Telomere Length Shortening: A Mini Review Article

Maryam Tavakolli *, Fatemeh Mahdavi 1, Alireza Rasa 1

1Guilan University of Medical Sciences, Department of Public Health, Guilan, Iran

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ABSTRACT

There is growing evidence that lifestyle factors might affect the health of individuals by affecting telomere length (TL). The objective of this review was to show the importance of telomeres in aging and to find out lifestyle factors that might affect health. Recent research findings show that TL can only allow an estimate of the aging rate and can be regarded as an important risk marker for age-related pathologies and mortality. Recent studies indicate that telomere length, which can be affected by different lifestyle factors, might affect the pace of aging and onset of various diseases. Telomere length shortens by aging. Shortening of telomeres is associated with increased incidence of diseases such as diabetes and cardiovascular diseases. The rate of telomere shortening might be either increased or decreased by different lifestyle factors. Choice of diet and activities can reduce the rate of telomere shortening, leading to delayed onset of age-associated diseases and increased lifespan. In this review, we discussed the role of telomeres in aging. Different lifestyle factors such as smoking and diet which can affect telomeres was discussed.

Keywords: Lifestyle; Smoking; Oxidative Stress; Telomere.

*Corresponding Author E-mail: martav@gums.ac.ir
Introduction

Telomeres are repetitive loci of DNA adhered by proteins at the end of linear chromosomes which prevent the ends of chromosomes from being known as DNA double-strand breaks [1-5]. Telomere function is protecting the chromosome ends and maintaining the stability of the genome. Telomeric DNA is repetitive sequences of the hexanucleotide TTAGGGn repeat unit, bound in a sequence-specific manner to the protein complex shelter in, and assembled into macromolecular structures called telomere-loops [6-8].

Telomere length (TL) has many properties which make it suitable to be used as a biomarker of aging. The advantages of TL being a biomarker of aging are a correlation with chronological age throughout the whole life course [9-11], predictive power of the disease condition and mortality, and also large responsiveness to either adverse or beneficial exposures [12-15]. Accelerated shortening of telomeres might induce a phenotype of cellular and age with concomitant failure of the body [16]. As a result, telomere length and shortening might have an association with a lower life expectancy [17]. Lifestyle factors such as diet, stress, and smoking have effects on the length of the telomere [18]. Diet is considered a process inherent to the human condition. Diet is either a protective or a detrimental factor for telomere length, depending on its composition. In this review article, we highlight different factors affecting telomere length [19-23].

Structure of Telomeres

Telomeres are the DNA–protein at the ends of the chromosome that protects the genome from degeneration and inter chromosomal fusion [24-26]. Telomeric DNA is with telomere-binding proteins. In addition, a loop structure that is mediated by TRF2 protects the ends of chromosomes against exonucleolytic degradation [27-29].

Telomere shortening happens at every DNA replication, and if continued will cause chromosomal degradation [30-32]. Telomerase activity is present in hematopoietic cells and germline, whereas somatic cells have undetectable levels of activity and their telomeres have a progressive shortening with replication [33-35]. Telomerase is reactivated in cancers and immortalized cells. But, a group of cancer cells doesn’t have telomerase activity and keep telomere length by alternative mechanisms [36-38].
Determinants of Telomere length

Telomere length and the rate of telomere shortening according to aging depend on both genetic and environmental factors. In twin studies, the heritability of TL was shown and specific loci related to TL were recorded [39-41]. For instance, in the study by Hjelmborg et al, the heritability of LTL was about 64% at baseline; the heritability of age-dependent LTL attrition rate was less (28%) [42-44]. Genetic mutations associated with short TL are found to cause to diseases such as pulmonary fibrosis, dyskeratosis congenital, and some other clinical conditions (33-36). Potential sources of TL heritability are inherited variation in non-telomeric loci (e.g., single nucleotide polymorphisms which affect telomere maintenance) and TL in gametes producing zygotes (the “direct” inheritance) [45-47]. Other evidence has supported the fact that TLs in parental germ cells might impact TL in children’s cells. As a result, might contribute to the heritability of TL [48-50]. TL was recorded to increase with the age of the father in sperm while higher maternal age appears to be associated with shorter children’s TL [51]. The effect of parental germ cells on TL is significant even the telomere “reprogramming” in embryonic development by the mechanisms and then through the effect of telomerase at the blastocyst phase and later [52].

