Ultra-processed food consumption and the risk of short telomeres in an elderly population of the Seguimiento Universidad de Navarra (SUN) Project

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ABSTRACT

Background: Telomere length (TL) is a marker of biological age that may be affected by dietary factors through oxidation and inflammation mechanisms. In addition, ultra-processed food (UPF) consumption has increased worldwide and it has been associated with the risk of developing several diseases.

Objectives: We aimed to evaluate the association between UPF consumption and the risk of having short telomeres in an elderly population of the Seguimiento Universidad de Navarra (SUN) Project.

Methods: This is a cross-sectional study of 886 participants (645 men and 241 women) aged 57–91 y recruited from the SUN Project (Spain, 1999–2018). TL was measured from saliva samples by real-time qPCR at baseline and UPF consumption was collected using a validated 136-item FFQ and classified according to the NOVA system. We evaluated the association between consumption of energy-adjusted UPF categorized into quartiles (low, medium-low, medium-high, and high consumption) and the risk of having short telomeres ($<20^{th}$ percentile) using logistic regression models.

Results: Those participants with the highest UPF consumption had almost twice the odds of having short telomeres compared with those with the lowest consumption (adjusted OR: 1.82; 95% CI: 1.05, 3.22; *P*-trend = 0.03).

Conclusions: A higher consumption of UPF (>3 servings/d) was associated with higher risk of having shorter telomeres in an elderly Spanish population of the SUN Project. This trial was registered at clinicaltrials.gov as NCT02669602. *Am J Clin Nutr* 2020;111:1259–1266.

Keywords: telomere length, ultra-processed food, SUN cohort, cross-sectional studies, diet

Introduction

Telomere length (TL) could be modified by both lifestyle (food intake, physical activity, smoking) (1) and genetic factors. In view of this, several studies have focused on studying the impact of diet on TL. Telomeres [from the Greek *telos* (end) and *meros* (part)] (2) are the noncoding sections located at the end of eukaryote chromosomes (3). Telomeres consist of tandem TTAGGG repeats with a length of 4–25 kb, associated with specialized proteins and involved in the protection of DNA through different mechanisms, preserving chromosome stability and integrity (3). TL gets shorter throughout the life span with each cell division losing thousands of bases (30–200 nucleotides/division) (3). Thus, telomeres are considered markers of biological age (3). Oxidative stress and inflammation are the mechanisms associated with telomere shortening. Specifically, telomeres that are rich in guanines—prone to oxidation to 8-oxo-2′-deoxyguanosine—are likely to be affected by those mechanisms (4).

Regarding dietary patterns, globally fresh-food consumption is decreasing together whereas ultra-processed food (UPF) consumption is increasing (5). UPFs are industrial formulations of food-derived substances (oils, fats, sugars, starch, protein isolates) that contain little or no whole food and often

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Supplemental Tables 1 and 2 and Supplemental Figure 1 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/ajcn/.

Data described in the article, code book, and analytic code will be made available upon request pending application and approval.

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Abbreviations used: CVD, cardiovascular disease; SSB, sugar-sweetened beverage; SUN, Seguimiento Universidad de Navarra; TL, telomere length; UPF, ultra-processed food.

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include flavorings, colorings, emulsifiers, and other cosmetic additives. Their low nutritional quality, high energy density (6), and unique nonnutritional attributes, assembled into ready-to-consume hyper-palatable foods, promote overconsumption (7).

UPFs have been associated with several diseases such as hypertension (8), obesity (9), metabolic syndrome (10, 11), depression (12), type 2 diabetes (13), and cancer (13). These age-related pathologies are also related to oxidative stress, inflammation, and cellular aging which could modify TL (3). However, few studies have described the effects of UPF consumption on TL (14–21). These studies found associations of sugar-sweetened beverages (SSBs) (22), alcohol consumption, processed meats, and other foods rich in SFAs and sugar with shorter telomeres (23). However, several others did not find an association between SSBs and TL (14, 17, 18, 24).

To our knowledge there has been no study that has evaluated the association of UPF consumption with TL using the NOVA classification. For this reason, our objective was to assess the relation between UPF consumption and the risk of shorter telomeres in an elderly population of the Seguimiento Universidad de Navarra (SUN) cohort.

