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Association of leisure-time physical activity and sedentary behavior with carotid atherosclerosis morphology: The ARIC carotid-MRI study

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A R T I C L E I N F O

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A B S T R A C T

Objective: We evaluated the prospective association of midlife leisure-time physical activity (LTPA) and sedentary behavior (SB), and their temporal patterns, with MRI-measured carotid atherosclerotic morphology.
Methods: Participants enrolled in the Carotid MRI substudy (2004–2006) of the Atherosclerosis Risk in Communities (ARIC) Study and with self-reported assessments of LTPA and SB at visits 1 (1987–1989) and 3 (1993–1995) were included in this study. LTPA was ascertained using the ARIC/Baecke physical activity questionnaire and categorized according to the American Heart Association's metric of poor, intermediate, or ideal physical activity. SB, measured as TV viewing frequency, was categorized as high, medium, and low. We used multivariable adjusted linear and logistic regression models to examine the associations between midlife (visit 3 only) and persistent (visit 1 to 3) LTPA and TV viewing with carotid artery plaque burden and components.
Results: Among the 1,582 (mean age: 59 years, 43% male, 18% Black) participants, 45.7%, 21.7%, and 32.6% reported ideal, intermediate, or poor LTPA, respectively. High TV viewing was reported in 33.8% of participants, with 46.4% and 19.8% reporting medium or low TV viewing, respectively. Compared to poor LTPA, ideal LTPA in midlife was not associated with total wall volume (β=0.01, 95% CI: -0.01, 0.03), maximum carotid wall thickness (β=0.06, 95% CI: -0.08, 0.21), normalized wall index (β=-0.01, 95% CI: -0.03, 0.01), or maximum stenosis (β=-0.11, 95% CI: -1.98, 1.76). Low or middle, compared to high, TV viewing was also not associated with carotid artery measures of plaque burden. Compared to poor LTPA or high TV viewing, ideal LTPA (odds ratio (OR): 0.82, 95% CI: 0.55, 1.23) and low TV viewing (OR=0.90, 95% CI: 0.56, 1.44) was not associated with odds of lipid core presence, respectively.
Conclusion: Overall, this study does not provide strong evidence for an association between LTPA and SB with carotid plaque measures.

1. Introduction

Habitual leisure-time physical activity (LTPA) has been associated with cardiovascular benefits through its favorable impact on various cardiometabolic risk factors. For example, higher LTPA has been associated with lower blood pressure, lower body mass index (BMI), as well as elevated high density lipoprotein (HDL) and to a lesser extent, lower triglyceride levels [1]. LTPA may also influence vasculature structure,

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[2,3] which can be measured via characteristics such as carotid wall thickness and luminal stenosis [2,4–6]. As higher levels of these adverse carotid artery remodeling metrics have been linked to a greater risk for cardiovascular disease and stroke, [7] some studies have suggested that LTPA may be associated with more favorable carotid artery measures. In contrast to LTPA, some studies have suggested that higher levels of sedentary behavior (SB), measured via accelerometry or self-reported time spent watching television (TV), are associated with greater carotid plaque, larger carotid intima-media thickness (CIMT), and greater arterial stiffness [5,8–10] as well as cardiometabolic risk factors (e.g., hypertension, high BMI) [11]. Most studies, however, have utilized a cross-sectional design and primarily used ultrasound to measure CIMT as a proxy for plaque burden [2,4,12–14]. Additionally, few studies have explored both LTPA and SB in the same sample or tested for the joint associations of low LTPA and high SB. In this study, we seek to address key research gaps by using prospective data from the well-characterized community-based atherosclerosis risk in communities (ARIC) study. Recognizing the importance of midlife risk factors as predictors of later life cardiovascular disease [15], our study seeks to understand the independent associations of LTPA and TV viewing, persistence in LTPA and TV viewing over 6 years during midlife, and the interaction between LTPA and TV viewing on carotid wall characteristics and plaque morphologic features. In addition, among studies that have examined associations between activity levels and carotid atherosclerosis, this is the first study to utilize MRI-measured characteristics of carotid atherosclerosis, which has the benefits of being able to identify plaque components and image the entire circumference of the carotid wall, unlike ultrasonagrophy [16]. This is valuable to evaluate as the vulnerability of an atherosclerotic plaque may be more related to its composition rather than its size or accompanying luminal narrowing [17–19]. We hypothesize that higher LTPA and lower TV viewing at midlife are independently associated with more favorable carotid artery measures. We also tested if higher LTPA will attenuate the hypothesized adverse associations of TV viewing on manifestations of carotid artery characteristics.

2. Methods

The ARIC study is a prospective observational cohort of 15,792 mostly White and Black participants, ages 45 to 64 years, originally recruited based on a probability sample from 4 U.S. communities (Forsyth County, NC; Jackson, MS; Minneapolis, MN; and Washington County, MD). Participants completed several in-person clinic examinations, beginning with a baseline visit between 1987 and 1989 followed by 3 triennial examinations (visit 2: 1990–1992, visit 3: 1993–1995, visit 4: 1996–1998), where extensive medical, social and demographic data were collected. The details of the ARIC Study have been previously described [20]. Based on the interest to examine LTPA levels and SB in midlife and their persistence, our study baseline was visit 3 (1993–1995) with a retrospective evaluation of persistence in LTPA and SB over 6 years from ARIC visit 1 (1987–1989) to visit 3 (1993–1995).

