Original Article

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The relationship between physical activity and oxidative stress biomarkers in older adults

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Abstract: *Objective:* In this study, we aimed to determine the relationship between physical activity and oxidative stress biomarkers in adults over 65 years of age. *Material and Methods:* A total of 176 older people were included in the study. Physical activity was determined using a DynaPort triaxial accelerometer measuring time in 6 activities, namely brisk walking, slow walking, lying down, sitting, standing, and moving. Advanced oxidation protein products (AOPP), Malondialdehyde (MDA), total antioxidant capacity (TRAP), and superoxide dismutase enzyme (SOD) levels, as well as glycemic level, body mass index (BMI), and abdominal circumference were determined. *Results:* SOD was found to correlate with brisk walking and moving. There was a correlation between AOPP and brisk walking, slow walking, standing, moving, and lying down. Blood glucose level correlated with brisk walking time, standing, moving, slow walking, and lying down. *Conclusions:* Increased duration of physical activity in everyday life is associated with higher antioxidant capacity, lower oxidative stress, glycemic level, and BMI.

Keywords: aging, antioxidants, oxidative stress, physical activity

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INTRODUCTION

The aging process is characterized by psychological and physical changes associated with social and biological factors. Aging occurs at the biological level due to the negative effects of various types of cellular damage, leading to a gradual decrease in physical capacity, increased risk of disease, and ultimately death [1]. Free radicals acting as mediators for the transfer of electrons in various biochemical reactions are among the biological factors related to aging. Their sufficient production enables energy production and activates defense mechanisms. However, their overproduction can lead to oxidative damage in different tissues. The increase in reactive oxygen derivatives is balanced by antioxidant enzymes, and the imbalance in this mechanism can create oxidative stress (OS) [2]. OS is defined as an imbalance between the formation of oxidant compounds and the effect of antioxidant defense systems. This imbalance is due to the increased production of oxidizing compounds and decreased antioxidant capacity [3].

OS is also considered to be the cause of various chronic diseases related to systemic inflammation, including respiratory diseases, skeletal muscle diseases, metabolic diseases, and cancer [4]. OS has systemic effects, starting in an organ or tissue and damaging different muscle and nerve structures by producing oxidative compounds through the bloodstream. This process leads to sarcopenia and fragility, which are causes of disability and death in older people [5, 6]. Moreover, aging cells undergo changes in redox homeostasis and produce high levels of reactive oxygen species. Similarly, an increase in one's body mass index (BMI), abdominal circumference, alcohol consumption, smoking, and disordered eating behavior can increase OS [7]. Therefore, examining intervention strategies to reduce or control the increase in OS is vital for positive health outcomes [8].

Adequate daily life physical activity (DLPA) and healthy lifestyle changes contribute to the control of OS in humans [9, 10]. However, for the aging population, there is little evidence in the literature regarding the relationship between the duration of DLPA and blood levels of OS biomarkers. Since an increase in one's physical activity level decreases the levels of inflammatory markers and cardiovascular risk, as well as causes metabolic and physiological effects, it is possible to assume that DLPA will also affect blood levels of OS markers. Therefore, the purpose of this study was to determine the relationship between oxidant and antioxidant biomarkers with different DLPA performance times, which are measured by an accelerometer in older people. The purpose of the research is to evaluate the difference in oxidative stress biomarkers among people with similar activity and the reasons for this difference by comparing people with similar DLPA levels, rather than measuring changes before and after exercise, as is commonly done in previous studies.Thus, the focus of the study is on examining the duration of daily activities rather than intensity. To the best of our knowledge, data regarding the effects of physical activity on oxidative stress parameters are limited in older people.

