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Leukocyte telomere length and ideal cardiovascular health in American Indians: the Strong Heart Family Study

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Abstract

Telomere length, a marker of biological aging, has been associated with cardiovascular disease (CVD) and its risk factors. Ideal cardiovascular health (CVH), defined by the American Heart Association (AHA), has also been associated with a reduced risk of CVD, but the relationship between telomere length and ideal CVH is unclear. We measured leukocyte telomere length (LTL) by qPCR in 2568 American Indians in the Strong Heart Family Study (SHFS). All participants were free of overt CVD at enrollment (2001–2003). CVH indices included four behavioral factors (smoking, physical activity, diet, BMI) and three health factors (blood pressure, cholesterol, fasting glucose). Each index was categorized as poor, intermediate, or ideal according to the AHA's guideline. CVH was further categorized into below average (0–1), average (2–3) and above average (≥4) based on the total number of ideal indices. Results showed that, 29, 50 and 21 % of study participants had below average, average, and above average CVH, respectively. Participants with above average CVH had significantly longer LTL than those with below average CVH (β = 0.034, $P = 0.042$) after adjusting for age, sex, education level, marital status, processed meat consumption, alcohol consumption, and study site. Compared to the U.S. general population, American Indians achieved lower rates for five out of the seven ideal CVH metrics, including smoking, BMI, physical activity, diet, and blood pressure. Achieving four or more ideal CVH

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metrics was significantly associated with longer LTL. This finding suggests that achieving an ideal CVH may prevent or delay CVD, probably through promoting healthy aging.

Keywords

American Indians; Biological aging; Ideal cardiovascular health; Leukocyte telomere length; Strong heart family study

Introduction

Telomeres are repetitive DNA sequences and their associated proteins on the distal ends of the chromosomes [1]. They are critical in maintaining chromosomal stability during mitotic cell proliferation. Telomere length shortens during each round of cell division and when it reaches a critical length, cells stop division and become senescent. Thus, telomere length has been considered a marker of biological aging. Telomere length is heritable [2] and shorter telomere length has been associated with a wide range of age-related disorders including cardiovascular disease (CVD), [3] type 2 diabetes, [4] as well as cancer [5]. A better understanding of the relationship between these disorders and telomeric aging will shed light on the mechanism underlying premature aging and is likely to promote healthy aging and prevent or delay the onset of age-related diseases.

The 2020 strategic goal for the American Heart Association (AHA) has identified Life's Simple 7 as the key risk factors aimed at achieving ideal cardiovascular health (CVH) [6]. It includes 4 behavioral factors (smoking, diet, physical activity, and body mass index [BMI]) and 3 health factors (blood pressure, total cholesterol, and fasting glucose). Ideal CVH has been associated with a reduced risk for age-related conditions, including CVD, [7–9] cognitive impairment, [10, 11] diabetes, [12] atherosclerosis, [13–16] and total mortality [17, 18]. Moreover, previous studies have demonstrated that behavioral factors (e.g. smoking, [19, 20] alcohol abuse, [21] sedentary lifestyle, [22] obesity [19, 23]) can accelerate telomere shortening, and shorter telomere length has been associated with several health disorders such as hypertension, [24, 25] hypercholesterolemia, [26] and diabetes [4, 27]. Among American Indians in the Strong Heart Family Study (SHFS), we have recently demonstrated that shorter leukocyte telomere length (LTL) significantly and independently predicts future onset of diabetes [4] and carotid atherosclerosis [28] beyond traditional risk factors. Shorter LTL has also been associated with obesity [23] and a higher dietary intake of processed meat in this high risk population [Amanda Fretts, Ph.D., unpublished data, 2016]. However, no study has examined the potential influence of ideal CVH indices on biological aging assessed by LTL. This study is to investigate the association between ideal CVH indices and LTL among American Indians participating in the SHFS (2001–2003).

