Letter to the Editor

Association between Physical Activity and Telomere Length in a North Chinese Population: A China Suboptimal Health Cohort Study*

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Several studies have demonstrated an association between physical activity and telomere length; however, the association remains inconsistent. A cross-sectional study consisting of 588 participants (375 females, median age of 33.8 years) was carried out to investigate the association between telomere length and physical activity in a general population from North China. The results show that relative telomere length is not significantly different in participants in the northern Chinese population with different levels of physical activity, either in the model only adjusted for age (F = 2.127, P = 0.120) or in the model adjusted for demographics and lifestyle (F = 1.227, P = 0.294). The gender-stratified analysis also produced insignificant results. Our study confirmed a non-significant association between physical activity and telomere length in the northern Chinese population, which adds to the inconsistent association between physical activity and telomere length across different ethnic populations.

Key words: Physical activity; Telomere length; Relative telomere length; Chinese

Physical activity refers to any body movement that works one's muscles and requires more energy than resting. There is a growing consensus that physical activity confers favorable health outcomes across the lifespan and is consistently associated with a reduction in obesity, weight gain, coronary heart diseases (CHD), type II diabetes mellitus and the age-related diseases of dementia and Alzheimer's disease; decreased all-cause mortality rates and higher probability of late survival; good health and functioning during older age; and higher cognitive performance[1]. Conversely, sedentary behavior is associated with an unfavorable biomarker profile in older age, all-cause mortality, cardiovascular disease (CVD) incidence and mortality, type II diabetes incidence and cancer[2]. Recently, we demonstrated that short relative telomere length (RTL) is associated with suboptimal health status (SHS), a physical state between health and disease that can be recognized as a subclinical and reversible stage of chronic health conditions[3].

Telomeres are the repetitive sequences that protect the ends of chromosomes, help to maintain genomic integrity and are of key importance to human health. Telomere length (TL) declines with age and varies in relation to factors such as smoking and obesity, as well as a number of common diseases, including cardiovascular disease and some cancers; however, its relationship with cancer appears complex, in that longer telomeres are associated with a higher risk of some cancers[4]. Conversely, longer TL is associated with better health and protection from age-related diseases[5]. Therefore, TL might be an indicator of healthy aging and serve as a candidate biomarker of chronic diseases.

Considering that physical activity contributes to healthy aging and that telomere length might be an indicator of healthy aging, physical activity might correlate with telomere length. A systematic review and meta-analysis including 37 original articles indicated that further research is needed to determine the existence of a significant association between physical activity and telomere length, with

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15 studies favoring a positive association, 2 studies indicating an inverted ‘U’ correlation, and 20 studies not showing statistically significant associations[6]. Recently, a cross-sectional analysis including 5,823 adults from the National Health and Nutrition Examination Survey (NHANES 1999-2002) showed that physical activity (PA) was significantly and meaningfully associated with telomere length in U.S. men and women[7]. Only one study was carried out to investigate the relationship between telomere length and physical activity in an elderly Chinese population of individuals 65 years and older, and the results showed that there was no significant association[8]. The present study was aimed at investigating the association between telomere length and physical activity in a general population from Northern China.

A cross-sectional analysis was performed as part of the baseline survey of the China Suboptimal Health Cohort Study (COACS), a prospective community-based cohort study, with participants aged 18-64 years at enrollment and free from any diseases at the baseline screening[9]. Participants currently suffering from diabetes (self-reported diabetes or FPG ≥ 7.0 mmol/L at the investigation), hypertension (self-reported hypertension, or SBP ≥ 140 mmHg, or DBP ≥ 90 mmHg at the investigation), hyperlipemia (self-reported), cardiovascular or cerebrovascular conditions (including self-reported atrial fibrillation, atrial flutter, heart failure, myocardial infarction, transient ischemic attack, and stroke), any type of cancer (self-reported) and gout (self-reported) were excluded in the present study. The Ethical Committees of the Staff Hospital of Jidong oil-field of Chinese National Petroleum, and Capital Medical University approved the study. The ethical guidelines of the Helsinki Declaration were also followed.

Descriptions of DNA extraction, quantification, dilution and the determination of relative telomere length measurement by qPCR can be referred to in our previous paper[3].