MATERIAL AND METHODS

Study Design and Participants

The study was conducted as a prospective cross-sectional study between January 2017 and January 2023 with male and female elderly volunteers in two different cities. 176 people over 65 years of age participated in the study; 72 (41%) of the participants were female and 104 (59%) were male. The mean age of the subjects in the study was 71± 6.0 years and the overall BMI was 29.16 kg/m^2. The participants included in the study were self-sufficient in their activities of daily life, lived in the same geographic region, consumed a Mediterranean diet, had no history of diabetes mellitus, hypertension, liver disease, kidney disease, or cardiovascular disease, did not take regular medication, had no smoking history, and had no malignancies. Patients with a history of estrogen or testosterone treatment within the previous six months were excluded. Subjects with

neurological, orthopedic, respiratory, cardiovascular, or psychiatric diseases limiting their mobility or assessment performance during the day, alcohol addiction, or current use of any type of anti-inflammatory drug were also excluded from the study. Furthermore, we excluded people who took more antioxidant supplements than a standard multivitamin equivalent and those with a history of hospitalization within the past six months.

Study Protocol

DLPA was assessed using an accelerometer. In this study, a DynaPort triaxial accelerometer was used for one week, from Monday to Friday. An accelerometer was placed on each participant's waist area and supported by a belt that was adjusted according to the individual's body size. Each participant was instructed to use the accelerometer throughout the day, except while bathing and sleeping. The approach used in this study is a validated and widely used tool for the assessment of DLPA. Since DLPA objectively measures the amount of time spent performing different types of activities, it is widely considered the gold standard for evaluating DLPA [11]. The accelerometer captured the motions and postures performed by each individual for one week on three different axes: x (longitudinal), y (mediolateral), and z (anteroposterior). The logarithmic recognition software of the DynaPort triaxial accelerometer was used to analyze the data collected by tracking these axes. This software expresses the results of the analysis of the axes in six different positions or activities: (1) brisk walking, (2) slow walking, (3) lying down, (4) sitting, (5) standing, and (6) moving. Time was calculated in terms of daily minutes.

To determine oxidative biomarkers, antioxidants, and metabolic variables, 10 ml of peripheral blood was collected from each participant after a fasting period of 10 hours. After collecting the blood, sera were separated for measurements of oxidant and antioxidant biomarkers. Advanced oxidation protein products [AOPP] and malondialdehyde [MDA] were determined as oxidation markers. The antioxidant biomarkers assessed in this study were total antioxidant capacity [TRAP] and enzyme superoxide dismutase [SOD]. Furthermore, each participant's glycemic level, BMI, and abdominal circumference were measured as metabolic variables.

Statistical Analysis

Microsoft Excel 2019 software was used for data tabulation, and statistical analysis was conducted using SPSS software version 20. The Shapiro-Wilk test was utilized to analyze the normality of the data distribution. Correlations were analyzed with Pearson or Spearman correlation coefficients. Statistical significance was set at $p < 0.05$. Finally, although no initial calculations were conducted for sample size, statistical power and effect size calculations were performed as a result on the highest correlation using GPower version 3.1 software.

RESULTS

As contain in Table 1, the average age of the subjects in the study was 71 and 59% were male, furthermore the overall BMI was 29.16 kg/m^2. The participants were monitored for an average of 15 hours per day. The subjects' demographic characteristics are presented in Table 1, while Table 2 contain the antioxidant capacity markers and blood levels of oxidation products and the participants' daily life physical activities are collectively.

The analysis of correlation between the variables (Table 3) reveals that the amount of time participants spent engaged in fast walking was positively correlated with SOD ($r = 0.54$, $p = 0.003$) and negatively correlated with AOPP ($r = -0.40$, $p < 0.03$). AOPP was positively correlated with the amount time spent lying down ($r = 0.53$, $p < 0.03$) and negatively correlated with the amount of time spent standing ($r = -0.41$, $p < 0.03$).

