Shiftwork and the Retinal Vasculature Diameters Among Police Officers

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Objective: To investigate associations of central retinal arteriolar equivalent (CRAE), a measure of retinal arteriolar width, and central retinal venular equivalents (CRVE), a measure of retinal venular width, with shiftwork in 199 police officers (72.9% men). **Methods:** Shiftwork (day, afternoon, night) was assessed using electronic payroll records. Four digital retinal images per officer were taken. Mean diameters of the retinal vasculature were compared across shifts using analysis of variance (ANOVA)/analysis of covariance (ANCOVA). **Results:** Among all officers (mean age $= 46.6 \pm 6.8$ years), shiftwork was not significantly associated with CRAE or CRVE. However, among current and former smokers, night-shift officers had a wider mean ($\pm$standard error [SE]) CRVE ($230.0 \pm 4.5 \, \mu m$) compared with day shift officers ($215.1 \pm 3.5 \, \mu m$); adjusted $P = 0.014$. **Conclusions:** Night shift schedule in current and former smokers is associated with wider retinal venules. Reasons for this association are not known. Longitudinal studies are warranted.

Cardiovascular disease (CVD) is the number one cause of mortality in many industrialized countries, although its prevalence appears to be declining in the United States.[1,2] Police officers are known to have a higher prevalence of CVD and CVD risk factors compared with the general population.[3–5] In addition, police officers belong to a profession that requires them to work shift schedules. Shiftwork is associated with cardiovascular disease, metabolic disorders, and several other adverse health outcomes.[6–9] Shiftwork is also known to be associated with endothelial dysfunction, atherosclerosis, and other adverse effects on the CVD system.[10–13]

Changes in the microvasculature are associated with and may precede CVD and CVD risk factors.[14,15] Narrowing of the arterioles in the retina has been shown to be associated with an increased risk of coronary heart disease,[15] stroke mortality,[16] metabolic syndrome,[14] chronic kidney disease,[17,18] and hypertension.[19–22] In addition, widening of the retinal venules has been found to be associated with endothelial dysfunction,[23] metabolic syndrome,[24] atherosclerosis, increased total serum cholesterol levels, and systemic inflammation.[21]

It is possible that shiftwork may be associated with changes in the microvasculature, particularly the retinal microvasculature, because exposure to shiftwork has been shown to increase biomarkers of systemic inflammation. In one study of Finnish airline workers, the authors found that exposure to 2nd and 3rd shifts may independently increase biomarkers of peripheral inflammation.[25] Their results also showed that inflammation was not elevated in former shiftworkers who had moved to day work, pointing to the presumably reversible effect of shiftwork on inflammation. Oxidative stress is known to play a role in atherosclerosis, arrhythmias, and other cardiac and vascular abnormalities.[26] In another study conducted among Japanese adults, oxidative stress and chronic inflammation were observed to promote arteriosclerosis in the retinal arteries.[27] Since shiftwork is mandatory in the occupation of law enforcement, it is important to identify as many of the health conditions associated with it to be better able to protect workers, or at least, mitigate the effects of this occupational exposure.

A review of the literature identified no studies that investigated associations between shiftwork and retinal vasculature. To the best of our knowledge, this study is the first to examine the association between shiftwork and retinal vasculature diameters. Our main objective was to investigate the association between shiftwork and the diameters of the retinal arterioles (ie, central retinal arteriolar equivalent [CRAE]) and venules (ie, central retinal vein equivalent [CRVE]) in police officers. Secondary objectives were to assess for effect modification by sex and smoking status. We hypothesized that officers working the afternoon and night shifts would show adverse effects (ie, narrowing) in the arterioles and (ie, widening) in the venules.