Physical activity was classified as ideal (≥ 150 min/week of moderate intensity or ≥ 75 min/week of vigorous intensity), intermediate (1-149 min/week of moderate intensity or 1-74 min/week of vigorous intensity), or poor (none). Covariates such as demographic variables (age, sex, marital status, education level, and family income), alcohol drinking, smoking history, and sleeping hours per night were included. In addition, body mass index (BMI), hip circumference, abdominal circumference, blood pressure and biochemistry measurements (FBG, TG, LDL, TC) were also included. Methods of collecting these data have been described previously[9].

Continuous variables with an underlying normal distribution were presented as a mean ± SD and analyzed by independent *t*-tests or analyses of variance (ANOVAs); otherwise, variables were presented as a median (interquartile range) and analyzed by nonparametric tests. The chi-square test was used to examine between-group differences in categorical variables. General linear models were used to compare the between-group differences of RTL after controlling for covariates. All statistical tests were 2-sided, and $P < 0.05$ was considered significant. All statistical analyses were carried out using IBM SPSS Statistics software (version 21.0 from Armonk, NY: IBM Corp, USA).

In total, 588 subjects (375 females, 63.8%) with a median age of 33.8 years (range 20-64 years) are included in the final analysis. The descriptive characteristics of the participants are listed in Table 1. The proportion of females, age, education, smoking and alcohol drinking are significantly different among participants with inactive, intermediate and active physical activity levels, while BMI is not significantly different. The results show that RTL is not significantly different among participants with different levels of physical activity in the northern Chinese, neither in the model only adjusted for age ($F = 2.127$, $P = 0.120$) nor in the model adjusted for demographics and lifestyle ($F = 1.227$, $P = 0.294$) (Table 2). Similarly, the stratified analysis shows that RTLs are not significantly different in participants with different levels of physical activity, either in males ($F = 1.016$, $P = 0.364$) or in females ($F = 0.350$, $P = 0.750$) (Table 3).

In the present study, we demonstrated that RTLs are not significantly associated with physical activity, either in males or in females. This is the first attempt to explore the association between telomere length and physical activity in a general population in mainland China. Our findings are consistent with the findings from an elderly Chinese population of individuals 65 years and older in Hong Kong, which showed no association between telomere length and physical activity[8]. However, our findings are contrary to the findings in NHANES 1999-2002, which demonstrated that telomere length does not differ among the sedentary and those engaged in low or moderate levels of physical activity; however,

Table 1. Descriptive Characteristics of the Participants (*n* = 588)

Variable	Physical Activity			$t/Z/\chi^2$	*P*
	Inactive (*n* = 450)	Intermediate (*n* = 70)	Active (*n* = 68)		
Female	316 (70.2)	35 (50.0)	24 (35.3)	36.66	< 0.001
Age (years)*	34.9 (29.7-43.7)	32.2 (27.1-36.6)	31.0 (26.7-42.2)	17.55	< 0.001
20-29	123 (27.3)	24 (34.3)	31 (45.6)	19.82	0.003
30-39	173 (38.4)	34 (48.6)	19 (27.9)		
40-49	90 (20.0)	9 (12.9)	14 (20.6)		
≥ 50	64 (14.2)	3 (4.3)	4 (5.9)		
Education				18.22	0.001
Iliteracy or compulsory education	38 (8.4)	1 (1.4)	4 (5.9)		
High school	102 (22.7)	5 (7.1)	9 (13.2)		
College or higher	310 (68.9)	64 (91.4)	55 (80.9)		
Body mass index				7.32	0.292
Underweight	24 (5.3)	5 (7.1)	4 (5.9)		
Normal	266 (59.1)	36 (51.4)	32 (47.1)		
Overweight	121 (26.9)	21 (31.4)	28 (41.2)		
Obese	39 (8.7)	7 (10.0)	4 (5.9)		
Smoking				19.05	0.001
Never	370 (82.2)	53 (75.7)	41 (60.3)		
Current	78 (17.3)	17 (24.3)	27 (39.7)		
Former	2 (0.4)	0	0		
Alcohol drinking				13.46	0.009
Never	344 (76.6)	46 (65.7)	41 (60.3)		
Moderate	66 (14.7)	11 (15.7)	15 (22.1)		
Heavy	39 (8.7)	13 (18.6)	12 (17.6)		

Note. *Data were presented as median (P_{25}-P_{75}).