Table 1. Demographic characteristics (n=176)

Variables	Mean ± SD	CI 95%
Age	71.0 ± 6.0	66.0 – 74.0
BMI (Kg/m^2)	29.1 ± 6.2	25.4 – 31.6
Abdominal circumference (cm)	98.2 ± 11.5	93.7 – 101.6

The data were presented as mean ± standard deviation. 95% CI means 95% confidence interval, BMI: Body Mass Index, SD: standard deviation

Table 2. Summary of selected indicators

Indicator	Variables	Mean ± SD	CI 95%
Levels of blood biomarkers	Glucose (mg/dL)	117.3 ± 41.9	99.4 – 135.4
	TRAP (µM Trolox)	954.1 ± 138.9	896.4– 1012.4
	SOD (U/mg Hb)	34.3 ± 11.9	28.7 – 39.5
	AOPP (µmoles/L)	113.7 ± 66	86.1 – 142.6
	Malondialdehyde (µmol/L)	2.65 ± 0.17	1.85 – 2.96
	Brisk walking (min)	130.8 ± 58.2	105.2 – 154.4
	Slow walking (min)	28.1 ± 10.8	20.6 – 31.5
	Lying down (min)	128.7 ± 102.4	88.8 – 171.6
	Sitting (min)	367.4 ± 105.4	320.3 – 206.8
	Standing (min)	177.4 ± 69.8	151.2 – 206.4
	Moving (min)	104.2 ± 50.3	84.42 – 124.8
Daily Life Physical Activities	Brisk walking (min)	130.8 ± 58.2	105.2 – 154.4
	Slow walking (min)	28.1 ± 10.8	20.6 – 31.5
	Lying down (min)	128.7 ± 102.4	88.8 – 171.6
	Sitting (min)	367.4 ± 105.4	320.3 – 206.8
	Standing (min)	177.4 ± 69.8	151.2 – 206.4
	Moving (min)	104.2 ± 50.3	84.4– 124.8

TRAP: Total antioxidant capacity, SOD: Superoxide dismutase enzyme, AOPP: Advanced Oxidation Protein Products MDA: Malondialdehyde, SD: standard deviation

Table 3. The relationship between oxidative, antioxidant, glycemic and BMI blood markers with time performance of different DLPA

Variables		Brisk walking	Slow walking	Lying down	Sitting	Standing	Moving
TRAP	r	-0.16	-0.15	0.18	0.22	-0.18	-0.16
	p	0.37	0.40	0.34	0.26	0.35	0.40
SOD	r	0.54	0.35	-0.16	-0.002	0.30	0.55
	p	0.003*	0.06	0.38	0.97	0.11	0.003*
AOPP	r	-0.40	-0.50	0.53	-0.12	-0.41	-0.38
	p	0.03**	0.007**	0.003*	0.58	0.03**	0.03**
MDA	r	-0.08	0.02	0.28	-0.12	-0.30	-0.10
	p	0.65	0.91	0.13	0.13	0.11	0.58
Glucose	r	-0.62	-0.61	0.53	-0.56	-0.58	-0.60
	p	0.001**	0.001**	0.003*	0.77	0.001**	0.001**
BMI	r	-0.20	-0.40	0.22	0.02	-0.32	-0.15
	p	0.28	0.033**	0.23	0.88	0.08	0.41
Abdominal Circumference	r	-0.23	-0.38	0.33	-0.05	-0.30	-0.20
	p	0.21	0.41	0.08	0.10	0.10	0.31

AOPP: Advanced Oxidation Protein product. BMI: body mass index. MDA: Malondialdehyde. SOD: superoxide dismutase enzyme. TRAP: total antioxidant capacity. * Significant positive correlation ($p < 0.05$). ** Significant negative correlation ($p < 0.05$), r: correlation coefficient

DISCUSSION

In this study, it was observed that performing daily life activities requiring increased energy expenditure, such as brisk and slow walking, was associated with higher antioxidant levels and lower oxidative stress levels, blood glucose levels, and BMIs in elderly patients. These correlations indicate that performing physical activity has a protective effect in preventing chronic diseases and geriatric syndromes. However, daily life activities requiring low levels of energy expenditure, such as lying down, were associated with higher levels of protein oxidation and blood glucose levels [12,13].