Methods

This is a cross-sectional study (NCT02669602) with 886 participants. This work was conducted within the SUN Project, which is a dynamic, permanently open prospective cohort of graduates, ≥20 y old, from the University of Navarra and other Spanish universities (25). This cohort study began recruitment in December 1999 and is permanently open (25). The design, methods, and cohort profile have been published in detail elsewhere (25). Data are collected by self-reported mailed questionnaires every 2 y (25).

In May 2008, 1921 elderly participants (>55 y old at baseline questionnaire) of the SUN Project were invited to participate in a genetic study (26). Participants received a kit designed to collect saliva (27); 1085 accepted to participate and 986 returned saliva samples (26), although only 953 samples could be correctly analyzed. In 67 participants, total energy intake was reported outside Willett's predefined values (<800 or >4000 kcal/d for men and <500 or >3500 kcal/d for women) and they were excluded (28). Data from 886 participants were available for the analyses. The mean age of the population was 67.7 y old and 72.8% were male. **Supplemental Figure 1** shows a flowchart of the study participants.

Dietary assessment: UPF consumption

A self-administered 136-item semiquantitative FFQ validated in Spain (29) was used to assess dietary intake. Nine categories were established for consumption frequencies (ranging from never/almost never to >6 servings/d). The FFQ included a typical portion size for each item. The estimated daily food consumption was calculated by multiplying the portion size in grams by the consumption frequency for each item.

We classified all FFQ items according to NOVA, a classification system based on the nature, extent, and purpose of industrial food processing (6). Unprocessed/minimally processed foods are parts of animals or plants (fruits, vegetables, eggs, milk, meat, etc.) which are fresh or processed in ways that do not add substances such as salt, sugar, oils, or fats, and infrequently contain additives (6). Substances extracted from unprocessed foods or nature are processed culinary ingredients (salt, oil, sugar, etc.) (6). Processed foods are simple products manufactured by adding processed culinary ingredients to unprocessed foods (i.e., canned fruit or vegetables, salted nuts, cured and smoked meats, cheese, etc.) (6). UPFs are industrial formulations of food-derived substances (oils, fats, sugars, starch, protein isolates) that contain little or no whole food and often include flavorings, colorings, emulsifiers, and other cosmetic additives (e.g., carbonated drinks; sweet and savory packaged snacks; ice-cream, chocolate, and candies (confectionery); mass-produced packaged bread and buns; margarines and spreads; cookies, pastries, cakes, and cake mixes; breakfast "cereals," "cereal" and "energy" bars; "energy drinks"; milk drinks, "fruit" yogurts, and "fruit" drinks; cocoa drinks; meat and chicken extracts and "instant" sauces; infant formulas, follow-on milks, and other baby products; "health" and "slimming" products such as powdered or "fortified" meal and dish substitutes; and many ready-to-heat products including preprepared pies and pasta and pizza dishes; poultry and fish "nuggets" and "sticks," sausages, burgers, hot dogs, and other reconstituted meat products; and powdered and packaged "instant" soups, noodles, and desserts) (6). The sum of UPF items was estimated using the frequency of UPF consumption per person (servings/d). The sample was divided into quartiles according to energy-adjusted UPF consumption (**Table 1**). The study protocol was written in accordance with the principles of the Declaration of Helsinki and was approved by the University of Navarra institutional review board.

Outcome assessment: TL

The primary outcome was TL. Participants' saliva samples were collected with specialized kits (DNA Collection - Oragene OG-250 Saliva Kit) and DNA was extracted according to the manufacturer's instructions and stored at −80°C. TL was measured with the use of a monochrome multiplex real-time qPCR method described elsewhere (30). Briefly, this method measures telomere signals and single copy gene signals, in experimental DNA samples, in 1 set of reaction wells and in separate wells, respectively (30). These 2 parameters are compared to a reference DNA to express a ratio that is proportional to average TL (30). The master mix contained 10 ng genomic DNA, a QuantiTect CYBR Green PCR kit (Qiagen), telomere and albumin primers, and nuclease-free water to complete the final volume (10 μL). Telomere primers (telc and teg) and albumin primers (albu and albd) were combined (final concentration 900 nM each). The primer sequences were telg (5′-ACACTAAGGTTTGGGTTTGGGTTTGGGTTTGGGTT AGTGT-3′), telc (5′ TGTTAGGTATCCCTATCCCTATCCCTA TCCCTATCCCTAACA-3′), albu (5′ -CGGCGGCGGGCGG CGCGGGCTGGGCGGAAATGCTGCACAGAATCCTTG-3′), and albd (5′-GCCCGGCCCGCCGCGCCCGTCCCGCCGGA AAAGCATGGTCGCCTGTT-3′). All primers were from Sigma Aldrich and were purified by the manufacturer via HPLC.

