Comparison of serum telomerase, CBC and insulin resistance and their relationship with physical fitness factors in active and sedentary elderly people under quarantine of coronavirus

Comparación de telomerasa sérica, CBC y resistencia a la insulina y su relación con factores de aptitud física en adultos mayores activos y sedentarios en cuarentena por coronavirus

Seyed Morteza Sajadi[1], Mohammad Reza Kordi[2*], Seyyed Reza Attarzadeh Hosseini[3], Hamzeh Akbari Bokani[4], Mahdi Aliakbari[5]
[1]PhD Student of Exercise Physiology, Sport Sciences Research Institute, Tehran, Iran. ORCID: 0000-0002-2139-2053. Email: morteza.sajadi60@yahoo.com
[2]Full Professor of Exercise Physiology, Department of Exercise Physiology, Faculty of Physical Education and Sports Sciences, University of Tehran, Tehran, Iran. ORCID: 0000-0002-6796-1696. Corresponding Author Email: mrkordi@ut.ac.ir
[3]Full Professor of Exercise Physiology, Department of Exercise Physiology, Faculty of Physical Education and Sports Sciences, University of Ferdowsi Mashhad, Mashhad, Iran. ORCID: 0000-0002-9059-3262. Email: attarzadeh@um.ac.ir
[4]Assistant Professor of Exercise Physiology, Department of Exercise Physiology, Faculty of Physical Education and Sports Sciences, University of Allameh Tabataba'i, Tehran, Iran. ORCID: 0000-0003-0050-632X. Email: mh_akbari1258@yahoo.com
[5]PhD of Exercise Physiology, Department of Sports Physiology, Islamic Azad University, South Tehran Branch, Tehran, Iran. ORCID: 0000-0002-5561-0282. Email: aliakbaribidokhti@yahoo.com
Received: 06/24/2022 Accepted: 10/19/2022 Published: 11/25/2022 DOI: https://doi.org/10.5281/zenodo.7626463

Abstract

The aim of this study was to compare serum telomerase, CBC and insulin resistance and their relationship with physical fitness factors in active and sedentary elderly people under quarantine of coronavirus. In this study, healthy men and women with a mean age of 61.43±6/07 in coronavirus pandemic conditions participated in this study voluntarily. Subjects were divided into three groups of physical activity: high, medium and low. The international Physical Activity Level Questionnaire (IPAQ) was used to assess the level of physical activity. Serum telomerase, CBC and insulin resistance were measured in different groups after measuring physical fitness factors. Results showed that BMI is higher in the sedentary group than the groups with moderate and high levels of physical activity; In addition, blood Hb and Hct levels were higher in the moderate physical activity group than in the sedentary group, but blood Plt levels were lower in the moderate physical activity group than in the sedentary group. Another result of the present study was the negative correlation of telomerase with BMI and the positive correlation of telomerase with Hb, Hct and RBC, although there was no correlation between telomerase and physical fitness factors. In addition, BMI was negatively correlated with fitness factors, glucose levels, insulin resistance and CBC. Physical fitness in the elderly people under quarantine of coronavirus has a positive relationship with some blood parameters but no correlation was observed between telomerase and insulin resistance with physical fitness.

Keywords: CBC, Covid -19, Physical activity, Telomere

Resumen

El objetivo de este estudio fue comparar la telomerasa sérica, el CBC y la resistencia a la insulina y su relación con factores de aptitud física en adultos mayores activos y sedentarios en cuarentena por coronavirus. En este estudio, participaron voluntariamente hombres y mujeres sanos con una edad media de 61,43 ± 6/07 en condiciones de pandemia de coronavirus. Los sujetos se dividieron en tres grupos de actividad física: alta, media y baja. Se utilizó el cuestionario internacional de nivel de actividad física (IPAQ) para evaluar el nivel de actividad física. La telomerasa sérica, el CBC y la resistencia a la insulina se midieron en diferentes grupos después de medir los factores de aptitud física. Los resultados mostraron que el IMC es mayor en el grupo sedentario que en los grupos con niveles moderados y altos de actividad física; Además, los niveles de Hb y Hct en sangre fueron más altos en el grupo de actividad física moderada que en el grupo sedentario, pero los niveles de Plt en sangre fueron más bajos en el grupo de actividad física moderada que en el grupo sedentario. Otro resultado del presente estudio fue la correlación negativa de la telomerasa con el IMC y la correlación positiva de la telomerasa con Hb, Hct y RBC, aunque no hubo correlación entre la telomerasa y los factores de aptitud física. Además, el IMC se correlacionó negativamente con factores de condición física, niveles de glucosa, resistencia a la insulina y CBC. La condición física en los adultos mayores en cuarentena por coronavirus tiene una relación positiva con algunos parámetros sanguíneos, pero no se observó correlación entre la telomerasa y la resistencia a la insulina con la condición física.