Our results reveal that a negative relationship exists between physical activity levels and oxidative stress, which supports the results of previous studies published by Accattato et al. and Carraro et al. [14,15]. Furthermore, physical activity is effective in preventing metabolic diseases and lowering body weight and blood glucose. Consistent with other studies indicating that physical activity has protective effects, the present study showed that physical activity is negatively correlated with blood glucose levels and BMI. In this respect, individuals performing higher levels of physical activity or regular exercise have a higher antioxidant capacity and a lower metabolic risk [16,17]. Regular physical activity can enhance immune function and dramatically prevent the spread of the inflammatory cytokine response and OS. The excessive release of cytokines is associated with the onset of chronic diseases, and physical activity can dramatically reduce the spread of these cytokines and their irreparable damage [19].

In this study, it was determined that walking, regardless of pace, was positively associated with lower levels of protein oxidation biomarkers. Protein oxidation biomarkers were found to correlate with the presence of various chronic comorbidities, such as diabetes, hypertension, and chronic obstructive pulmonary disease. Based on the results obtained in the current study, an increase in these oxidative biomarkers is associated with periods of longer immobility. In this sense, the inverse proportional relationship found between protein oxidation and DLPA in elderly patients may be reflective of a biological factor that could be helpful in understanding the role of DLPA in muscle building. This finding also supports previous data indicating that oxidative stress causes oxidative damage in muscle proteins, decreases the mass and function of muscle tissue, and is associated with the presence of sarcopenia and frailty [20,21].

Moraes [22] showed that moderate exercise is associated with a decrease in OS and an increase in antioxidant activity. The increase in antioxidant capacity was observed by Fraile-Bermúdez [23] as an increase in superoxide dismutase and catalase enzymes in elderly patients. In the present study, we observed that antioxidant capacity was positively correlated with the amount of time spent walking. Although specific data regarding the participants' physical exercise were not collected in the current study, it was determined that the time distribution of daily life activities, such as standing, walking, and sitting, was associated with the balance of OS biomarkers.

Most studies conducted on this topic link the effects of exercise to blood biomarkers. In this sense, it is important to mention the conflicting effects of oxidant and antioxidant levels related to exercise and OS reported by Kawamura, who stated that the results depend on the exercise type and intensity, as well as on the individual characteristic of each participant [24]. Although some studies have demonstrated the positive effects of exercise in reducing OS, the effects of exercise are not well understood. Therefore, the results of this study are scientifically and clinically important because they indicate the beneficial effects of physical activity for older people. However, as in the present study, it is important to track activity levels and monitor changes in the biological levels of important blood biomarkers [25,26].

Since the results obtained indicate that there was a correlation between time spent moving, standing, and walking and low glycemic levels, it may be suggested that maintaining a good DLPA level may be effective in the treatment of hyperglycemia. However, it should be taken into consideration that the effects of physical activity and

exercise depend on other factors, such as the individual's nutritional status and body composition. In this sense, the dietary intake of antioxidant nutrients contributes to defense against oxidation by increasing the antioxidant response of individuals engaged in physical activity. Furthermore, increased amounts of free radicals cause a tendency toward higher levels of oxidation in individuals. Therefore, assessing the nutritional level, diet, and body composition of individuals, mainly in older people, is important for the analysis of biomarkers [26]. This approach should be considered in future research.

The present study has some limitations and strengths that should be mentioned. The small sample size and cross-sectional study design are among the limitations of the study; therefore, it is not possible to analyze causality in the results. Furthermore, the study did not assess the participants' nutritional status and diet, which may affect the results of blood biomarkers. The assessment of the effects of exercise for different time periods on oxidative stress would also be more informative. Finally, although participants with chronic diseases that could alter daily activities were not included in the study, all the participants' chronic diseases and medications that they were taking were not recorded, which may have had some effects on the results. Despite these limitations, through the use of different blood biomarkers, we were able to provide a nearly complete view of the oxidant/antioxidant capacity of each participant. The study also found a moderate correlation between variables with high statistical power (99%, $\alpha = 0.05$) and a 0.74 effect size. Additionally, physical activity is often determined using questionnaires in studies linking DLPA and OS. Since the use of instruments to assess DLPA is considered the gold standard, physical activity was monitored using a DynaPort triaxial accelerometer in the current study. The determination of physical activity was conducted for one week, which was sufficient for the objective and direct instrumental evaluation of DLPA. Future studies should include a comparison of different levels of physical activity, such as sedentary and active, and their effects on other blood biomarkers in elderly patients while considering differences in other variables, such as nutritional status, diet, and gender [16-18].

