.8±3.5*	-2.46%	0.018 (0.27)	0.82 (003)	0.000 (0.62)
	CON	28.7±3.3	29.00±3.3	1.05%			

*Significant difference compared to the pre-test; #Significant difference compared to the control group in the post-test; P<0.05.

Relative change=([post-test value–pre-test value]/pre-test value)×100.

Abbreviations: HAE: Home-based aerobic exercise; CON: Control; *8-OHDG*, 8-hydroxy-2′-deoxyguanosine; *TERT*: Telomerase reverse transcriptase; BMI: Body mass index.

compared to the pre-test (MD=1.91, P=0.000, 95% CI, 1.21%-2.16%) (Figure 1). The main effect of time ($F_{(1, 18)}$=6.76, P<0.05) and the interaction of time×group effect ($F_{(1, 18)}$=29.78, P<0.05) on BMI was significant (Table 3). However, the group's main effect on BMI was not significant ($F_{(1, 18)}$=0.011, P=0.91). The post hoc test also showed that, unlike the CON group (MD=0.26, P=0.06, 95% CI, -0.011%-0.53%), in the HAE group, BMI decreased significantly in the post-test compared to the pre-test (MD=0.73, P=0.000, 95% CI, 0.46%-1.00%) (Figure 1). In the pre-test, there was no significant difference between the HAE and CON groups regarding body weight (MD=0.99, P=0.74, 95%CI, -5.24%-7.22%) and BMI (MD=0.16, P=0.91, 95% CI, -3.06%-3.38%). Also, in the post-test, there was no significant difference between the two groups in body weight (MD=1.59, P=0.57, 95% CI, -5.24%-7.42%) and BMI (MD=0.83, P=0.58, 95% CI, -2.27%-3.94%). However, the comparison of the difference in body weight and BMI (difference between the post-test and the pre-test) showed that the body weight (t_{18}=4.28, MD=2.76, P=0.000, 95% CI, 1.40%-4.11%) and BMI (t_{18}=4.37, MD=1.01, P=0.000, 95% CI, 0.54%-1.56%) in the HAE group decreased significantly compared to the CON group.

Discussion

The present study showed that 4 weeks of HAE significantly decreased body weight and BMI in the HAE group compared to the CON group (P<0.05). In addition, HAE increased *TERT* gene expression (40%) in the HAE group compared to the CON group (P<0.05). Also, the interaction effect of the time×group on body weight, BMI, and *TERT* gene expression was significant (P<0.05). Although the *8-OHDG* level in the HAE group significantly increased in the post-test compared to the pre-test (P<0.05), no significant difference was observed between the CON and HAE groups. Also, the interaction effect of the time×group on *8-OHDG* was not significant (ES=0.11, P>0.05).

Weight and BMI loss after HEA were the expected findings, as previous studies had reported the positive effect of regular exercise (without caloric restriction) on weight loss [17, 18]. It should be stressed that the HEA protocol has been implemented for only 4 weeks, and its significant effect on weight loss suggests its effectiveness in improving health indicators (such as body weight and body mass index). Negative energy balance, one of the most important mechanisms, can explain the weight loss caused by HAE in the present study. Unfortunately, the present study did not evaluate the variables related to body composition (percentage of fat, muscle mass) and metabolism (basal metabolic ratio), so the exact mechanism of weight loss in the HAE group is unknown. Nevertheless, some studies have reported that aerobic exercise can cause weight loss by changing body fat content, regulating energy metabolism, lipid metabolism, insulin metabolism, and obesity gene expression [19]. It is sug-