METHODS

Study Design and Participants

Participants were police officers employed by the Buffalo, New York, Police Department. The Buffalo Cardio-Metabolic Occupational Police Stress (BCOPS) study was undertaken to investigate associations between work-related stressful exposures and subclinical measures of CVD.[28] The Institutional Review Boards at the University at Buffalo and the National Institute for Occupational Safety and Health approved the studies. Female officers who were pregnant at the time of examination were excluded ($n = 2$). From June 2004 through October 2009, 464 active-duty and retired police officers (from an estimated 710 officers in 2004) were recruited and examined in the baseline BCOPS study. The 464 officers reviewed and signed informed consent forms before the examinations. Data for all exams were collected at the Center for Health Research, School of Public Health and Health Professions, University at Buffalo, State University of New York.[28]

The police officers also participated in two subsequent examinations: a follow-up examination and a microvascular study (in which retinal photos and some CVD-related biomarkers were collected) during 2011 to 2014 and 2012 to 2016, respectively. All data for the current investigation were taken from the microvascular examination (only retinal vessel diameters) and the follow-up examination (shiftwork and all other variables). Retinal data were not available in the follow-up examination. In the follow-up study (2011 to 2014), 281 officers participated after signing consent forms (Fig. 1). Of the 281 officers, 243 consented to participate in the microvascular study