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Original Research Article

Inverse Association Between Adiposity and Telomere Length: The Fels Longitudinal Study

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Objectives: To assess the relationship between telomere length and adiposity, using dual-energy X-ray absorptiometry (DXA) and magnetic resonance imaging (MRI), in addition to conventional anthropometric proxies including body mass index (BMI) and cardiovascular disease risk factors.

Methods: A cross-sectional sample of 309 non-Hispanic white participants in the Fels Longitudinal Study aged 8 to 80 yr (52% female) was included. Average telomere length was measured by quantitative PCR.

Results: Telomere length was negatively correlated with age ($r = -0.32$, $P < 0.0001$) and had numerous significant correlations with established cardiovascular disease risk factors including waist circumference ($r = -0.33$), apolipoprotein B ($r = -0.26$), systolic blood pressure ($r = -0.28$), and fasting serum glucose ($r = -0.15$); all $P < 0.0025$. In backward selection linear regression models of telomere length, adiposity measures were consistently retained in the best models; BMI, waist circumference, hip circumference, total body fat, and visceral adipose tissue volume were all inversely associated with telomere length at the nominal $P < 0.05$ level or lower, independent of age, sex, systolic blood pressure, and fasting serum lipid, lipoprotein, and glucose concentrations. The negative association of BMI with telomere length was stronger among younger than older participants (P for interaction, 0.03).

Conclusions: Individuals with higher total and abdominal adiposity have lower telomere length, a marker of cellular senescence, suggesting obesity may hasten the aging process. Longitudinal studies are required to establish the causal association of early life adiposity with biological aging. Am. J. Hum. Biol. 23:100–106, 2011.

Telomeres are noncoding repeat sequences at the ends of chromosomes [5′-$(TTAGGG)_n$−3′] that function to stabilize the chromosome during mitosis, prevent aberrant recombination, and protect the chromosomes from end-degrading enzymes (Moyzis et al., 1988). In somatic cells, telomere repeats are lost at each cell division due to the inability of DNA polymerase to fully replicate chromosome ends (Levy et al., 1992; Olovnikov, 1973), leading to declines in telomere length with age. When telomere length reaches a critically short length in one or more chromosomes (the "Hayflick limit"), the cell is signaled to arrest replication and becomes senescent, with eventual apoptosis (Di Leonardo et al., 1994). Thus, telomere attrition is a fundamental aspect of senescence at the cellular level.

Telomere length varies greatly between individuals at birth, partially reflecting their inherited genetic potential related to replicative senescence (Andrew et al., 2006; Njajou et al., 2007; Okuda et al., 2002). The telomere attrition is also dependent on aging-related exposure to physiological and pathophysiological environments (Aviv, 2008; Epel, 2009). Oxidative stress and inflammation are major contributors to aging and aging related chronic diseases such as cardiovascular disease, and also play important roles in accelerated telomere attrition (Herbert et al., 2008; Minamino et al., 2009). Thus, the key premise of telomere length and attrition as a biomarker of human aging and related disease is that they reflect the cumulative burden of oxidative stress and inflammation occurring over the life course.

At the epidemiologic level, telomere length and attrition may be a useful biomarker to examine aging related process and diseases. Individuals with shorter leukocyte telomere length tend to have greater incidence of all-cause (Cawthon et al., 2003) and cardiovascular disease-specific mortality (Benetos et al., 2001; Jeanclos et al., 2000) and greater risk of age-related diseases including atherosclerosis (O'Donnell et al., 2008; Samani et al., 2001), coronary artery disease (Brouilette et al., 2003, 2007, 2008; Fitzpatrick et al., 2007), dementia (Martin-Ruiz et al., 2006; von Zglinicki et al., 2000), and certain cancers (McGrath et al., 2007; Risques et al., 2007; Wu et al., 2003). Given the role of adiposity, particularly abdominal adiposity, in the development of insulin resistance and chronic diseases (Banerji et al., 1997; Despres and Lemieux 2006; Festa et al., 2000), the documented changes in adiposity level over the life-course (Cameron and Demerath, 2002; Jorgensen et al., 1997) and the relationship of declines in muscle mass with senescence and frailty (Miller and Wolfe, 2008), individuals with greater total and abdominal adiposity and lower lean body mass would be expected to exhibit shorter telomeres (Kim et al., 2009). However, no published studies to date have focused on the role of total body and abdominal adiposity in telomere attrition; they have relied almost exclusively on BMI or other indirect anthropometric measures.