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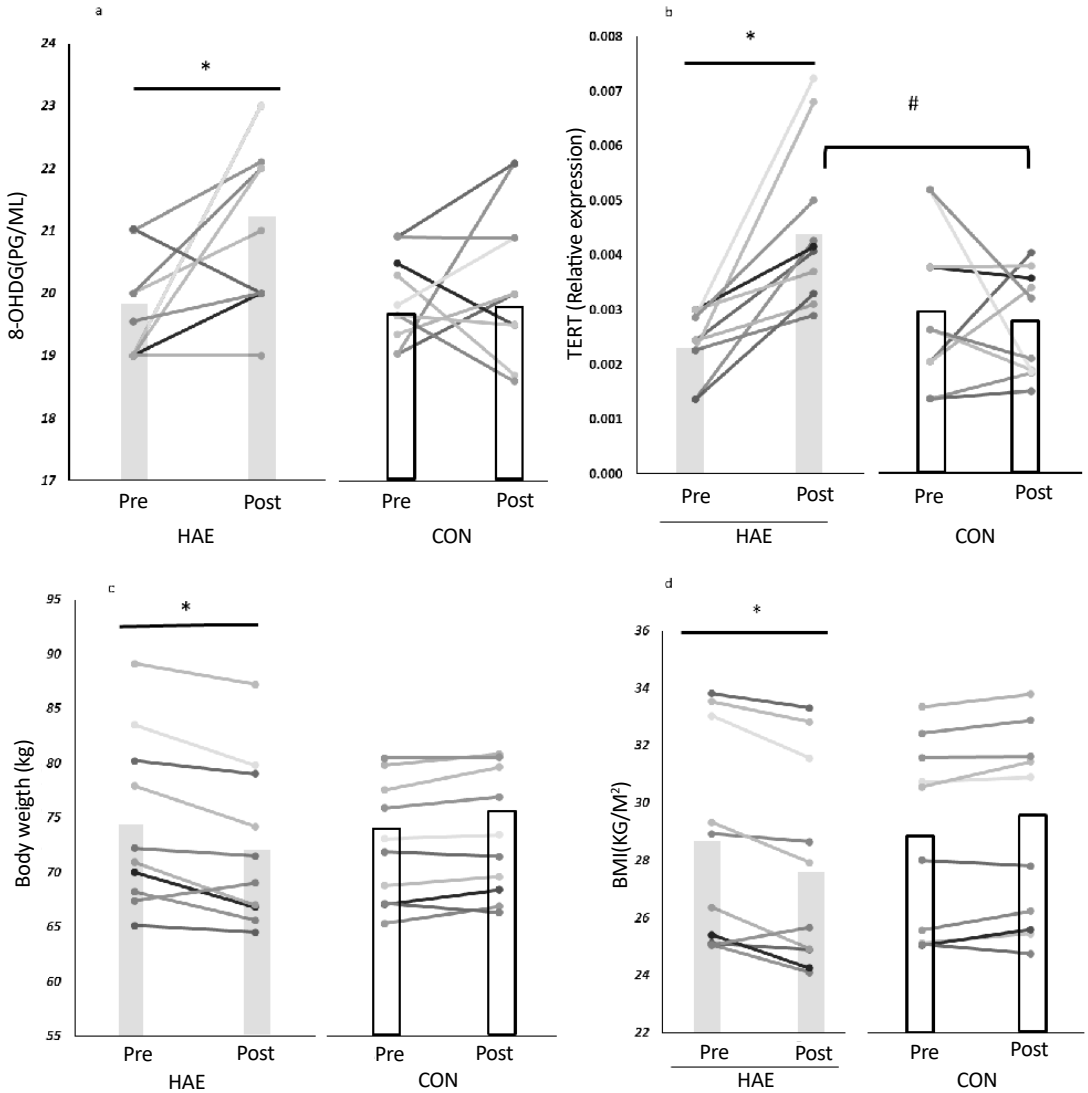

Figure 1. Individual (line segment) and group (mean, bars) changes *8*-- (a), *TERT* (b), body weight (c) and body mass index (d) in pre-test and post-test.

*Within group significant difference, #Between group significant difference, P<0.05.

gested that the effect of HAE on weight loss and its related mechanisms should be explored in future studies.