and had complete data on retinal photography. We merged all data from the follow-up examination and the microvascular examination, and retained only those officers who were active-duty and had complete information on shiftwork and retinal photos. As in the baseline examination, officers underwent a 6-hour examination which usually occurred on one of their training days. Our final sample size was 199 police officers, 54 women, and 145 men.

Assessment of Shiftwork

Electronic work history data from the City of Buffalo, NY payroll records were available for each day from May 1994 to the date of each officer's retinal photographic examination. The database contained information regarding the activities for each officer and included the start and end time of work, the type of activity (ie, regular work, overtime work, court appearances), the type of leave (ie, weekend, vacation, work-related injury, other types of sick leave), and the number of hours worked on each activity. All officers worked weekdays and weekends and were scheduled 4 days on and 3 days off. The time officers started their shift for the regular time work was used to classify each record into one of the following three shifts: day shift, if the start time of the record was between 04:00 and 11:59; afternoon shift, if the start time was between 12:00 and 19:59; and night shift, if the start time was between 20:00 and 03:59. An officer's dominant shift was defined as the shift on which he/she worked the highest percentage of hours. For example, the dominant shift would be night shift for an officer who worked 10% on the day
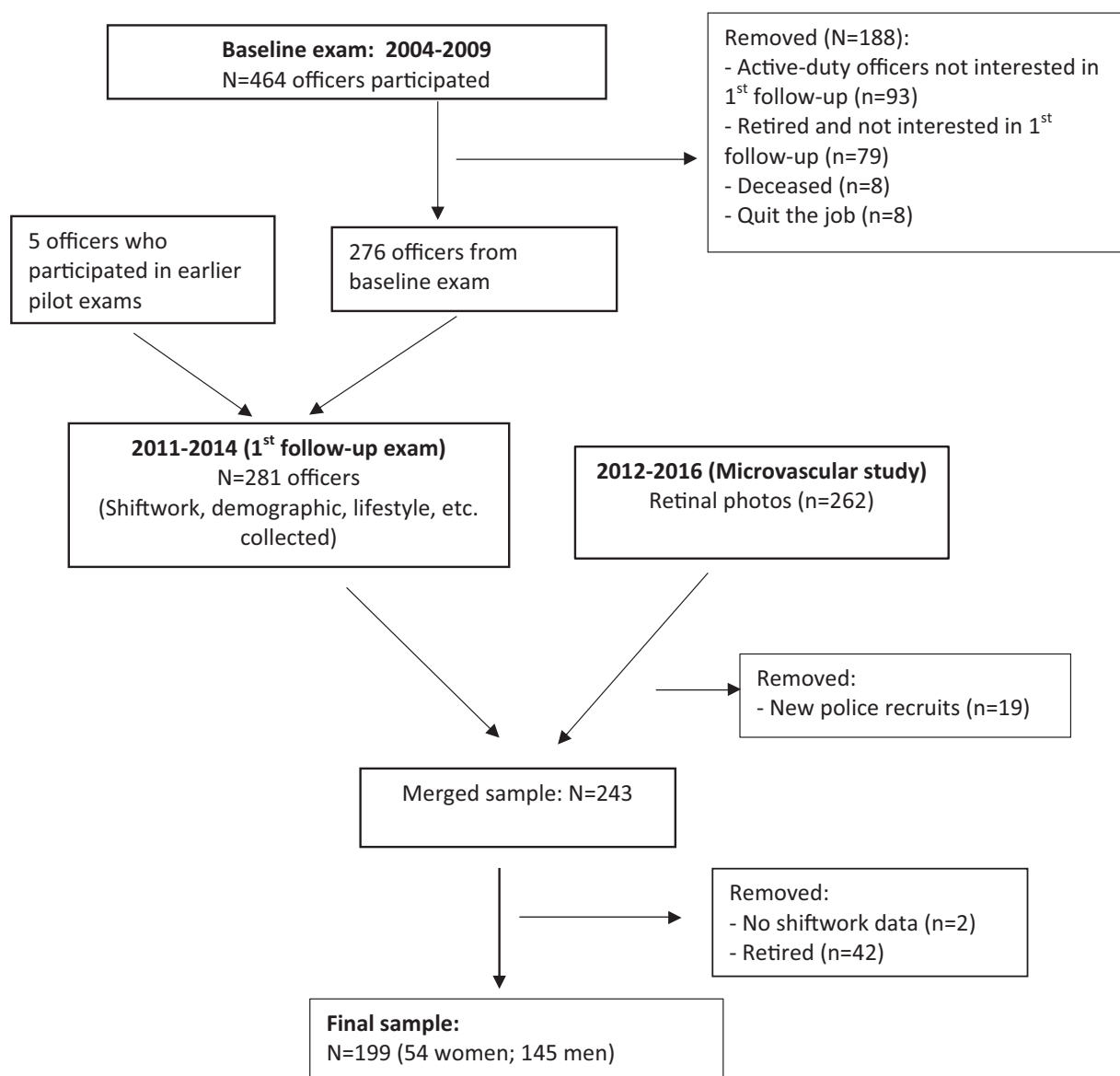