CONCLUSION

In conclusion, the results obtained in the present study indicate that the amount of time spent in DLPA requiring higher levels of energy expenditure is significantly associated with higher antioxidant capacity and lower OS, glycemic levels, and BMIs in elderly patients. Appropriate energy expenditure programs, especially those that include fast walking, should be scheduled for elderly patients to reduce oxidative stress. Further studies are warranted to determine the effects of continuous exercise programs for different periods on oxidative stress parameters in elderly patients.

Ethics: The study received ethical approval from the Non-Interventional Research Ethics Committee of Bezmialem University with approval number 2011-KAEK-42 2017702-01 and was conducted in accordance with the Helsinki declaration. Informed consent was obtained from all subjects involved in the study.

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REFERENCES

1. Vina J, Borras C, Abdelaziz KM, Garcia-Valles R, Gomez-Cabrera MC. The free radical theory of aging revisited: the cell signaling disruption theory of aging. Antioxid Redox Signal. 2013;19(8): 779-787. doi: 10.1089/ars.2012.5111
2. Venkataraman K, Khurana S, Tai TC. Oxidative stress in aging--matters of the heart and mind. Int J Mol Sci. 2013; 14(9): 17897-17925. doi: 10.3390/ijms140917897
3. Kregel KC, Zhang HJ. An integrated view of oxidative stress in aging: basic mechanisms, functional effects, and pathological considerations. Am J Physiol Regul Integr Comp Physiol. 2007; 292(1): R18-36. doi: 10.1152/ajpregu.00327.2006
4. Jacob KD, Noren Hooten N, Trzeciak AR, Evans MK. Markers of oxidant stress that are clinically relevant in aging and age-related disease. Mech Ageing Dev. 2013; 134(3-4): 139-157. doi: 10.1016/j.mad.2013.02.008
5. Hubbard RE, Woodhouse KW. Frailty, inflammation and the elderly. Biogerontology. 2010; 11(5): 635-641. doi: 10.1007/s10522-010-9292-5
6. Barzilay JI, Blaum C, Moore T, Xue QL, Hirsch CH, Walston JD, Fried LP. Insulin resistance and inflammation as precursors of frailty: the Cardiovascular Health Study. Arch Intern Med. 2007; 167(7): 635-641. doi: 10.1001/archinte.167.7.635
7. Ruiz M, Cefalu C, Reske T. Frailty syndrome in geriatric medicine. Am J Med Sci. 2012 Nov;344(5):395-8. doi: 10.1097/MAJ.0b013e318256c6aa
8. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, Cooper C, Landi F, Rolland Y, Sayer AA, Schneider SM, Sieber CC, Topinkova E, Vandewoude M, Visser M, Zamboni M; Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019; 48(4): 601. doi: 10.1093/ageing/afz046. Erratum for: Age Ageing. 2019; 48(1): 16-31
9. Visser M, Kritchevsky SB, Goodpaster BH, Newman AB, Nevitt M, Stamm E, Harris TB. Leg muscle mass and composition in relation to lower extremity performance in men and women aged 70 to 79: the health, aging and body composition study. J Am Geriatr Soc. 2002; 50(5): 897-904. doi: 10.1046/j.1532-5415.2002.50217.x
10. Stephens JW, Khanolkar MP, Bain SC. The biological relevance and measurement of plasma markers of oxidative stress in diabetes and cardiovascular disease. Atherosclerosis. 2009; 202(2): 321-329. doi: 10.1016/j.atherosclerosis.2008.06.006
11. Kotani K, Sakane N. C-reactive protein and reactive oxygen metabolites in subjects with metabolic syndrome. J Int Med Res. 2012;40(3):1074-81. doi: 10.1177/147323001204000326
12. Higashi Y, Maruhashi T, Noma K, Kihara Y. Oxidative stress and endothelial dysfunction: clinical evidence and therapeutic implications. Trends Cardiovasc Med. 2014 May;24(4):165-9. doi: 10.1016/j.tcm.2013.12.001
13. Bohannon RW. Comfortable and maximum walking speed of adults aged 20-79 years: reference values and determinants. Age Ageing. 1997 Jan;26(1):15-9. doi: 10.1093/ageing/26.1.15
14. Accattato F, Greco M, Pullano SA, Carè I, Fiorillo AS, Pujia A, Montalcini T, Foti DP, Brunetti A, Gulletta E. Effects of acute physical exercise on oxidative stress and inflammatory status in young, sedentary obese subjects. PLoS One. 2017 Jun 5;12(6):e0178900. doi: 10.1371/journal.pone.0178900
15. Carraro E, Schilirò T, Biorci F, et al. Physical Activity, Lifestyle Factors and Oxidative Stress in Middle Age Healthy Subjects. Int J Environ Res Public Health. 2018;15(6):1152-60. doi: 10.3390/ijerph15061152
16. Mulero J, Zafrilla P, Martinez-Cacha A. Oxidative stress, frailty and cognitive decline. J Nutr Health Aging. 2011 Nov;15(9):756-60. doi: 10.1007/s12603-011-0130-5
17. Sies H. Oxidative stress: oxidants and antioxidants. Exp Physiol. 1997 Mar;82(2):291-5. doi: 10.1113/expphysiol.1997.sp004024
18. Pippi R, Prete D, Ranucci C, Ministrini S, Pasqualini L, Fanelli C. Physical activity level and mediterranean diet adherence evaluation in older people - observational, uncontrolled, pilot study. Phys Act Rev 2022; 10(1): 119-129. doi: 10.16926/par.2022.10.13
19. Gomes EC, Silva AN, de Oliveira MR. Oxidants, antioxidants, and the beneficial roles of exercise-induced production of reactive species. Oxid Med Cell Longev. 2012;2012:756132. doi: 10.1155/2012/756132.
20. Korsager Larsen M, Matchkov VV. Hypertension and physical exercise: The role of oxidative stress. Medicina (Kaunas). 2016;52(1):19-27. doi: 10.1016/j.medici.2016.01.005.
21. Niki E. Biomarkers of lipid peroxidation in clinical material. Biochim Biophys Acta. 2014 ; 1840(2): 809-817. doi: 10.1016/j.bbagen.2013.03.020

