American Journal of Epidemiology

Vol. 173, No. 5
DOI: 10.1093/aje/kwq412
Advance Access publication: February 7, 2011

Original Contribution

Physical Activity, Television Viewing Time, and Retinal Microvascular Caliber

The Multi-Ethnic Study of Atherosclerosis

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Initially submitted July 23, 2010; accepted for publication October 27, 2010.

Physical activities and sedentary behaviors are 2 broad classes of behavior that may be clearly distinguished from each other and have different patterns of determinants. The authors examined the associations of physical activity and television viewing time with retinal vascular caliber among US adults ($n = 5,893$) from 4 racial/ethnic groups in the Multi-Ethnic Study of Atherosclerosis (2002–2004) that included non-Hispanic whites, blacks, Hispanics, and Chinese. Physical activity and television viewing time were assessed by using a questionnaire, and vascular calibers (arteriolar and venular) were measured from digital retinal photographs. Those in the lowest quartile of physical activity had wider retinal venular caliber compared with those in the highest quartile in multivariate models adjusted for demographic, cardiovascular, behavioral, and inflammatory risk factors. This was noted in non-Hispanic whites and Hispanics but not in blacks or Chinese. For television viewing time, non-Hispanic whites (but not the other racial/ethnic groups) who were in the highest quartile of television viewing time had wider retinal venular caliber compared with those in the lowest quartile. No associations were noted with arteriolar caliber. Lower levels of physical activity (among non-Hispanic whites and Hispanics) and higher levels of television viewing time (among whites) are associated with wider retinal venules.

arterioles; microvessels; motor activity; retina; sedentary lifestyle; venules

Abbreviations: CI, confidence interval; CRAE, central retinal artery equivalent; CRVE, central retinal vein equivalent; MESA, Multi-Ethnic Study of Atherosclerosis; MET, metabolic equivalent.

Lack of regular moderate-to-vigorous intensity physical activity is a well-known modifiable risk factor for cardiovascular disease, as well as for a wide variety of other chronic diseases. Public health guidelines for physical activity recommend a minimum of 30 minutes of moderate-intensity physical activity for 5 days of each week or 20 minutes of vigorous intensity physical activity for 3 days of each week (1) with those not meeting these guidelines classified as insufficiently active. Recent findings, by use of objectively derived measures of physical activity and sedentary time (accelerometry), have indicated that less than 5% of the US population meets these physical activity guidelines (2) with the majority of the day spent sedentary (3). Sedentary behaviors are characterized by their low energy expenditure (4) and occur across the domains of work, travel, and leisure time (5). Television viewing time is a highly prevalent and commonly measured leisure-time sedentary behavior (6). A consistent relation between television viewing time and adverse health outcomes has been observed, including premature mortality in adults independent of physical activity levels (7–10).

Physical activity has been shown to improve endothelial function in both healthy individuals and disease states including heart failure and coronary heart diseases (11–13), and microvascular changes in the retina of the eye are thought to represent a directly visible microvascular

phenotype of endothelial dysfunction (14). Advances in retinal imaging technology allow not only the measurement of the retinal microvasculature in a noninvasive fashion but also provide accurate and reproducible estimates of arteriolar and venular caliber (15). Narrow retinal arteriolar caliber is associated with hypertension (16), and wider retinal venular caliber has been shown to be associated with diabetes, obesity, stroke, smoking, and systemic inflammation (17, 18).

The Atherosclerosis Risk in Communities (ARIC) Study from the United States showed beneficial associations of sport-related physical activity with the venular caliber (19). A recent study in a predominantly white Australian population showed greater levels of television viewing time to be associated with wider retinal venules in men (20). However, no studies have examined potential racial/ethnic variations in the relations of physical activity and sedentary behavior with the microvasculature. The Multi-Ethnic Study of Atherosclerosis (MESA) allows us to examine physical activity and television viewing time with retinal vascular caliber in 4 racial/ethnic groups (non-Hispanic white, black, Hispanic, and Chinese).