The qPCR used was the CFX 384™ Real Time System (BioRad) with the following protocol: 15 min at 95°C for enzyme activation followed by 2 cycles of 95°C at 15 s and 49°C at 15 s, and 35 cycles of 15 s at 95°C, 10 s at 63°C, 15 s at 74°C (first

TABLE 1 Baseline characteristics of elderly subjects of the SUN study according to UPF consumption (1999–2014)[1]

Characteristics	Quartiles of energy-adjusted UPF consumption				
	Low (<2 servings/d) (n = 222)	Medium-low (2 to <2.5 servings/d) (n = 221)	Medium-high (2.5 to <3 servings/d) (n = 222)	High (≥3 servings/d) (n = 221)	P values (low vs. high quartiles)
Total UPF consumption, servings/d	1.1 ± 0.5	2.1 ± 0.2	2.8 ± 0.2	4.1 ± 1.1	<0.001
Short telomere risk (<20th percentile)	37 (16.5)	41 (18.5)	50 (22.7)	52 (23.5)	0.032
Age, y	68.3 ± 5.9	67.8 ± 6.5	67.0 ± 5.5	67.5 ± 6.5	0.151
Men	143 (64.4)	159 (71.9)	166 (74.8)	177 (80.1)	<0.001
Married	182 (82.0)	164 (74.0)	170 (76.5)	151 (68.4)	0.001
Baseline BMI, kg/m^2	25.7 ± 3.1	25.5 ± 3.1	26.1 ± 3.2	26.1 ± 3.2	0.064
Years at university	5.3 ± 2.0	5.4 ± 1.8	5.2 ± 1.7	5.4 ± 1.9	0.579
Educational level					
Graduate	174 (78.7)	175 (79.1)	181 (81.7)	172 (77.7)	0.755
Postgraduate	2 (0.6)	6 (2.8)	6 (2.7)	4 (1.9)	0.193
Doctorate	46 (20.7)	40 (18.1)	35 (15.6)	45 (20.3)	0.927
Family history of diabetes	35 (16.0)	42 (19.0)	52 (23.3)	39 (17.7)	0.590
Family history of cardiovascular disease	44 (19.8)	50 (22.6)	58 (26.0)	62 (28.2)	0.045
Cancer prevalence	22 (9.8)	22 (9.9)	19 (8.4)	17 (7.8)	0.433
Diabetes prevalence	9 (4.3)	25 (11.3)	25 (11.0)	22 (10.1)	0.014
Special diet at baseline	30 (13.5)	38 (17.1)	36 (16.5)	28 (12.7)	0.926
Smoking status					
Current	28 (12.5)	32 (14.6)	40 (17.9)	34 (15.4)	0.405
Former smoker	116 (52.3)	111 (50.1)	119 (53.5)	111 (50.5)	0.703
Lifelong smoking, packs/y	15.5 ± 18.2	13.8 ± 18.0	16.1 ± 19.9	14.2 ± 17.2	0.449
Physical activity, MET-h/wk	24.0 ± 19.1	22.0 ± 19.4	22.9 ± 20.2	21.3 ± 20.6	0.108
Computer use, h/d	1.4 ± 1.5	1.4 ± 1.5	1.5 ± 1.5	1.5 ± 1.6	0.524
Car driving, h/d	0.9 ± 1.0	0.9 ± 1.1	0.9 ± 0.7	0.9 ± 0.9	0.442
Television watching >3 h/d	19 (8.6)	15 (6.8)	24 (10.6)	29 (13.2)	0.152
Sedentarism, h/d	4.1 ± 2.6	3.9 ± 2.4	4.1 ± 1.9	4.2 ± 2.4	0.801
Sleeping/siesta, h/d	0.4 ± 0.9	0.4 ± 0.8	0.4 ± 0.6	0.4 ± 0.7	0.436
Hypercholesterolemia	96 (43.3)	94 (42.4)	100 (44.9)	77 (35.1)	0.088
