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THE ASSOCIATION BETWEEN OBJECTIVELY MEASURED SEDENTARY BEHAVIOR AND RED BLOOD CELL DISTRIBUTION WIDTH IN A NATIONAL SAMPLE OF US ADULTS

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Red blood cell distribution width (RDW), an indicator of anisocytosis, is a novel biomarker of cardiovascular disease (CVD) and all-cause mortality (1). Although findings are inconclusive, the pathophysiology linking RDW with morbidity/mortality may pertain to inflammation and/or disordered iron homeostasis (2). Consequently, identification of modifiable behaviors for prevention of unequal RDW, particularly in the general population, is needed.

Emerging research demonstrates that sedentary behavior (SB), even independently of physical activity, is predictive of CVD and premature mortality (3). Although results have been inconclusive, potential mechanisms for explaining this relationship include SB-induced inflammation and modulation of metabolic risk (4). Consequently, it is plausible to suggest that SB may be related to CVD and mortality via SB-induced anisocytosis. However, to our knowledge, no study has yet examined the association between SB and RDW. Identification of such an association may help to delineate a potential mechanism through which SB may influence CVD. Therefore, we decided to evaluate this possible association.

METHODS

Design

Data from the 2003–2006 cycles of the National Health and Nutrition Examination Survey (NHANES) were used (http://www.cdc.gov/nchs/nhanes.htm). During NHANES 2003–2006, 4,538 participants aged ≥20 years provided data on the study variables. All study procedures were approved by the National Center for Health Statistics review board; all participants provided informed consent.

Conflict of interest: none declared.

Red blood cell distribution width

RDW was derived from the coefficient of variation of the NHANES RDW histogram and recorded as a percentage.

Sedentary behavior

Accelerometers were initialized to collect data in 1-minute epochs. SB was measured during waking hours and was assessed here among participants with ≥10 hours/day of monitoring on at least 4 days (in a 1-week period) using the ActiGraph 7164 accelerometer (ActiGraph LLC, Pensacola, Florida). An activity level of less than 100 counts per minute was classified as SB (6), and to control for physical activity, counts/minute greater than or equal to 2,020 were classified as moderate-to-vigorous physical activity. Nonwear was defined as a period of at least 60 consecutive minutes of zero activity counts, with the allowance of 1–2 minutes of activity counts between 0 and 100 (5).

Covariates

Covariates included age, sex, race/ethnicity, poverty-to-income ratio, body fat percentage (as determined by dual-energy x-ray absorptiometry (DEXA)), cotinine level, history of diabetes, history of cancer, history of coronary artery disease, mean arterial blood pressure, estimated glomerular filtration rate, high-density lipoprotein cholesterol level, diet, accelerometer-determined physical activity, accelerometer wear time, serum iron level, and C-reactive protein level.

Total body fat percentage was estimated from whole-body DEXA scans (Hologic, Inc., Bedford, Massachusetts). Serum cotinine concentration was measured by means of isotope dilution–high-performance liquid chromatography/atmospheric pressure chemical ionization tandem mass spectrometry. Blood pressure was measured up to 4 times, and the average mean arterial pressure ([diastolic blood pressure × 2 + systolic blood pressure]/3) was calculated. Iron concentration was measured from a blood sample using the LX20 Pro Chemistry Analyzer (Beckman Coulter Inc., Brea, California), with high-density lipoprotein cholesterol measured enzymatically directly in serum. Dietary behavior was assessed using the 2005 Healthy Eating Index (6–8). Glomerular filtration rate was assessed from the Chronic Kidney Disease Epidemiology equation (9). High-sensitivity C-reactive protein concentration was quantified using latex-enhanced nephelometry.

Analysis

Analyses were performed using survey data procedures in Stata (StataCorp LP, College Station, Texas) to adjust for the complex survey design. Multivariable logistic regression was used to examine the association between 5 SB quintiles (independent variable) and elevated RDW (≥75th percentile; ≥13.1%). Four logistic regression models were fitted, including an unadjusted model (model 1), a minimally adjusted model (model 2), a further adjusted model (model 3), and a fully adjusted model (model 4). The minimally adjusted model (model 2) controlled for age, sex, race/ethnicity, poverty level, and DEXA-determined body fat percentage. The further adjusted model (model 3) controlled for the same covariates as model 2 plus cotinine, diabetes, cancer, coronary artery disease, mean arterial blood pressure, estimated glomerular filtration rate, high-density lipoprotein

cholesterol, diet (2005 Healthy Eating Index), accelerometer-determined physical activity, and accelerometer wear time. The fully adjusted model (model 4) controlled for the same covariates as model 3 plus serum iron and C-reactive protein. Statistical significance was established as a 2-sided *P* value less than 0.05.