FIGURE 1. Schematic diagram of study sample.

shift, 5% on the afternoon shift, and 85% on the night shift. We used data on the dominant shift worked during the entire career.[10]

Assessment of Retinal Microvasculature

Research associates from the University at Buffalo SUNY, NY were trained and certified to perform retinal imaging. Retinal imaging is a simple, noninvasive technology for assessing microvascular abnormalities that may be associated with CVD development. A non-mydriatic ophthalmic digital imaging system was used to take two digital images per eye (four images total per participant) through a non-pharmacologically dilated pupil. Participants were seated in a windowless room with the lights turned off to allow the pupils to dilate naturally in preparation for the retinal imaging examination. One image was centered on the macula and the second on the optic nerve. The digital images were sent to the University of Wisconsin Department of Ophthalmology Ocular Epidemiology Reading Center to be graded using a standardized protocol. Retinal vessel diameters were measured at the Reading Center using a

TABLE 1. Descriptive Statistics of the Study Population, by Sex

	All ($n = 199$)	Women ($n = 54$)	Men ($n = 145$)	P
	Mean ± SD	Mean ± SD	Mean ± SD	
Age (yrs)	46.60 ± 6.84	47.31 ± 6.57	46.33 ± 6.94	0.368
Years of service	19.52 ± 7.17	18.91 ± 6.76	19.74 ± 7.33	0.466
Systolic blood pressure (mm Hg)	116.05 ± 11.59	111.9 ± 12.44	117.6 ± 10.90	0.002
Diastolic blood pressure (mm Hg)	78.46 ± 7.88	74.78 ± 6.95	79.82 ± 7.79	<0.0001
Body mass index (kg/m^2)	29.27 ± 4.41	26.50 ± 3.89	30.29 ± 4.15	<0.0001
Triglyceride (mg/dL)	118.37 ± 84.15	81.72 ± 40.28	132.0 ± 91.91	<0.0001
Total cholesterol (mg/dL)	198.59 ± 36.41	199.9 ± 35.32	198.1 ± 36.92	0.757
HDL cholesterol (mg/dL)	48.83 ± 13.98	59.39 ± 16.86	44.90 ± 10.34	<0.0001
LDL cholesterol (mg/dL)	126.31 ± 33.72	124.2 ± 30.92	127.1 ± 34.77	0.588
Sleep duration (hrs/24 hr)	6.05 ± 1.12	5.94 ± 1.26	6.09 ± 1.06	0.377
Vitamin D3 25 (OH) (ng/mL)	28.81 ± 11.28	30.77 ± 12.29	28.09 ± 10.84	0.136
Retinal arteriolar diameter (μm)	154.78 ± 13.16	157.2 ± 15.55	153.9 ± 12.08	0.156
Retinal venular diameter (μm)	222.69 ± 19.76	224.6 ± 21.62	222.0 ± 19.04	0.411
White blood cell count (WBC)	5.80 ± 1.65	5.45 ± 1.40	5.93 ± 1.72	0.069
	N (%)	N (%)	N (%)	
Race/ethnicity				0.029
White/Hispanic	157 (78.9)	37 (68.5)	120 (82.8)	
African American	42 (21.1)	17 (31.5)	25 (17.2)	
Education				0.351
≤HS/GED	16 (8.0)	3 (5.6)	13 (9.0)	
<4 yrs college	101 (50.8)	32 (59.3)	69 (47.6)	
≥4 yrs college	82 (41.2)	19 (35.2)	63 (43.5)	
Rank				0.824
Patrol officer	110 (55.8)	32 (59.3)	78 (54.6)	
Sergeant/Lieut/Capt	42 (21.3)	11 (20.4)	31 (21.7)	
Det/Exec/other	45 (22.8)	11 (20.4)	34 (23.8)	
BMI (kg/m^2)				<0.0001
Normal (<25.0)	28 (14.1)	22 (40.7)	6 (4.1)	
Overweight (25–29)	91 (45.7)	22 (40.7)	69 (47.6)	
Obese (≥30)	80 (40.2)	10 (18.5)	70 (48.3)	
Smoking status				0.011
Current	20 (10.1)	5 (9.4)	15 (10.3)	
Former	55 (27.8)	23 (43.4)	32 (22.1)	
Never	123 (62.1)	25 (47.2)	98 (67.6)	
Sleep quality				0.559
Good	94 (48.7)	24 (45.3)	70 (50.0)	
Poor	99 (51.3)	29 (54.7)	70 (50.0)	
Hypertension				0.014
No	144 (72.4)	46 (85.2)	98 (67.6)	
Yes	55 (27.6)	8 (14.8)	47 (32.4)	
Metabolic syndrome				0.064
Yes (>3 components)	52 (26.1)	9 (16.7)	43 (29.7)	
No	147 (73.9)	45 (83.3)	102 (70.3)	
Diabetes				0.111
No	191 (96.0)	54 (100.0)	137 (94.5)	
Yes	8 (4.0)	0 (0.0)	8 (5.5)	
Shiftwork (entire career)				<0.0001
Day	88 (44.2)	40 (74.1)	48 (33.1)	
Afternoon	72 (36.2)	9 (16.7)	63 (43.5)	
Night	39 (19.6)	5 (9.3)	34 (23.5)	

Results were obtained from the *t* test (continuous variables) and the chi-squared test (categorical variables).
BMI, body mass index; HDL, high density lipoprotein; HS/GED, high school/general education development; LDL, low density lipoprotein; SD, standard deviation.

TABLE 2. Covariates by Shiftwork (Entire Shiftwork History Up to Retinal Examination)