For the current study, we were interested in a subsample of ARIC participants who were selected and consented to participate in the Carotid MRI ancillary study conducted from 2004 to 2006 [21]. Participants in the ARIC Carotid MRI study were selected using a stratified sampling design intended to oversample for plaque based on CIMT at a prior ultrasound assessment (1993–1998), with the goal of recruiting approximately 1200 participants with ‘thick’ walls and a random sample of 800 additional participants. CIMT cutpoints to define thick carotid artery walls ranged from 1.00 mm to 1.28 mm (69th to 73rd percentile) across field centers to allow for an approximately equal distribution of participants across field centers [21]. Participants with contraindications to MRI or contrast media were excluded, as well as participants who did not provide informed consent. Those who had a prior carotid endarterectomy were also excluded [21]. Among the 2066 participants enrolled, 1939 completed a carotid MRI exam, of which 1769 had a complete set of MRI parameters. We additionally excluded 187 who had missing data on carotid MRI variables of interest and LTPA and TV viewing exposures at both visits 1 and 3, resulting in a final analytic sample of 1582 participants (Supplemental Figure 1). Institutional review boards at all study sites approved the study and all study participants provided written informed consent at each clinic visit.

LTPA was ascertained at visits 1 (1987 – 1989) and 3 (1993 – 1995) with the interviewer-administered ARIC/Baecke questionnaire [22]. Participants were asked to report up to 4 leisure-time physical activities they participated in the past year and to provide the number of hours per week (duration) and months per year (frequency) for each activity. The Baecke questionnaire has moderate to good reliability (test-retest reliability ranging from 0.74 to 0,88) [22] and has also been shown to have moderate validity (Spearman correlation coefficient 0.54) against energy expenditure measured with doubly labeled water [23]. Several strengths of the questionnaire have been identified, including ease of administration, high reliability, and assessment of light to vigorous intensity physical activities that are not well-captured by other self-reported questionnaires [24]. Furthermore, modified versions of this questionnaire have been used in several population-based studies, including the Study of Women's Health Across the Nation and the Jackson Heart Study [25,26]. Activities were assigned a metabolic equivalent of task (MET) value ranging from 1 to 12 based on the Compendium of Physical Activities [27]. MET values $\geq$3 to <6 were considered moderate intensity physical activity and METs $\geq$6 were categorized as vigorous intensity physical activity. The frequency and duration of each activity were used to estimate minutes/week spent in moderate or vigorous LTPA at each visit, which was further categorized according to the American Heart Association's (AHA) cardiovascular health metrics for physical activity [28]: “ideal” ($\geq$75 min/week of vigorous intensity or $\geq$150 min/week of any combination of moderate + vigorous intensity exercise), “intermediate” (1–74 min/week of vigorous intensity or 1–149 min/week of any combination of moderate + vigorous intensity exercise), or “poor” (0 min/week of moderate or vigorous exercise). Persistence in LTPA (n = 849) was measured by identifying participants as stable ideal (ideal LTPA at visits 1 and 3), stable intermediate (intermediate LTPA at visits 1 and 3) or stable poor (poor LTPA at visits 1 and 3).

TV viewing was also ascertained at both visit 1 and visit 3 with a question asking participants how often they viewed TV during leisure-time. Response options included never, seldom, sometimes, often, and very often, which were further classified as high (“often”/ “very often”), medium (“sometimes”), and low (“never”/“seldom”), consistent with prior published ARIC studies [29]. Persistence in TV viewing (n = 954) was measured by categorizing participants as having stable low [“never”/“seldom” at visits 1 and 3], stable medium [“sometimes” at visits 1 and 3], or stable high [“often”/ “very often” TV viewing at visits 1 and 3].

A standard MRI protocol as described previously [21] was used for all participants who were selected for the ARIC Carotid MRI ancillary study and performed on 1.5 Tesla scanners (Excite platform, GE Medical Systems, Forsyth County, Jackson, and Washington County, USA; Symphony Maestro, Siemens Medical Solutions, Minneapolis, USA) using bilateral 4-element phased array carotid coils (Machnet, The Netherlands) [21]. Total protocol time was less than 1 hour. A 3-dimensional time-of-flight magnetic resonance angiogram (MRA) was acquired through both carotid bifurcations, followed by T1-weighted carotid vessel wall MRI (VWMRI) images oriented perpendicular to the vessel and centered at the thickest part of the internal or common carotid artery wall [21]. The image parameters were repetition time/ echo time of 1 RR/ 5 msec, turbo factor of 10, in-plane resolution =0.51 × 0.58 mm^2 and thickness=2 mm with total longitudinal coverage of 3.2 cm. The VWMRI images were repeated 5 min after the intravenous gadodiamide injection (Omniscan, GE Amersham). Seven readers were trained to interpret the MRI images with semiautomated software (VesselMASS; Division of Image Processing, Radiology Department, Leiden University Medical Center, Leiden, the Netherlands). All examinations were assigned quality scores based on image quality and protocol adherence; exams that failed were not analyzed.