MATERIALS AND METHODS

Study population

MESA is a prospective cohort study of men and women aged 45–84 years without history of clinical cardiovascular disease and living in 6 US communities (Baltimore, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles County, California; northern Manhattan, New York; and St. Paul, Minnesota) (21). At the first MESA examination (July 2000–July 2002), 6,814 participants were recruited from these 6 sites, by using lists of residents, dwellings, and telephone-company customers. In the last few months of the recruitment period, participants were also recruited from lists of Medicare beneficiaries obtained from the Centers for Medicare and Medicaid Services, and by referrals from other participants, to ensure the enrollment of adequate numbers of elderly participants and members all 4 ethnic groups. Participants identified themselves as non-Hispanic white, black, Hispanic, or Chinese at the time of enrollment. Participation rates among those screened were approximately 70% for non-Hispanic whites, 61% for blacks, 59% for Hispanics, and 48% for Chinese (22). Tenets of the Declaration of Helsinki were followed, and institutional review board approval was granted at each study site. Written, informed consent was obtained from each participant.

Retinal photography and measurement of retinal vascular caliber

Fundus photography was done at the second examination (August 2002–January 2004). Forty-four of the original 6,814 participants died, leaving 6,770 enrolled for the second examination. Of these, 162 (2%) refused participation, and 373 (6%) were not examined for other reasons. Of the 6,235 examined, 6,176 (99%) had retinal photographs and, for 5,979 (96%), the photographs were suitable for caliber measurement. A standardized protocol (22) was followed at each site, wherein retinas of both eyes of the participants were photographed with a 45° 6.3-megapixel digital nonmydriatic fundus camera. Two fields were taken of each eye, one centered on the optic disc and the other on the fovea. The images were sent to the University of Wisconsin, Madison, for measurement of retinal vascular calibers. A computer-based program was used by trained graders masked to the participants' characteristics to measure the caliber based on a detailed protocol (23). For each photograph, all retinal arterioles and venules coursing through an area from one-half to one-disc diameter from the margin of the optic disc were measured and summarized as the central retinal artery equivalent (CRAE) and the central retinal vein equivalent (CRAE). These calculations were made by using formulas developed by Hubbard et al. (23) and later modified by Knudtson et al. (15). Reproducibility of these measurements has been reported with intra- and intergrader intraclass correlation coefficients ranging from 0.78 to 0.99 (18). For this study, the mean of the CRAE and CRVE values for the 2 eyes was used.

Measurement of physical activity and television viewing time

Data from the second examination in MESA were used for this study. The typical weekly time and frequency of physical activities were assessed by using a modified Typical Week Physical Activity Survey, adapted from the Cross-Cultural Activity Participation Study (24). This was designed to identify the time spent in and frequency of various physical activities during a typical week of the past month. These included walking (not at work) to get places, walking for exercise, dancing and sport activities, and conditioning activities. Respondents were asked whether they participated in the different categories of activities and, if yes, they answered further questions regarding the average number of days per week and time per day that they were engaged in these activities. To obtain metabolic equivalent (MET)-minutes/week (4), we then multiplied minutes of activity by metabolic equivalents. The intentional physical activity variable was the sum of walking for exercise, sports/dancing, and conditioning activities in MET-minutes/week. The Typical Week Physical Activity Survey also questioned participants about the amount of time spent watching television, either sitting or reclining. Television viewing time in hours/week was used as the measure of sedentary behavior.

Other measures

Information about age, gender, ethnicity, educational status, and cigarette smoking was obtained by a self-administered questionnaire. Resting blood pressure was measured 3 times in the seated position by using a Dinamap model Pro 100 automated oscillometric sphygmomanometer (Critikon, Tampa, Florida), and the average of the last 2 measurements was used. ''Hypertension'' was defined as systolic blood pressure $\geq$140 mm Hg, diastolic blood pressure $\geq$90 mm Hg, or current use of antihypertensive medications (18). ''Diabetes'' was defined as fasting plasma glucose of $\geq$7.0

mmol/L (126 mg/dL) or use of medication for diabetes. "Impaired fasting glucose" was defined as a fasting glucose level of 6.1–6.9 mmol/L (110–125 mg/dL) (25). Height and weight were measured with participants wearing light clothing and no shoes, and the body mass index was calculated as weight (kg)/height $(m)^2$. Fasting blood samples were drawn from participants, and aliquots were prepared for central analysis and storage at the University of Vermont and the University of Minnesota (21). These samples were analyzed for plasma triglycerides, plasma glucose, and high-sensitivity C-reactive protein. Standardized protocols, described elsewhere (26), were used for assaying these measures.