22. Fraile-Bermúdez AB, Kortajarena M, Zarrazquin I, Maquibar A, Yanguas JJ, Sánchez-Fernández CE, Gil J, Irazusta A, Ruiz-Litago F. Relationship between physical activity and markers of oxidative stress in independent community-living elderly individuals. Exp Gerontol. 2015; 70: 26-31. doi: 10.1016/j.exger.2015.07.005. Epub 2015 Jul 11. PMID: 26173055.
23. Kawamura T, Muraoka I. Exercise-Induced Oxidative Stress and the Effects of Antioxidant Intake from a Physiological Viewpoint. Antioxidants (Basel). 2018; 7(9): 119. doi: 10.3390/antiox7090119
24. Picard M. Pathways to aging: the mitochondrion at the intersection of biological and psychosocial sciences. J Aging Res. 2011; 2011: 814096. doi: 10.4061/2011/814096.
25. Khansari N, Shakiba Y, Mahmoudi M. Chronic inflammation and oxidative stress as a major cause of age-related diseases and cancer. Recent Pat Inflamm Allergy Drug Discov. 2009; 3(1): 73-80. doi: 10.2174/187221309787158371
26. El Assar M, Angulo J, Rodríguez-Mañas L. Oxidative stress and vascular inflammation in aging. Free Radic Biol Med. 2013; 65: 380-401. doi: 10.1016/j.freeradbiomed.2013.07.003