Atherosclerosis 282 (2019) 154–161

Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

The impact of sedentary behavior patterns on carotid atherosclerotic burden: Implications from the Corinthia epidemiological study

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HIGHLIGHTS

- Physical activity is associated with a reduction of cardiovascular events.
- Few data exist about the association of sedentary behavior with atherosclerosis.
- Association between hypertension prevalence and increasing TV-viewing-time.
- TV-viewing-time was associated with increased mean cIMT and carotid atheromatic plaque.
- Sedentary behavior may provoke atherosclerotic progression.

ARTICLE INFO

Keywords:
Corinthia study
Physical activity
Sedentary behavior
Television viewing
Atherosclerosis
Carotid intima-media thickness

ABSTRACT

Background and aims: Sedentary lifestyle, unlike leisure time physical activity (PA), is associated with atherosclerosis progression. Regarding the interrelationship between television watching, as a sedentary behavior pattern, and cardiovascular disease burden, few data exist.

Methods: In this cross-sectional epidemiological study based on 2043 inhabitants of the Corinthia region, in Greece, ultrasonography was used to measure carotid intima-media thickness (IMT) in both carotid arteries. The average (meanIMT) and maximum thickness (maxIMT) were determined as representative values of subclinical atherosclerosis. We evaluated PA using the self-reported International Physical Activity Questionnaire (IPAQ). Based on specific questions, the average hours per week spent on watching television (TV), videos or DVD was calculated for each participant.

Results: According to TV viewing time, subjects were categorized into the low (≤7 h/week), moderate (7> TV hours/week ≤21) and high (>21 h/week) TV viewing time groups. Prevalence of carotid atheromatic plaque was lower in the low TV viewing time group compared to the moderate and high TV viewing time groups ($p = 0.02$). TV viewing time was associated with increased carotid IMT ($p = 0.03$) and the prevalence of carotid atheromatic plaque ($p = 0.02$), even after adjustment for age, body mass index, cardiovascular risk factors or history of cardiovascular disease. Subjects in the high TV viewing time group have 80% increase odds of carotid atheromatic plaque compared to patients categorized in the low TV viewing time group ($p = 0.01$).

Conclusions: The present findings have important public health implications, providing a better understanding of the components of sedentary behavior that are associated with atherosclerotic progression.

1. Introduction

The beneficial effects of regular exercise on cardiovascular and overall health as well as all-cause mortality are well established [1]. Increasing levels of PA have been linked to a reduction of cardiovascular events and this effect holds true for individuals with and without heart disease [2]. Interestingly, moderate intensity PA (approximately 60–75 min per day) appears to counterbalance or even eliminate any harm (including risk of death) associated with prolonged sitting time and sedentary lifestyle in general [3].

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https://doi.org/10.1016/j.atherosclerosis.2019.01.026
Received 23 August 2018; Received in revised form 27 December 2018; Accepted 15 January 2019
Available online 29 January 2019
0021-9150/

Possible mechanisms involved in exercise associated health benefits include, among others, a better control of arterial hypertension, plasma lipoproteins, insulin sensitivity, state of mood [2].

In contrast to the active attitude, any sedentary behavior (e.g. television watching, sitting in front of a screen, reading and low energy expenditure in general) appears to have detrimental effects on health and well-being [4–7]. For example, television viewing which is an extremely common habit worldwide (with particular emphasis in the Western world), has been linked to heart disease, cancer and six additional causes of death [6].

Although several biological mechanisms (including higher rates of type 2 diabetes mellitus, metabolic syndrome, obesity, higher prevalence of cardiovascular disorders, etc.) have been encountered as responsible for sedentary life harms, further investigation is required to shed more light on these associations [8]. A matter of concern relevant to this topic is whether different sedentary behaviors are associated with different cardiovascular and mortality risk rates. In particular, little is known whether television watching, working on computers, reading and so on, have a varying impact on cardiometabolic risk and health outcomes. In this line, initial research efforts have been already addressed this issue by investigating the impact of replacing a certain type of sedentary task with another [5]. Another challenging topic needing further clarification regards the potential elimination (either complete or partial) of sedentary life risks when engagement in regular PA is implemented [3].

Accordingly, in the context of the Corinthia epidemiological study we examined the impact of different components of sedentary lifestyle on carotid atherosclerotic burden in an effort to generate new clues in the role of sedentary behavior on cardiovascular health.

2. Materials and methods

2.1. Study design

The Corinthia study has been carried out from October 2015 to February 2017. Two thousand forty-three permanent inhabitants of Corinthia region (822 males), aged 40 years old or older, have been voluntarily enrolled in this cross-sectional survey. Based on the latest national Census a multistage sampling method was used to achieve balance recruitment across different areas, census blocks, age categories (per decades) and gender, as previously described [9–11]. All participants have been interviewed by the investigator group consisted of physicians, cardiologists, nurses and social scientists [12].