The primary outcomes of interest (Supplemental Table 1) used in this study were continuous measures of MRI internal carotid artery (ICA) plaque burden defined by total wall volume (mL) - calculated by integrating area measurements over 8 pre-contrast contiguous slices, selected to include the thickest wall, covering 1.6 cm; maximum wall thickness (mm) - maximum segmental wall thickness of 12 segments measured at the slice with the largest lipid core area of the maximum segmental wall thickness if no core was present; normalized wall index – calculated as lumen area (mm^2)/ total vessel wall area (mm^2); and maximum stenosis (%). Binary measures of ICA MRI plaque characteristics included presence of a lipid core (present on at least 1 slice) and a lipid core in 2 or more adjacent slices. Measures of plaque components included total lipid core volume (mL), maximum lipid core area (cm^2), calcification presence/absence (binary), and maximum calcification area (cm^2) and were limited to those participants with a lipid core present. In addition, maximum calcification area was only analyzed among those with calcification present.

We used multivariable linear regression for continuous outcomes, and present regression coefficients (β) and 95% confidence intervals (CI). For all categorical outcomes, we used multivariable logistic regression and present odds ratios (OR) and 95% CI. All analyses adjusted for age, race-ARIC field center (White adults from Minneapolis, Washington County, or Forsyth County or Black adults from Forsyth County and Jackson) to reflect the race-geographic distribution of the ARIC cohort, sex, height squared (m^2) as previous studies in this cohort have demonstrated the association between height and lumen diameter, [30–32] education (< high school, high school, > high school), smoking pack-years (0 pack-years for never smokers and mean imputation for $n = 90$ participants with missing pack-years data), and hyperlipidemia (defined as total cholesterol level higher than 240 mg/dL, high-density lipoprotein cholesterol level lower than 40 mg/dL, low-density lipoprotein cholesterol level higher than 160 mg/dL, triglyceride level higher than 200 mg/dL, or use of cholesterol-lowering medications) obtained at visit 3. Analyses examining lipid core measures were also adjusted for maximum segmental wall thickness. Sensitivity analyses considered additional adjustment for comorbidities presumed to be on the causal pathway (i.e., hypertension, diabetes, and body-mass index measured at visit 3). For baseline (visit 3) analyses, the "high" and "poor" TV viewing and LTPA groups were used as the reference groups respectively. Similarly, for the persistence analyses (visit 1 to 3), the "stable high" and "stable poor" TV viewing and LTPA groups were used as the reference groups respectively. In secondary analyses, we examined LTPA as a continuous variable, in MET-min/ week, as well as by using a linear spline model. In additional analyses, we also examined the interaction between TV viewing and LTPA at baseline (visit 3) with continuous and categorical measures of plaque burden by specifying models that included LTPA ("poor", "intermediate", and "ideal"), TV viewing ("high", "medium", and "low"), and the interaction between the two, adjusted for the same covariates indicated above. Sampling weights were used in all analyses to account for the oversampling of participants with thick carotid artery walls and to provide estimates referable to the overall ARIC population. A p-value of <0.05 was considered statistically significant. Analyses were performed with Stata, version 15.0.

3. Results

Among the 1582 participants included, the mean weighted age at visit 3 was 59 years (standard deviation [SD]: 5.4 years), 43% were male and 18% were Black. Overall, approximately 43% of the weighted sample had reported ideal LTPA based on the AHA guidelines and 23% reported low TV viewing (responded "never" or "seldom"). Participants classified as having ideal LTPA compared to poor or intermediate LTPA, as well as those who reported low levels of TV viewing, were more often White, had a higher education, and had fewer comorbidities (e.g., diabetes, hypertension) (Table 1).

At visit 3, there were no associations between LTPA or TV viewing and continuous (Table 2) or categorical (Fig. 1) measures of carotid artery plaque burden as assessed by total wall volume, maximum wall thickness, normalized wall index, and maximum stenosis. There were no significant associations between persistence in LTPA or TV viewing over 6 years with measures of plaque burden (Table 2, Fig. 2).

Associations between LTPA and TV viewing with plaque components were also assessed among the subset of participants who had a lipid core present. For these analyses, we additionally adjusted for maximum wall thickness. There were no significant associations across all exposure/ outcome combinations (Table 3). Sensitivity analyses that excluded subjects with coronary heart disease (defined as participants who had a reported history of CHD at visit 1, or a myocardial infarction, coronary artery bypass surgery, or angioplasty by 1997, $n = 1466$) or statin use ($n = 1411$) did not significantly change results or inferences (Supplemental Table 2, Supplemental Table 3). Sensitivity analyses that additionally adjusted for comorbidities hypothesized to be on the casual pathway (i.e., hypertension, diabetes, and BMI measured at visit 3) also did not appreciably change the results or inferences (Supplemental Table 4).