Palabras clave: CBC, Covid -19, Actividad física, Telómero

Introduction

Aging is an important factor for promoting chronic diseases such as cardiovascular, neurological, Parkinsons, cancer, and health restrictions[1]. Telomeres are regions of duplicate DNA that play a vital role in protecting the ends of chromosomes [2]. The telomere is made up of thousands of replicates of TTAGGG, located on the end of the chromosome. Telomere length is inversely related to chronological age and has been considered for years as a potential cell marker for aging [3]. Telomerase is an enzyme that prevents telomere shortening by adding duplicate TTAGGG sequences and stimulates telomere synthesis. It is a ribonucleus enzyme that uses its own internal RNA components as a template to synthesize DNA at the ends of chromosomes during cell division [4]. A number of premature aging syndromes with short telomeres have been identified. All genes that have been mutated in related diseases have been implicated in repairing DNA damage and have played an important role in maintaining telomere length [5]. Aging is associated with extensive changes such as changes in blood profile. Immunological and hematological functions have been reported to be reduced, leading to increased risk of disease. The fact that aging reduces the ability to maintain an effective immune response has been accepted [6]. Aging-related diseases also include metabolic syndrome, which includes a set of metabolic risk factors such as abdominal obesity, harmful fats, high blood pressure, and glucose intolerance [7]. Insulin resistance is usually seen in the elderly, but it is increasingly common in people who are overweight and sedentary that with increasing insulin resistance, a chronic inflammatory condition develops that results in release of proinflammatory cytokines is noted and β cells continuously stimulate insulin production in an attempt to reduce severe hyperglycemia, but this action is ineffective and may affect the additional status of hyperinsulinemia [8]. Studies have shown that older people suffer from a chronic inflammatory condition called inflammatory aging, which is closely related to age-related diseases, may now play a role in the pathogenesis of diseases or as a consequence. Inflammatory aging is closely related to the age-related immune system [9]. Certain diseases, such as Covid-19, may accelerate metabolic immune disorders in the elderly. One study suggested that there are at least four mechanisms associated with aging (Aging speed of the immune system, inflammation rate, decreased ACE2 receptor anti-inflammatory activity, aging cell density, and telomere shortening), which may influence the severity of COVID -19 affect [10]. In the elderly, the amount of extracellular mtDNA released by cells was considered as a key factor in inflammatory aging and circulating mtDNA levels were considered as a predictor of COVID-19 severity [11,12]. In another study, extracellular telomere DNA (telDNA) was considered as an important source of extracellular anti-inflammatory DNA that decreases significantly with age [13]. Short telomeres have been reported to indicate adverse outcomes in patients with COVID-19 [14]. In general, extracellular DNA in the elderly may further stimulate inflammation due to the concomitant decrease in extracellular telDNA and the increased release of extracellular mtDNA. Consequently, the release of proinflammatory mtDNA, which intensifies during the course of COVID-19, along with the loss of age-related extracellular anti-inflammatory telDNA repository, may lead to systemic hyperinflammation [14]. It has been suggested that telomerase-based therapies can be used to treat diseases such as cancer, as well as to extend human lifespan [15]. Risk factors such as diet, smoking, physical activity, stress or sleep can be associated with the aging process and related diseases [16]. Therefore, knowledge of effective strategies to slow down the aging process is one of the important priorities of researchers [1]. Exercise is used as