Dyslipidemia prevalence	40 (18.1)	33 (14.9)	51 (23.0)	52 (23.6)	0.014
Total energy intake, kcal/d	2418.3 ± 571.8	2152.2 ± 601.8	2093.7 ± 662.8	2332.2 ± 710.4	0.147
Macronutrients, % energy					
Carbohydrate intake	45.0 ± 9.0	44.1 ± 7.9	43.0 ± 8.6	43.4 ± 8.0	0.026
Protein intake	18.5 ± 3.7	19.5 ± 3.7	19.1 ± 3.7	17.6 ± 3.8	0.011
Fat intake	33.3 ± 7.2	33.8 ± 6.4	34.7 ± 6.9	35.7 ± 6.2	<0.001
SFA	10.4 ± 3.5	11.1 ± 3.2	11.9 ± 3.6	12.7 ± 3.1	<0.001
MUFA	15.2 ± 4.4	14.9 ± 4.1	15.0 ± 3.8	15.3 ± 3.6	0.859
PUFA	4.9 ± 1.8	5.0 ± 1.6	5.2 ± 1.6	5.3 ± 1.6	0.011
Total dietary fiber intake, g/d	37.8 ± 16.8	31.2 ± 11.6	26.9 ± 11.4	27.6 ± 11.7	<0.001
Mineral intake					
Sodium intake, mg/d	3377.7 ± 1692.0	3356.9 ± 2023.4	3806.8 ± 2817.0	4972.5 ± 3498.4	<0.001
Potassium intake, mg/d	5742.1 ± 2064.6	4940.8 ± 1483.3	4528.5 ± 1679.4	4604.3 ± 1669.5	<0.001
Magnesium intake, mg/d	488.5 ± 142.4	429.7 ± 122.7	393.2 ± 133.0	408.3 ± 135.3	<0.001
Calcium intake, mg/d	1311.1 ± 568.4	1189.1 ± 538.9	1107.5 ± 492.8	1154.2 ± 528.9	0.001
Phosphorus intake, mg/d	2086.3 ± 577.5	1900.7 ± 559.1	1782.7 ± 560.5	1874.2 ± 612.4	<0.001
Caffeine intake, mg/d	32.4 ± 41.0	34.7 ± 37.1	33.5 ± 39.6	37.2 ± 37.2	0.161
Alcohol consumption, g/d	10.8 ± 15.1	8.5 ± 10.0	9.5 ± 11.6	10.7 ± 15.8	0.970
Olive oil intake, g/d	24.4 ± 21.4	17.6 ± 14.3	15.9 ± 13.5	14.3 ± 13.4	<0.001
Low-fat dairy consumption, servings/d	0.5 ± 1.0	0.5 ± 1.0	0.5 ± 0.9	0.5 ± 1.0	0.771
Whole-fat dairy consumption, servings/d	0.4 ± 1.0	0.3 ± 0.6	0.3 ± 0.6	0.3 ± 0.6	0.185
Dietary cholesterol intake, mg/d	383.6 ± 142.2	373.6 ± 127.1	379.1 ± 149.0	418.1 ± 148.3	0.008
Fruit consumption, servings/d	3.6 ± 2.6	2.8 ± 1.8	2.6 ± 2.4	2.3 ± 1.8	<0.001
Vegetable consumption, servings/d	3.5 ± 2.8	2.8 ± 1.5	2.4 ± 1.4	2.5 ± 1.5	<0.001
Sugar-sweetened beverage consumption, servings/d	0.05 ± 0.1	0.1 ± 0.2	0.1 ± 0.3	0.3 ± 0.5	<0.001
Fast-food consumption,[2] servings/d	0.05 ± 0.1	0.07 ± 0.1	0.08 ± 0.1	0.1 ± 0.2	<0.001
Processed meat consumption,[3] g/d	8.4 ± 10.9	11.6 ± 13.1	14.1 ± 16.0	18.8 ± 17.1	<0.001
Fried-food consumption, servings/d	0.6 ± 0.8	0.5 ± 0.6	0.6 ± 0.8	0.6 ± 0.7	0.243
Mediterranean dietary pattern[4] (0–9 points)	5.6 ± 1.5	5.2 ± 1.6	4.6 ± 1.8	4.3 ± 1.7	<0.001
Snacking	41 (18.7)	41 (18.5)	49 (22.2)	58 (26.1)	0.040