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The aim of this study was to test the cross-sectional association of telomere length with both total and abdominal body composition measures in healthy adults and children. Because the relationship of adiposity to health changes with age, we secondarily hypothesized that these associations would differ between younger and older individuals.

METHODS

Sample

The Fels Longitudinal Study is a study of normative growth and aging in approximately 1,000 healthy children and adults in the greater Dayton, Ohio area (Roche, 1992). This cross-sectional analysis focused on an initial subset of 345 subjects aged 8 to 90 yr (including 66 children, aged ≤18 yr), who visited the center during 2002–2004 and who were randomly selected to participate in a pilot study examining the association of telomere length with cardiovascular disease risk factors (including lipids, lipoproteins, blood pressure, physical activity level, and body composition). There were no significant differences between this subset and the entire cohort in body mass index (BMI), waist circumference, or other body composition measures.

Measurements

Anthropometrics included weight, stature, and waist and hip circumferences using standard protocols and methods (Lohman et al., 1988). Total body fat and fat-free mass were measured using dual energy X-ray absorptiometry (DXA) from a Hologic QDR 4500 Elite densitometer (Hologic, Bedford, MA). In a subset of 177 subjects, multiple image magnetic resonance imaging (MRI) of the abdomen was conducted to assess total visceral and abdominal subcutaneous adipose tissue volumes (VAT and SAT, respectively), as previously described (Demerath et al., 2007). The group with MRI data were younger, had lower BMI, lower telomere length, and lower waist circumference than those without MRI data. Triplicate measurements of systolic blood pressure (SBP) and fifth phase diastolic blood pressure (DBP) were taken when the patient was seated and at rest. Pulse pressure was calculated as the difference between SBP and DBP. Fasting plasma concentrations of triglycerides, total cholesterol, high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) were measured following standard protocols. The levels of apolipoprotein B levels in plasma were determined by immunoturbidimetric assay (Behring-Nephelometer-100, Medical Research Laboratories International, Inc., Cincinnati, OH). Homeostasis model assessment insulin resistance (HOMA-IR) index was calculated by the formula: HOMA-index = fasting serum blood glucose (mg/dl) × immunoreactive insulin (μU/ml)/405 (Matthews et al., 1985).

Obesity was defined as age and sex matched BMI at or above the 95th percentile in children (aged ≤18 yr) and BMI at or above 30 in adults. Physical activity levels were self-reported using the Baecke Habitual Physical Activity questionnaire (Baecke et al., 1982). Cigarette smoking (coded as current vs. former/never) and alcohol consumption (coded as current vs. former/never) were also assessed by self-reported questionnaire. Current alcohol consumption was defined as 12 oz. beer, 4 oz. wine, or 1 oz. hard liquor once or more weekly. College graduates among adults were those who reported completing a college or 4-yr technical school degree or beyond.

Telomere length

Telomere length was measured using DNA extracted from frozen (−80°C) buffycoat samples collected for that purpose and stored for less than 1 yr. Even though there exists great interindividual variation in telomere length at birth, literature suggests that telomere length attrition is less tissue-specific and the measurement of telomere length in peripheral blood leukocytes may accurately reflect systemic telomere length and aging (Okuda et al., 2002; Proctor and Kirkwood, 2002; Takubo et al., 2002). DNA sample integrity was evaluated by gel electrophoresis; samples that suggested DNA degradation ($N = 10$) were excluded from the study. Using a real-time quantitative polymerase chain reaction (qPCR) method, as described by Cawthon (2002), concentrations of telomere repeat copy number (T) and single-copy gene (*36B4*, acidic ribosomal phosphoprotein P0) copy number (S) were measured. Three replicate reactions were conducted for each sample and the mean T and S copy number was determined. We then standardized individual T and S copy numbers to a single reference DNA sample (pooled from all samples in the study) and then normalized T to S by taking the ratio (T/S ratio) for each sample. This procedure was done twice (two complete experiments), approximately one week apart, and the mean of the two T/S ratios was used for the analysis. The T/S ratio indicates the average telomere length in peripheral leukocytes and a lower T/S ratio suggests shorter telomere length. Of the 335 samples run, 15 samples did not amplify and 11 samples had outlying values for one of the duplicate measures (T/S ratio <0.02 or >2.0), leaving a final sample of 309 for analysis. The qPCR method has been validated against the more common Southern blot method for assessing terminal restriction fragment length (Cawthon, 2002; Cawthon et al., 2003). In this study, the intraclass correlation between the two repeated measures was 0.90 ($P < 0.0001$) and the coefficient of variation (CV) was 10.1%.