a special strategy to prevent or treat various diseases that are related to age in the elderly as an effective mechanism [17]. In observational studies, higher levels of physical activity were associated with longer telomere lengths in different populations, and athletes showed longer telomere lengths than non-athletes. This relationship is particularly evident in older individuals, indicating the role of physical activity in combating normal age-related reductions during telomere [3]. Also, leukocyte telomere length has a positive correlation with the number of years of healthy life, which may be a biomarker of leukocyte telomere length for healthy aging [18]. Most research has shown that higher physical activity has a positive relationship with longer skeletal muscle or leukocyte telomere lengths compared to a sedentary lifestyle. However, conflicting results have been reported, and such discrepancies may be due to different exercise protocols (such as intensity and duration of exercise), different measured cells, and self-reported activities, suggesting that conflicting results may be due to sources. Different telomerase (PBMC vs. leukocytes) and differences in sample size in studies [19]. Research in sports hematology and blood cell counts has shown that blood composition can be changed as a result of exercise [20]. Changes such as increased hemoglobin, decreased hematocrit or platelet count in the elderly and young have been shown to be associated with exercise [21]. An acute and chronic effect of physical activity on improving glucose metabolism has also been reported in a review article [8]. In general, to date, few studies have examined the relationship between physical activity and telomerase. Also, according to our survey, there was no study that looked at elderly people under quarantine of coronavirus in this area and examined the correlation of blood factors with telomerase.

Methods

This study was a cross-sectional study with quasi-experimental method. Their mean body mass, age, and body mass index were 71.8 ± 10.7 kg, 61.43 ± 6.07 years old, height 160.38±10.12 and 27.74 ± 3.99 kg/m^2, respectively. General characteristics and health records of all subjects were collected through a personal health records questionnaire. All subjects participated in a briefing session and the process were explained to them and after knowing the purpose of the research and how to do the work, written consent was obtained from them to participate in the research. This study was approved by the Research Ethics Committee of the Institute of Physical Education and Sport Sciences with the ID IR.SSRI.REC.1400.1041. Anthropometric factors including height were measured and recorded using a wall altimeter with an accuracy of one millimeter, weight by a scale with an accuracy of approximately 0.1 kg with a minimum of clothing. Body mass index was also calculated by dividing weight (kg) by height (m) and WHR by dividing waist circumference (cm) by hip circumference (cm).

Assess the level of physical activity

To assess the level of physical activity, the International Physical Activity Level Questionnaire (IPAQ) consists of 27 questions in four parts (physical activity related to working with seven questions; physical activity to travel in different directions with six questions; homework, affairs home repairs and family care with six questions; leisure activities, sports and entertainment with six questions) and low, medium and walking physical activity during the seven days before scoring and class review Classifies; was used. The questionnaire allowed researchers to consider physical activity in the workplace, home and leisure; be able to have a good classification of active, semi-active and inactive people during the corona pandemic. The total physical activity of a person in a week before completing the questionnaire is measured in units of metabolic equivalent of activity (MET). In this study, the following criteria were used to classify physical activity (high, medium and low):

Excessive physical activity: do any combination of low, medium, or walking activity seven days a week or more on weekdays totaling about 3,000 MET (minutes per week). Moderate physical activity: 5 days a week or more on a combination of walking, moderate or low activity, at least 600 MET (minutes per week). Low physical activity: means that the person does not report any activity or the reported physical activity does not meet the criteria of high and moderate physical activity [22]. The validity of the questionnaire in the study of Vashghani Farahani et al. (2011) was 0.63 and its reliability was 0.83 [23]. The mentioned tool was suitable for determining the physical activity of adults aged 15-69 years and its application in the present study is to determine the level of physical activity (high, medium and low) of the subjects participating in the study.

Protocol for measuring physical fitness factors for the elderly

The subjects first warmed up their bodies on a bicycle for 5 minutes and then did a general warm-up. They participated in special standardized tests after the warm-up program to determine the factors of physical fitness. Functional tests including sitting and brush test with chair, back traction test, 30-second test of getting up from a chair, 30-second test of forearm, test of getting up and going 8 feet, 6-minute walking test were performed in a separate session in all subjects. All performance tests are shown in the pictures.

