DIFFERENT TYPE AND INTENSITIES OF EXERCISE CORRELATES WITH TELOMERE LENGTH

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ABSTRACT

In the current generation, physical activity is a trend. Many people only do physical activity as a modern thing without knowing the limits. Recent studies have shown that mechanisms of physical activity influence the aging process, one of which is telomere biomarkers. Telomeres are repetitive DNA sequences which serve to protect genomic DNA from degradation and are highly relevant in the cellular aging process and the shortening of telomeres that occurs with increasing age is considered an important benefactor to aging in organisms. There are many factors that affect telomere length such as oxidative stress, chronic inflammation, BMI, lifestyles like smoking, alcohol intake, stress, increased insulin resistance, and exercise. This study aims to determine different types and intensities of exercise correlates with telomere length. The method used in this study is an internet search for journals and articles through several websites like Mendeley Search, Proquest, Pubmed, Science Direct, and Scopus. We reviewed and compared the latest journals that discuss the correlation between physical exercise and telomere length. As a result, the people who perform moderate physical activity more in their leisure time, have longer leukocyte telomere length (LTL) and 30 minutes of resistance training for 24 weeks may exert a protective effect on muscle telomere length in the elderly. Several studies have reported a correlation between prevention of leukocyte telomere length shortening and exercise at a certain intensity successfully.

Keywords : telomere; telomere length; exercise

INTRODUCTION

Several studies have shown a link between exercise and telomere length with mixed results. Telomeres are structures spotted at the end of human chromosomes that help to protect genomic DNA from enzymatic degradation. Telomeres had tandem sequences sheltered by protein complexes. Besides the cell fusion process, two main factors that can expedite telomere shortening are oxidative stress and inflammatory processes. In addition, physical activity also affects refinement in various aspects of human life. The beneficial effects of physical activity on cellular regeneration and deterioration have been observed[1].

There is still some doubt that physical activity has been found to improve quality of life, can minimize oxidative damage, and prevent the onset of several metabolic disorders and cardiovascular diseases. There are several reports of beneficial effects on the antioxidant system, but there is still a constant debate on exercise type, intensity, frequency, and duration, on the health of a person[1]. A study showed, there was a relationship between physical activity and oxidative stress, it was stated that superoxide dismutase increased in the exercise group and correlated with strenuous exercise. Superoxide dismutase is a powerful antioxidant that acts as a detoxifying enzyme that converts oxygen radicals generated during intense exercise into hydrogen peroxide, a prooxidant that can cause damaging effects on various cellular structures. Oxidative stressinduced damage to telomeres is caused by G-rich nucleotide sequences. There are two types of exercise, aerobic and anaerobic exercise [2–4].

Another study showed no interactivity between long-term resistance training and telomere length, but the negative collision has been found between heavy-resistance training and telomere length. In highly active adults, exercise can cause muscle breakdown, proliferation of satellite cells, and telomere length shortening in skeletal muscle tissue[5–9]. Usually, moderate exercise like easy swimming, jogging, bicycling, and faster walking can make telomere lengthening while mild and vigorous exercise can shorten telomeres. Recent studies have shown the relationship between telomere length shortening and increasing age is interrelated. On the other hand, exercise at a certain intensity is correlated with good health and improved quality of life, also dynamic effects of exercise are proven to have correlation with the aging process. This literature review is aimed to discuss different views and research findings concerning different type and intensities of exercise correlates with telomere length[3,5,7,10–12].

METHODS

The method used in this literature review is internet search for journals and articles through several websites such as Mendeley Search, ProQuest, Pubmed, Science Direct, and Scopus using the keywords "exercise" and "telomere length" or "telomere". The eligible criteria include studies in the English language published between 2012 and 2022. The studies that report the correlation between different types and intensities of exercise with telomere length were selected for the literature review. Reference lists from selected literature were also checked to identify additional relevant reports. The selected journals are checked through the Scimago Journal & Country Rank website,and we only select journals that are accredited from Q1 to Q3.

DISCUSSION

Telomere and Telomerase Activity

Many studies have been conducted to establish the connection between exercise and telomere length, but still have varying results[5,13–15]. Telomeres are reiterative DNA sequences (5'-TTAGGGn-3') that function to protect genomic DNA from enzymatic degradation[2,5,16–18]. These repeated TTAGGG sequences are located at the end of chromosomes and tied up by a protective protein complex called Shelterin[19–21]. Furthermore, shelterin and the proteins that are involved in chromatin remodeling form telomere structure[4,6,20]. Telomeres form large loop structures at the ends of chromosomes called T-loops where the G-rich strand protrudes and forms a single strand called the G-overhang. This G-overhang reforms a T-loop and invades the 5' double stranded telomeric duplex to form a D-loop. The formation of this circular structure is an important mechanism that protects telomeres from premature degradation[16]. Telomeres can be actively transcribed to form telomeric repeat-containing RNA (TERRA)[1,16]. These molecules play important roles in the regulation of telomerase activity and the formation of heterochromatin at the end of chromosomes[4,5,10,16,22].