Statistical analysis

Retinal vascular calibers (CRAE and CRVE) were examined as continuous variables. Intentional physical activity (MET-minutes/week) and television viewing time (hours/week) were examined in quartile ranges. General linear modeling was used to determine the associations of the physical activity and television viewing time measures with retinal vascular calibers. Two models were constructed. Model 1 was adjusted for age (in years), gender, and race/ethnicity. Model 2 was further adjusted for clinic site, level of educational attainment (less than high school, high school, university education), smoking status (former and never/current), presence of hypertension, diabetic status (absent, present, impaired fasting glucose), body mass index, serum triglyceride levels (mg/dL), C-reactive protein, and CRVE (in models that examined CRAE) and CRAE (in models that examined CRVE). Additionally, Model 2 was also adjusted for television viewing time in models that examined physical activity levels and for physical activity in models that examined television viewing time. Unstandardized regression coefficients (β) for CRAE and CRVE were calculated with the reference category being the highest quartile of intentional physical activity for analyses involving physical activity and the lowest quartile of television viewing time for that involving sedentary behavior. Data are reported as estimated marginal means of CRAE and CRVE for the quartiles of intentional physical activity and television viewing time. The analyses were undertaken for the total study population initially and then stratified by gender and by race/ethnicity. Gender-specific and race/ethnicity-specific quartiles of physical activity and television viewing time variables were used for the analyses involving Models 1 and 2. A criterion of $P < 0.05$ was used for statistical significance. Analyses were performed by using SPSS, version 17.0.1, for Windows (SPSS, Inc., Chicago, Illinois).

RESULTS

Characteristics of participants

Table 1 presents relevant attributes of all MESA participants, as well as stratified by race/ethnicity. There were significant differences in arteriolar and venular calibers and physical activity and sedentary measures among the 4 racial/ethnic groups. The mean CRAE was larger in blacks and Hispanics than in non-Hispanic whites and Chinese; the

Table 1. Selected Characteristics of all MESA Participants[a] and Stratified by Race/Ethnicity,[b] United States, 2002–2004

	All Participants (n = 5,893)			Non-Hispanic Whites (n = 2,348)			Blacks (n = 1,586)			Hispanics (n = 1,269)			Chinese (n = 690)		
	Mean (SD)	No.	%	Mean (SD)	No.	%	Mean (SD)	No.	%	Mean (SD)	No.	%	Mean (SD)	No.	%
Age, years	63.1 (9.9)			63.7 (10.0)			62.9 (9.6)			62.1 (9.8)			2.9 (9.9)		
Gender, males		2,814	47.8		1,138	48.5		713	45		618	48.7		345	50
Smoking, current		684	11.6		258	11		252	15.9		134	10.6		40	5.8
Diabetes, present		869	14.7		191	8.1		309	19.5		262	20.6		107	15.5
Hypertension, present		2,861	48.5		1,014	43.2		991	62.5		585	46.1		271	39.3
Body mass index, kg/m^2	28.4 (5.5)			27.8 (5.1)			30.2 (5.8)			29.7 (5.3)			24.1 (3.3)		
Triglycerides, mmol/L[c]	1.27 (0.91)			1.27 (1.09)			1.04 (0.64)			1.51 (1.03)			1.46 (0.99)		
hs-CRP, mg/L[c]	1.89 (3.39)			1.67 (3.24)			2.5 (4.47)			2.43 (3.78)			0.87 (1.31)		
Television time, hours/day	2.1 (1.5)			1.9 (1.4)			2.4 (1.7)			2.2 (1.5)			1.8 (1.2)		
Intentional physical activity, MET-minutes/week	1,405 (2,118)			1,528 (1,990)			1,547 (2,596)			1,088 (1,692)			1,247 (1,956)		
CRVE, μm	214.2 (21.9)			206.8 (21.0)			222.1 (21.3)			217.5 (20.8)			215.7 (20.5)		
CRAE, μm	144.2 (14.1)			142.8 (14.2)			145.5 (13.8)			146.0 (13.4)			143.1 (14.5)		