Blood samples

Blood samples were taken from the anterior vein of the arm (anticubital) at 10 to 12 o'clock at night at 7 to 8 in the morning and left sitting. Five ml of whole blood was taken from the subjects and 3 ml of blood samples were placed at room temperature for 15 minutes to separate the serum to form a clot, then using a centrifuge (15 min-

utes and serum was isolated at 3000 rpm and used for biochemical experiments. It should be noted that 2 ml of blood samples were poured into special containers containing EDTA anticoagulant and immediately mixed with anticoagulants using special shakers to prevent the sample from clotting; this sample was used for CBC testing. The kit made in Iran by Pars Azmoun Company was used by enzymatic colorimetric method with a sensitivity of 5 mg/dL to measure serum glucose concentration and serum insulin concentration was used by Arba Company in the United States by ELISA method with a sensitivity of 1.76 µl. It was measured in mg. insulin resistance method was also used to measure insulin resistance. Serum telomerase concentration was determined by ELISA method and sensitivity of 0.63 international units per milliliter using the kit made in Germany by Zelbaio Company.

Statistical methods

One-way analysis of variance, Bonferroni post hoc test and Pearson correlation coefficient test were used to test the research hypotheses. Statistical significance level was determined as p≥0.05 and statistical analysis was performed using SPSS software version 20.

Results

The results of the present study showed that there was a significant difference in BMI between groups with high, moderate and low physical activity and the analysis of multiple post hoc comparisons showed that all pairwise comparisons were statistically significant. (P <0.05). BMI in the sedentary group was higher than the groups with moderate (P = 0.01) and high (P = 0.000) physical activity levels (Table 1).

Table 1: significant difference between the groups for the BMI

	groups	Mean±SE	F	p
BMI	Low physical activity (LA) *	30.59896±0.77041	21.613	0.000
	Moderate physical activity (MA)	27.3655±0.47595		
	High physical activity (HA)	23.9488±0.67856		

*Different with MA (p=0.001), Different with HA (p=0.000).

There was no significant difference in telomerase (p = 0.255) and insulin resistance (p = 0.242) between groups with high, medium and low physical activity.

In relation to CBC, the data showed that between different groups in WBC (p = 0.76), RBC (p = 0.283), MCV (P=0.691), MCH (p = 0.660), MCHC (p = 270), FBS (p = 0.363), insulin (p = 0.62), there was no significant difference, but in Hb, Hct and Plat, a significant difference was observed between the groups. Analysis of multiple follow-up comparisons showed that all pairwise comparisons of the results were statistically significant (P <0.05). Blood Hb and Hct levels were higher in the moderate physical activity group than the sedentary group (P = 0.018, P=0.016), but blood Plt levels were lower in the moderate physical activity group than in the sedentary group (P = 0.024) (Tabl 2).

Table 2: significant difference between the groups for the HB, HCT, PLT

	groups	Mean±SE	F	p
HB	Low physical activity (LA)	13.542±0.22859	4.58	0.021
	Moderate physical activity (MA) *	13.8286±00.99486		
	High physical activity (HA)	2529.6±13.3875		
HCT	Low physical activity (LA)	39.192±0.57107	4.124	0.20
	Moderate physical activity (MA) *	41.2286±0.49374		
	High physical activity (HA)	40.3812±79657		
PLT	Low physical activity (LA)	245.923±10.93488	4.215	0.18
	Moderate physical activity (MA) *	214.0.4571±6.73138		
	High physical activity (HA)	215.2500±5.51471		

*HB:Different with LA (p=0.018), *HCT Different with LA(P=0.016),* PLT Different with LA(0P=0.024)

Pearson correlation coefficient test showed negative correlation of telomerase with BMI (P = 0.031; r = -0.247) and positive correlation of telomerase with Hb (p = 0.000; r = 0.461), Hct (p = 0.000; r = 0.498) and RBC (p = 0.027; r = 0.253) respectively. There was also no correlation between telomerase and physical fitness factors. In addition, BMI was negatively correlated with fitness factors, glucose levels, insulin resistance and CBC.