In supplemental analyses, we examined LTPA as a continuous measure in MET-min/week at visit 3. There were no significant associations of LTPA measured continuously with measures of plaque burden or plaque components (Supplemental Table 5). Due to the high proportion (~32%) of participants reporting not engaging in any physical activity (i.e., 0 MET-min/ week), we also used a linear spline model to analyze the association between LTPA measured continuously at visit 3 to estimate the combined association of not reporting any physical activity as well as the linear association of MVPA for those with >0 MET-min/ week. This model did show an isolated, positive association of LTPA with maximum lipid core area (Supplemental Table 6). However, these results did not reach statistical significance after a Bonferroni correction considering the number of outcomes examined. Due to the nature of the response options for the question on television viewing as "never," "seldom," "sometimes," "often," or "very often," we were unable to examine this measure as a continuous variable.

As a secondary analysis, we examined interactions between visit 3 LTPA (poor, intermediate, ideal) and TV viewing (low, medium, high) for all measures of plaque burden and plaque components. No significant interactions were observed (Supplemental Table 7).

4. Discussion

Though we hypothesized that higher LTPA would be associated with favorable carotid artery characteristics and higher TV viewing would be associated with higher atherosclerotic burden, the results of this study did not provide strong evidence to support an association. Though the linear spline model showed an isolated, positive association between LTPA and maximum lipid core area, it did not reach statistical significance after a Bonferroni correction for multiple comparisons. Overall, there were no clinically significant associations with LTPA and TV viewing with measures of atherosclerosis in this study. It is possible that long-term sustained high LTPA, perhaps at higher intensity and throughout mid- to late-life, is needed to see measurable differences in carotid plaque burden. Furthermore, it is understandable that there were not clinically significant associations for LTPA and TV viewing with plaque components as the participants included in these sub-analyses by default, have significant atherosclerotic burden given the presence of a lipid core. In this case, perhaps the effects of LTPA and SB on lipid core characteristics are not as impactful and other factors, such as genetic predisposition and comorbidities may be more predictive of disease.

Prior studies on this topic, which have been largely cross-sectional and used ultrasonography to measure characteristics of the carotid wall, have demonstrated inconsistent findings regarding the association

Table 1
Weighted visit 3 (1993–1995) characteristics of study participants by leisure-time physical activity levels and television viewing frequencies ($N = 1582$).

	Overall	Leisure-Time Physical Activity			Television Viewing		
Demographics							
Weighted Mean (SD) or%	$n = 1582$	Poor ($n = 515$)	Intermediate ($n = 344$)	Ideal ($n = 723$)	High ($n = 534$)	Medium ($n = 734$)	Low ($n = 314$)
Mean age, years	58.72 (5.42)	58.05 (5.33)	58.05 (5.03)	59.60 (5.58)	59.13 (6.09)	58.51 (5.23)	58.65 (4.92)
Mean height, meters	1.68 (0.09)	1.67 (0.09)	1.67 (0.09)	1.70 (0.10)	1.69 (0.10)	1.67 (0.09)	1.69 (0.08)
% Male sex	43.2	38.3	36.3	50.8	48.3	39.4	44.9
% Black race	18.0	26.9	16.3	12.3	26.4	15.6	12.3
% <HS education	13.2	19.1	10.6	10.3	15.0	12.2	13.1
Lifestyle Behaviors							
% Ever smoker	55.0	57.0	52.2	55.0	60.6	53.4	51.1
Smoking pack-years	269.47 (367.99)	279.43 (373.50)	254.12 (341.47)	270.55 (378.12)	306.21 (414.45)	253.59 (362.28)	255.79 (319.62)
% Ever drinker	76.8	74.2	75.9	79.2	79.1	78.0	71.3
Comorbidities*							
Mean BMI, kg/m2	27.51 (4.69)	28.64 (5.32)	27.22 (4.07)	26.83 (4.34)	27.93 (4.86)	27.36 (4.54)	27.30 (4.68)
Mean LDL-C	125.27 (34.26)	125.98 (38.11)	126.42 (31.94)	124.10 (32.29)	129.54 (35.38)	124.13 (32.77)	122.25 (34.70)
Mean HDL-C	54.00 (18.83)	51.08 (16.74)	56.69 (17.82)	54.67 (20.54)	51.57 (19.93)	55.07 (19.06)	54.87 (16.53)
% Hyperlipidemia	43.5	47.1	43.1	41.0	50.0	41.7	39.0
% Diabetes	9.5	12.9	10.3	6.5	11.6	9.5	6.8
% Hypertension	32.4	38.6	30.0	29.1	38.5	31.1	27.1
% CHD	3.0	2.5	2.2	3.7	4.8	2.4	1.9
% Taking anti-hypertensives	27.7	30.1	29.2	25.0	31.3	26.3	25.9
% Taking statins	4.1	4.9	2.2	4.5	5.4	3.8	2.8
Leisure-Time Physical Activity & Sedentary Behavior							
% Ideal PA/ Meeting Guidelines	43.4	0	0	100	36.1	46.3	46.7
Mean Moderate to Vigorous Intensity PA, MET-min/week	736.95 (870.67)	0	377.70 (179.83)	1487.39 (848.72)	618.85 (882.15)	770.22 (862.35)	817.99 (842.74)
% Low TV Viewing	22.9	19.2	24.7	24.7	0	0	100
Carotid Artery Measures of Plaque Burden							
Total wall volume (mL)	0.42 (0.16)	0.40 (0.15)	0.40 (0.16)	0.44 (0.18)	0.42 (0.19)	0.41 (0.15)	0.42 (0.16)
Max carotid wall thickness (mm)	2.11 (1.12)	2.04 (1.03)	2.02 (1.10)	2.22 (1.18)	2.15 (1.28)	2.07 (1.06)	2.17 (1.04)
Normalized wall index	0.56 (0.14)	0.57 (0.14)	0.57 (0.12)	0.55 (0.15)	0.57 (0.16)	0.56 (0.13)	0.55 (0.13)
Max stenosis (%)	7.39 (13.76)	7.48 (14.51)	6.86 (11.51)	7.61 (14.42)	8.18 (16.33)	6.52 (12.57)	8.20 (12.77)
Lipid core presence	26.4%	27.8%	21.4%	28.2%	29.0%	24.5%	27.1%
Lipid core in 2+ adjacent sites	22.6%	24.3%	18.3%	23.7%	24.5%	21.2%	23.1%