Abbreviations: CRAE, central retinal artery equivalent; CRVE, central retinal vein equivalent; hs-CRP, high-sensitivity C-reactive protein; MESA, Multi-Ethnic Study of Atherosclerosis; MET, metabolic equivalent; SD, standard deviation.

[a] Values are means (standard deviations) for continuous variables and number and percent for categorical variables.

[b] P values based on racial/ethnic differences for individual variables were calculated by using analysis of variance for continuous variables and the χ^2 statistic for categorical variables; for all comparisons, $P < 0.001$.

[c] Values are median (interquartile range).

Table 2. Association of Quartiles of Intentional Physical Activity With CRVE and CRAE Measures for All MESA Participants and Stratified by Race/Ethnicity, United States, 2002–2004

Intentional Physical Activity (MET-minutes/week)	CRVE, μm				CRAE, μm			
	Model 1[a]		Model 2[b]		Model 1[a]		Model 2[b]	
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI
All participants								
Quartile 4 (≥1,838)	213.4	212.3, 214.5	217.8	216.5, 219.1	143.8	143.0, 144.5	144.5	143.6, 145.3
Quartile 3 (751–1,837)	214.3	213.2, 215.4	217.8	216.5, 219.1	144.3	143.6, 145.0	144.8	144.0, 145.7
Quartile 2 (53–750)	215.6*	214.5, 216.7	218.8	217.5, 220.0	143.8	143.1, 144.6	144.1	143.3, 144.9
Quartile 1 (<53)	218.4**	217.3, 219.4	220.1*	218.9, 221.3	145.1*	144.3, 145.8	144.3	143.5, 145.1
Non-Hispanic whites								
Quartile 4 (≥2,070)	205.2	203.5, 206.9	208.2	205.9, 210.4	142.8	141.7, 143.9	144.4	142.9, 145.9
Quartile 3 (976–2,069)	205.1	203.5, 206.8	208.3	208.1, 212.6	142.7	141.6, 143.8	144.3	142.8, 145.8
Quartile 2 (248–975)	206.6	204.9, 208.3	209.9	206.1, 210.5	141.6	140.5, 142.7	143.5	141.9, 144.4
Quartile 1 (0–247)	210.1**	208.4, 211.7	210.7*	208.6, 212.8	143.7	142.6, 144.9	143.9	142.5, 145.3
Blacks								
Quartile 4 (≥1913)	220.8	218.7, 222.9	226.1	223.5, 228.6	145.3	144.0, 146.7	145.4	143.7, 147.1
Quartile 3 (736–1,912)	220.4	218.3, 222.5	225.0	222.5, 227.5	145.2	143.8, 146.6	145.6	144.0, 147.2
Quartile 2 (1–735)	223.8	221.6, 226.0	227.3	224.8, 229.7	145.6	144.2, 147.0	145.4	143.8, 147.0
Quartile 1 (0)	223.3	221.3, 225.4	226.4	224.1, 228.7	145.5	144.2, 146.9	145.2	143.7, 146.7
Hispanics								
Quartile 4 (≥1,470)	212.5	210.2, 214.8	217.4	214.7, 220.2	143.9	142.4, 145.4	145.8	144.0, 147.5
Quartile 3 (496–1,469)	218.5**	216.3, 220.7	220.1	217.5, 222.6	146.9*	145.5, 148.4	147.2	145.5, 148.8
Quartile 2 (1–495)	218.0*	215.1, 220.8	219.6	216.6, 222.6	146.1	144.2, 147.9	146.5	144.6, 148.5
Quartile 1 (0)	220.3**	218.3, 222.2	221.1*	218.7, 223.6	146.6*	145.3, 147.8	146.4	144.8, 148.0
Chinese								
Quartile 4 (≥1,670)	214.5	211.5, 217.6	217.9	214.0, 221.9	143.6	141.5, 145.7	143.3	140.5, 146.1
Quartile 3 (736–1,669)	214.5	211.3, 217.7	218.8	214.9, 222.8	141.8	139.6, 144.0	141.8	139.0, 144.6
Quartile 2 (105–735)	214.6	211.7, 217.5	218.3	214.6, 221.9	142.4	140.4, 144.4	142.3	139.7, 144.9
Quartile 1 (<105)	219.0**	215.9, 222.0	221.4	217.6, 225.2	144.4	142.3, 146.5	142.2	139.5, 144.9