Statistical analysis

Raw and age-adjusted (partial) Pearson correlation coefficients were calculated between T/S ratio and adiposity and cardiovascular disease risk factors for continuous variables, and analysis of variance (ANOVA) analysis was used to examine differences between educational status, tobacco use, and alcohol use groups. Backward multiple linear regression analysis was used to examine the association of body composition measures (BMI, waist circumference, hip circumference, waist-hip ratio, total body fat, fat free mass, VAT, and SAT) with T/S ratio. All initial models for backward regression modeling included an adiposity variable (e.g., BMI), age and all factors identified in the bivariate correlation analysis as having significant association with T/S ratio (e.g., total cholesterol/HDL-C ratio). An interaction term examining effect modification by age was also tested in each model (adiposity × age group), where age group was defined as <30 yr, 30–60 yr, or >60 yr. The best model for each adiposity measure was chosen by maximizing R^2 while minimizing Mallows' $C(P)$ statistic as a measure of the goodness of fit for a selected

TABLE 1. Adiposity and cardiovascular disease risk factor levels, and their associations with T/S ratio

Variable	*N*	Mean	SD	Range	Pearson *r*, unadjusted	Pearson *r*, age-adj.
Age (yr)	309	39.7	19.8	18.0–80.0	-0.319^{***}	–
Weight (kg)	309	73.5	20.3	22.0–142.0	-0.271^{***}	-0.185^{*}
Height (cm)	309	169.2	12.5	122.0–198.0	−0.101	−0.053
BMI (kg/m^2)	309	26.4	5.1	12.0–46.0	-0.315^{***}	-0.227^{***}
BMI percentile[a]	52	50.4	31.4	0.1–99.5	−0.213	–
Total body fat (kg)	294	20.7	9.9	3.7–54.2	-0.262^{***}	-0.155^{*}
Fat free mass (kg)	294	51.9	13.1	18.5–86.6	-0.160^{*}	−0.105
Waist circumference (cm)	309	91.2	16.4	53.4–139.5	-0.333^{***}	-0.238^{**}
Hip circumference (cm)	309	102.2	12.6	62.7–136.9	-0.297^{***}	-0.191^{**}
Waist to hip ratio	309	0.9	0.1	0.7–1.2	-0.255^{***}	-0.168^{**}
VAT (l)	177	2.3	2.0	0.1–10.5	-0.228^{**}	-0.164^{*}
SAT (l)	177	4.44	2.9	0.4–15.8	-0.238^{**}	-0.209^{**}
Total cholesterol (mg/dl)	300	187.6	36.8	110.0–333.0	-0.201^{**}	−0.097
HDL-C (mg/dl)	300	51.3	13.5	27.0–107.0	0.074	0.123^{*}
Total cholesterol/HDL-C ratio	300	3.9	1.2	1.8–7.9	-0.221^{**}	-0.178^{**}
Apolipoprotein B (mg/dl)	300	101.2	25.3	42.0–252.0	-0.262^{**}	-0.190^{**}
Log triglycerides (mg/dl)	309	4.75	0.6	2.9–6.9	-0.224^{***}	-0.162^{**}
SBP (mm Hg)	306	116.3	18.0	74.0–200.0	-0.283^{**}	−0.143
DBP (mm Hg)	304	71.1	11.1	37.0–118.0	-0.160^{**}	−0.059
Pulse pressure (mm Hg)	304	45.4	13.6	20.0–104.0	-0.242^{***}	−0.113
Log insulin (μIU/ml)	299	1.94	0.7	0.1–3.8	−0.027	0.004
Serum glucose (mg/dl)	309	92.2	16.7	59.0–287.0	-0.148^{**}	−0.034
Current alcohol use (yes, %)[b]	303	20.1%	–	–	$\beta = 0.01$	$\beta = 0.01$
Current tobacco use (yes, %)[b]	284	48.9%	–	–	$\beta = -0.05$	$\beta = -0.06$
College/university degree (yes, %, among adults)[b]	258	49.2%	–	–	$\beta = 0.03$	$\beta = 0.04$
HOMA-IR index	299	2.1	2.0	0.2–14.0	−0.061	−0.008
Sports activity index	307	2.4	0.7	1.0–4.5	0.111	−0.008
T/*S* ratio (relative telomere length)	309	0.95	0.3	0.26–1.89	–	–