Methods

Study population

The SHFS is a family-based longitudinal study designed to identify metabolic, genetic and behavioral factors for CVD, diabetes and their risk factors in American Indians in tribes and communities residing in Arizona, North/South Dakota, and Oklahoma. The SHFS recruited 3665 tribal members from 94 multigenerational families (14–93 years) between 2001 and 2003. All participants underwent a clinical examination including a personal interview and physical examination. Information on socio-demographic factors, medical history, medication use, and lifestyle factors was collected by personal interview using standard questionnaires. A physical examination was conducted, and fasting blood samples were collected for laboratory tests, including fasting glucose and lipids. The SHFS protocol was approved by the Institutional Reviews Boards from the Indian Health Service and the participating institutions. Study design and methods of the SHFS have been described elsewhere [29]. In the current study, 874 participants from one community were removed due to withdraw of consent. However, the subsample of 2791 participants did not differ significantly from the total sample of 3665 participants in the distribution of demographics. After excluding participants with overt CVD (n = 135) or missing LTL data (n = 88), a total of 2568 participants were included in the final data analysis.

Assessments of behavioral factors

Cigarette smoking was classified as current smoking, past smoking and never smoking. Current smoking was defined as having smoked at least 100 cigarettes in the subject's entire life, having smoked cigarettes regularly, and smoking currently. Past smoking was defined as having smoked at least 100 cigarettes in the subject's entire life, having smoked cigarettes regularly in the past, and not smoking currently. Never smoking was defined as never smoked or having smoked fewer than 100 cigarettes in their life time. Each participant received a pedometer, instructions for wearing the pedometer, and an activity diary at their clinical examination. They were asked to wear the pedometer for seven consecutive days and to record the number of the steps taken daily in the activity diary. Physical activity was assessed by the mean number of steps per day calculated by averaging the total number of steps recorded each day during the 7-day period. Dietary intake was assessed using a Block food frequency questionnaire and an American Indian supplemental foods questionnaire which collected data regarding reported "usual" intake of 119 foods over the past year. Body weight (kg) and height (cm) were measured when participants wore light clothes and no shoes by trained research staff. BMI was calculated by dividing weight in kilograms by the square of height in meters (kg/m^2).

Assessments of health factors

Systolic and diastolic blood pressure were measured three times by trained staff using a standard mercury sphygmomanometer after the participants had been resting for at least 5 min and the mean of the last two measurements was used in statistical analysis. Fasting glucose and blood lipids were measured by standard laboratory methods [30]. Medical history and medications for hypertension, dyslipidemia, and diabetes were obtained by standard questionnaires.

Indices of ideal cardiovascular health

Methods for the calculation of ideal CVH indices in the SHFS have been described previously [12] and were listed in Table 1. Briefly, each of the 7 indices was categorized as poor, intermediate, or ideal in accordance to the AHA's definitions [6]. A composite score (ranging from 0 to 7) was calculated by summing the total number of ideal indices. This score was further categorized as below average (0–1), average (2–3) and above average (≥ 4) and used in statistical analysis.

Measurement of leukocyte telomere length

Detailed methods for LTL measurement in the SHFS have been described previously [4]. Briefly, genomic DNA from peripheral blood was isolated according to standard protocols. LTL was measured using quantitative PCR at Dr. Blackburn's lab at the University of California, San Francisco using a high-throughput telomere length assay system. The telomere length assay determines the ratio of telomeric product/single copy gene (T/S) obtained using quantitative PCR according to protocols reported previously [31]. T/S ratio was calculated by taking the difference between the mean of two T values and two S values attained for each of the three replicates. Three of these T/S ratios were averaged, and standard deviation and percent for coefficient of variation (% CV, standard deviation/mean) were calculated. T/S ratios were normalized to the mean of all samples. For quality control, we included seven control DNA samples from various cancer cell lines in each assay plate. These control samples allowed us to create standard curves, which were then integrated into a composite standard curve, used for T and S concentration calculations. In addition, about 20 % of the samples selected randomly were measured twice. Intra- and interassay % CV was 4.6 and 6.9 %, respectively.