*Sample sizes were lower for comorbidities due to missing data: LDL-C ($n = 1558$), HDL-C ($n = 1577$), Diabetes ($n = 1574$), Hypertension ($n = 1574$), Coronary Heart Disease (CHD) ($n = 1550$).

between LTPA and TV viewing with atherosclerosis [33]. Some studies have demonstrated an inverse correlation between LTPA levels and atherosclerotic measures [2]. Other studies have demonstrated associations between self-reported LTPA and lower CIMT among specific sub-groups only, including non-smokers [34] or males [35]. In the Jackson Heart Study, Diaz et al. found that higher self-reported frequency of TV viewing was associated with greater CIMT, though higher occupational sitting was associated with lower CIMT among African Americans, suggesting that there may be differences in associations across subgroups as well as by activity domain [8]. Still others, like our study, found no significant associations overall [36]. Reasons for these discrepancies may include recall bias and differences in ascertainment of physical activity levels by different questionnaires that are based on self-reported activity levels as well as varied demographics (e.g., age) of the participants samples.

Our study has some limitations. First, given the methodology, we acknowledge the possibility that the results of the study may have been biased towards the null. LTPA and TV viewing were ascertained via self-report and may be subject to information (e.g., recall) bias and do not adequately capture certain intensities of physical activity, such as light-intensity activity, that is more commonly performed in an aging population. Furthermore, as we focused on TV viewing as a measure of SB, we were unable to distinguish between passive versus active SB. Future studies should explore the range of behaviors in both domains of LTPA and SB, possibly through device-based measures. In this study, we examined persistence in LTPA and TV viewing, as a majority reported maintenance over time, and did not examine those who increased (25% increased LTPA, 22% increased TV viewing) or decreased (21% decreased LTPA, 17% decreased TV viewing) activity levels over time. In addition, we did not examine duration of physical activity and TV viewing before midlife; therefore we are unable to determine the accrued benefits, or lack of benefit due to lower engagement in physical activity, over the life course. While we used two time points over 6 years to assess for persistence in physical activity, it may not be entirely reflective of cumulative, mid-life LTPA. However, the Baecke questionnaire asks participants to report on their activity levels over the last year providing a better indication of habitual levels of physical activity compared to other self-report measures. While our sample included both Black and White men and women, small sample sizes precluded our ability to assess for interactions by race and sex. In addition, attrition and selection biases are of concern when analyzing longitudinal data since those who drop out are typically less healthy and less physically active, likely further biasing our associations towards the null. Lastly, there is the potential for residual confounding. Specifically, dietary

Table 2
Weighted, adjusted association of midlife (visit 3) and persistent (visit 1 to 3) leisure-time physical activity and TV viewing with continuous carotid artery measures of plaque burden ($N = 1582$).

			Total wall volume (mL)	Maximum carotid wall thickness (mm)	Normalized wall index	Maximum stenosis (%)
Visit 3	LTPA ($n = 1582$)	Poor ($n = 515$)	0 (Ref)	0 (Ref)	0 (Ref)	0 (Ref)
		Intermediate ($n = 344$)	−0.01 (−0.03, 0.02)	−0.04 (−0.21, 0.14)	0.01 (−0.01, 0.03)	−0.55 (−2.49, 1.38)
		Ideal ($n = 723$)	0.01 (−0.01, 0.03)	0.06 (−0.08, 0.21)	−0.01 (−0.03, 0.01)	−0.11 (−1.98, 1.76)
		p-trend	0.270	0.357	0.268	0.928
	TV Viewing ($n = 1582$)	High ($n = 534$)	0 (Ref)	0 (Ref)	0 (Ref)	0 (Ref)
		Medium ($n = 734$)	−0.01 (−0.03, 0.01)	−0.05 (−0.20, 0.10)	−0.01 (−0.02, 0.01)	−1.11 (−2.84, 0.63)
		Low ($n = 314$)	−0.002 (−0.02, 0.03)	0.02 (−0.16, 0.21)	−0.02 (−0.04, 0.01)	0.25 (−1.97, 2.47)
		p-trend	0.945	0.855	0.167	0.914
Persistence (Visit 1 – 3)	LTPA ($n = 849$)	Poor ($n = 294$)	0 (Ref)	0 (Ref)	0 (Ref)	0 (Ref)
		Intermediate ($n = 126$)	−0.01 (−0.04, 0.03)	−0.02 (−0.25, 0.22)	0.01 (−0.02, 0.04)	−0.14 (−2.86, 2.59)
		Ideal ($n = 429$)	0.02 (−0.01, 0.05)	0.12 (−0.05, 0.30)	−0.01 (−0.03, 0.01)	0.43 (−1.93, 2.79)
		p-trend	0.146	0.144	0.285	0.706
	TV Viewing ($n = 954$)	High ($n = 313$)	0 (Ref)	0 (Ref)	0 (Ref)	0 (Ref)
		Medium ($n = 453$)	−0.01 (−0.04, 0.02)	−0.10 (−0.31, 0.11)	−0.0005 (−0.02, 0.02)	−1.94 (−4.45, 0.57)
		Low ($n = 188$)	−0.01 (−0.04, 0.03)	0.04 (−0.22, 0.30)	−0.01 (−0.05, 0.02)	−0.42 (−3.50, 2.66)
		p-trend	0.713	0.820	0.397	0.714