Diseases associated with Telomere Length

Recently, so many diseases have been found to be associated with short telomere length. stress exposures during prenatal and early postnatal can make the telomere biology that promotes cellular senescence [53]. As a result, lead to an accelerated rate of aging. The possibility of programming TL and the rate of erosion of telomeres related to age can be vital in aging and also aging-associated pathology [54]. According to a developmental model of aging shorter TL in life might be associated with health status later [55]. Others assumed that lengthened telomeres might increase the risk for diseases linked to increased proliferation rate such as cancer, while shortened telomeres might increase the risk for diseases related to a limited cellular proliferation and tissue degeneration, including atherosclerosis-associated cardiovascular diseases [56]. In epidemiological studies, Telomere length was found to show the risk for chronic pathological conditions [57]. In patients affected with coronary heart disease, telomere lengths were significantly shorter compared to those in controls [58]. In addition, TL was inversely associated
with the severity. Convincing evidence was found that short telomeres are indicative of a higher risk for atherosclerosis and related vascular complications [5]. Low telomerase activity was shown to be with atherosclerotic plaque instability and a higher risk for heart disease, myocardial infarction, or stroke. Many associations were seen between the high rate of age-related LTL and hypertension [64].

There are no available consistent data on TL in neurodegenerative disorders. In the meta-analysis by Forero et al, there was no evidence for shorter TLs in patients with Parkinson's disease [61]. In other studies, the association between shorter telomere length and Alzheimer’s disease was observed [62]. One explanation for this might be the increased level of oxidative stress in these patients.

**Smoking and Telomere length shortening**

Smoking has adverse effect on aging and telomere length. Telomere shortening can lead to tumorigenesis. Telomeres in many cancer cells are shorter comparing to normal cells. Smoking is associated with telomere shortening. Higher smoking rate is associated with lower telomere length. An increase in telomere shortening has been seen in blood cells of smokers. Telomere length can use as a biomarker to evaluate the oxidative damage that is caused by smoking. It may also predict the pace at which each person is aging. It is observed that the oxidative damage that leads to telomere shortening might be inhibited by antioxidant therapy. In other words, the smoking can increase oxidative stress, expediting telomere shortening, and might increase the pace of aging process [63].

**Diet and Telomere length shortening**

Diet also has an important role in determining the length of telomeres. Obesity is associated with oxidative stress and damage to DNA. In a meta-analysis study done by Khosravaniardakani et al., the most category of telomere length was associated with an approximate 0.75 kg/m² reduction in body mass index. In addition, obese patients had shorter telomere lengths compared with non-obese adults [60]. sources of heterogeneity were continent, age, and sample size. In a study done by Furukawa et al., it is revealed that a high BMI increases the elevated plasma and urinary levels of reactive oxygen species. In another study by Song et al higher BMI was
strongly associated with biomarkers of DNA damage. It is mainly because of the production of adipocytokines. Obese KKAY mice show higher reactive oxygen species and lipid peroxidation in their plasma, compared to control C57BL/6 mice [65]. These higher levels of reactive oxygen in obese mice were seen in white adipose tissue but it was not seen in other tissues, showing that the oxidative stress in plasma might be because of oxidizing agents produced in fat tissue [66].

**Conclusion**

Telomeres shorten with age and can cause senescence and/or apoptosis. Shorter telomeres have been seen in genomic instability and oncogenesis. Older people with shorter telomeres have an increased risk to die due to heart and infectious diseases. Smoking, obesity, stress, and an unhealthy diet increase oxidative burden and the rate of telomere shortening. The measurement of TL can be used as a biomarker of obesity. It can also be used as a response marker to the treatment of obesity. Weight loss is associated with an increase in TL. The initial longer TL can be a predictor of response to treatment. Longer TL is accompanied by better fasting glucose levels. TL at the beginning of intervention might predict changes in decreasing the weight, improving fasting glucose levels, and lowering inflammatory biomarkers after treatment.

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