Statistical analyses

To examine the association between each individual ideal CVH index and LTL, we constructed generalized estimating equation (GEE) model with independent correlation structure, in which LTL was the dependent variable and each individual ideal CVH index (ideal vs. intermediate vs. poor, using poor level as reference) was the independent variable, adjusting for age and sex. GEE model was used here to account for the family relatedness among study participants. To examine whether socioeconomic information, lifestyle and study site influence the associations between LTL and ideal CVH indices, we further adjusted for education level, marital status, processed meat consumption, alcohol consumption, and study site in the GEE model described above. The association between the composite score of ideal CVH and LTL was similarly examined. To examine whether sex influences the association between ideal CVH and LTL, we conducted a separate analysis by stratifying by sex. Further, we generate an interaction term "ideal CVH 9 sex" to examine the interaction between ideal CVH and sex. A two-tailed P value <0.05 was considered statistically significant. All statistical analysis was conducted using SAS statistical software (version 9.4, Cary, North Carolina).

Results

The current analysis included 2568 American Indians (1549 women and 1019 men) free of overt CVD at enrollment. The mean age was 39 ± 16 years (14–93 years). Figure 1 shows the distribution of the 7 ideal CVH metrics. About 40 % participants never smoked, 13 % walked >10,000 steps/day, and 20 % achieved ideal BMI. No participant achieved ideal diet. In contrast, ideal health factors were better achieved. 69 and 61 % participants achieved ideal cholesterol and fasting glucose, respectively, but only 37 % achieved ideal blood pressure. Collectively, only 21 % participants achieved 4 or more ideal CVH components and no one achieved all 7 ideal CVH metrics. About 29–50 % participants achieved 0–1 and 2–3 ideal CVH indices, respectively.

Table 2 shows the clinical characteristics of study participants according to LTL quartiles. Compared to participants with longer LTL, those with shorter LTL had significantly higher BMI and fasting glucose and were more likely to be men (all $P < 0.05$). No significant difference in other listed characteristics was observed.

Association between LTL and ideal cardiovascular health

Table 3 shows the associations between individual ideal CVH indices and LTL. Among the 7 ideal CVH indices, longer LTL was significantly associated with ideal BMI ($\beta = 0.027$, $P =$ 0.0.026) and ideal fasting glucose ($\beta =$ 0.0.031, $P = 0.030$) but not the other 5 ideal CVH metrics after adjusting for age, sex, study site, education level, marital status, processed meat consumption, alcohol consumption and other CVH metrics. Table 4 shows the association between LTL and a composite score of ideal CVH metrics. Participants who achieved above average CVH had significantly longer LTL than those with below average CVH after adjusting for age and sex ($\beta = 0.038$, $P = 0.021$). After further adjusting for education level, marital status, processed meat consumption, alcohol consumption, and study site, an achievement of above average ideal CVH remained significantly associated with longer LTL ($\beta = 0.034$, $P = 0.042$). We further examined the associations of LTL with the composite CVH score, health factor score, and behavior factor score, separately. The results showed a significant association of LTL with health factor score ($\beta = 0.013$, $P = 0.006$) but not behavior factor score ($P = 0.637$) and CVH score ($P = 0.107$).

Sex-specific association between LTL and ideal cardiovascular health

Stratification analysis by sex showed that the association between ideal CVH and LTL was still significant in women ($P = 0.044$) but not in men (Table 5). However, the effect size of the association was similar in men and women (0.032 vs. 0.039). We did not find a significant interaction between ideal CVH and sex on LTL ($P = 0.762$). These results indicated that the association between ideal CVH and LTL may not be influenced by sex.