	Day ($n = 88$)	Afternoon ($n = 72$)	Night ($n = 39$)	P
	Mean ± SD	Mean ± SD	Mean ± SD	
Age (yrs)	49.0 ± 6.33	44.8 ± 6.38	44.7 ± 7.28	<0.0001
Years of service	21.5 ± 6.91	18.4 ± 6.78	16.9 ± 7.38	0.001
Systolic blood pressure (mm Hg)	117.0 ± 12.51	115.8 ± 11.34	114.4 ± 9.80	0.493
Diastolic blood pressure (mm Hg)	78.56 ± 7.69	78.20 ± 8.51	78.70 ± 7.27	0.934
Body mass index (kg/m²)	28.57 ± 3.86	30.32 ± 5.02	28.89 ± 4.09	0.037
HDL cholesterol (mg/dL)	50.89 ± 15.46	47.5 ± 13.42	46.6 ± 10.82	0.173
LDL cholesterol (mg/dL)	125.8 ± 31.12	124.9 ± 31.85	130.2 ± 42.32	0.722
Sleep duration (hrs/24 hr)	6.15 ± 1.15	6.08 ± 1.06	5.78 ± 1.15	0.229
Vitamin D3 25 (OH) (ng/mL)	27.58 ± 11.73	31.37 ± 11.63	26.89 ± 8.72	0.052
White blood cell count (WBC)	5.60 ± 1.54	5.74 ± 1.33	6.36 ± 2.23	0.052
	N (%)	N (%)	N (%)	
Sex				<0.0001
Women	40 (45.5)	9 (12.5)	5 (12.8)	
Men	48 (54.6)	63 (87.5)	34 (87.2)	
Race/ethnicity				<0.0001
White/Hispanic	56 (63.6)	67 (93.1)	34 (87.2)	
African American	32 (36.4)	5 (6.9)	5 (12.8)	
BMI (kg/m²)				0.165
Normal (<25.0)	17 (19.3)	7 (9.7)	4 (10.3)	
Overweight (25–29)	36 (40.9)	32 (44.4)	23 (59.0)	
Obese (≥30)	35 (39.8)	33 (45.8)	12 (30.8)	
Smoking status				0.186
Current	6 (6.9)	6 (8.3)	8 (20.5)	
Former	24 (27.6)	22 (30.6)	9 (23.1)	
Never	57 (65.5)	44 (61.1)	22 (56.4)	
Sleep quality				0.321
Good	46 (54.8)	32 (45.1)	16 (42.1)	
Poor	38 (45.2)	39 (54.9)	22 (57.9)	
Hypertension				0.391
No	66 (75.0)	48 (66.7)	30 (76.9)	
Yes	22 (25.0)	24 (33.3)	9 (23.1)	
Metabolic syndrome				0.996
Yes (>3 components)	23 (26.1)	19 (26.4)	10 (25.6)	
No	65 (73.9)	53 (73.6)	29 (74.4)	
Diabetes				0.552
No	86 (97.7)	68 (94.4)	37 (94.9)	
Yes	2 (2.3)	4 (5.6)	2 (5.1)	

Results were obtained from ANOVA (continuous variables) and the chi-squared test (categorical variables). HDL, high density lipoprotein; LDL, low density lipoprotein; SD, standard deviation.

computer-assisted technique based on a standard protocol and using the Parr–Hubbard–Knudtson formula.[29,30] Trained graders, masked to participant characteristics, using a computer software program measured the diameters of all arterioles and venules coursing through a specified area one-half to one disc diameter surrounding the optic disc. On average, between 7 and 14 arterioles and an equal number of venules were measured per eye. Individual arteriolar and venular measurements were combined into summary indices that reflected the average CRAE and CRVE diameters of an eye based on the Parr–Hubbard–Knudtson formula.[19,31]

Covariates

Demographic characteristics, lifestyle behaviors, medical history, and medication use were obtained from all officers through self- and interviewer-administered questionnaires. Body mass index (BMI) was calculated as weight (in kilograms) divided by height (in meters) squared. Blood pressure was determined using the average of the second and third of three separate measurements of resting systolic and diastolic blood pressure obtained with a standard

sphygmomanometer. Hypertension was defined as a systolic blood pressure of greater than or equal to 140 mm Hg or a diastolic blood pressure of greater than or equal to 90 mm Hg, or use of antihypertensive medications. The metabolic syndrome criteria were based on the National Cholesterol Education Program Adult Treatment Panel III guidelines with recent modifications from the American Heart Association and the National Heart, Lung, and Blood Institute.[32] 25-hydroxy (OH) vitamin D was measured by liquid-phase Radioimmunoassay technique (ImmunoDiagnostic-Systems, Fountain Hills, AZ). White blood cell (WBC) count was obtained from a complete blood count using standard laboratory procedures.