Telomeres will shorten by 15-200 bp (base pair) in each cycle of somatic cell division because of the inability of DNA polymerase to fully replicate the lagging C-strands (this phenomenon is called "the end-replication problem")[1,3,6,16]. Apart from the process of cell division, two major factors that can accelerate the shortening of telomeres are oxidative stress and chronic inflammation[3,10,23]. In addition, several other factors that affect telomeres are BMI, lifestyles such as smoking, alcohol intake, stress, increased insulin resistance, and exercise[6,24]. The G-rich nucleotide sequences are sensitive to damage caused by oxidative stress which leads to single strand telomere breaking and further shortening of telomeres[2,3]. Chronic inflammation also causes telomere shortening by increasing cell turnover, particularly in peripheral leukocytes. Therefore, the shortening of telomeres is often associated with cellular aging and physical aging[3,6,16,25].

In cells that require high replication activity, these cells will express telomerase, an enzyme that adds repeating DNA sequences in the telomere region[16,26]. In humans, this enzyme has been expressed in early development in utero and then inactivated in most adult cells except in the germ line, embryonic stem cells, and immune cells[16,27]. But even though stem cells express telomerase, this is not enough to keep normal telomere length, so that telomere shortening also occurs in these cells[2,16,18,26,28].

Several criteria for aging biomarkers according to American Federation for Aging Research are as follows:

1) Can predict the rate of aging, so that it can tell exactly where the people are in their total lifespan and must be a better predictor of lifespan than chronological age,
2) Must be able to reflect and monitor the basic process of aging, not the effect of diseases,
3) Can be done repeatedly without harming the person,
4) Can be tested on laboratory animal and human models[16,18].

Telomere length can be used as a biomarker of aging because its repeating structures are known to be highly involved in the cellular aging process and the shortening of telomeres that occurs with increasing age is considered an important contributor to aging in organisms[16,18,29]. Although telomere length meets the criteria number 3 and 4 above, adjustment for criteria 1 and 2 is still questionable. The results of examining the relationship between exercise and telomere length were also inconsistent, which may be due to methodological differences[16,18].

Oxidative Stress

Oxidative stress and inflammation are two very closely related things that can cause increased telomere friction in all cell types[3,10,30]. The damage caused by oxidative stress to telomeres is due to the G-rich nucleotide sequence. Due to the rapid erosion of telomeres, this can result in single-stranded telomere damage and of course shortening of subsequent telomeres[2–4].

Oxidative stress itself is included as a confounding variable to assess its close relationship with telomere length. An unhealthy lifestyle and oxidative stress will increase the risk of a decrease in body fitness, a faster aging process, and trigger the onset of diseases[5,22]. To inhibit telomere shortening, several physical sports activities can be carried out that will stimulate antioxidant and anti-inflammatory responses. Physical exercise activity will increase telomerase activity and lengthen telomere length and increase mRNA expression as well[12,31–33]. LTL is often included in cross-sectional and longitudinal analyzes by comparing individual age and sex, but until now due to differences in the measurement of telomere length methods and differences in statistical calculations, there are still many questions whether the aging process is related to telomere length[18,34].

Telomere shortening, one of which is caused by oxidative stress, can cause problems, such as obesity and cardiometabolic problems, which will reduce the life expectancy of individuals[15,35]. With moderate to high intensity physical exercise, it will increase metabolism in everyone which is indicated to produce good results for telomeres[34,35].

Effect of Exercise on Oxidative Stress and Telomere Length

Oxidative stress (damage to cells, tissues, and organs) occurs due to excessive production of reactive oxygen species (ROS). This can lead to DNA damage and aging of cells, tissues, and organs. Oxidative stress can cause telomere shortening, but chronic exercise can reduce oxidative stress. This is because chronic exercise reduces ROS production, therefore it can reduce oxidative stress. It is recommended to do chronic exercise and consume high antioxidant foods[2,27,32,36].