Discussion

In a large, family-based population cohort of American Indians, we studied the effects of ideal CVH on leukocyte telomere length, independent of traditional cardiovascular risk factors. We found that an achievement of four or more ideal CVH indices was significantly associated with longer leukocyte telomere length, independent of established cardiovascular risk factors.

The AHA's 2020 goal to improve CVH by 20 % [6] is bold and forward thinking, but achievement of this goal could be challenging for some populations including American Indians. Our analysis in American Indians and those from other ethnic groups indicated that very few adults achieved ideal CVH [7, 9–12, 17, 18]. Compared to the U.S. general population as reported in the NHANES 2005–2006, [6] American Indians appeared to have poorer ideal CVH. For example, lower proportions of American Indians in the SHFS achieved ideal levels of smoking (40 vs. 73 %), physical activity (13 vs. 45 %), diet (none vs. <0.5 %), BMI (20 vs. 33 %), and blood pressure (37 vs. 42 %). Although direct comparison may bring some concerns due to the different distribution of demographics between these two samples of population, the data may indicate a high challenge in promotion of ideal CVH for American Indians. None of the SHFS participants achieved all seven ideal indices. About 40 % of the SHFS participants achieved ideal health factors, but less than 20 % achieved ideal behavioral factors, indicating that ideal health factors could be more achievable than ideal behavioral factors in American Indians. It is noteworthy that, similar to U.S. general population, none of the American Indian participants achieved healthy diet. Developing optimal strategies for healthy eating, smoking cessation, and physical activity is the key to promote healthy aging and prevent or delay CVD.

Previous studies have reported associations of shorter telomere length with behavioral factors (e.g. smoking, [19, 20] alcohol consumption, [21] inactive lifestyle, [22] obesity [19, 23]) and health factors (e.g. hypertension, [24, 25] hypercholesterolemia, [26] and diabetes [4, 27]). In the SHFS, we have demonstrated that shorter telomere length significantly predicted the risk of diabetes [4] and carotid atherosclerosis, [28] independent of traditional risk factors. We have also reported significant associations of LTL with obesity [23] and processed meat and unprocessed red meat [Amanda Fretts, Ph.D., unpublished data, 2016] in this high risk population. However, we failed to find significant associations of telomere length with smoking, physical activity, and diet in our study. The reasons of the discrepant findings are unclear. While these findings provide valuable information for the relationship between biological aging and cardiovascular health factors, previous studies have largely focused on the association of telomere length with each individual behavioral or health factor. However, because many of these factors often coexist and are interwoven in multiple biologically related pathways, modeling their joint effects should reflect true biological processes and thus provide more accurate information compared to studying each factor individually. To our knowledge, no study has investigated the combined effects of all seven behavioral and health factors on biological aging assessed by LTL in American Indians or other ethnic groups as well.

Since the release of AHA's definition for ideal CVH, several epidemiological studies have consistently reported associations of achieving ideal CVH with reduced risk of age-related disorders such as CVD, [7–9, 32] cognitive impairment, [10, 11], disability, [33] cancer, [32, 34] and all-cause mortality [17, 18]. For example, in the CARDIA study [35] including participants aged 18–30 years, an achievement of ideal CVH predicted a decreased risk of cardiac dysfunction after 25 years of follow-up (OR 0.52, 95 % CI 0.37–0.73). In the NHANES in 1988–1994 (with mortality assessment through 2006), achieving a higher degree of ideal CVH metrics reduced the risk of CVD and total mortality among adults (≥20 years) [18]. In the Women's Health Initiative study [32] including postmenopausal women aged over 50 years, participants who achieved 6–7 ideal CVH metrics had significantly lower risk for CVD and cancer compared to those who achieved 0–1 ideal CVH metrics. Among participants aged 45–64 years in the ARIC study, [36, 37] ideal CVH attainment or improvement through mid- to later-life was associated with lower CVD prevalence and better cardiac structure and function in later-life. Similar beneficial effects of achieving an above-average ideal CVH were also observed among participants in the REGARDS study [38]. Moreover, ideal CVH has been associated with various measures of subclinical CVD, including arterial stiffness, [39–41] carotid atherosclerosis, [14–16] and coronary artery calcium, [42–44] as well as cardiovascular risk factors such as diabetes, [12] hypertension, [45] and depression [46]. While these results provide strong evidence for a protective effect of achieving ideal CVH on CVD and related conditions, previous investigations did not include American Indians, a minority group suffering from high rates of CVD, diabetes, and other risk factors. In addition, to the best of our knowledge, no study has examined the impact of ideal CVH on biological aging in American Indians or other ethnic groups. Here we identified that achieving four or more ideal CVH metrics was associated with longer telomere length. This finding may improve our understanding of the relationship between healthy aging and CVD.