$^{*}P < 0.05$,
$^{**}P < 0.0025$,
$^{***}P < 0.0001$.
[a]Percentile based on CDC US 2000 growth charts, age ≤ 18 yr ($N = 52$).
[b]For categorical variables (current alcohol use, current tobacco use, college/university degree), the estimate of their unadjusted and age-adjusted effects on *T*/*S* ratio are from ANOVA (standardized β coefficient), where the referent is the group stating "no."
BMI, body mass index; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue; HDL-C, high density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; HOMA-IR index, Homeostasis model assessment insulin resistance index.

model (which should be less than the number of parameters in the model) (Kleinbaum et al., 1988). All variables with P value less than 0.10 were retained in the best model. Only significant variables from the best model for each individual adiposity variable were presented as "final model estimates."

Given the multiple tests (seven models with different body composition measures), we used a Bonferonni correction of 0.05/7 to obtain critical $\alpha = 0.007$. At $\alpha = 0.007$, our sample size of ∼ 300 individuals provided statistical power >80% to detect a bivariate correlation as low as $r = 0.20$, and an R^2 as low as 0.04 attributable to an independent variable (i.e., BMI), adjusting for an additional four covariates which together explain 10% of the trait variance in multiple linear regression models (Cohen, 1988). All analyses were performed using SAS, version 9.1.3.

Review of the literature

Finally, we conducted a three-stage review of the literature. The search included: (1) PubMed and Medline electronic databases using the search terms "telomere length" with "obesity," "adiposity," "overweight," "BMI," or "cardiovascular disease" for dates spanning from 1950 to December 2008; (2) articles obtained from personal archives and reference lists; and (3) all relevant references from retrieved papers. We examined these documents to find estimates of the association between telomere length and any adiposity traits in humans. Of the 79 articles originally retrieved, 24 studies reported testing the association of telomere length and adiposity, and 13 of these had >100 subjects, which we set as conservative minimum thresholds for sample size and the age range (∼ 20 yr) to have sufficient statistical power to detect the association in question as previously suggested (Aviv et al., 2006; Nordfjall et al., 2008).

RESULTS

Characteristics of the study sample (means and standard deviations for study variables) and correlations between *T*/*S* ratio and other study variables are presented in Table 1. As expected, chronological age was inversely correlated with *T*/*S* ratio ($r = -0.319$, $P < 0.0001$). However, mean *T*/*S* ratio did not differ by sex (0.95 ± 0.30 in males and 0.95 ± 0.29 in females; $P = 0.78$), and so all subsequent analyses were conducted with sexes combined. Once adjusted for the effect of age, only body composition and lipid, lipoprotein, and glucose concentrations remained significantly associated with *T*/*S* ratio. The strongest of these was waist circumference (unadjusted $r = -0.333$, $P < 0.0001$; age-adjusted $r = -0.238$, $P < 0.0001$). The total cholesterol/HDL-C ratio, log of triglycerides and apolipoprotein B were also negatively correlated with telomere lengths (all $P < 0.01$ age-adjusted). There was no association between *T*/*S* ratio and fat free mass, current alcohol or tobacco use, educational attainment, or

TABLE 2. Backwards selection linear regression analysis of T/S ratio on individual adiposity measures: Final model estimates[a]