Consistent with these results, an increase in *8-OHDG* serum level in response to exercise training has also been shown in previous studies [8, 20]. Contrary to our findings, some studies reported that chronic aerobic or resistance training decreases the serum levels of *8-OHDG* in older women [8]. These inconsistencies can be attributed to the differences in the blood sampling timing and exercise training protocols. In this regard, in a new meta-analysis review study, Tryfidou et al. examined the acute effects of aerobic exercise on DNA oxidative damage (*8-OHDG*) [20]. The studies in this meta-analysis comprised those with human samples (peripheral blood mononuclear cells) aged 18-70 years without studies on animal samples [20]. This review shows that acute aerobic exercise can induce oxidative DNA damage, and DNA repair probably takes at least 3 days after exercise [20]. Therefore, since the present study blood samples were collected 48 hours after the last session of HAE, it is unlikely that the residual effect of the last session of aerobic training has elevated *8-OHDG* in the training group [20]. In addition, it has been suggested that increasing the intensity of aerobic exercise up-regulates DNA damage dose-dependently [20]. Therefore, another

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reason for the increase in *8-OHDG* in the training group could be the higher intensity of training in the final sessions of the training period compared to the pre-test. Although many studies have shown an increase in *8-OHDG* under conditions of oxidative stress, the biological role of *8-OHDG* has received less attention. It probably has a mutagenic or at least a harmful effect on cells, so it must be eliminated from the body and cells [21]. However, it has recently been suggested that this molecule can be one of the defense mechanisms of cells against inflammation caused by oxidative stress [21]. For example, inhibition of RAC1 by exogenous *8-OHDG* has significantly inhibited ROS-induced inflammation [22]. Also, *8-OHDG* has a strong anti-inflammatory effect compared to other nucleoside products. For example, *8-OHDG* is more effective than aspirin in reducing tumor necrosis factor (TNF-α), interleukins, myeloperoxidase activity, and neutrophil recruitment in severe lipopolysaccharide-induced pneumonia in mice [23]. Therefore, the slight increase of *8-OHDG* in the HAE group may relate to the anti-inflammatory effects caused by regular exercise. In addition, it should be noted that the rate of change of *8-OHDG* shows a minimal increase (1.68%) with a small effect size (Eta^2=0.29), probably due to the activation and up-regulation of repair systems (antioxidants and base excision repair) [24]. However, one of the limitations of the present study was the lack of assessing antioxidant factors, which is recommended to be considered in future studies. Therefore, according to the findings of the present and previous studies, significant oxidative damage may not occur due to HAE in sedentary postmenopausal women. Also, considering the wide range of individual differences in the postmenopausal period, it is suggested that more studies be conducted in this area.

This study showed a significant increase in *TERT* gene expression in the HAE group compared to the control group (a 91% increase for the HAE and a 7% decrease for the control group). A longitudinal study investigating the effect of 12 weeks of low-intensity resistance training with high repetitions (body-pump exercises for 12 weeks, 2 sessions per week for 1 hour) on telomere length and *TERT* gene expression in sedentary middle-aged adult blood leukocytes (16 women and 7 men) showed that the telomere length of leukocytes did not change significantly. However, *TERT* gene expression was significantly increased [25]. The study found that after 12 months of monitoring and re-examining the subjects, the telomere length of the blood leukocytes of those who had returned to an inactive lifestyle was significantly reduced compared to before exercise [25]. It seems that although the molecular parameters associated with telomere length (*TERT* gene expression) improve in response to short-term periods (12 weeks) of low-intensity resistance training with high repetitions, long-term periods of sports training (more than 12 months) should be observed to observe the significant effects of sports training on telomere length [25]. Based on a meta-analysis study, exercise training as an inexpensive lifestyle factor has increased *TERT* expression and telomerase activity [26]. This study indicated that acute (high heterogeneity) and chronic (moderate heterogeneity) exercise can both increase the expression of the *TERT* gene and telomerase activity in humans and rodents [26]. However, most studies in this meta-analysis focused on the effect of exercise on telomerase activity, and only two studies examined the impact of regular exercise on the expression of the *TERT* gene in human blood leukocytes. In addition, Laye et al. reported that *TERT* gene expression in blood leukocytes of endurance runners (7 male, 1 female) did not show significant changes after 7 days of long-distance running training [27]. The contradiction between the findings of this study and the results of Laye et al. could be due to the difference in the gender of the participants (predominantly male vs postmenopausal women), the type of exercise (long-distance running vs HAE), and the period of training (7 days vs 4 days per week for 4 weeks). Therefore, studies on the long-term effect of exercise on regulating the expression and function of *TERT* in blood leukocytes (especially in postmenopausal women) are limited, and considering the inconsistency of the results, it seems that more studies should be done in this regard.