Recently, a sex difference was found in the association between sex hormones and ideal CVH, [47] indicating a probable effect of sex on the association between ideal CVH and telomere length. Therefore, we conducted a sex-specific analysis to examine whether sex influences the association between ideal CVH and telomere length. We found that the effect size of the association between ideal CVH and LTL was similar in men and women, although the association was not significant in men. Further, we did not find a significant interaction between ideal CVH and sex in our study. These results indicated that sex may not influence the association between ideal CVH and telomere length.

Strengths of this study include the high quality telomere data, the detailed clinical phenotypes on CVH metrics for all study participants, and the extensive adjustments of known cardiovascular risk factors. However, several limitations should also be mentioned. First, our dietary data were obtained from a self-reported food frequency questionnaire, which may be subject to measurement error. Second, the ideal CVH was assessed by a crude additive scoring method based on achievement of the key behavioral and health factor goals; however, the magnitude of the association of each individual index is not the same, and thus this scoring method may oversimplify the association of ideal CVH with telomere length. Third, our findings were derived from American Indians whose cardiovascular health profiles could be different from those with other ethnic backgrounds. Thus, the generalizability of our results to other populations is unknown. Lastly, the cross-sectional nature of our analysis precludes any causal inference for the relationship between telomere length and cardiovascular health factors.

In summary, compared to the U.S. general population, American Indians achieved lower rates for five out of the seven ideal CVH metrics including smoking, BMI, physical activity, diet, and blood pressure. Achieving four or more ideal CVH metrics is associated with longer telomere length, a marker of biological aging and age-related disorders. This finding may deepen our understanding of the biological mechanisms behind aging and cardiovascular disease.