[1] Values are means ± SDs (for quantitative variables) or n (%) (for qualitative variables). P values were obtained using linear multivariable regression (for quantitative variables) and logistic regression (for qualitative variables) models adjusted for age and sex. Each variable was adjusted for age and sex, except these 2, through inverse probability weighting. MET, metabolic equivalent of tasks; SUN, Seguimiento Universidad de Navarra; UPF, ultra-processed food.

[2] Sum of hamburgers, sausages, and pizza.

[3] Sum of ham, sausages, chorizo, salami, mortadella, and hamburgers.

[4] Higher scores indicate greater adherence.

signal acquisition), and 15 s at 88°C (second signal acquisition). For each sample, we generated a melting curve from 45 to 95°C, ramped at 0.2°C/s. Three hundred and eighty-four-well plates were used and samples were run in triplicate for quality control. Moreover, a calibration curve of reference DNA samples (150–2.34 ng/mL in 2-fold dilutions; linearity agreement $R^2 > 0.99$) was included on each high-throughput plate.

Assessment of covariates

The baseline questionnaire of the SUN cohort gathers information on a wide array of characteristics previously validated including sociodemographic, lifestyle-related, anthropometric (such as BMI) (25), and clinical variables including age, sex, marital status, years at university, educational level, family history of diabetes or cardiovascular disease (CVD), smoking status, lifelong smoking, physical activity, hours of computer use, hours driving, special diets, television viewing, prevalence of cancer, diabetes, dyslipidemia and hypercholesterolemia, sedentary lifestyle, napping, and dietary cholesterol intake. Adherence to the Mediterranean dietary pattern was assessed using a well-known score (31). Intakes of total energy, macronutrients, fats, fiber, minerals (sodium, potassium, magnesium, calcium, and phosphorus), caffeine, and alcohol were calculated by multiplying the frequency of consumption of each food item by the nutrient composition of the specified portion sizes, then summing, using the FFQ (8). The FFQ was also used to assess the consumption of daily fruits, vegetables, SSBs, fast foods (sausages, hamburgers, and pizza), processed meat (sausages, hamburgers, and ham), fried foods, and snacks (8).

Statistical analyses

Descriptive statistics were used to analyze baseline characteristics among participants. We used inverse probability weighting to evaluate age- and sex-adjusted baseline characteristics of participants according to quartiles of UPF consumption (Table 1). Means ± SDs were used for continuous variables and percentages for categorical variables. UPF consumption was adjusted for energy intake through the residual methods (32) and subsequently categorized into quartiles: low consumption (first quartile: <2 serving/d), medium-low consumption (second quartile: 2 to <2.5 servings/d), medium-high consumption (third quartile: 2.5 to <3 servings/d), and high consumption (fourth quartile: ≥3 servings/d). *P* values were obtained using linear multivariable regression (for quantitative variables) and logistic regression (for qualitative variables) models adjusted for age and sex comparing the first quartile with the fourth quartile.

We calculated the contribution of each food group to the total consumption of UPF by dividing the amount of each food group in grams by the total grams of UPF consumption and multiplying by 100.

We defined short telomeres as a TL below the 20th percentile, as was previously reported (33–35). To assess the association between UPF consumption and the odds of having short telomeres, logistic regression models were fitted to estimate the OR and 95% CI considering the first quartile (low UPF consumption) as the reference category. We ran a crude model and 2 adjusted models: Model 1 adjusted for age and sex and Model 2 further adjusted for BMI (kg/m^2, continuous); smoking status (never, current, and former); lifelong smoking (pack-years of smoking, continuous); physical activity (metabolic equivalent of tasks in h/wk, continuous); television viewing (≥3 h/d, dichotomous); cancer, diabetes, and dyslipidemia prevalence (dichotomous); family history of diabetes and CVD (dichotomous); and educational level (years at university, continuous). A linear trend across the quartiles of UPF consumption was calculated by assigning the median value to each category and considering the variable as continuous.