RESULTS

The median age of participants was 49 years. The adjusted (adjusted for covariates in model 2) percentages of participants with an elevated RDW (≥75th percentile; 13.1%) in the 5 quintiles of SB (lowest to highest) were 18.6%, 17.8%, 20.4%, 20.7%, and 26.1%, respectively.

The fully adjusted regression model (model 4) showed that persons in the fifth quintile of SB, as compared with the first quintile, had 63% increased odds of an elevated RDW (odds ratio = 1.63, 95% confidence interval: 1.13, 2.33; *P* = 0.009; using the median values of the quintiles, *P* for linear trend = 0.04) (Table 1); when the referent group was changed to the fourth quintile, persons in the fifth quintile versus those in the fourth quintile had 45% increased odds (odds ratio = 1.45, 95% confidence interval: 1.03, 2.04; *P* = 0.03) (data not shown).

DISCUSSION

The main finding of this study was that SB was positively associated with RDW. SB was still associated with RDW after controlling for serum iron, C-reactive protein, and other established CVD risk factors, suggesting that SB may be associated with RDW via other pathways yet to be investigated. Although the conclusion is speculative, SB may be associated with RDW via SB-facilitating cytokine-induced erythropoietin resistance (10). Future work is needed to help clarify the potential mechanisms through which SB influences RDW.

A 63% increase in the odds of elevated RDW (≥13.1%) was observed among persons in quintile 5 versus those in quintile 1, which is a concern, because elevated RDW predicts premature mortality (e.g., RDW greater than or equal to 13.3% increased mortality risk by 19% among critically ill patients (11), and RDW greater than or equal to 13.0% increased mortality risk by 20% in a general population aged ≥45 years (1)). This, coupled with the fact that the majority of adults spend most of their waking hours in SB (12), underscores the importance of minimizing SB among adults.

The main limitation of this study was the cross-sectional design. Further, although accelerometer-determined information on SB overcomes many of the limitations associated with self-reported SB, lack of consensus regarding the most appropriate accelerometer data-processing protocol limits evidence synthesis and comparability between studies (13). Major strengths of this study include the novel association, the use of an objective measure of SB, the national sample, and the inclusion of several robust measures of covariates (e.g., DEXA-determined body fat percentage). Future mechanistic and prospective work is needed, but these findings suggest that prolonged SB may induce unequal RDW, which may ultimately increase risk of CVD and all-cause mortality.

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Table 1

Odds of Having an Elevated (≥75th Percentile; 13.1%) Red Blood Cell Distribution Width According to Quintile of Accelerometer-Determined Sedentary Behavior (Weighted Association) Among US Adults (*n* = 4,538), National Health and Nutrition Examination Survey, 2003–2006

Analytical Model	Quintile of Sedentary Behavior[a]							
	1 (321.6 minutes/day)	2 (420.1 minutes/day)		3 (480.8 minutes/day)		4 (543.3 minutes/day)		5 (646.6 minutes/day)	
		OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
1[b]	Referent	0.97	0.74, 1.25	1.27	1.00, 1.60	1.32	1.05, 1.67	1.96	1.53, 2.51
2[c]	Referent	0.94	0.70, 1.24	1.14	0.87, 1.50	1.16	0.86, 1.55	1.58	1.25, 2.00
3[d]	Referent	0.93	0.71, 1.23	1.14	0.86, 1.52	1.16	0.85, 1.59	1.65	1.18, 2.31
4[e]	Referent	0.91	0.68, 1.22	1.09	0.80, 1.49	1.12	0.81, 1.54	1.63	1.13, 2.33

Abbreviations: CI, confidence interval; OR, odds ratio.

[a] Sample sizes for the 5 quintiles were 908, 908, 907, 908, and 907, respectively. The reported number of minutes/day for each quintile is the mean number of sedentary minutes/day in that quintile.

[b] Unadjusted model.

[c] Model 2 (minimally adjusted) controlled for age, sex, race/ethnicity, poverty level (poverty-to-income ratio), and body fat percentage (as determined by dual-energy x-ray absorptiometry).

[d] Model 3 (further adjusted) controlled for the same covariates as model 2 plus cotinine level, history of diabetes, history of cancer, history of coronary artery disease, mean arterial blood pressure, estimated glomerular filtration rate, high-density lipoprotein cholesterol level, diet (2005 Healthy Eating Index (6)), accelerometer-determined moderate-to-vigorous physical activity, and accelerometer wear time.

[e] Model 4 (fully adjusted) controlled for the same covariates as model 3 plus serum iron and C-reactive protein.