Telomere Length and Cardiorespiratory Fitness in Marathon Runners

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Background and Aim: Physical exercise up-regulates telomere-stabilizing proteins in mice, suggesting that physical activity affects telomere length. Several human studies assessing the relationship between physical activity, measured by health or activity surveys, and telomere length have produced conflicting results. The present study sought to explore the association between telomere length and physical fitness measured objectively as maximal oxygen uptake in endurance-trained athletes and sedentary controls.

Methods: Seventeen marathon runners and 15 age- and sex-matched healthy, sedentary control subjects participated in the study. Medical history, demographic information, maximal oxygen uptake (VO_2 max), and peripheral blood lymphocyte telomere length were measured in all subjects. Statistical analysis was performed to examine the relationship between telomere length and measured variables.

Results: Athletes and sedentary controls had similar lymphocyte (0.97 ± 0.20 vs 1.01 ± 0.18; $P = 0.6$) and granulocyte (0.89 ± 0.11 vs 0.89 ± 0.12; $P = 0.9$) telomere lengths. Linear regression analysis showed age as the only variable significantly associated with telomere length ($P = 0.007$). There was no correlation between VO_2 max and telomere length.

Conclusion: In a cohort of healthy adult athletes and sedentary controls, there was no association between physical activity measured by VO_2 max and peripheral blood lymphocyte and granulocyte telomere length.

Key Words: telomere, exercise tolerance, athletes, aging

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Telomeres are noncoding repetitive sequences (TTAGGG)n that form a protective cap at the end of chromosomes. The best characterized function of the telomeric complex is to protect the chromosomal ends from degradation. During somatic cell division, DNA polymerase cannot completely replicate the ends of linear DNA causing an "end replication problem" and resulting in progressive loss of telomeric repeats.[1] Telomerase is a ribonucleoprotein that maintains telomere length. Adult mammalian somatic cells typically exhibit low or absent telomerase activity, and thus, such cells display progressive telomere attrition with each mitotic cycle. Accordingly, telomere length in somatic cells reflects their replicative history, decreases progressively with aging, and can predict their remaining proliferative potential.

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Cells with critically short telomeres undergo chromosomal end-to-end fusions, replicative senescence, and apoptosis.[2,3] Short telomere length has been associated with cardiovascular morbidity and mortality and has emerged as a novel marker of biological age.[4–8] Telomere length is highly variable among individuals of the same age, and environmental factors may help determine the rate of telomere attrition and consequently the telomere length in adulthood.[9]

Physical exercise has been shown to up-regulate telomere-stabilizing proteins in mice, suggesting that physical activity may be a determinant of telomere length.[10] Several human studies assessing the relationship between physical activity, measured by health or activity surveys, and telomere length have shown conflicting results.[11–13] Consequently, the aim of the present study was to explore the association between telomere length and physical fitness measured objectively as maximal oxygen uptake in endurance-trained athletes and sedentary controls.

MATERIALS AND METHODS

Study Subjects

Seventeen marathon runners and 15 age- and sex-matched healthy, sedentary control subjects were recruited for the study. None of the subjects had a history of smoking or any chronic medical problem. The runners had practiced long distance running for at least 5 years, and all ran on an average of more than 21 miles/wk. The study was approved by the Hartford Hospital Institutional Review Board.

Study Protocol

The participants provided demographic details and a medical history and had vital signs, height, and weight measured. Psychological stress has been proposed to affect telomere length in previous studies.[11] The subjects' perception of stressful situations was measured using a 10-question 0- to 40-point scale using Perceived Stress Survey.[14]

The participants underwent a physician-supervised metabolic treadmill exercise test using the modified Balke protocol. Expired oxygen, carbon dioxide, and ventilatory volume were measured using a Parvomedics TrueOne 2400 metabolic cart (ParvoMedics Corp, Sandy, UT) and a breath-by-breath method. Maximal oxygen uptake (VO_2 max) was determined by averaging the 2 highest consecutive 30-second values.

Serum lipids and C-reactive protein levels were measured (Clinical Lab Partners, Hartford, CT). Telomere length was measured in granulocytes and lymphocytes by the fluorescence in situ hybridization technique in a commercial laboratory (Repeat Diagnostics, Vancouver, Canada).

Statistical Analysis

Categorical variables were compared using χ^2 analysis and continuous variables using the Student t test. Linear regression analysis was used to assess any significant associations between telomere length and measured variables. $P < 0.05$ was

TABLE 1. Demographic Characteristics of Athletes and Sedentary Subjects

Variable	Athletes n = 15	Sedentary n = 17	*P*
Age	54 ± 4	55 ± 5	0.3
Sex, male	67%	53%	0.4
Hypertension	14%	0	0.1
Premature coronary artery disease in family	14%	17%	0.8
History of cancer in family	30%	35%	0.7
BMI	22 ± 5	26 ± 3	0.01*
Education level (scale 0–5)	2.4 ± 0.7	2.2 ± 0.5	0.5
Income level (scale 0–5)	3.9 ± 0.8	3.7 ± 0.7	0.5
Stress score	46 ± 3	46.9 ± 3	0.8
VO_2 max	43.9 ± 6.4	33.4 ± 5.9	<0.001*

BMI indicates body mass index.

* indicates statistically significant difference between the 2 groups.

considered significant. Statistical Package for the Social Sciences version 17 (Chicago, IL) was used for all statistical analyses.

RESULTS

Study Subjects

The mean age and sex distribution was similar between the athletes and the sedentary controls as planned (Table 1). The mean ± SD running duration among athletes was 14 ± 11 years, and the mean running distance among the group was 32 ± 9 miles/wk. Athletes had significantly lower body mass index as well as lower low-density lipoprotein and C-reactive protein values but a higher VO_2 max (Tables 1 and 2).