Abbreviations: CI, confidence interval; CRAE, central retinal artery equivalent; CRVE, central retinal vein equivalent; MESA, Multi-Ethnic Study of Atherosclerosis; MET, metabolic equivalent.

* $P < 0.05$; ** $P < 0.001$ for the difference in marginal means in μm compared with quartile 4, which is the reference category.

[a] Adjusted for age, gender, and race/ethnicity.

[b] Adjusted for age, gender, race/ethnicity, clinic site, educational attainment, current smoking, diabetic status (present/absent/impaired fasting glucose), presence of hypertension, body mass index, serum triglycerides, C-reactive protein, television viewing time, and venular caliber (in models of arteriolar caliber) and arteriolar caliber (in models of venular caliber).

mean CRVE was largest in blacks, intermediate in Hispanics and Chinese, and smallest in non-Hispanic whites; non-Hispanic whites and blacks reported the highest measure of intentional physical activity, while Chinese were intermediate and Hispanics reported the least intentional physical activity. Self-reported television viewing was highest among the blacks and lowest among the Chinese.

Physical activity and retinal vascular calibers

Table 2 shows the multivariate-adjusted marginal means for CRVE and CRAE by quartiles of intentional physical activity for all participants and stratified by race/ethnicity.

Compared with those in the highest quartile of intentional physical activity, those in the lowest quartile had CRVE that was 2.3 μm (95% confidence interval (CI): 0.94, 3.57) wider after full adjustment (Model 2). Testing revealed significant interaction with race/ethnicity ($P = 0.02$) but not with gender, so race/ethnicity-specific analyses were done. Non-Hispanic whites and Hispanics showed the strongest association among all ethnic groups in that those in the lowest quartile of intentional physical activity had wider CRVE (non-Hispanic whites: 2.5 μm, 95% CI: 0.5, 4.5; Hispanics: 3.6 μm, 95% CI: 1.1, 5.9) compared with those in the highest quartile in multivariate models adjusted for demographic, cardiovascular, behavioral, and inflammatory risk factors. No statistically significant associations were noted in blacks or Chinese.

No statistically significant association was noted in the multivariate models, either overall or in the analyses by race/ethnicity, of physical activity and CRAE.

Table 3. Association of Quartiles of Television Viewing Time With CRVE and CRAE Measures for All MESA Participants and Stratified by Race/Ethnicity, United States, 2002–2004