	β coefficient (SE)	*P*
BMI (model $R^2 = 0.176$)		
Intercept	1.765 (0.151)	<0.0001
Chronological age	−0.010 (0.004)	0.004
BMI	−0.021 (0.006)	0.001
Age × BMI	0.0003 (0.0001)	0.040
Apolipoprotein B	−0.029 (0.015)	0.011
Waist circumference (model $R^2 = 0.170$)		
Intercept	1.634 (0.105)	<0.0001
Chronological age	−0.003 (0.0009)	0.001
Waist circumference	−0.004 (0.001)	0.001
Apolipoprotein B	−0.002 (0.0007)	0.004
Glucose group (≥100 vs. <100)	−0.090 (0.044)	0.041
Hip circumference (model $R^2 = 0.155$)		
Intercept	1.666 (0.140)	<0.0001
Chronological age	−0.003 (0.0009)	0.001
Hip circumference	−0.004 (0.001)	0.007
Apolipoprotein B	−0.002 (0.0007)	0.004
Total body fat (model $R^2 = 0.145$)		
Intercept	1.356 (0.071)	<0.0001
Chronological age	−0.003 (0.0009)	0.0002
Total body fat	−0.004 (0.002)	0.045
Apolipoprotein B	−0.002 (0.0007)	0.009
Waist to hip ratio (model $R^2 = 0.156$)		
Intercept	1.827 (0.190)	<0.0001
Chronological age	−0.004 (0.0009)	<0.0001
Waist to hip ratio	−0.592 (0.228)	0.098
Apolipoprotein B	−0.002 (0.0007)	0.004
Glucose group (≥100 vs. <100)	−0.096 (0.046)	0.036
VAT (model $R^2 = 0.115$)		
Intercept	1.385 (0.193)	<0.0001
Log VAT	−0.059 (0.025)	0.021
Log triglycerides	−0.088 (0.041)	0.033
SAT (model $R^2 = 0.085$)		
Intercept	1.252 (0.082)	<0.0001
Chronological age	−0.002 (0.001)	0.048
SAT	−0.0015 (0.0008)	0.055
Total cholesterol/HDL-C ratio	−0.038 (0.018)	0.040

[a]The final estimates (β coefficient and standard error) of significant variables are from backward selection regression models including initially adiposity variables, age, interaction between adiposity variable and age, total cholesterol/HDL-C ratio, HDL-C, log transformed triglycerides, apolipoprotein B, SBP, and a categorized variable for glucose level.
BMI, body mass index; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue; HDL-C, high density lipoprotein cholesterol.

sports activity score either before, or after, adjusting for age.

Multivariate models identifying significant independent predictors of *T*/*S* ratio are shown in Table 2. There was no significant relationship between fat free mass and *T*/*S* ratio in the multivariate model (data not shown). All adiposity measures other than waist to hip ratio and SAT were significantly negatively associated with *T*/*S* ratio at the nominal $P < 0.05$ level, independent of age and apolipoprotein B and glucose concentrations. Using the more stringent $P < 0.007$ level considering multiple comparisons, only BMI, waist circumference, and hip circumference were significant. An interaction term for age × BMI was nominally significant ($P = 0.04$), and a similar trend toward age interaction was seen for age × waist circumference ($P = 0.08$, not shown). This interaction is illustrated graphically in Figure 1, showing that the relationship between *T*/*S* ratio and adiposity was stronger in younger than older participants. In the youngest age group ($n = 114$, age < 30 yr), obese subjects had significantly lower *T*/*S* ratio than normal weight subjects ($P = 0.005$), whereas in the oldest age group ($n = 61$, age > 60 yr), *T*/*S* ratio did not differ by BMI status ($P = 0.66$).