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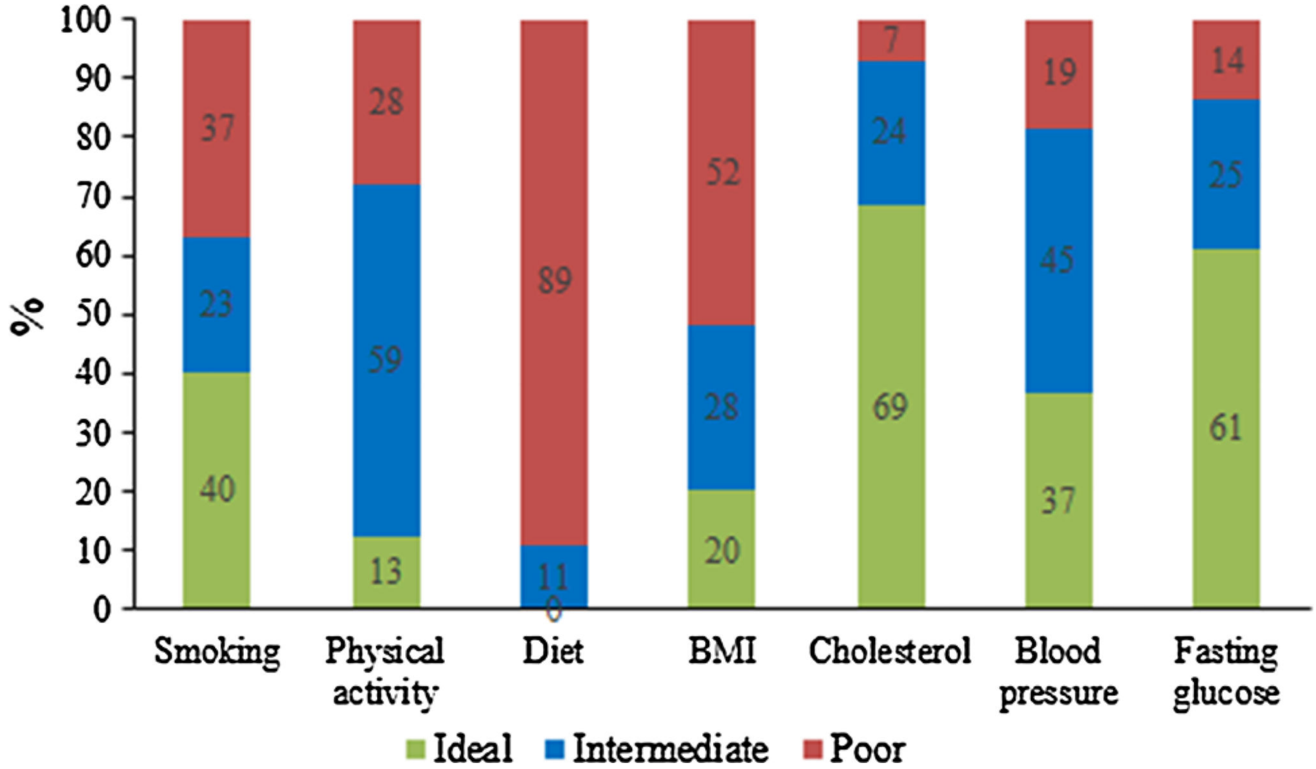

Fig. 1.

Distribution of ideal cardiovascular health indices among American Indians in the strong heart family study

Table 1

Definition of ideal, intermediate, and poor levels of ideal cardiovascular health indices

Metrics	Poor	Intermediate	Ideal
Smoking	Current smoker	Former smoker	Nonsmoker
Physical activity[a]	<3500 steps/day	3500–10,000 steps/day	>10,000 steps/day
Healthy diet[b]	0–1 component	2–3 components	4–5 components
Body mass index	≥30 kg/m^2	25–29.9 kg/m^2	<25 kg/m^2
Blood pressure	SBP ≥ 140 or DBP ≥ 90 mmHg	SBP 120–139 or DBP 80–89 mmHg or treated to ideal	SBP<120 and DBP<80 mmHg
Total cholesterol	≥240 mg/dL	200–239 mg/dL or treated to ideal	<200 mg/dL
Fasting glucose	≥126 mg/dL	100–125 mg/dL or treated to ideal	<100 mg/dL

[a]The AHA's definitions [6] classify physical activity levels based on total activity time (minutes per day), but in the SHFS, physical activity was assessed with pedometers (steps per day). As several studies suggest that individuals who accumulate at least 10,000 steps per day have a decreased risk of obesity and hypertension compared with individuals who accumulate fewer steps per day, [48]>10,000 steps per day was considered an ideal level of activity

[b]Includes (1) fruits and vegetables: ≥4.5 servings per day; (2) fish: ≥200 g per week; (3) fiber-to-carbohydrate ratio:>1 g of fiber per 10 g of carbohydrate; (4) sodium:<1500 mg per day; and (5) sugar-sweetened foods and beverages: ≤450 kcal per week. The 5 healthy diet components here were adapted from the AHA's definitions of the 5 components, which were "(1) fruits and vegetables: ≥4.5 cups per day; (2) fish: ≥two 3.5-oz servings per week (preferably oily fish); (3) fiber-rich whole grains (≥1.1 g of fiber per 10 g of carbohydrate): ≥three 1-oz-equivalent servings per day; (4) sodium:<1500 mg per day; (5) sugar-sweetened beverages: ≤450 kcal (36 oz) per week."