In addition, we conducted subgroup analyses for the association between consumption of UPF and the odds of short telomeres by rerunning all the models under different a priori stratifications: sex, years at recruitment (only participants 75 y old or younger, and only participants >75 y old), BMI (only participants with BMI ≤ 25, and only participants with BMI > 25), and smoking status (only participants who were never smokers and only former and current smokers). The *P* value for interaction was calculated using the likelihood ratio test for each scenario.

Sensitivity analyses were conducted by rerunning the models with additional adjustments: using the 5th and 95th percentiles as limits for allowable total energy intake; and excluding participants with cancer, diabetes, and dyslipidemia. We also adjusted for alcohol consumption, antidepressant use, and adherence to the Mediterranean diet using Trichopoulou's score (31).

We considered 2-tailed *P* values < 0.05 to be statistically significant. Analyses were performed using STATA version 14.0 (StataCorp).

Results

A total of 645 men and 241 women were included in this analysis (Supplemental Figure 1) with a mean ± SD age of 67.7 ± 6.1 y. Table 1 shows baseline characteristics according to quartiles of total UPF consumption adjusted for sex and age.

Participants in the fourth quartile (>3 servings/d) compared with participants in the first quartile (<2 servings/d) of UPF consumption were more likely to have family history of CVD, diabetes, and dyslipidemia prevalence, and to snack more in between meals. Moreover, participants in the fourth quartile (>3 servings/d) compared with those in the first quartile (<2 servings/d) consumed on average more fats, SFAs, PUFAs, sodium, dietary cholesterol, SSBs, fast food, and processed meat. These participants also consumed less carbohydrates, proteins, fiber, potassium, magnesium, calcium, phosphorus, olive oil, fruits, and vegetables. A lower adherence to the Mediterranean diet (Table 1) was observed along with the increase in UPF consumption.

Supplemental Table 1 shows the percentage each food contributed to the total amount of UPF consumed in the SUN cohort. Dairy products, processed meats, pastries, and cookies were the main foods contributing to the total UPF consumed.

Table 2 presents the odds of having short TL according to UPF consumption. Those participants with the highest UPF consumption almost doubled their risk of presenting short TL (adjusted OR: 1.82; 95% CI: 1.05, 3.22; *P*-trend = 0.03).

Supplemental Table 2 shows subgroup analyses for the association between consumption of UPF and the odds of short telomeres, comparing the lowest with the highest quartiles in the different scenarios. None of the *P* values for interactions was statistically significant.

TABLE 2 Multivariable adjusted ORs (95% CIs) for short telomeres (<20th percentile) in elderly subjects of the SUN cohort[1]

	Quartiles of energy-adjusted ultra-processed food consumption				
	Low (<2 servings/d) ($n = 222$)	Medium-low (2 to <2.5 servings/d) ($n = 221$)	Medium-high (2.5 to <3 servings/d) ($n = 222$)	High (≥3 servings/d) ($n = 221$)	*P*-trend
Participants with short telomere length, *n* (%)	36 (16)	41 (19)	48 (22)	52 (24)	
Crude model	1 (ref)	1.18 (0.72, 1.93)	1.43 (0.88, 2.30)	1.58 (1.00, 2.55)	0.04
Age- and sex-adjusted model	1 (ref)	1.23 (0.74, 2.03)	1.62 (0.99, 2.65)	1.71 (1.04, 2.78)	0.02
Multiple-adjusted model 2	1 (ref)	1.29 (0.73, 2.32)	1.40 (0.80, 2.51)	1.82 (1.05, 3.22)	0.03

[1]Crude and adjusted logistic regression models. Values are ORs (95% CIs) unless otherwise indicated. Model 2 adjusted for age; sex; education level (years at university, continuous); BMI (linear and quadratic terms); family history of diabetes and cardiovascular disease (dichotomous); prevalence of cancer, diabetes, and dyslipidemia (dichotomous); lifelong smoking (pack-years of smoking, continuous); smoking status (never, current, former); physical activity (metabolic equivalent of tasks-h/wk, continuous); and television viewing (≥3 h/d, dichotomous). SUN, Seguimiento Universidad de Navarra.