Discussion

MtDNA release is a basic mechanism of cellular damage and is considered as the main stimulus of local and systemic inflammation. In this process, TLR4 stimulates NF-κB expression, which transcribes several proinflammatory genes such as Il-6, COX2 and TNF -α initiates, mediates the inflammatory process. The proinflammatory capacity of mtDNA is expected to increase in the elderly, especially those with Covid-19, because most of the released mtDNA is oxidized and therefore more resistant to the cytoplasmic DNaseIII / TREX enzyme. Previous evidence suggests that telDNA fragments have anti-inflammatory activity and can inhibit TLR-9, cGAS and AIM2 [14,24]. Exercise affects the biology of telomeres and telomerases by preventing a variety of diseases and as a mechanism for delaying age-related diseases [17]. The results of the present study showed that there was no correlation between telomerase and physical fitness factors in different groups, but telomerase had a negative correlation with BMI and a positive correla-

tion with Hb, Hct and Rbc. Some studies have reported a positive effect of exercise on telomere length and telomerase activity [25,26]. However, some other studies have not reported a significant effect that may be related to the severity, duration or type of populations studied [2,27]. Previous evidence has reported that regular physical activity leads to telomerase activation and telomere length stabilization [3]. In a study, stress levels were measured in physically active and sedentary individuals. The results showed that perceived stress in sedentary individuals was negatively correlated with telomere length, but in active individuals, no correlation was observed between perceived stress and telomere length [25]. According to this study, physical activity may protect against stress-induced telomere shortening. Exercise has been reported to cause the secretion of the enzyme telomerase, which causes the telomeres to be shorter in some types of white blood cells [3]. Related with the mechanisms involved, it has been reported that after exercise, the expression of Telomere-repeat binding protein 2 (TRF2) mRNA increases, which binds directly to the telomere sequence and in addition to regulating telomerase activity causes Prevents telomere erosion. It is possible that the increase of this protein is mediated by IGF-1, TERT, eNOs [28]. In another study, exercise increased the activity of telomerase, increased TRF2 and decreased the levels of Chk2, p16 and p53 in athletes compared to sedentary individuals, and these changes were shown by TERT and Enos [29]. Spallarossa et al. (2009) showed that MAPK p38 is involved in regulating Trf2 gene expression in response to doxorubicin treatment in cardiomyocytes. Hence, the MAPK pathway may have to influence telomere biology as a possible mechanism through exercise [30]. In the present study, there was no significant difference between telomerase and physical fitness factors in different groups, it may be necessary to increase the intensity of physical activity such as exercise in the daily program for changes in telomerase. Other results of this study showed that blood Hb and Hct levels were higher in the moderate physical activity group than the sedentary group, but blood Plt levels were lower in the moderate physical activity group than the sedentary group. A positive correlation of telomerase with Hb, Hct and Rbc was shown. Also, no significant difference was observed in the insulin resistance index between groups with high, medium and low activity. Aging reduce the ability to maintain an effective immune response. Changes in blood parameters in old age indicate that they can have a physiological effect on immune defense [31]. Therefore, interventions such as physical activity and sports have been suggested to minimize and improve these changes and improve hematological parameters, such as increasing hemoglobin or platelet count and decreasing hematocrit in the elderly and young [21]. The positive effect of endurance training on increasing the number of red blood cells has been documented. However, in a study consistent with our study, there was no significant change in red blood cell counts after a training period in the elderly. In this study, it was stated that a resistance training course may not have a positive effect on leukocytes and their number in older men and women, and older people may not be sensitive to resistance training in terms of intensity, duration, frequency or method of training [6]. Studies on the effect of exercise on blood cell changes in the elderly and the mechanisms involved have been limited and require further investigation, especially in cases of covid-19.

Conclusions

In general, according to the results of the present study and the negative correlation of telomerase with BMI, the positive correlation of telomerase with Hb, Hct and RBC and the lack of correlation between telomerase and physical fitness factors, it can be said that the level of physical fitness in the elderly people has a positive relationship with some blood parameters and may indirectly affect telomerase, and suggesting mechanisms involved in future research is suggested.

Acknowledgments
The authors thank all the volunteers for their enthusiastic participation in this study.