Table 2

Baseline characteristics of SHFS participants according to LTL quartiles (N = 2568)

Characteristics	LTL quartiles				*P* for trend[a]
	Q1	Q2	Q3	Q4	
No. of participants	633	626	678	631	–
Age, years (mean ± SD)	47.5 ± 16.0	42.9 ± 15.9	36.8 ± 15.4	31.7 ± 14.7	<0.001
Male, n (%)	253 (39.97)	244 (38.98)	281 (41.45)	241 (38.19)	0.026
Current drinking, n (%)	343 (54.19)	350 (55.91)	407 (60.03)	417 (66.09)	0.486
Education level, years (mean ± SD)	12.3 ± 2.3	12.3 ± 2.3	12.1 ± 2.3	11.9 ± 2.2	0.960
Processed meat consumption (g/day, mean ± SD)[b]	38.6 ± 41.5	37.1 ± 39.7	47.4 ± 65.0	41.2 ± 48.1	0.761
Ideal cardiovascular health indices					
Current smoking, n (%)	217 (34.34)	230 (36.86)	261 (38.50)	239 (37.88)	0.722
BMI (kg/m^2, mean ± SD)	32.18 ± 7.62	31.92 ± 7.82	31.26 ± 7.41	29.50 ± 7.15	<0.001
Physical activity (steps/day, mean ± SD)	5275.2 ± 3859.5	5701.3 ± 3809.2	6235.4 ± 3905.2	6555.1 ± 4023.0	0.079
Diet, healthy score (mean ± SD)	0.7 ± 0.7	0.6 ± 0.7	0.5 ± 0.6	0.5 ± 0.7	0.983
SBP (mmHg, mean ± SD)	124.5 ± 17.5	124.1 ± 17.1	122.9 ± 16.5	118.8 ± 15.0	0.053
DBP (mmHg, mean ± SD)	76.5 ± 10.6	76.6 ± 11.3	77.0 ± 11.4	74.8 ± 10.5	0.803
TC (mg/dL, mean ± SD)	187.3 ± 38.6	185.7 ± 36.2	183.0 ± 37.1	174.9 ± 37.8	0.561
FPG (mg/dL, mean ± SD)	116.5 ± 52.9	112.7 ± 47.8	105.3 ± 44.1	100.1 ± 33.5	0.003

LTL leukocyte telomere length, *Q* quartile, *BMI* body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *TC* total cholesterol, *FPG* fasting plasma glucose

[a]Adjust for age and sex using GEE regression model to account for family relatedness of participants

[b]Processed meat included breakfast sausage, spam, hotdogs, and lunchmeat

Table 3

Association between cardiovascular health indices and LTL among SHFS participants