Figure 1 shows the sensitivity analyses. The association between UPF consumption and odds of short telomeres was not reduced after also changing the energy limits to the 5th and the 95th percentiles; after excluding participants with prevalent cancer, diabetes, and dyslipidemia at baseline; and after also adjusting for alcohol consumption.

Discussion

In this cross-sectional study, UPF consumption (>3 servings/d) was associated with higher odds for short TL in an elderly Spanish population within the SUN cohort. This result supports previous studies evaluating risks associated with UPF consumption (36–38) and the reported effects of diet on TL (14, 15, 17, 23, 24, 39–42). A Brazilian longitudinal cohort study showed associations of UPF consumption with body weight gain (1.68 kg/y) and larger waist circumference (2.52 cm/y) (43). In addition, Hall et al. (44) observed that participants consuming a diet rich in UPF increased their body weight but participants consuming an unprocessed diet did not. Moreover, several authors observed in a cohort with young (mean age: 22.8 y) adults that UPF consumption was positively correlated with

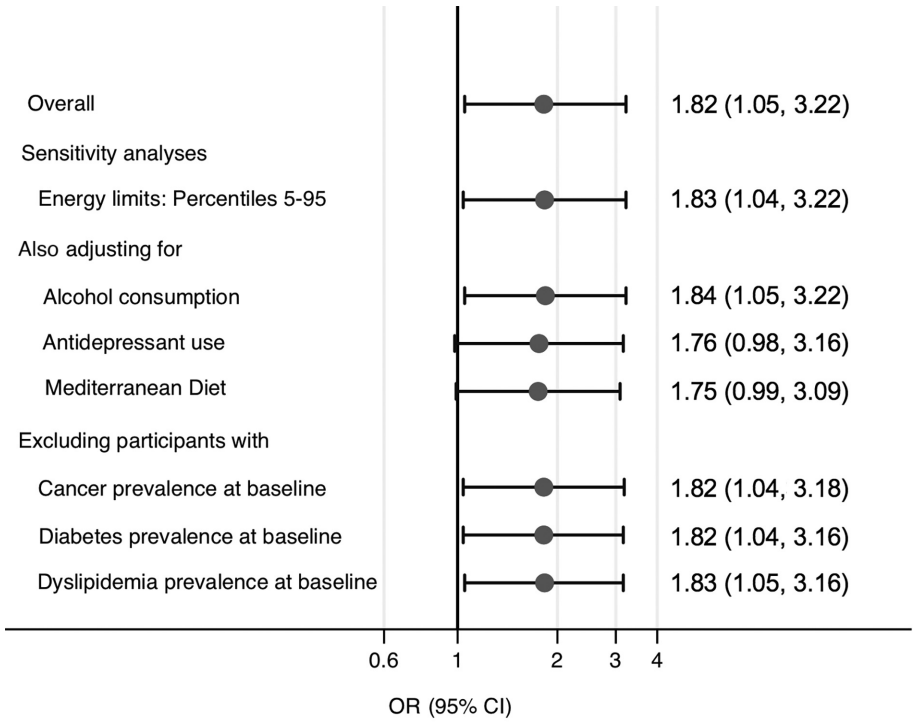

FIGURE 1 Sensitivity analyses for the association between UPF consumption and the odds of having short telomeres (<20th percentile) (high vs. low quartile of UPF consumption). Logistic regression models adjusted for age; sex; education level (years at university, continuous); BMI (linear and quadratic terms); family history of diabetes and cardiovascular disease (dichotomous); prevalence of cancer, diabetes, and dyslipidemia (dichotomous); lifelong smoking (pack-years of smoking, continuous); smoking status (never, current, former); physical activity (metabolic equivalent of tasks-h/wk, continuous); and television viewing (≥3 h/d, dichotomous). UPF, ultra-processed food.

the intake of fat, cholesterol, sodium, iron, calcium, and calories and negatively correlated with the intake of carbohydrates, protein, and dietary fiber (45).