Authors' contributions: All authors contributed equally to data collection. They read and approved the final manuscript. Finally, all authors agreed to be accountable for all aspects of the work.

Conflicts of Interest: The authors declare no conflicts of interest.

Ethical approval: This study was approved by the Research Ethics Committee of the Institute of Physical Education and Sport Sciences with the ID IR.SSRI.REC.1400.1041

Funding: This research received no external funding.

References

1. Barragán R., Ortega-Azorín .C, Sorlí J.V., Asensio E.M., Coltell .O, St-Onge M.P., Portolés .O., Corella. D., 2021. Effect of Physical Activity, Smoking, and Sleep on Telomere Length: A Systematic Review of Observational and Intervention Studies. Journal of Clinical Medicine.11(1),76.

2. Laye M.J., Solomon T.P., Karstoft .K., Pedersen K.K., Nielsen S.D., Pedersen B.K., Nielsen S.D., Pedersen B. K., 2012. Increased shelterin mRNA expression in peripheral blood mononuclear cells and skeletal muscle following an ultra-long-distance running event. Journal of applied physiology. 112(5),773-81.

3. Arsenis N.C., You T., Ogawa E.F., Tinsley G.M., Zuo L., 2017. Physical activity and telomere length: Impact of aging and potential mechanisms of action. Oncotarget. 8(27), 45008.

4. Meyer T.D., Rietzschel E.R., Buyzere M.D., Bacquer D. D., Criekinge W. V., Backer G. D., Gillebert T. C., Oostveldt P. V., Bekaert S., 2007.

Paternal age at birth is an important determinant of offspring telomere length. Human molecular genetics. 16(24), 3097-102.

5. Blasco M.A., 2005. Telomeres and human disease: ageing, cancer and beyond. Nature Reviews Genetics. 6(8), 611-22.

6. Bobeuf F., Labonté M., Khalil A., Dionne I.J., 2009. Effect of resistance training on hematological blood markers in older men and women: a pilot study. Current gerontology and geriatrics research. 2009, 156820.

7. Veronica G., Esther R.R., 2012. Aging, metabolic syndrome and the heart. Aging and disease. 3(3) ,269.

8. Keshel T.E., Coker R.H., 2015. Exercise training and insulin resistance: a current review. Journal of obesity & weight loss therapy. 5(0 5).

9. Storci G., De Carolis S. D., Olivieri F., Bonafe M., 2018. Changes in the biochemical taste of cytoplasmic and cell-free DNA are major fuels for inflamm-aging. Seminars in Immunology. 40, 6-16.

10. Bonafè M., Prattichizzo F., Giuliani A., Storci G., Sabbatinelli J., Olivieri F., 2020. Inflamm-aging: why older men are the most susceptible to SARS-CoV-2 complicated outcomes. Cytokine & Growth Factor Reviews. 53, 33-7.

11. Iske J., Seyda M., Heinbokel T., Maenosono R., Minami K., Nian Y., Quant M., Falk C.H., Azuma H., Martin F., Passos G.F., Niemann C.U., Tchkonia T., Kirkland j.l., Elkhah A., Tulius S. G., 2020. Senolytics prevent mt-DNA-induced inflammation and promote the survival of aged organs following transplantation. Nature communications. 11(1), 1-13.

12. Scozzi D., Cano M., Ma L., Zhou D., Zhu J.H., O'Halloran J.A., Goss C., Rauseo A. M., Liu Z., Sahu S. K.,, Peritore V., Rocco M., Ricci A., Amodeo R., Aimati L., Ibrahim M., Hachem R., Kreisel D., Mudd P. A., Kulkarni H. S., Gelman A. E., 2021.Circulating mitochondrial DNA is an early indicator of severe illness and mortality from COVID-19. JCI insight, 6(4).

13. Bonafè M., Sabbatinelli J., Olivieri F., 2020. Exploiting the telomere machinery to put the brakes on inflamm-aging. Ageing Research Reviews. 59, 101027.

14. Storci G., Bonifazi F., Garagnani P., Olivieri F., Bonafè M., 2021. The role of extracellular DNA in COVID-19: Clues from inflamm-aging. Ageing Research Reviews. 66, 101234.