*Models adjusted for age, race-center, sex, height squared (m^2), education, smoking pack-years, and hyperlipidemia at visit 3.
†Models for p-trend were obtained by including LTPA and TV viewing as continuous rather than categorical variables in the statistical model.
‡LTPA: leisure-time physical activity.

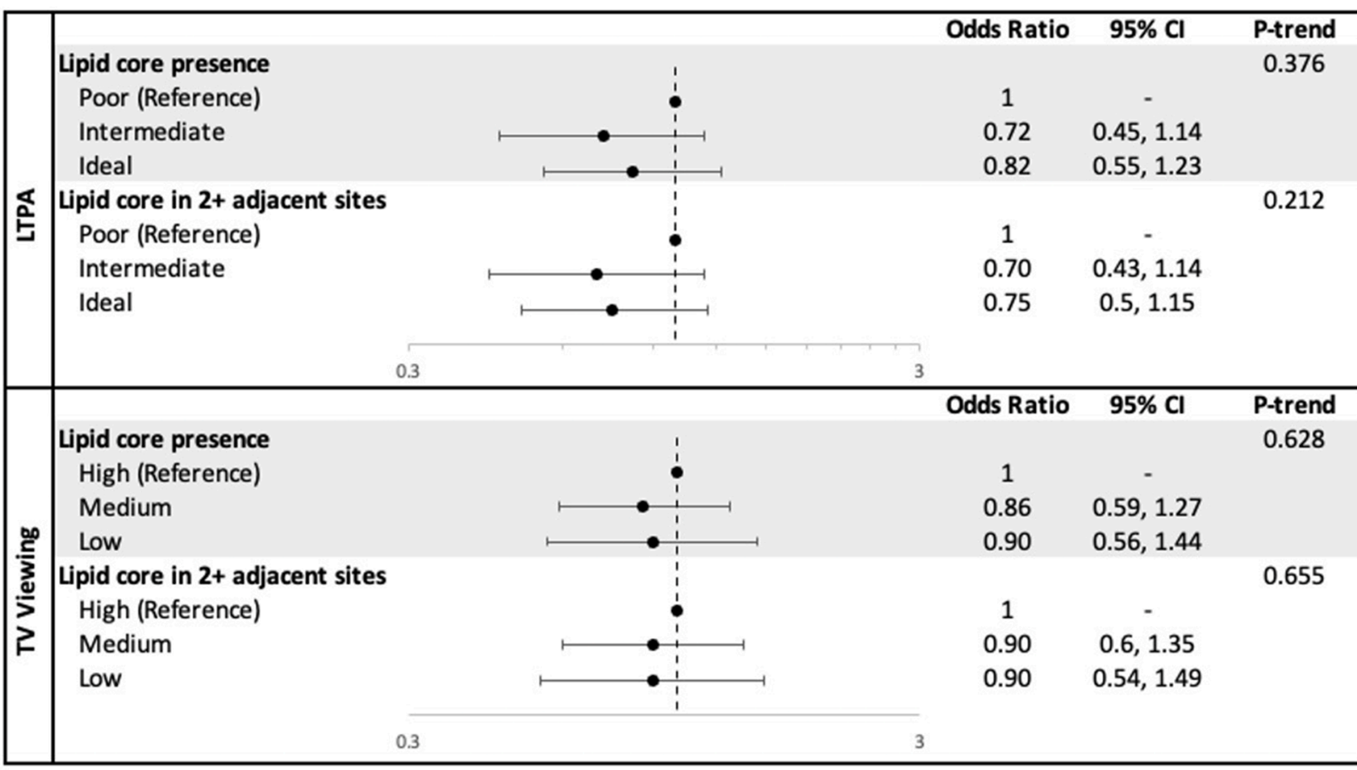

Fig. 1. Weighted, adjusted association of midlife leisure-time physical activity and TV viewing at visit 3 with binary carotid artery measures of plaque burden ($N = 1582$).
*Models adjusted for age, race-center, sex, height squared (m^2), education, smoking pack-years, and hyperlipidemia at visit 3 as well as maximum segmental wall thickness (mm)
†Models for p-trend were obtained by including LTPA and TV viewing as continuous rather than categorical variables in the statistical model
‡LTPA: leisure-time physical activity.

information was not captured at ARIC visit 3 and may be an important confounder of LTPA.