The Medical Research Ethics Committee of the First Cardiology clinic of Athens Medical School approved the study which was carried out in accordance with the Declaration of Helsinki (1989) of the World Medical Association. An inform consent was signed by all subjects before participation after detailed information for the purpose, aims and procedure of the study.

2.2. Clinical, biochemical and anthropometric characteristics

Standard procedures were used to measure weight and height. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). Accordingly, subjects were grouped according to standard BMI categories [13] as follows: normal weight, BMI 18.5–24.9 kg/m^2; overweight, BMI 25.0–29.9 kg/m^2; and obese BMI ≥ 30.0 kg/m^2. At the end of the physical examination, an electronic sphygmomanometer was used to measure resting arterial blood pressure with the subject in a sitting position according to the current recommendations. The average of three measurements was used to define arterial blood pressure. Individuals under anti-hypertensive medication or with blood pressure levels greater or equal to 140/90 were classified as hypertensive subjects according to the contemporary ESH/ESC Guidelines for the management of arterial hypertension [12]. Blood samples were collected between 8.00 and 10.00 a.m. after an overnight fast. Serum total cholesterol, high-density lipoprotein (HDL) cholesterol and triglycerides were measured using a chromatographic enzymic method in an automatic analyzer (RA-1000). The Friedewald formula: Low-density lipoprotein (LDL) = cholesterol (total cholesterol) - (HDL cholesterol) - 1/5 (triglycerides) was used to calculate LDL cholesterol levels [14]. The intra and inter-assay coefficients of variation of cholesterol levels did not exceed 3%, of triglycerides 4% and of HDL-cholesterol 4%. Individuals under lipid-lowering treatment or with total serum cholesterol levels greater than 200 mg/dl were classified as having hypercholesterolemia.

We classified individuals as having type 2 diabetes mellitus based on fasting blood glucose levels > 126 mg/dl, according to American Diabetes Association diagnostic criteria [15], or when subjects where under regular use of anti-diabetic medication.

As regarding smoking habits, current smokers were defined as those who smoked at least one cigarette per day or had stopped smoking for less than a year, while non-current smokers were defined as those who had never smoked or had stopped smoking for at least one year.

2.3. Evaluation of carotid intima media thickness (cIMT)

High resolution B-mode images of the right and left common carotid arteries were obtained using a Vivid e ultrasound system (General Electric, Milwaukee, Wisconsin, USA) equipped with a 5.0–13.0 MHz (harmonics) linear array ultrasound. cIMT was measured at 3 paired segments: in the right and left common carotid artery, the carotid bulb, and the internal carotid artery, as described previously [16]. In each segment, 3 measurements of the cIMT in the far wall were averaged; and the average cIMT was calculated for each of the 2 carotid arteries. The average value of right and left cIMT was defined as mean cIMT. The maximum-cIMT was also studied. Thickness of cIMT > 1.5 mm or protrusion > 50% compared to adjacent segments was considered as atherosclerotic plaque [17]. If plaque was present in the distal territory of the examined segment, it was included in the cIMT measurement [18].

2.4. Evaluation of sedentary activities

PA was evaluated using the shortened version of the self-reported International Physical Activity Questionnaire (IPAQ) for the elderly [19]. Frequency (times per week), duration (minutes per time) and intensity of PA during sports, occupation and/or free-time activities were assessed. In accordance with the standard IPAQ scoring procedures [19], participants were classified into one of the following groups: upper tertile: "vigorous" PA [a) vigorous-intensity activity on at least 3 day, achieving a minimum of at least 1500 MET/min/week or b) seven or more days of any combination of walking, moderate-intensity activity, or vigorous-intensity activity achieving a minimum of at least 3000 MET/min/week], middle tertile: "moderate" PA [a) three or more days of vigorous activity of at least 20 min/day or b) five or more days of moderate intensity activity or walking of at least 30 min/day or c) five or more days of any combination of walking, moderate-intensity activity, or vigorous-intensity activity achieving at least 600 MET/min/week] or lower tertile: "low" PA (individuals who do not met criteria for vigorous or moderate PA).

Total sitting time was estimated as a continuous measure in response to the 7th question of the shortened version of the self-reported IPAQ ‘About how many hours do you sit during an average day? (including work hours and leisure time). Daily time spend watching TV, videos or DVD (TV-viewing time) was assessed by two extra questions “About how many hours do you watch TV, videos or DVD an average working day?” and “About how many hours do you watch TV, videos or DVD at weekend?” Based on these responses the average hours per week spent on watching TV, videos or DVD was calculated for each participant.