It is worth mentioning that in another analysis within the SUN cohort, we found that UPF consumption was associated with the risk of depression (especially in patients with low levels of physical activity) (12), hypertension (8), overweight/obesity (9), and all-cause mortality (46). Strong consistency in the association with mortality suggests a causal relationship (47).

We believe that the observed association between UPF consumption and the risk of having short telomeres could be explained by higher total intakes of salt, saturated fat, and sugar, as well as inadequate intakes of fiber and micronutrients (48). Participants who consumed a greater amount of UPF in our cohort had higher intakes of salt, fats, SFAs, PUFAs, SSBs, and processed meats; lower intakes of fiber, potassium, phosphorus, magnesium, calcium, fruits, and vegetables; and a lower adherence to the Mediterranean dietary pattern.

Our results support previous cross-sectional (14–19) and case-control studies (20, 21) associating TL with the consumption of some specific UPFs. Higher SSB consumption was associated with shorter TL in a middle-aged and an older Korean population (15) as well as in a systematic review studying 17 articles regarding the effects of dietary patterns and various food groups on TL (22). However, other studies did not find an association between SSB consumption and TL (14, 17, 18, 24). Processed meats were associated with shorter telomeres in individuals aged 25–40 y (15, 19, 22). Moreover, regular fried-food consumption, deep-fried potatoes, soya milk, salty biscuits, and margarine were also associated with shorter telomeres in individuals aged 35–70 y (17, 20). Alcohol consumption was negatively associated with TL in a study including alcohol abusers (high alcohol consumption defined as >3 drink-units/d) and social drinkers (21) and in a study including volunteers aged 35–55 y (16). All these studies support the evidence of the unbeneficial effects of UPF on human health, which affects our morbidity and mortality (46).

Strengths and limitations

To the best of our knowledge, this is the first cross-sectional study evaluating the relation between UPF consumption and TL using the NOVA classification. One of the main strengths related to TL is the method used (monochrome multiplex real-time qPCR), which allows the quantification of TL and the single copy gene in the same well in a single reaction, which reduces potential measurement errors. We used validated methods and a variety of sensitivity analyses to support the robustness of the results; and we adjusted for a wide range of potential confounders. Even if the findings were self-reported, we can consider that the data are high-quality because the participants are university graduates and previous validation studies were carried out. This restriction of university graduate participants was applied to control for confounding by socioeconomic status, being "an excellent technique for preventing or at least reducing confounding by known factors" (25). Furthermore, the NOVA classification ranks food categories according to the extent and purpose of food processing, instead of in terms of nutrients. It is recognized as a valid tool for research on nutrition and public health research. It involves physical, biological, and chemical processes occurring in food after being separated from nature and before its consumption. It is a clear, simple, and understandable classification (49).

Our study has also limitations. First, the FFQ was not exactly designed to collect data for the NOVA classification of UPF consumption. Second, although we adjusted for several potential confounders, other potential confounders may exist and we cannot rule out the existence of residual confounding. Third, there could be a misclassification because we used servings of UPF as an indicator for consumption. However, there was a validation of the SUN cohort which confirmed that the intraclass correlation coefficients were in the established ranges usually used for nutritional epidemiological studies (50). Fourth, our population was not representative of the general population. This is due to the fact that the SUN cohort was found to have a healthier profile, probably because participants were graduates and more aware of the importance of a good diet and lifestyle (25). Fifth, the DNA was isolated from saliva samples. Saliva is a diagnostic fluid that contains leukocytes and epithelial cells at varying proportions (51). Moreover, it is reported that TL measures in leukocytes and saliva are positively correlated (51). It is nevertheless an attractive alternative DNA source because it is less expensive and less invasive for participants.

Sixth, cereal and energy bars, energy drinks, health and slimming products, and meat or vegetable nuggets were not included because the FFQ and the food records used in the validation study did not collect information on these items. Seventh, because the design of the study is cross-sectional, causal effects cannot be inferred. Eighth, the relatively small sample size may have limited our ability to detect small associations where they truly exist, especially in the stratified analyses.

Conclusion

In this cross-sectional study of elderly Spanish subjects we showed a robust strong association between UPF consumption and TL. However, further research in larger longitudinal studies with baseline and repeated measures of TL is needed to confirm these observations.

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