Television Viewing Time (hours/day)	CRVE, μm				CRAE, μm			
	Model 1[a]		Model 2[b]		Model 1[a]		Model 2[b]	
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI
All participants								
Quartile 1 (0–1)	214.4	213.4, 215.3	218.2	217.0, 219.4	144.2	143.6, 144.9	144.5	143.7, 145.3
Quartile 2 (1.1–2)	215.0	214.0, 216.0	218.5	217.3, 219.7	143.7	143.1, 144.4	144.0	144.3, 146.0
Quartile 3 (2.1–3)	215.6	214.3, 216.8	217.8	216.4, 219.1	144.7	143.8, 145.5	145.0	143.2, 144.8
Quartile 4 (>3)	218.4**	217.1, 219.8	219.9*	218.6, 221.3	144.7	143.9, 145.6	144.2	143.3, 145.1
Non-Hispanic whites								
Quartile 1 (0–0.9)	204.0	202.3, 205.7	208.1	205.9, 210.4	141.8	140.7, 143.0	143.8	142.3, 145.4
Quartile 2 (1–1.9)	207.2	205.5, 208.9	209.3	208.1, 212.6	142.5	141.4, 143.7	143.4	141.9, 145.0
Quartile 3 (2–2.9)	206.0	204.3, 207.7	208.3	206.1, 210.4	142.7	141.5, 143.8	144.3	142.8, 145.8
Quartile 4 (>2.9)	209.9**	208.2, 211.5	210.4*	208.3, 212.5	143.8*	142.7, 144.9	144.0	142.6, 145.5
Blacks								
Quartile 1 (0–1)	221.6	219.5, 223.7	226.1	223.6, 228.6	145.4	144.0, 146.8	145.5	143.8, 147.1
Quartile 2 (1.1–2)	221.0	219.0, 223.0	225.4	223.0, 227.9	144.9	143.6, 146.2	145.1	143.5, 146.7
Quartile 3 (2.1–3.2)	222.5	220.2, 224,7	226.3	223.7, 228.9	146.1	144.6, 147.5	146.0	144.3, 147.7
Quartile 4 (>3.2)	223.7	221.6, 225.8	226.9	224.5, 229.3	145.4	144.1, 146.8	145.0	143.4, 147.9
Hispanics								
Quartile 1 (0–0.9)	216.8	214.7, 218.8	218.7	216.1, 221.3	146.8	145.5, 148.2	147.4	145.7, 149.1
Quartile 2 (1–1.9)	217.8	215.8, 219.9	220.4	217.9, 222.8	145.3	144.0, 146.6	145.8	144.2, 147.4
Quartile 3 (2–2.9)	215.7	213.1, 218.3	217.9	215.0, 220.8	145.2	143.5, 146.8)	146.5	144.6, 148.4
Quartile 4 (>2.9)	220.5*	217.8, 223.2	221.3	218.5, 224.2	146.4	144.6, 148.1	146.2	144.3, 148.0
Chinese								
Quartile 1 (0–0.9)	214.6	211.5, 217.6	219.2	215.3, 223.1	142.9	140.8, 145.0	142.0	139.2, 144.8
Quartile 2 (1–1.5)	215.4	212.4, 218.4	219.8	216.0, 223.6	142.4	140.3, 145.9	141.5	138.8, 144.2
Quartile 3 (1.6–2.1)	217.9	214.9, 225.7	219.8	216.1, 223.5	143.8	141.8, 144.5	142.4	139.8, 145.0
Quartile 4 (>2.1)	215.4	212.3, 218.5	217.6	213.8, 221.5	143.6	141.4, 145.7	143.7	141.0, 146.4

Abbreviations: CI, confidence interval; CRAE, central retinal artery equivalent; CRVE, central retinal vein equivalent; MESA, Multi-Ethnic Study of Atherosclerosis.

*$P < 0.05$; **$P < 0.001$ for the difference in marginal means in μm compared with quartile 1, which is the reference category.

[a] Adjusted for age, gender, and race/ethnicity.

[b] Adjusted for age, gender, race/ethnicity, clinic site, educational attainment, current smoking, diabetic status (present/absent/impaired fasting glucose), presence of hypertension, body mass index, serum triglycerides, C-reactive protein, television viewing time, and venular caliber (in models of arteriolar caliber) and arteriolar caliber (in models of venular caliber).

Television viewing time and retinal vascular calibers

Table 3 shows the multivariate-adjusted marginal means for CRVE and CRAE by quartiles of television viewing time for all participants and stratified by race/ethnicity.

In Model 2 analyses (adjusted for age, gender, race/ethnicity, clinic site, education, smoking, hypertension, diabetic status, body mass index, serum triglycerides, high-sensitivity C-reactive protein, intentional physical activity, and CRAE), those in the highest quartile of television viewing time (>3 hours/day) had a statistically significant wider CRVE (1.8 μm, 95% CI: 0.4, 3.2) than those in the lowest quartile (≤1 hour/day). Again, significant interactions were noted with race/ethnicity ($P < 0.1$) but not with gender. When analyzed by race/ethnicity, in Model 2, we noted that non-Hispanic whites who were in the highest quartile of television viewing time had a significantly wider CRVE (2.3 μm, 95% CI: 0.2, 4.3) than those in the lowest quartile. There were no statistically significant associations between television viewing time and CRVE in the other 3 ethnic groups.