2.5. Statistical analysis

Data are presented as mean ± standard deviation (SD) for continuous variables and as valid percentages for categorical variables. Continuous variables were tested for normality of distribution with Kolmogorov-Smirnov test and by visual inspection of P-P plots. To examine the differences in demographic and clinical characteristics and in carotid atheromatic burden according to tertiles of total sitting time and the three categories of TV-viewing time chi-square test and one-way analysis of variance (ANOVA) were used for categorical and continuous variables respectively. The same statistical tests (ANOVA and chi-square test for continuous and categorical data respectively) were used to examine the differences in demographic and clinical characteristics according to age groups. Linear regression analysis and logistic regression analysis were applied to examine, -independently from confounders established in bibliography or from covariates proved significant by the univariate analysis-the association of increasing TV-viewing time and total sitting time with the mean cIMT and the odds ratio of atheromatic carotid plaque, respectively. Data of the linear regression and logistic regression analysis were graphically represented in a forest plot consisted from the correlation coefficients or odds ratio (for linear regression and for logistic regression respectively) and 95% confidence intervals. All reported p-values were based on two-sided tests. Exact values of $p < 0.05$ were considered statistically significant. Data analysis was performed with SPSS software, version 18.0 (SPSS Inc., Chicago, IL).

3. Results

3.1. Basic characteristics of the participants

From the study participants, 60% were women, 26% were current smokers, 80% were overweight or obese, 80% were hypertensive, 18% had diabetes mellitus, 46% had hypercholesterolemia and 13% suffered from cardiovascular disease (Table 1). The total sitting time/week was 25 ± 18 h and the total TV-viewing time/week was 18 ± 13 h.

3.2. Total sitting time association with demographic and clinical characteristics

According to tertiles of total sitting time, subjects were categorized in three groups low (< 14 h/week), moderate (14–28 h/week) and high (≥28 h/week). As it is shown in Table 2, more men than women were categorized in the first tertile (low total sitting time), while increased percentage of current smokers were categorized in the third tertile (high total sitting time), compared to non-smokers. There was no difference in other demographic and clinical characteristics according to total sitting time neither in other cardiovascular risk factors or cardiovascular diseases. Especially concerning carotid atheromatic burden there was no difference in the prevalence of carotid atheromatic plaque (low total sitting time: 24% *vs*. moderate sitting time: 28% *vs.* high total sitting time: 29%, $p = 0.10$), in mean cIMT (low total sitting time: 0.97 ± 0.42 mm *vs*. moderate sitting time: 1.03 ± 0.48 mm *vs*. high total sitting time: 1.02 ± 0.47 mm, $p = 0.17$) and in maximum cIMT (low total sitting time: 1.29 ± 0.84 mm *vs.* moderate sitting time: 1.41 ± 0.93 mm *vs.* high total sitting time: 1.37 ± 0.91 mm, $p = 0.18$) (Table 2, Fig. 1). Moreover, even when the analysis was stratified by age decade there was no difference in the prevalence of carotid atheromatic plaque, in mean cIMT and in maximum cIMT through total sitting time tertiles (Supplementary Table 1). Additionally, we found that even after adjustment for multiple possible confounders (i.e. age, gender, BMI, hypertension, diabetes mellitus, hypercholesterolemia, cardiovascular disease and smoking habits) for every hour increase of total sitting time/week there is borderline statistical significant increase in the odds of carotid atheromatic plaque [Odds ratio: 1.01, 95% Confidence interval (0.998, 1.030), $p = 0.08$] (data not shown). After adjustment for the aforementioned confounders association of total sitting time/week was not found to be associated with mean cIMT [b coefficient: 0.003, 95% Confidence interval (−0.002, 0.002), $p = 0.72$] (data not shown).

3.3. TV-viewing time association with demographic and clinical characteristics

According to TV-viewing time, subjects were categorized into the low TV-viewing time group (≤7 h/week), the moderate TV-viewing time group (7> TV hours/week ≤21) and the high TV-viewing time group (>21 h/week). As it is shown in Table 2, there was no difference in the sitting time spend on watching TV, DVD, etc. according to gender. Interestingly, there was an association between hypertension prevalence and increasing TV-viewing time (low TV-viewing time group: 79% *vs.* moderate TV-viewing time group 86% *vs*. high TV-viewing time group 87%, $p = 0.05$). Importantly, prevalence of carotid atheromatic plaque was lower in the low TV-viewing time group compared to the moderate and high TV-viewing time groups (low TV-viewing time group: 21% *vs*. moderate TV-viewing time group: 29% *vs.* high TV-viewing time group: 30%, $p = 0.02$). There was also an association between increasing TV-viewing time and mean cIMT (low TV-viewing time group: 0.93 ± 0.40 mm *vs.* moderate TV-viewing time group: 1.02 ± 0.47 mm *vs.* high TV-viewing time group: 1.05 ± 0.48 mm, $p = 0.002$) and between increasing TV-viewing time and maximum cIMT (low TV-viewing time group: 1.22 ± 0.79 mm *vs.* moderate TV-viewing time group: 1.39 ± 0.90 mm *vs.* high TV-viewing time group: 1.44 ± 0.97 mm, $p = 0.005$) (Table 2 and Fig. 2). There was no difference in other demographic and clinical characteristics according to TV-viewing time. When the analysis was stratified by age decade, although there was an increase in the prevalence of carotid atheromatic plaque according to TV-viewing time, in mean cIMT and in maximum cIMT, this difference did not reached statistical significance (Supplementary Table 2).