In exercise, telomere length can be assessed on skeletal muscle cells and white blood cells (leukocytes)[18]. According to previous studies, exercise has a positive effect on telomere length. Short-time exercise has not been shown to affect LTL. However, strenuous exercise training has been shown to affect LTL. In most studies that try to evaluate the impact of physical exercise on telomere length, for example, in the form of endurance training or aerobic-type training, it can have a positive effect on LTL[7,37]. However, there is no clear evidence from research about anaerobic exercise like sprinting[38].

There was no interaction between long-term resistance training and telomere length, but a negative impact was found between heavy-resistance training and telomere length when telomeres in skeletal muscle were measured[7,14]. In highly active individuals, exercise can cause muscle damage, satellite cell proliferation (precursor cells), and telomere length shortening in skeletal muscle tissue[6,9,39]. Breathing exercises and meditation such as yoga have also shown positive effects on telomere length as they have been shown to have effects on psychological health, such as reducing stress, anxiety, and depression which shorten telomeres[7].

Another study found that low and high activity were associated with shorter telomeres, while moderate activity had an impact on longer telomeres[5,8]. For gender, there is an effect between men and women who did physical exercise on telomere length. Women have longer telomeres than men, but this varies depending on the measurement method[40]. Another study found that men have longer telomeres than women[41]. Many factors are associated with shortening of telomere length, including aging process and chronic disease, but according to studies, by exercising, individuals can maintain telomere length[12,32]. However, according to research by Sun et al., there is no correlation between physical activity and telomere length[3].Shadyab et al. observed in the last 2 years that the higher the intensity of physical activity, the longer the telomeres[11].

We included 6 journals that have been analyzed in the table below.

Table 1. The correlation between different type and intensities of exercise and telomere length

Author and year of publication	**Design**	**Sample**	**Exercise**	**Method of Evaluation**	**Conclusion**
Shadyab et al, 2017[11]	Cross-sectional study	1,476 post-menopausal women Age 50-79	Robust: ≥17 MET-h/week Moderate: 1.25-17 MET-h/week	Southern blot	After 2 years of observation, higher levels of moderate to robust exercise ($p=0.04$) and faster walking speed ($p=0.03$) were associated with longer telomere length
Østhus et al, 2012[5]	Cross-sectional study	20 men Age 22-27 and 66-77	Low, moderate, robust exercise	qPCR	Long term endurance exercise training may regulate telomeres in old age ($p<0.05$)
Werner et al, 2018[12]	Cohort study	124 men and women Age 30-60	ET, IT, and RT	qPCR	After 6 months of training, ET ($p=0.024$) and IT ($p=0.026$) increased telomerase activity and telomere length
Mason et al, 2013[10]	Cohort study	106 post-menopausal women Age 50-75	Moderate intensity aerobic exercise	qPCR	After 12 months of exercise, it did not change telomere length ($p=0.51$)
Sun et al, 2012[3]	Case-control study	5,862 women Age 58.7±0.09	Robust: >2.5 MET-h/week Moderate: 1-1.5 MET-h/week	qPCR	There was no correlation between physical activity and telomere length ($p=0.18$)
Laine et al, 2015[7]	Cohort study	599 men Age 72.3±6.0	Robust: ≥22.6 MET-h/week Moderate: 6.1-22.5 MET-h/week	qPCR	After 3 months, there was no significant differences regarding telomere length ($p=0.666$)

*Statistically Significant (p <0,05).MET:Metabolic Equivalent for Task; qPCR: quantitative Polymerase Chain Reaction; ET: Endurance Training; IT: Interval Training; RT: Resistance Training

Table 2. Different intensities and type of exercise correlates with telomere length[3,11]

Exercise Intensities	Exercise Type	Frequency	Telomeres Effect
Low	Yoga, walking, light jogging, bicycling, hiking outdoor, lap swimming, tennis, aerobic dance	30 min/day, 3-5 times/week	Shortening
Moderate	Fast walking, jogging, easy swimming, bicycling	30 min/day, 3-5 times/week	Lengthening
High	Jogging, running, bicycling, swimming, tennis, aerobic activities	30-50min /day, 3-5 times/week	Shortening

CONCLUSION

Telomere length shortens with age and can be a potential marker of biological aging. Several studies have managed to see a correlation between the prevention of LTL shortening and exercise at a certain intensity. Understanding risk factors and determining the right intensity of exercise can prevent telomere length shortening. The results of our literature review show that moderate intensity exercise has the effect of lengthening telomeres. Generally, moderate exercise like easy swimming, jogging, bicycling, and faster walking can longer telomere length while mild and vigorous exercise can shorten telomeres. But this is also influenced by the duration of exercise, different population, age, and sample size. Further research is needed regarding the type, intensity, and duration of exercise that is more specific to prevent telomere length shortening.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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