Table 2. Differences in Mean RTL by Level of Physical Activity in Northern Chinese Participants, after Adjusting for Covariates

Covariate	Physical Activity			*F*	*P*
	Inactive	Intermediate	Active		
Age	0.912 ± 0.012	0.917 ± 0.031	0.980 ± 0.031	2.127	0.120
Demographics	0.913 ± 0.012	0.918 ± 0.031	0.969 ± 0.032	1.340	0.263
Demographics and lifestyle	0.913 ± 0.012	0.919 ± 0.031	0.967 ± 0.032	1.227	0.294

Note. Means on the same row were adjusted for the covariates in the left column. The demographic covariates were: age, sex and education. The lifestyle covariates were: body mass index, cigarette smoking, and alcohol use. Data were presented as mean ± SE.

Table 3. Differences in Mean RTL by Level of Physical Activity in Northern Chinese Males by Gender, after Adjusting for Covariates

Covariate	Physical Activity			*F*	*P*
	Inactive	Intermediate	Active		
Male					
Age	0.932 ± 0.024	0.945 + 0.048	1.010 + 0.042	1.264	0.285
Demographics	0.931 ± 0.024	0.958 ± 0.047	1.004 ± 0.041	1.184	0.308
Demographics and lifestyle	0.932 ± 0.024	0.960 ± 0.047	0.999 ± 0.041	1.016	0.364
Female					
Age	0.903 ± 0.014	0.889 + 0.040	0.924 + 0.049	0.152	0.859
Demographics	0.904 ± 0.014	0.887 ± 0.041	0.924 ± 0.049	0.169	0.844
Demographics and lifestyle	0.904 ± 0.013	0.878 ± 0.040	0.929 ± 0.049	0.350	0.750

Note. Means on the same row were adjusted for the covariates in the left column. The demographic covariates were: age and education. The lifestyle covariates were: body mass index, cigarette smoking, and alcohol use. Data were presented as mean ± SE.

adults who participate in high levels of physical activity tend to have significantly longer telomeres than their counterparts[10]. The present study further addresses the complex and inconsistent association between telomere length and physical activity.

The inconsistent association between telomere length and physical activity might be attributable to the differences in the ethnicities of the study populations, the methods for the determination of telomere length or the measurement of physical activity. In addition, bias due to confounding factors or covariates might also contribute to this inconsistency among studies. Although the same covariates were adjusted in our study and in the U.S. study[7], the imbalance of potential confounding factors in different studies may result in an insignificant association in one study and a significant association in another study. Unmeasured variables, such as depression, psychosocial stress, sleep disturbances, and intake of vitamins and minerals had been reported to be associated with telomere length and may also be affected by levels of physical activity[2]. These differences could partly explain the inconsistent associations across the multiple studies.

The precise mechanism linking physical activity and telomeres remains unknown, aside from the pathway of inflammation and oxidative stress. Telomere length and cell senescence are closely related to inflammation and oxidative stress, while chronic physical activity suppresses inflammation and oxidative stress[10]. Furthermore, most longitudinal cohort studies have consistently indicated that physical activity is positively associated with healthy aging and serves as a protective factor against chronic diseases, as well as that short telomere length is consistently correlated with chronic diseases, except for cancers. Taking into account the inconsistent association between physical activity and telomere length, it is possible to speculate that physical activity benefits healthy aging *via* multiple related pathways, not only through the shortening of telomere length. Another possible explanation of these inconsistencies may be the intensity of the exercise and classification of individuals into the current groups. For instance, recent data indicates that greater exercise levels, above and beyond that of the American College of Sports Medicine (ACSM) recommendations are needed to modify telomere biology[7]. Further, running specifically has been shown to have a greater impact on modifying telomere biology as well[11].

The present study has several limitations. First, the study design did not enable us to establish a temporal or causal association between RTL and physical activity. Second, although several confounding factors are controlled in the analysis, other possible confounding factors might lead to bias in the association between physical activity and telomere length. Third, the study lacks any measurement of telomerase activity and information on the genetic contribution to TL. Forth, our study includes only individuals of Chinese ethnicity, thus restricting the generalization of the findings. Fifth, the participants in this study are relative young (20-64 years), which might lead to the failure to observe a significant association between telomere length and physical activity. This result is urgent to be validated in other independent cohorts. Finally, in this study, mean telomere length determined by the q-PCR, but not the shortest telomere length determined by was Single telomere length analysis (STELA), might decrease the statistical power in exploring the association between telomere length and physical activity.

In brief, the present study confirmed a non-significant association between physical activity and telomere length in the Chinese population. Considering that this finding is not consistent with results from several cross-sectional studies in other ethnic populations, the association needs to be validated in cross-sectional studies in other independent populations or in longitudinal cohort studies.

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