Since many confounders may interfere to the association of TV-viewing time with carotid atherosclerotic burden, atheromatic plaque prevalence and cIMT, we proceed to a multivariate regression model for the association of carotid atherosclerosis with sedentary habits after adjustment for possible confounders proved significant by the univariate analysis or based on bibliographic data on the risk factors of atherosclerosis [17,20,21] (Table 3, Supplementary Fig. 1). As it is shown in Table 3, TV-viewing time was significantly associated with increased mean cIMT [b-coefficient = 0.002, 95% Confidence intervals (0.0002, 0.005), p = 0.03] and the prevalence of carotid atheromatic plaque [Odds-ratio = 1.01, 95% Confidence intervals (1.002, 1.030), p = 0.02], independently from age, gender, BMI, arterial hypertension, diabetes mellitus, hypercholesterolemia, cardiovascular diseases and smoking habits. Interestingly, subjects in the high TV-viewing time group (>21 h/week) have 80% increase odds of carotid atheromatic plaque compared to patients categorized in the low TV-viewing time group (≤7 h/week), independently of the aforementioned confounders [Odds-ratio = 1.83, 95% Confidence intervals (1.12, 2.94), p = 0.01] (Supplementary Table 3).

3.4. Interrelationship between total sitting time, TV-viewing time and carotid atherosclerosis

Since based on our findings the association between total sitting time, TV-viewing time and carotid atherosclerosis is not straightforward we tried to explore the role of this balance by a composite index the ratio of TV-viewing time to total sitting time (TV/Total-sitting time) with increasing values of this ratio expressing a higher percentage of sedentary activities spent watching TV, DVD, etc.

Mean cIMT (r = 0.11, $p < 0.001$) and maximum cIMT (r = 0.11, $p < 0.001$) were significantly associated with increased ratio of TV-viewing/Total-sitting time.

Table 1
Baseline demographic and clinical characteristics of the total study population (N = 2043) and according to age groups.

	Total study population N = 2043	Age group 1 (40 ≥ age < 50 years) (19% of the total study population)	Age group 2 (50 ≥ age < 60 years) (22% of the total study population)	Age group 3 (60 ≥ age < 70 years) (27% of the total study population)	Age group 4 (70 ≥ age < 80 years) (25% of the total study population)	Age group 5 (age ≥ 80 years) (7% of the total study population)	*p*-value
Mean age (years)	64 ± 12						
Male gender (%)	40	37	39	41	41	45	0.46
BMI (kg/m^2)[a]	28.74 ± 4.59	27.84 ± 4.96	28.66 ± 4.84	29.05 ± 4.53	28.51 ± 3.94	27.59 ± 4.36	< 0.001
Normal weight (%)	21	32	22	16	19	28	< 0.001
Overweight (%)	43	35	43	45	47	49	
Obese (%)	36	32	34	38	34	23	
Current smokers (%)	26	35	32	25	25	15	< 0.001
Hypertensive (%)	80	58	74	80	86	88	< 0.001
Diabetes mellitus (%)	18	14	20	16	23	24	0.005
Hypercholesterolemia (%)	46	36	45	48	53	46	0.009
Cardiovascular disease	13	12	12	13	13	15	0.89
Physical activity							0.65
Low (%)	59	58	60	59	63	60	
Moderate (%)	31	31	30	32	28	29	
Vigorous (%)	11	12	10	10	9	11	
Total sitting time (hours/week)	25 ± 18	26 ± 18	24 ± 16	26 ± 18	26 ± 18	22 ± 15	0.11
TV-viewing time (hours/week)	18 ± 13	19 ± 13	17 ± 13	19 ± 14	19 ± 13	18 ± 9	0.67
Low [TV-viewing time (hours/week) < 7 (%)]	28	28	31	29	28	18	0.19
Moderate [TV-viewing time (hours/week) ≥ 7, < 21 (%)]	45	47	46	43	44	59	
High [TV-viewing time (hours/week) ≥21 (%)]	26	25	24	28	28	24	
Mean cIMT (mm)	1.00 ± 0.46	1.00 ± 0.42	0.99 ± 0.48	0.99 ± 0.46	1.00 ± 0.44	1.04 ± 0.47	0.04
Maximum cIMT (mm)	1.35 ± 0.89	1.37 ± 0.80	1.35 ± 1.00	1.31 ± 0.82	1.37 ± 0.93	1.39 ± 0.86	0.73
Carotid plaque (%)	27%	33	25	26	26	27	0.27

BMI: body mass index; cIMT: carotid intima-media thickness.
Continuous variables are presented as mean ± standard deviation; categorical variables are presented as valid percentages; for dichotomous variables, percentages represent the category listed in the table – variable list (first column). The other category of each dichotomous variable is calculated by subtracting the provide percentage from 100%.
p-values are referred to the differences among age groups calculated with one way analysis of variance or Chi square test for continuous and categorical data, respectively.
[a] According to BMI, subjects were grouped as: normal weight, BMI 18.5–24.9 kg/m^2; overweight, BMI 25.0–29.9 kg/m^2; and obese BMI ≥30.0 kg/m^2.