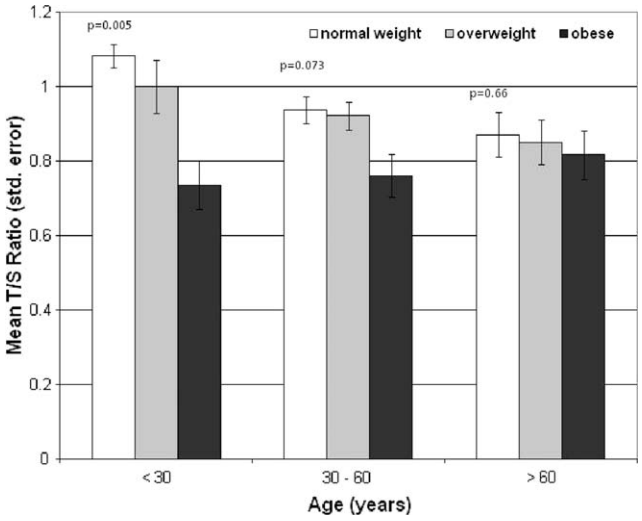

Fig. 1. Telomere length by age and weight status: interaction effect. Interaction between weight status and age on *T*/*S* ratio ($P = 0.04$). *P* values refer to post hoc Tukey-Kramer tests comparing least square means between weight status groups within age group.

DISCUSSION

This study is the first to examine the association of telomere length with total body adiposity and visceral and subcutaneous abdominal adipose tissue. Significant inverse associations were found between telomere length and BMI, waist circumference, and hip circumference ($P < 0.007$) in this sample of healthy children and adults, independent of sex, age, fasting glucose, insulin, lipid and lipoprotein concentrations, habitual physical activity, smoking status, and other cardiometabolic risk factors. A similar inverse relationship ($P < 0.05$) for total and visceral adiposity (total body fat and VAT) was found while there was no significant relationship between lean mass and telomere length. We found that not only BMI or waist circumference measured using anthropometry, but also adipose tissue quantity measured using more sophisticated body composition techniques such as DXA and MRI was associated with shorter telomere length. Even considering the limitation of DXA measurement such as weight limitation and the small number of participants ($n = 177$) with MRI data in the present study, it is likely that adiposity, but not lean mass, is adversely related to telomere length and attrition.

We also found that an atherogenic lipid and lipoprotein pattern (i.e., higher total cholesterol/HDL-C ratio and apolipoprotein B concentration) was independently negatively associated with telomere length. This supports previous findings regarding reduced telomere length in atherosclerosis (O'Donnell et al., 2008; Okuda et al., 2000; Samani et al., 2001). Higher levels of apolipoprotein B are linked to atherosclerosis and increased oxidative stress (Di Angelantonio et al., 2009; Pan et al., 2004). We did not find significant effects of selected behavioral factors on telomere length as has been reported in some studies (e.g., cigarette smoking (Valdes et al., 2005), physical activity (Cherkas et al., 2008), and socioeconomic status (Cherkas et al., 2006)).

Accumulated exposure to oxidative stress and inflammatory process have been linked to accelerated telomere

attrition and "stress-induced premature senescence" (Herbert et al., 2008; Houben et al., 2008; Minamino et al., 2009; Toussaint et al., 2000). Obesity is regarded as a crucial factor in the regulation of adipose tissue aging and further metabolic outcomes such as increased proinflammatory cytokines, insulin resistance, and further diabetes and cardiovascular disease (Despres and Lemieux, 2006; Minamino et al., 2009; Trayhurn and Wood 2004). For example, researchers found that the p53 pathway in adipose tissue, which is key in the aging process of adipose tissue and increased inflammation, may play an important role in relation to obesity and obesity-mediated aging (Minamino et al., 2009). In the same vein, a recent *in vitro* study showed that telomere length measured from subcutaneous adipocytes in formerly obese patients was significantly lower than in never-obese patients (Moreno-Navarrete et al., 2010). This relationship may be partially responsible for the observed inverse association with telomere length, as oxidative stress is thought to accelerate telomere attrition (Houben et al., 2008), but the deleterious effect of adiposity on telomere length could be mediated by multiple different mechanisms (Epel, 2009).

As noted by Nordfjäll et al. (2008), the literature on the relationship of telomere length to adiposity is mixed. Including our study, 5 of 13 studies reviewed reported significant negative relationships between adiposity measures and telomere length (Fitzpatrick et al., 2007; Nordfjall et al., 2008; O'Donnell et al., 2008; Valdes et al., 2005), while 8 did not (Bekaert et al., 2007; Benetos et al., 2001; Bischoff et al., 2006; Brouilette et al., 2007, 2008; McGrath et al., 2007; Nettleton et al., 2008; Risques et al., 2007; Valdes et al., 2005). Our review did not find evidence that inconsistent results in literature are due to measurement methods (qPCR vs. southern blot) of telomere length or sample characteristics in the study.