Telomere Length

Athletes and sedentary controls had similar lymphocyte (0.97 ± 0.20 vs 1.01 ± 0.18; $P = 0.6$) and granulocyte (0.89 ± 0.11 vs 0.89 ± 0.12; $P = 0.9$) telomere lengths. Linear regression analysis showed age as the only variable with significant association with telomere length ($P = 0.007$; Fig. 1). There was no correlation between relative VO_2 max (calculated as a percentile referenced to age- and sex-predicted norms[15]) and age-adjusted telomere length (Fig. 2).

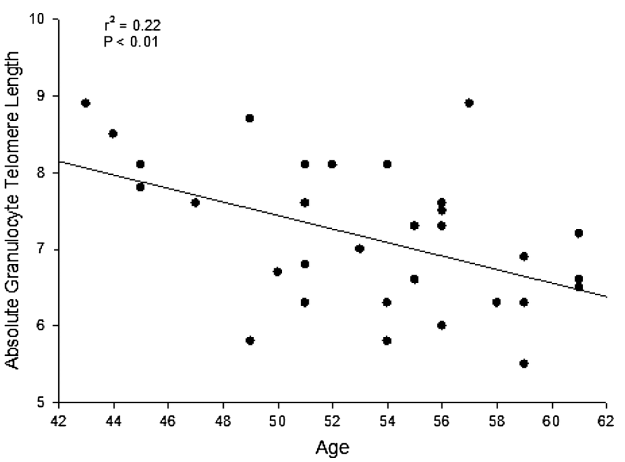

FIGURE 1. Correlation curve between granulocyte telomere length and age. This graph shows a significant decline in telomere length with advancing age.

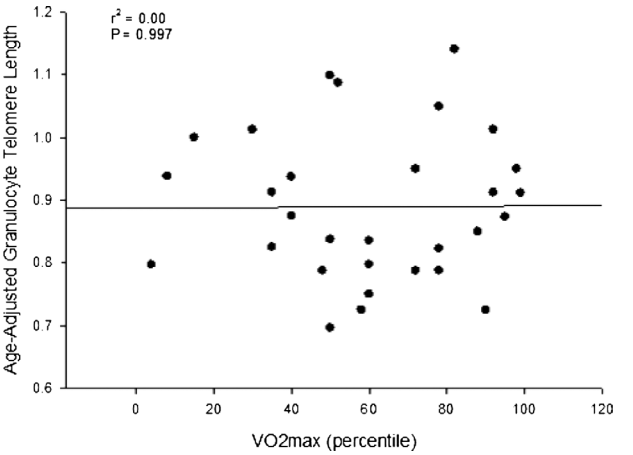

FIGURE 2. Correlation curve between telomere length and maximal exercise capacity (VO_2 max). This graph shows that there is no correlation between telomere length and exercise capacity.

DISCUSSION

Athletes in the present study had significantly lower body mass index and low-density lipoprotein values and a higher VO_2 max than the sedentary subjects but similar telomere length. There was also no relationship between VO_2 max and telomere length, although there was an association between age and telomere length ($P = 0.007$). Previous studies have produced conflicting data on the relationship of physical activity to telomere length. Self-reported physical activity assessed by questionnaires has been reported to be associated with telomere length,[12] but this was not confirmed by other studies.[11,13] Werner et al.[16] found that telomere length was preserved in middle-aged athletes and was significantly shorter in middle-aged control subjects compared to young subjects. LaRocca et al.[17] studied young and old sedentary and endurance-trained subjects (n = 57) and found a positive association between VO_2 max and telomere length. In their study VO_2 max, and not age, was the only independent predictor of telomere length. Ponsot et al.[18] found no difference in skeletal muscle telomere length in young and old healthy, physically active men and women. In a recent prospective cohort study, multiple patient factors including exercise capacity measured by symptom-limited exercise treadmill test revealed that omega-3 fatty acid levels were associated with the rate of telomere shortening with time.[19]

TABLE 2. Differences in Clinical lab Results in Athlete and Sedentary Groups

Variable	Athletes	Sedentary	*P*
CRP	0.6 ± 0.5	1.7 ± 1.4	0.01*
LDL	101 ± 30	132 ± 33	0.01*
HDL	69 ± 20	57 ± 16	0.3
Triglycerides	80 ± 32	98 ± 64	0.1
Lymphocyte telomere length	0.975 ± 0.203	1.011 ± 0.181	0.6
Granulocyte telomere length	0.894 ± 0.116	0.897 ± 0.120	0.9

CRP indicates C-reactive protein; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Notably, there was no association between exercise capacity and telomere length even after adjusting for multiple variables in this study.

Several other factors could explain the conflicting results among studies examining telomere length and physical activity. Telomere length is associated with several environmental and biological variables[9,20] such as psychological stress, socioeconomic status, vitamin D levels, and atherosclerotic coronary artery disease. Statins have been found to attenuate the increased cardiovascular risk associated with shorter telomeres.[21] It is also possible that other yet-to-be-determined factors affect telomere length and obscure any relationship between physical activity and telomere length. Telomere length shortens with age process,[22,23] and our study confirmed an inverse relationship between age and telomere length. Furthermore, individuals with shorter telomere length may have reduced survival due in part to higher mortality from heart disease and infectious diseases.[5]

Our study was limited by variation in running history and present activity level among the athletes.

In conclusion, the present study did not find a relationship between objectively measured exercise performance or running history and telomere length in a cohort of healthy adult athletes and sedentary controls. These results do not support the hypothesis that exercise training preserves telomere length.

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