Table 2
Demographic and clinical characteristics of participants according to tertiles of total sitting time and TV-viewing time groups.

	Tertiles of total sitting time				TV-viewing time groups			
	1st tertile (low total sitting time) < 14 h/week	2nd tertile (moderate total sitting time) 14–28 h/week	3rd tertile (high total sitting time) ≥28 h/week	*p*-value	Low TV-viewing time group (≤7 h/week)	Moderate TV-viewing time group (7 > TV hours/week ≤21)	High TV-viewing time group (> 21 h/week)	*p*-value
Mean age (years)	64 ± 12	63 ± 12	63 ± 12	0.89	63 ± 11	64 ± 13	64 ± 12	0.65
Male (%)	45	34	41	0.006	42	40	39	0.77
BMI (kg/m^2)[a]	28.73 ± 4.59	28.72 ± 4.38	28.76 ± 4.83	0.99	28.81 ± 4.54	28.67 ± 4.63	28.78 ± 4.60	0.90
Normal weight (%)/Overweight (%)/Obese (%)	15/46/39	21/42/37	21/40/39	0.51	21/44/35	21/43/36	20/43/37	0.90
Current smokers (%)	30	22	27	0.30	29	26	24	0.32
Hypertensive (%)	81	80	81	0.74	79	86	87	0.05
Diabetes mellitus (%)	15	21	19	0.34	14	20	20	0.08
Hypercholesterolemia (%)	46	47	43	0.66	42	47	48	0.30
Cardiovascular disease	11	15	14	0.16	12	14	11	0.54
Mean cIMT (mm)	0.97 ± 0.42	1.03 ± 0.48	1.02 ± 0.47	0.17	0.93 ± 0.40	1.02 ± 0.47	1.05 ± 0.48	0.002
Maximum cIMT (mm)	1.29 ± 0.84	1.41 ± 0.93	1.37 ± 0.91	0.18	1.22 ± 0.79	1.39 ± 0.90	1.44 ± 0.97	0.005
Carotid plaque (%)	24	28	29	0.10	21	29	30	0.02

BMI: body mass index; cIMT: carotid intima-media thickness.
Continuous variables are presented as mean ± standard deviation.
Categorical variables are presented as valid percentages; for dichotomous variables, percentages express the category of the dichotomous variable listed in the table-variable list (first column), in each tertile of sitting time or in each group of TV-viewing time respectively. The other category of each dichotomous variable is calculated by subtracting the provide percentage from 100% in each tertile of sitting time or in each group of TV-viewing time, respectively.
[a] According to BMI, subjects were grouped as: normal weight, BMI 18.5–24.9 kg/m^2; overweight, BMI 25.0–29.9 kg/m^2; and obese BMI ≥30.0 kg/m^2.