Statistical Methods

Descriptive statistics were obtained for all variables using the chi-squared test of independence and the Student's *t* test. Associations between selected variables and shiftwork were obtained using analysis of variance (ANOVA) and the chi-squared test. We used Pearson's correlation coefficients and analysis of covariance

TABLE 3. Age-Adjusted Associations of Covariates With Retinal Arteriolar and Venular Diameters

	Arteriolar Diameter (CRAE)	Venular Diameter (CRVE)
	Correlation/*P* Value	Correlation/*P* Value
Years of service	−0.122, 0.099	0.022, 0.771
Systolic blood pressure (mm Hg)	−0.330, <0.0001	−0.073, 0.322
Diastolic blood pressure (mm Hg)	−0.361, <0.0001	−0.064, 0.389
Body mass index (kg/m^2)	−0.073, 0.323	0.073, 0.322
HDL cholesterol (mg/dL)	−0.018, 0.808	−0.185, 0.012
LDL cholesterol (mg/dL)	−0.128, 0.082	−0.014, 0.848
Sleep duration (hrs/24 hr)	−0.020, 0.789	−0.006, 0.940
Vitamin D3 25 (OH) (ng/mL)	−0.151, 0.040	−0.340, <0.0001
White blood cell count (WBC)	0.099, 0.164	0.212, 0.003
	Mean ± SE	Mean ± SE
Sex		
Women	157.40 ± 1.77	224.61 ± 2.70
Men	153.79 ± 1.09	221.97 ± 1.65
P value	0.084	0.406
Race/ethnicity		
White/Hispanic	154.16 ± 1.05	220.37 ± 1.55
African American	157.05 ± 2.02	231.31 ± 2.99
P value	0.204	0.001
BMI (kg/m^2)		
Normal (<25.0)	155.70 ± 2.48	219.48 ± 3.75
Overweight (25–29)	155.64 ± 1.38	223.16 ± 2.08
Obese (≥30)	153.45 ± 1.48	223.30 ± 2.24
P value	0.511	0.652
Smoking status		
Current	159.75 ± 2.92	227.54 ± 4.45
Former	152.59 ± 1.77	220.02 ± 2.70
Never	154.89 ± 1.18	223.13 ± 1.80
P value	0.113	0.333
Sleep quality		
Good	154.34 ± 1.37	220.03 ± 2.07
Poor	155.24 ± 1.33	224.66 ± 2.01
P value	0.642	0.112
Hypertension		
No	155.95 ± 1.09	222.75 ± 1.66
Yes	151.72 ± 1.75	222.53 ± 2.68
P value	0.041	0.945
Metabolic syndrome		
Yes (>3 components)	153.82 ± 1.82	226.51 ± 2.75
No	155.12 ± 1.09	221.33 ± 1.64
P value	0.542	0.107
Diabetes		
No	154.78 ± 0.95	222.16 ± 1.43
Yes	154.76 ± 4.64	235.38 ± 6.96
P value	0.997	0.064

Results were obtained from the Partial Pearson's correlation (continuous variables) and the ANOVA (categorical variables). HDL, high density lipoprotein; LDL, low density lipoprotein; SE, standard error.

(ANCOVA) to assess age-adjusted associations for the same selected variables with CRAE and CRVE. There were strong correlations between left and right eyes for the arteriolar diameters (Pearson's $r = 0.743$, $P < 0.0001$) and the venular diameters ($r = 0.789$, $P < 0.0001$), therefore we used the average of the two eyes in our analyses as has been done in other large studies.[22,33]