No statistically significant associations between television viewing time and CRAE were noted in the overall, gender-specific, or race/ethnicity-specific analyses.

Analyses involving television viewing time and retinal vascular caliber were repeated for those in the sample who worked ($n = 3,113$). No difference in the associations was found after adjustment for the amount of time spent doing work that involved light, moderate, or heavy effort.

DISCUSSION

MESA provides a unique opportunity to examine the associations of physical activity and sedentary behavior with retinal vascular caliber among 4 racial/ethnic groups in a large US population without clinical cardiovascular disease. Although the association of higher levels of physical activity with a reduced prevalence of wider venules (19) and the association of greater television viewing time with wider venules among men (20) have been previously demonstrated in a predominantly white population, this is the first study to explore racial/ethnic differences in the associations of physical activity and television viewing time with retinal vascular caliber. After adjusting for sociodemographic, behavioral, and other cardiovascular risk factors, we found that lower levels of physical activity were associated with wider retinal venular caliber in non-Hispanic whites and Hispanics but not in blacks or Chinese. Again, the association of prolonged television viewing with wider retinal venular caliber was noted in non-Hispanic whites but not in the other racial/ethnic groups.

Studies on retinal microcirculation have shown that assessment of retinal vascular caliber provides insights into the contribution of subclinical vascular processes to the development of systemic disease (18). A larger retinal venular caliber has been shown to be associated with hyperglycemia, hypertriglyceridemia, current smoking, obesity, renal disease, and higher fibrinogen levels, and it is predictive of stroke and coronary heart disease (14, 27, 28). Our findings of an association of lower levels of physical activity and greater time spent in sedentary behavior with wider retinal venules could possibly result from vascular processes that lead to adverse cardiometabolic outcomes. These microvascular associations suggest a possible deleterious effect of reduced physical activity and sedentary behavior on the microvasculature. Cardiovascular disease morbidity and mortality vary widely across different ethnic groups (29), and the differences noted in our study could highlight potential pathophysiologic mechanisms underlying these race/ethnic variations. Clearly, there is a need for additional prospective studies to examine further the clinical significance of these associations.

Our findings are consistent with evidence from the population-based Atherosclerosis Risk in Communities Study, comprising a population of blacks and whites that has shown higher levels of sport- and work-related physical activity to be associated with lower prevalence of retinal microvascular signs including that of wider retinal venular caliber (19). The association of sedentary behavior with the microcirculation is similar to the findings from the Australian Diabetes, Obesity, and Lifestyle Study on Caucasian adults aged 25 years or more, which has shown associations of prolonged television viewing time with wider retinal venular caliber in men (20). However, the lack of statistically significant associations of physical activity with vascular caliber in this Australian study could be a spurious finding due to the nature of the physical activity variables (leisure-time physical activity only) used, smaller sample size in comparison with the current study, and lack of an ethnically diverse population.

The underlying pathophysiologic mechanisms for these associations remain speculative. Physical activity is known to protect the vascular endothelium (13, 30), as well as to reduce inflammatory markers associated with endothelial dysfunction (31). A recent large population-based study has shown that higher levels of physical activity are associated with lower urinary albumin excretion, possibly mediated by its effects on the renal vascular endothelium (32, 33). Data from several epidemiologic studies have shown an association of larger venular caliber with specific and nonspecific inflammatory markers, as well as systemic markers of endothelial dysfunction (18, 34, 35). Retinal microvascular changes result from underlying endothelial damage and have the potential to act as surrogate markers of endothelial function (14). Hence, it is likely that the association of lower levels of physical activity and larger venular caliber noted in our study would be mediated by endothelial dysfunction. Physical activity also induces a reduction in inflammatory markers (36, 37) that could play a role. Moreover, experimental evidence on the effects of physical activity on the molecular biology of circulating blood cells (38) and the elastic properties of the vessel wall (39) suggests that these could also influence the microvascular caliber. The cellular and molecular mechanisms underlying the relations of sedentary behavior on health outcomes still remain largely unknown and are an emerging area of research (33).