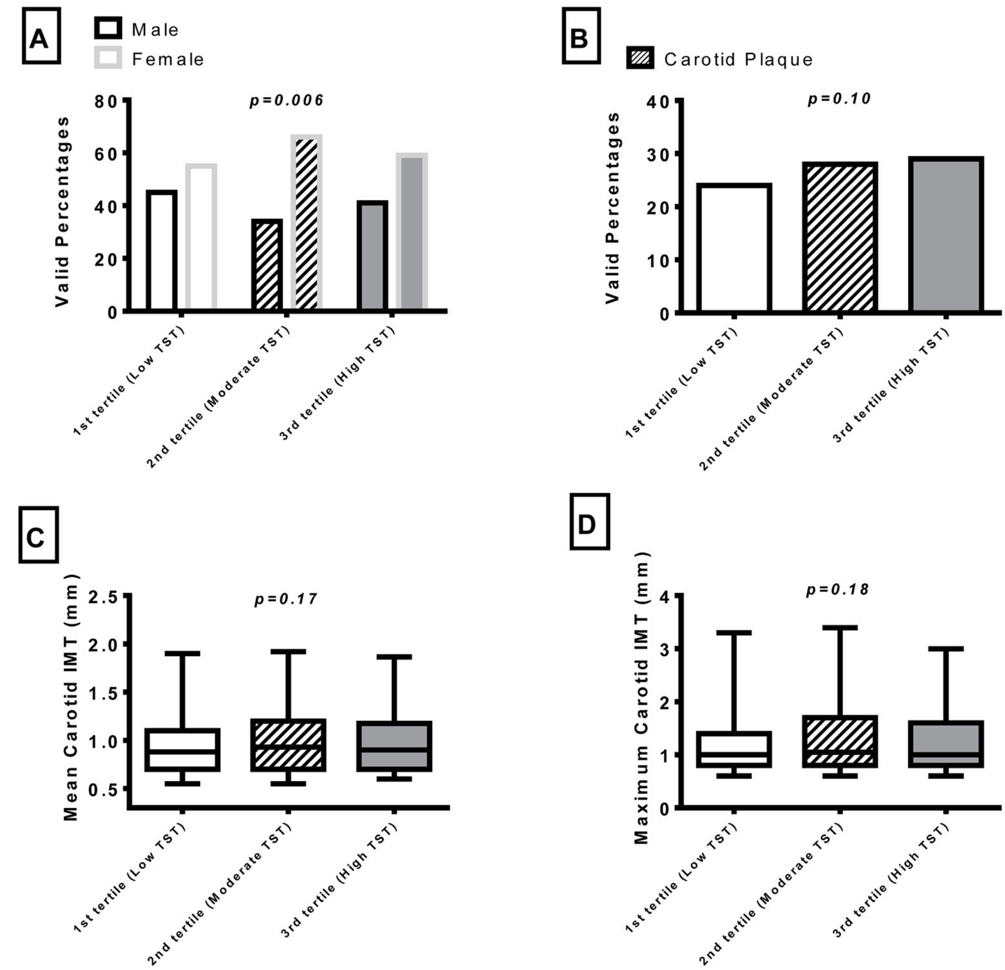

Fig. 1. Subjects characteristics according to tertiles of total sitting time.
(A) Bars representing valid percentages of female and male subjects in each tertile of total sitting time. (B) Box-plots representing mean carotid intima media thickness according to tertile of total sitting time. (C) Box-plots representing maximum carotid intima media thickness according to tertile of total sitting time. (D) Bars representing valid percentages of patients with carotid plaque according to tertiles of total sitting time breakfast consumption. TST: total sitting time; IMT: intima media thickness.

4. Discussion

Although there is persuasive data about an inverse relationship between time spent in PA and cIMT [22,23], evidence about the association between sedentary behavior and carotid wall thickness is scarce. As it is already known, cIMT, and/or the presence of plaques can predict the occurrence of cardiovascular diseases, such as myocardial infarction or stroke, independently from traditional cardiovascular risk factors and constitutes a marker of subclinical atherosclerosis [12,24–26]. The Corinthia study is one of the very few epidemiological, prospective studies evaluate the effect of a sedentary behavior, such as watching TV, on this early atherosclerotic marker.

Our cross-sectional analysis indicates that the prevalence of carotid atheromatic plaque was lower in the low TV-viewing time group compared to the moderate and high TV-viewing time groups, while there was also an association between increasing TV-viewing time and mean and maximum cIMT. Interestingly, in the regression analysis, TV-viewing time was significantly associated with increased mean cIMT and the prevalence of carotid atheromatic plaque independently from confounders such as age, gender, BMI, cardiovascular risk factors or cardiovascular diseases.

A rather unanticipated finding in this study was the higher prevalence and odds of carotid atheroma burden in the subjects aged < 50 years as compared with the older counterpart, although a stepwise increase in plaque burden was observed in the latter subgroup. A possible (albeit speculative) explanation may be offered by the over-representation of classical risk factors in younger subjects (such as smoking, increased total sitting and TV-viewing time, unhealthy diet, etc.) and the change overtime of environmental factors, lifestyle habits, working and occupational activities.

Our study comes along with other prospective studies regarding the impact of sedentary lifestyle and especially TV-viewing time in cIMT. According to Kozakova et al. [27] in healthy, young-to-middle age men and women, the proportion of time spent in sedentary lifestyle was directly associated with baseline cIMT, while, the progression in cIMT was influenced by vigorous activity. In the same way, in 623 healthy individuals of the EVIDENT study, total sedentary time and sedentary time in bouts longer than 10min, were positively, although weakly, associated with cIMT [28]. In the recent Jackson Heart Study, in 3140 African-American subjects, longer TV viewing time (> 4 h a day) was significantly, associated with greater cIMT, while occupational sitting was correlated with lower cIMT [29]. Of course, one should be aware of the racial differences in cardiovascular system, as African-American individuals tend to have increased cIMT and risk for cardiovascular diseases [30,31]. According, to a meta-analysis of 8 observational prospective studies, Grontved et al. [32] showed that increased time spent in TV viewing is associated with an increased risk of diabetes mellitus type 2, fatal and non-fatal cardiovascular diseases, and all-cause mortality. On the contrary, findings from the epidemiological National Heart, Lung, and Blood Institute Family Heart Study, in 1778