Cardiovascular health indices	**Age- and sex-adjusted**		**Multivariate-adjusted**[a]	
	β (SE)	***P*-value**	**β (SE)**	***P*-value**
Smoking				
Poor (ref)	–	–	–	–
Intermediate	−0.016 (0.012)	0.189	−0.009 (0.013)	0.489
Ideal	−0.010 (0.011)	0.352	−0.014 (0.010)	0.161
Physical activity				
Continuous (steps/day)	0.000 (0.000)	0.049	0.000 (0.000)	0.267
Categorical				
Poor (ref)	–	–	–	–
Intermediate	0.025 (0.012)	0.033	0.013 (0.011)	0.242
Ideal	0.023 (0.017)	0.172	0.007 (0.017)	0.684
Healthy diet				
Poor (ref)	–	–	–	–
Intermediate	0 (0.013)	0.984	-0.007 (0.013)	0.610
Ideal	–	–	–	–
Body mass index				
Continuous (kg/m^2)	−0.003 (0.001)	<0.001	−0.002 (0.001)	0.001
Categorical				
Poor (ref)	–	–	–	–
Intermediate	0.046 (0.011)	<0.001	0.029 (0.011)	0.005
Ideal	0.041 (0.011)	<0.001	0.027 (0.012)	0.026
Blood pressure				
Continuous (mmHg)				
Systolic blood pressure	0.001 (0.000)	0.169	0.001 (0.000)	0.087
Diastolic blood pressure	0.000 (0.001)	0.513	0.001 (0.000)	0.085
Categorical				
Poor (ref)	–	–	–	–
Intermediate	−0.027 (0.013)	0.029	−0.032 (0.013)	0.013
Ideal	−0.006 (0.016)	0.687	−0.021 (0.017)	0.223
Total cholesterol				
Continuous (mg/dL)	−0.000 (0.000)	0.291	−0.000 (0.000)	0.548
Categorical				
Poor (ref)	–	–	–	–
Intermediate	−0.006 (0.022)	0.796	−0.015 (0.023)	0.527
Ideal	−0.004 (0.022)	0.872	−0.007 (0.025)	0.763
Fasting glucose				
Continuous (mg/dL)	−0.000 (0.000)	<0.001	−0.000 (0.000)	0.007
Categorical				

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Cardiovascular health indices	Age- and sex-adjusted		Multivariate-adjusted[a]	
	β (SE)	*P*-value	β (SE)	*P*-value
Poor (ref)	–	–	–	–
Intermediate	0.037 (0.016)	0.020	0.021 (0.015)	0.149
Ideal	0.048 (0.015)	0.001	0.031 (0.014)	0.030

[a]Adjust for age, sex, education level, marital status, processed meat consumption, alcohol consumption, study site, and other CVH indices

Table 4

Association between ideal cardiovascular health and LTL among SHFS participants

Ideal cardiovascular health	Age (years)	Mean LTL (T/S ratio)	Age- and sex-adjusted		Multivariate-adjusted[a]	
			β (SE)	*P*-value	β (SE)	*P*-value
Categorical						
Below average (ref)	47.5 ± 13.9	0.95 ± 0.22	–	–	–	–
Average	40.3 ± 16.0	0.99 ± 0.23	0.010 (0.012)	0.419	0.009 (0.012)	0.450
Above average	27.2 ± 11.9	1.08 ± 0.23	0.038 (0.017)	0.021	0.034 (0.016)	0.042
P for trend				0.028		0.051
Continuous						
Composite CVH score			0.008 (0.004)	0.057	0.007 (0.004)	0.107
Behavior factor score			0.004 (0.005)	0.417	0.003 (0.005)	0.637
Health factor score			0.011 (0.006)	0.041	0.013 (0.006)	0.032

CVH cardiovascular health

[a]Adjust for age, sex, education level, marital status, processed meat consumption, alcohol consumption, and study site

Table 5

Sex-specific association between ideal cardiovascular health and LTL among SHFS participants

Ideal cardiovascular health	Mean LTL (T/S ratio)	Age-adjusted		Multivariate-adjusted[a]	
		β (SE)	*P*-value	β (SE)	*P*-value
Men					
Below average (ref)	0.95 ± 0.22	–	–	–	–
Average	0.98 ± 0.23	0.000 (0.019)	0.994	−0.001 (0.019)	0.943
Above average	1.07 ± 0.23	0.038 (0.023)	0.129	0.032 (0.024)	0.280
P for trend			0.201		0.371
Women					
Below average (ref)	0.95 ± 0.23	–	–	–	–
Average	1.00 ± 0.24	0.017 (0.015)	0.252	0.017 (0.015)	0.255
Above average	1.08 ± 0.24	0.042 (0.020)	0.033	0.039 (0.019)	0.044
P for trend			0.034		0.045

[a] Adjust for age, education level, marital status, processed meat consumption, alcohol consumption, and study site