The mechanisms that exercise regulates *TERT* gene expression in blood leukocytes have not been identified. However, one of the possible mechanisms could be the activation of the PPAR-γ/PGC-1α/β signaling pathway. Previous studies have shown that PPAR-γ levels are higher in blood leukocytes of people with higher VO_2max [28]. These results indicate that PPAR-γ is strongly expressed in the leukocytes of trained individuals [28]. In another study, it was shown that 8 weeks of low-intensity exercise has a positive effect on increasing the expression of PPAR-γ and PGC-1α/β leukocytes in middle-aged men and women (9 men and 8 women). Also, some studies have reported that PPAR-γ activity decreases in aging mononuclear leukocytes [29]. Considering the positive role of PPAR-γ/PGC-1α/β on *TERT* expression in other tissues or cells [30], the increase observed in the present study can also be due to this mechanism. In addition, although Ramlee et al. [31] determined some other positive and negative regulatory factors of *TERT* transcription, their exact role in response to regular exercise activity and blood leukocytes requires further studies.

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Reducing systemic inflammation and oxidative stress caused by regular exercise can also be another mechanism [3]. Based on previous observations, high inflammatory loads and oxidative stress are both associated with shorter telomere length in human leukocytes [32, 33]. Also, it has been shown that menopause is associated with an increase in systemic inflammation and senescent T cells (one type of leukocytes), which can be due to an increase in visceral fat mass and a decrease in the level of sex hormones [2]. However, some studies have reported that exercise reduces inflammation and related body composition parameters in postmenopausal women [34]. In addition, in postmenopausal women's blood leukocytes, the anti-inflammatory effect of exercise is associated with longer telomeres [35]. Also, exercise training in postmenopausal women can modulate and reduce psychophysiological stress and related hormones such as cortisol [36]. In succession, psychophysiological stress can play a role in reducing *TERT* expression and telomere length [37]. Therefore, stress reduction through HAE could be another possible mechanism for increasing *TERT* expression compared to the control group. It is suggested that the role of these mechanisms and their relationship with the effect of exercise on the regulation of *TERT* expression be considered in future studies.

Some methodological limitations may influence the observed results, such as the small sample size and lack of assessing protein activity and concentration. Additionally, participants' diet and psychophysiological stress levels were not fully controlled. Also, telomere length and its relationship with other oxidative stress indicators have not been measured. Therefore, in addition to measuring the expression of *TRET* and *8-OHDG*, it is suggested that future studies investigate the effect of various training methods and their relationship with oxidative stress and telomere regulation.

Conclusions

Taken together, the findings of this study show that although HAE has increased *TERT* expression, it does not significantly affect oxidative DNA damage in postmenopausal women. Also, HEA serves as a cost-effective strategy to help lose weight in postmenopausal women. As a result, the role of HEA in reducing telomere erosion and improving the health of postmenopausal women should be given more attention.

Ethical Considerations

Compliance with ethical guidelines

The study proposal and procedures were approved by the Ethics Committee of the Institute of Physical Education and Sports Sciences (Code: IR.SSRC.REC.1399.102).

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The paper was extracted from the master's thesis of Fahime Khairabadi, approved by Department of Sport physiology, Faculty of Physical Education and sport Sciences, University of Tehran.

Authors' contributions

Conceptualization, supervision, funding acquisition and resources: Fahime Khairabadi and Abbas Ali Gaeini; Methodology: Abbas Ali. Gaeini; Investigation, Writing: All authors; Data collection: Fahime Khairabadi; Data analysis: Fahime Khairabadi and Mohammadreza. Kordi.

Conflict of interest

The authors declared no conflict of interest.

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