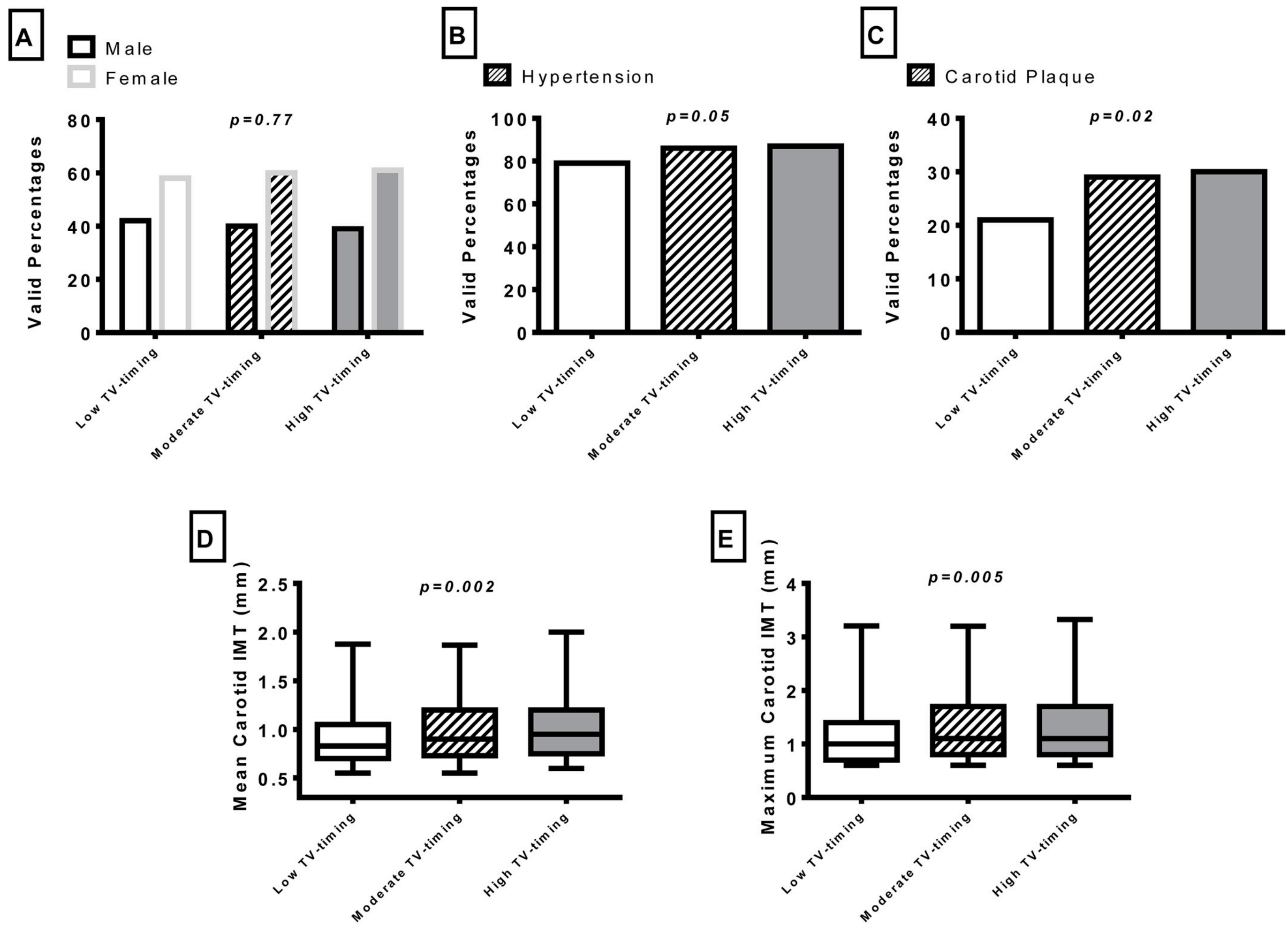

Fig. 2. Subjects characteristics according to TV-viewing time groups.
(A) Bars representing valid percentages of female and male subjects in each group of TV-viewing time. (B) Bars representing valid percentages of hypertensive subjects in each group of TV-viewing time. (C) Bars representing valid percentages of carotid plaque in each group of TV-viewing time. (D) Box-plots representing mean carotid intima media thickness according to groups of TV-viewing time. (E) Box-plots representing maximum carotid intima media thickness according to groups of TV-viewing time. IMT: intima media thickness.

adults without cardiovascular risk factors, demonstrated no significant relationship between everyday TV viewing time and cIMT [33]. However, a strong limitation of this study was that the TV viewing time was ≤2h/day in the majority of participants, which does not increase health risk according to the above mentioned meta-analysis [32]. Similarly, in the CARDIA study, the time spent in front of a screen (TV or DVDs viewing and/or computer use) had no significant impact of the function of left ventricle systolic function [34]. Accordingly, evidence from the NHANES survey demonstrated no significant association between accelerometer-measured sedentary time measured by accelerometer and cardiovascular risk factors [35].

The mechanisms underlying the cross-sectional association between

Table 3
Regression analysis for the association of mean cIMT (linear regression) and carotid atheromatic plaque (logistic regression) with TV-viewing time and other confounders.