Despite these limitations, our study has several strengths. To our knowledge, this is the first study to examine associations between physical activity and sedentary behavior with MRI-measured characteristics of carotid atherosclerosis. MRI has the benefits of being able to image the entire circumference of the carotid wall, identify plaque components, and include the adventitia in wall thickness measurements, unlike CIMT [16]. Furthermore, a previous study suggested that carotid artery wall thickness measured by MRI may be a better

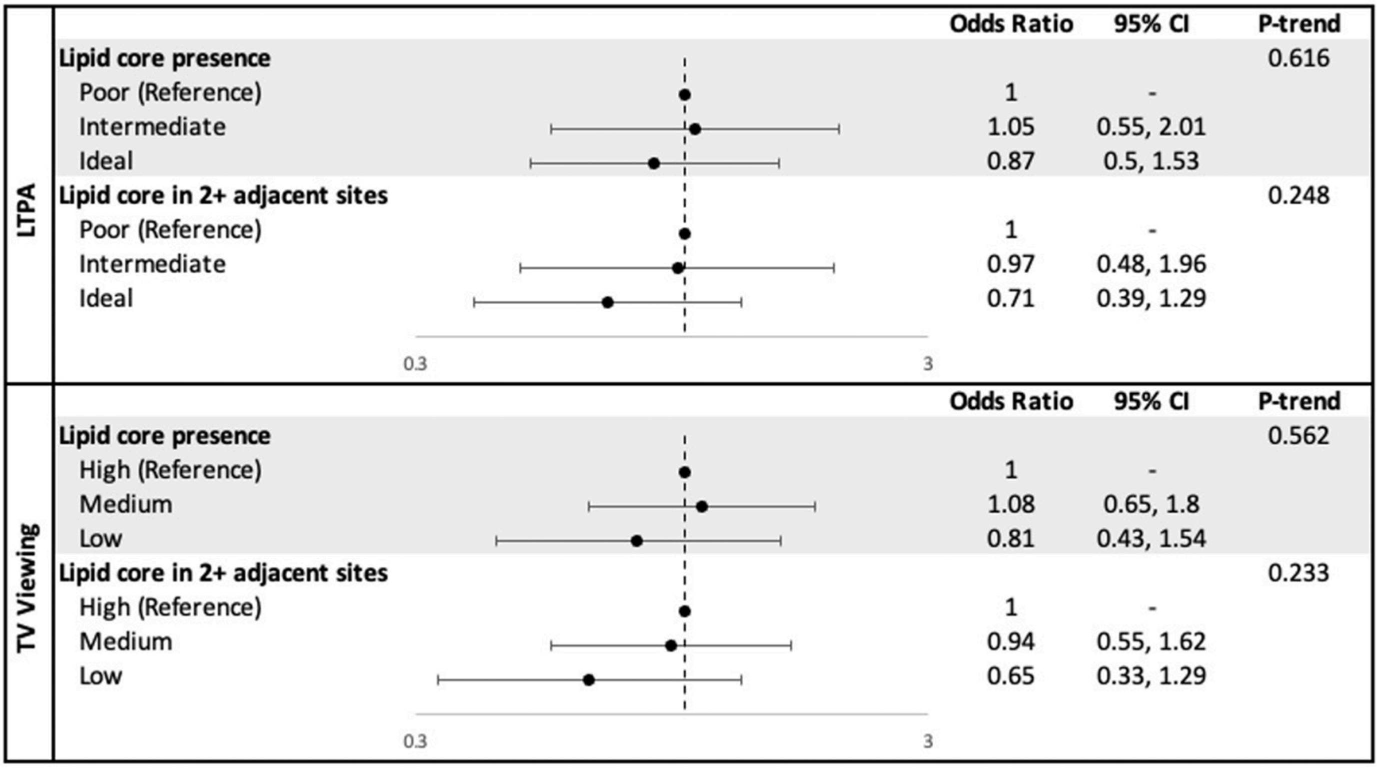

Fig. 2. Weighted, adjusted association of persistent midlife leisure-time physical activity ($N = 849$) and TV viewing ($N = 954$) from Visits 1 to 3 with binary carotid artery measures of plaque burden.

*Models adjusted for age, race-center, sex, height squared (m^2), education, smoking pack-years, and hyperlipidemia at visit 3 as well as maximum segmental wall thickness (mm)

†Models for p-trend were obtained by including LTPA and TV viewing as continuous rather than categorical variables in the statistical model

‡LTPA: leisure-time physical activity.

Table 3
Weighted, adjusted association of midlife leisure-time physical activity and TV viewing at visit 3 with plaque components among those with a lipid core.