15. Flanary B. Cells. 2004. Aging, and Human Disease. Mary Ann Liebert, Inc.

16. Zhang W., Song M., Qu J., Liu G.H., 2018. Epigenetic modifications in cardiovascular aging and diseases. Circulation research. 123(7), 773-86.

17. Jin K., 2010. Modern biological theories of aging. Aging and disease. 1(2), 72.

18. Njajou O.T., Hsueh W.C., Blackburn E.H., Newman A.B., Wu S.H., Li R., Simonsick E. L., Harris T. M, Cummings S.R, Cawthon R.M., 2009. Association between telomere length, specific causes of death, and years of healthy life in health, aging, and body composition, a population-based cohort study. Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences. 64(8), 860-4.

19. Ludlow A.T., Zimmerman J.B., Witkowski S., Hearn J.W., Hatfield B.D., Roth S.M., 2008. Relationship between physical activity level, telomere length, and telomerase activity. Medicine and science in sports and exercise. 40(10), 1764.

20. Szygula Z., 1990. Erythrocytic system under the influence of physical exercise and training. Sports Medicine. 10(3),181-97.

21. El-Sayed M.S., Sale C., Jones P., Chester M., 2000. Blood hemostasis in exercise and training. Medicine and science in sports and exercise. 32(5), 918-25.

22. Wu, C.Y., Hu, H.Y., Chou, Y.C., Huang, N., Chou, Y.J. and Li, C.P., 2015. The association of physical activity with all-cause, cardiovascular, and cancer mortalities among older adults. Preventive medicine. 72, 23-29.

23. Vasheghani-Farahani, A., Tahmasbi, M., Asheri, H., Ashraf, H., Nedjat, S. and Kordi, R., 2011. The Persian, last 7-day, long form of the International Physical Activity Questionnaire: translation and validation study. Asian journal of sports medicine. 2(2), p.106.

24. Calle M.C., Fernandez M.L., 2010. Effects of resistance training on the inflammatory response. Nutrition research and practice. 4(4), 259-69.

25. Puterman E., Lin J., Blackburn E., O'donovan A., Adler N., Epel E., 2010. The power of exercise: buffering the effect of chronic stress on telomere length. PloS one. 5(5), e10837.

26. Østhus I.B.Ø., Sgura A., Berardinelli F., Alsnes I.V., Brønstad E., Rehn T., Støbakk P. K., Hatle H., Wisløff U., Nauman J., 2012. Telomere length and long-term endurance exercise: does exercise training affect biological age? A pilot study. PloS one. 7(12), e52769.

27. Mason C., Risques R.A., Xiao L., Duggan C.R., Imayama I., Campbell K.L., Kong A., Foster-Schubert K. E., Wang C., Alfano C. M., Blackburn G. L., Rabinovitch P. S., McTiernan A. M., 2013. Independent and combined effects of dietary weight loss and exercise on leukocyte telomere length in postmenopausal women. Obesity. 21(12), E549-E54.

28. Ludlow A.T., Roth S.M., 2011. Physical activity and telomere biology: exploring the link with aging-related disease prevention. Journal of aging research. 790378.

29. Werner C., Fürster T., Widmann T., Pöss J., Roggia C., Hanhoun M., Scharhag J., Büchner N., Meyer T., Kindermann W., Haendeler J., Böhm M., Laufs U., 2009. Physical exercise prevents cellular senescence in circulating leukocytes and in the vessel wall. Circulation. 120(24), 2438-47.

30. Spallarossa P., Altieri P., Aloi C., Garibaldi S., Barisione C., Ghigliotti G., Fugazza G., Barsotti A., Brunelli C., 2009. Doxorubicin induces senescence or apoptosis in rat neonatal cardiomyocytes by regulating the expression levels of the telomere binding factors 1 and 2. American Journal of Physiology-Heart and Circulatory Physiology. 297(6), H2169-H81.

31. Kohut M.L., Senchina D.S., 2004. Reversing age-associated immunosenescence via exercise. Exerc Immunol Rev. 10(6), 41.