The reasons underlying the racial/ethnic differences in the study are not completely understood. Racial/ethnic differences in retinal vascular calibers in MESA have previously been noted; blacks, Hispanics, and Chinese have a larger mean venular caliber than non-Hispanic whites do, while blacks and Hispanics have a larger mean arteriolar caliber (18). Self-reported physical activity levels in our study varied among the different racial/ethnic groups in that non-Hispanic whites and blacks had the highest measure of intentional physical activity followed by the Chinese and then the Hispanics. This was similar to findings from the Third National Health and Nutrition Examination Survey that showed that whites and blacks had lower levels of physical inactivity than did Mexican Americans (40). Other cardiovascular risk factors also differed by race/ethnicity, with obesity, diabetes, and systemic inflammation more likely in blacks and Hispanics than in non-Hispanic whites. Some hemostatic factors and endothelial markers have been shown to differ within the racial/ethnic groups in the MESA population. For instance, intercellular adhesion molecule 1 (ICAM-1) protein, involved in leukocyte endothelial adherence and transmigration and a marker of cardiovascular disease risk, was highest in non-Hispanic whites and Hispanics, followed by blacks and Chinese (41). True biologic variation and genetic factors could also play a role (42). In effect, these do not fully explain the racial differences noted in associations of these behavioral measures with the microvasculature, and further studies are needed to elucidate these relations.

MESA is a unique resource with its inclusion of a large percentage of blacks, Hispanics, and Chinese. The strengths of the study include the high frequency of digital retinal photographs and the availability of extensive data on cardiovascular risk factors. The comprehensive nature of the

physical activity questionnaire used in MESA makes the measures used in this study to characterize the exposure variables unique. These features make the study different from the Australian Diabetes, Obesity, and Lifestyle Study that has previously looked at associations of these behavioral measures with the vascular caliber (20). However, several limitations should also be noted. First, temporality of the association cannot be ascertained given the cross-sectional nature of the study. Second, the relatively small numbers of participants in some ethnic groups could bias the results. Third, the self-reported nature of the physical activity and sedentary behavior data can be subject to recall and social desirability bias (43). Furthermore, participants with known cardiovascular risk factors such as diabetes, hypertension, or dyslipidemia may have received medical advice on increasing their physical activity levels that could have led to potential misclassification. Fourth, the presence of uncontrolled confounders could have introduced bias to the results. Intentional physical activity is only one component of physical activity in which participants were involved. Similarly, we used data on television viewing time only as a marker of sedentary time in our analyses. Although it is the most common leisure-time sedentary behavior (44), it raises questions about whether it reflects the true nature of the time spent sedentary. Recent analyses of data on race-specific, objectively measured sedentary time in a large US cohort have shown differences from data collected by self-report measures (3). Further studies using objective measures of physical activity and time spent in sedentary behaviors are needed to overcome this discrepancy.

In summary, our study has shown that lower levels of physical activity and higher levels of television viewing time are associated with wider retinal venules, independent of known sociodemographic, cardiovascular, and behavioral risk factors.

ACKNOWLEDGMENTS

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This study was supported by contracts N01-HC-95159 through N01-HC-95165 and N01-HC-95169 and by grant HL69979-03 from the National Heart, Lung, and Blood Institute. S. A. is supported by National Health and Medical Research Council (NHMRC) Public Health Postgraduate Scholarship 569764. D. W. D. is supported by a Victorian Health Promotion Foundation Public Health Research Fellowship. G. N. H. is supported by NHMRC Scholarship 569861 and by National Heart Foundation of Australia Fellowship PH 08B 3905. N. O. is supported by a Queensland Health Core Research Infrastructure grant and by NHMRC Program Grant 301200.

The authors thank the other MESA investigators and staff for their valuable contributions. A full list of participating MESA investigators and institutions can be found at http://mesa-nhlbi.org/.

Conflict of interest: none declared.

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