			Beta or Odds Ratio (95% CI) Maximum lipid core volume (mL)	Maximum lipid core area (cm^2)	Calcification presence	Calcification area (cm^2)
Visit 3	**LTPA**	**Poor**	0 (Ref)	0 (Ref)	1 (Ref)	0 (Ref)
		Intermediate	0.0004 (−0.02, 0.02)	−0.004 (−0.02, 0.01)	1.80 (0.86, 3.76)	−0.01 (−0.01, 0.004)
		Ideal	0.005 (−0.005, 0.02)	0.0005 (−0.01, 0.01)	1.11 (0.65, 1.90)	0.004 (−0.003, 0.01)
		p-trend	0.337	0.895	0.805	0.187
		n	523	523	523	302
	TV Viewing	**High**	0 (Ref)	0 (Ref)	1 (Ref)	0 (Ref)
		Medium	−0.002 (−0.01, 0.01)	−0.003 (−0.02, 0.01)	0.96 (0.56, 1.65)	−0.001 (−0.01, 0.01)
		Low	0.004 (−0.01, 0.02)	0.002 (−0.01, 0.02)	1.09 (0.56, 2.12)	0.004 (−0.01, 0.01)
		p-trend	0.686	0.892	0.821	0.413
		n	523	523	523	302
Persistence (Visit 1 – 3)	**LTPA**	**Poor**	0 (Ref)	0 (Ref)	1 (Ref)	0 (Ref)
		Intermediate	0.002 (−0.02, 0.02)	−0.01 (−0.03, 0.01)	1.96 (0.58, 6.65)	−0.003 (−0.02, 0.01)
		Ideal	0.001 (−0.01, 0.01)	−0.002 (−0.02, 0.01)	0.97 (0.44, 2.14)	0.01 (−0.01, 0.02)
		p-trend	0.869	0.877	0.784	0.274
		n	295	295	295	170
	TV Viewing	**High**	0 (Ref)	0 (Ref)	1 (Ref)	0 (Ref)
		Medium	−0.001 (−0.01, 0.01)	−0.001 (−0.02, 0.02)	1.67 (0.82, 3.37)	−0.001 (−0.01, 0.01)
		Low	−0.01 (−0.03, 0.01)	−0.01 (−0.02, 0.01)	0.97 (0.38, 2.44)	0.01 (−0.01, 0.02)
		p-trend	0.515	0.470	0.934	0.424
		n	314	314	310	178

*Models adjusted for age, race-center, sex, height squared (m^2), education, smoking pack-years, and hyperlipidemia at visit 3 as well as maximum segmental wall thickness (mm).

†Models for p-trend were obtained by including LTPA and TV viewing as continuous rather than categorical variables in the statistical model.

‡Sample sizes are smaller and varied as measures of plaque components were limited to those participants with a lipid core. Additionally, maximum calcification area was only analyzed among those with calcification present.

§LTPA: leisure-time physical activity.

predictor of cardiovascular disease and stroke compared to CIMT measured by ultrasound [37]. Another study also demonstrated that the presence of a lipid core on MRI was associated with incident cardiovascular events independent of wall thickness [38]. By using MRI, this study allowed for a more thorough investigation of various measures of plaque burden and plaque components. In addition, most studies have examined associations between activity levels and carotid atherosclerosis at one time point. In this study, we examined LTPA as well as TV viewing in the same sample at both baseline as well as across a 6 year time frame to ascertain sustained or persistent levels of LTPA and TV viewing. In addition, we evaluated for interactions between LTPA and TV viewing.

Data from our study suggest that the association between LTPA and TV viewing with MRI-measured features of carotid atherosclerosis remains unclear. Device-based measures of physical activity and sedentary behavior levels may better capture time spent in sedentary behavior and across the entire physical activity intensity spectrum. It would also be beneficial to assess for differences by domain of physical activity, e.g., occupational versus leisure-time. Furthermore, the benefits of ideal LTPA and low TV viewing likely accumulate over several years, therefore future work should further disentangle the role of duration, frequency, and intensity of LTPA prospectively to guide appropriate public health recommendations. Lastly, there is a need for further characterization of how carotid atherosclerotic measures differ among those with symptomatic disease to determine if there are any clinically significant thresholds of measures of plaque burden and components that lifestyle modifications may be able to modify. In conclusion, although this study addresses gaps by including simultaneous assessment of LTPA and TV viewing and utilizes more sensitive carotid MRI measures, this study does not provide strong evidence for a consistent association between LTPA and SB with carotid plaque measures.

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Disclosures

None

Supplemental Figure 1. flowchart of study exclusions and analytic sample.

*ICA: internal carotid artery

CRediT authorship contribution statement

Aarti Kumar: Conceptualization, Methodology, Data curation, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Ye Qiao:** Methodology, Data curation, Formal analysis, Writing – review & editing. **Bruce Wasserman:** Methodology, Data curation, Formal analysis, Writing – review & editing. **Kelley Pettee Gabriel:** Writing – review & editing. **Pablo Martinez-Amezcua:** Writing – review & editing. **Erin E. Dooley:** Writing – review & editing. **Keith M. Diaz:** Writing – review & editing. **Kelly R. Evenson:** Writing – review & editing. **A. Richey Sharrett:** Writing – review & editing. **Yiyi Zhang:** Writing – review & editing. **Priya Palta:** Conceptualization, Methodology, Data curation, Formal analysis, Writing – original draft, Writing – review & editing, Supervision.

Declaration of Competing Interest

The authors have no conflicts of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ajpc.2023.100505.

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