One of the negative studies (Epel et al., 2006), however, did find a significant inverse association between adiposity and telomerase activity, a regulator of telomere length. Furthermore, among smaller studies not included in our review, there were suggestive findings of a negative association of serial BMI changes with telomere length in young adults in the Bogalusa Heart Study (Gardner et al., 2005) and with BMI in a study of Italian adults (Zannolli et al., 2008). No clear differences in sample size, method of telomere length assessment, or proportion of subjects that were male or female emerged between studies that did, or did not, report significant relationships between telomere length and adiposity. We did note that no case–control study found significant relationships, which may reflect the problem of detecting low to moderate level associations typically seen between telomere length and other risk factors using a categorical approach (obese/not obese; cancer case/control). This may also suggest insufficient statistical power resulting from the reduced variation in adiposity and telomere length, observed in matched case–control designs.

The structure and function of adipose tissue changes with age (Wehrli et al., 2007; Zafon, 2007), which may reflect changes in the genetic control of different adipocyte lineages across the lifespan (Gesta et al., 2007). It would be expected, therefore, that the relationships between adiposity and health will also change with age. In this regard, the association between BMI and telomere length differed in younger versus older individuals in the present study, as was also found in the Cardiovascular Health Study (Fitzpatrick et al., 2007). Specifically, we found that the mean telomere length of obese subjects <30 yr of age was similar to that subjects >60 yr of age. Accumulated damages due to inflammatory and oxidative stress resulting from obesity or other unfavorable risk factors, such as smoking, over the life course may be greater in the elderly. Given increased prevalence of childhood obesity in recent years (Ogden et al., 2008), the elderly included in our analysis likely had lower lifetime exposure to obesity and its related risk factors. While it has been suggested that inclusion of a wide age range in studies of telomere dysfunction is helpful (Aviv, 2008), a cross sectional study with participants having wide age range, like ours, is subject to bias by including survivors in the elderly. It is possible that older healthy individuals in our study are different from individuals who are likely to suffer from chronic diseases and environmental hardships at younger ages. In addition, these older "survivors" with longer telomeres than expected in the general population may have had lower exposure to aging-associated chronic disease risks. This bias would result in diminished association between telomere length and age.

In a recent review of the epidemiology of telomeres, Aviv (2008) made the important point that the claims and counterclaims about associations between telomere length and indices of aging and longevity are often based on cross-sectional findings based on relatively small samples and therefore without sufficient statistical power to assess these associations (Aviv, 2008). For that reason, we limited our formal review of the literature to those with >100 subjects and reasonable age range studied and examined the presence or absence of significant telomere length-adiposity associations with regard to the number of subjects in each study. Our study was powered to detect linear correlation as low as $r = 0.18$–0.22, below which we would argue associations are of relatively low clinical significance. A second cautionary note raised in that review concerned the use of the qPCR method. It is not clear that the qPCR method is less reliable than the Southern blot method, but the relatively high CV% (10%) in the present study, while similar to that found by others (e.g., Risques et al., 2007) (interassay CV = 7%), does caution that future studies of telomere length must design their studies accounting for the expected reliability of the method used, particularly given the moderate level of correlation with other risk factors ($r < 0.3$) reported thus far (Nordfjall et al., 2008). Our study finding suggests that the deleterious consequences of obesity on mechanisms of aging and telomere dysfunction may be particularly important in children and young adults.

In conclusion, telomere length was lower in adults who had greater total and abdominal adiposity, independent of other established cardiometabolic risk factors. This finding, combined with the independent effects of apolipoprotein B, which is firmly associated with systemic inflammation and atherosclerosis, supports a role of oxidative stress and inflammation in telomere attrition. Longitudinal studies may clarify the temporal order of this relationship and how adiposity, chronic stress, insulin resistance, diet, systemic inflammation, and adipose-tissue derived hormones interplay in the premature attrition of telomeres, particularly in the young.

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