	Linear regression			Logistic regression		
	b-coefficients	95% confidence intervals	*p*-value	Odds ratio	95% confidence intervals	*p*-value
Age (years)	−0.002	−0.005, 0.001	0.11	0.97	0.96, 0.99	0.003
Male gender	0.04	−0.02, 0.11	0.20	1.09	0.77, 1.53	0.62
BMI (kg/m^2)	0.003	−0.004, 0.011	0.38	1.00	0.96, 1.04	0.82
Hypertension	0.11	0.02, 0.21	0.02	2.06	1.14, 3.70	0.02
Diabetes mellitus	0.16	0.08, 0.24	< 0.001	1.81	1.22, 2.69	0.003
Hypercholesterolemia	0.04	−0.03, 0.11	0.27	1.40	0.98, 1.99	0.06
Cardiovascular disease	0.35	0.25, 0.44	< 0.001	2.87	1.86, 4.44	< 0.001
Current smokers	0.05	−0.03, 0.12	0.22	1.19	0.81, 1.77	0.36
TV-viewing time (hours/week)	0.02	0.0002, 0.005	0.03	1.01	1.002, 1.030	0.02

The female gender was set for gender as reference category.
BMI: body mass index; cIMT: carotid intima-media thickness.

TV-viewing time and cIMT cannot be elucidated by this study, but there are a number of possible explanations. First of all, time spent on TV viewing may displace time for leisure activities and lead to physical inactivity [36,37]. The degree of substitutability of PA for sedentary behaviors may prove to be an important individual difference variable that may predict shifts in energy balance. Secondly, the TV-viewing time is a low energy activity in comparison to PA [38]. Thirdly, TV or DVDs viewing is associated with unhealthy behaviors, such as increased calorie intake from consumption of full-fat food and sugar-sweetened beverages, alcohol consumption, frailty and limitation in physical function independently of physical activity which may unfavorably affect metabolism [39,40]. In fact, this seems to be also the case in our study population since the majority of participants are either overweight or obese with possible impact on arterial atheromatosis and cIMT progress. According to experimental studies, prolonged sedentary behavior (such as TV viewing), results in deleterious postprandial glucose responses [41]. Observational studies indicate that prolonged TV viewing is associated with weight gain [42] and increased risk for developing diabetes mellitus [43]. Moreover, TV viewing has been associated with a prothombotic/inflammatory state, increased C-reactive protein levels [44], tumor necrosis factor-a levels [45], and interleukin-6 levels [46], factors which, in turn, have been linked with the inflammatory mechanisms of atherosclerosis. Finally, TV viewing time has been associated inversely with lower cardiorespiratory fitness, and adverse effects on energy balance [47] and reduce one's ability to withstand acute cardiovascular events later in life.

4.1. Limitations

Potential limitation of this study could be that PA and sedentary behavior, especially TV-viewing time, were self-reported, by using the given PA questionnaires. The administration of PA questionnaires is a cost-effective measurement, which can assess all types of PA and can be used in large populations. The incorporation of device-based measures of sitting time and PA, like accelerometers or pedometers, may provide more objective evaluation of duration and intensity of locomotion [48] and slightly more consistent results in addition to self-reported PA, however can be difficult applied in cross-sectional epidemiological studies. Moreover, our results are based on subjects living in semi-rural regions and it may be difficult to extrapolate these findings in inhabitants of urban cities where the patterns of activities and sedentary time differentiate. Furthermore, as with most such studies, the possibility of residual confounding, by lifestyle or behavioral factors must be considered. Such a confounder could be the presence of osteomuscular diseases, i.e. hip or knee osteoarthtis, arthritis or a past surgery, situations which consist a frequent cause of disability and immobility. Unfortunately, the lack of these data in the present analysis may be interfere with the findings present in this manuscript and pose a limitation. Finally, the cIMT and the presence of plaques were evaluated by B-mode images in carotid ultrasonography, while three-dimensional ultrasound could provide more accurate measurements of the plaque [49,50].

4.2. Conclusions

In the context of the Corinthia study, we found an association between sedentary behavior and particularly TV-viewing time with cIMT, a phenotype of subclinical atherosclerosis, independently of other established risk factors. The present findings have important public health implications, providing a better understanding of the components of sedentary lifestyle that are associated with atherosclerotic progression. Moreover, our results suggest the importance of reducing sitting time and avoiding prolonged periods of sedentary behavior among less active individuals, in order to reduce atherosclerotic burden. More research is needed to fully understand the relations between TV viewing, inflammation, and subclinical atherosclerosis and the biologic pathways through which sedentary behavior may affect cardiovascular health.

Conflicts of interest

The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

Author contributions

Evangelos Oikonomou had design the study, analyzed the data and wrote the manuscript.

George Lazaros and Georgia Vogiatzi had collected the data, performed research and wrote the manuscript.

Evangelia Christoforatou, Sotirios Tsalamandris, Athina Goliopoulou, Maria Tousouli, Vasiliki Mystakidou, had perform research and measurements and analyzed the data.

George Lazaros, Christos Chasikidis, and Dimitris Tousoulis had design the study, analyzed the data and revised critically the manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.atherosclerosis.2019.01.026.

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