Effect modification was assessed for sex and smoking status in the association of shiftwork with CRAE and CRVE. Cigarette smoking has been shown to be associated with wider CRVE, with the association being stronger in current than in former smokers.[34] In another study, former and current smoking status were independently associated with markers of inflammation (high sensitivity C-reactive protein and interleukin-6) and subclinical atherosclerosis (carotid intima media thickness, ankle-brachial index, and coronary artery calcium).[35] Confounders were selected based on evidence from the literature and/or whether they showed significant associations with both the independent and dependent variables, but were not on the pathway (ie, mediators) in the association. Confounders included age, sex, and race/ethnicity. We also included in the final model, risk factors for atherosclerosis and CVD which included metabolic syndrome, hypertension, smoking status, vitamin D3, and white blood cell (WBC) count. WBC count was also shown to be associated with wider CRVE.[34] Mean diameters of the retinal vasculature were compared across shifts using ANOVA and ANCOVA. Poisson regression was used to obtain prevalence ratios and 95% confidence intervals. Statistical significance was indicated if the *P* value was <0.05. All analyses were conducted in SAS v. 9.3 (SAS Institute, Cary, NC).

TABLE 4. Mean Values of Retinal Venular Diameter Across Shiftwork (Entire Work History) Among Police Officers, Stratified by Smoking Status; BCOPS 2010–2015

	Day ($n = 88$)	Afternoon ($n = 72$)	Night ($n = 39$)	*P*
All officers				
Model 1	222.9 ± 20.9	219.9 ± 18.9	227.2 ± 18.1	0.182
Model 2	220.3 ± 2.2	223.7 ± 2.3	226.3 ± 3.0	0.298
Never smokers	$N = 57$	$N = 44$	$N = 22$	
Model 1	225.9 ± 20.1	219.4 ± 20.2	223.0 ± 18.7	0.273
Model 2	223.2 ± 2.8	222.8 ± 3.1	223.6 ± 4.3	0.987
Current and former smokers	$N = 30$	$N = 28$	$N = 17$	
Model 1	217.3 ± 21.9	220.7 ± 17.1	232.6 ± 16.3	**0.031**
Model 2	215.1 ± 3.5	224.6 ± 3.6	230.0 ± 4.5	**0.040**

P values were obtained from ANCOVA.
Model 1: Unadjusted.
Model 2: Adjusted for age, sex, race/ethnicity, metabolic syndrome, hypertension, vitamin D3, and WBC.
Interaction by smoking status (Model 2): $P = 0.198$.
Multiple comparison (Model 2 for current and former smokers):
Day versus afternoon: $P = 0.087$
Day versus night: ***P = 0.014***
Afternoon versus night: $P = 0.362$.

RESULTS

Police officers ($n = 199$) ranged in age from 28 to 65 years (mean ± standard deviation = 46.6 ± 6.8 years) (Table 1). The majority of officers were men (72.9%), white or Hispanic (78.9%), and held the rank of patrol officer (55.8%). The mean values for the CRAE and CRVE for all officers were $154.8 \pm 13.2 \, \mu m$ and $222.7 \pm 19.8 \, \mu m$, respectively, with women and men having similar mean values. Approximately, 44% of the officers worked on the day shift, 36.2% on the afternoon shift, and 19.6% on the night shift. Sex was significantly associated with shiftwork, with a smaller percentage of women (9.3%) compared with men (23.5%) working the night shift; $P < 0.0001$. On average, officers who worked afternoon and night shifts were significantly younger, had fewer years of service, and were more likely to be man than those who worked the day shift (Table 2). Sleep duration and quality were not significantly associated with shiftwork.

Table 3 presents the age-adjusted associations between selected covariates and the retinal diameter measurements. Systolic and diastolic blood pressures and waist circumference were strongly and inversely correlated with CRAE; -0.321, $P < 0.0001$; -0.344, $P < 0.0001$; -0.157, $P = 0.033$, respectively. High density lipoprotein (HDL) cholesterol and 25-hydroxyvitamin D (25(OH)D) (vitamin D3) were inversely correlated with CRVE.

Shiftwork was not significantly associated with CRAE among officers after adjustment for age, sex, race/ethnicity, metabolic syndrome, hypertension, diabetes, smoking status, 25(OH)D levels, and WBC count (data not shown). Shiftwork was also not significantly associated with CRVE among officers overall (Table 4). Smoking status significantly modified the association between shiftwork and CRVE at the 20% level; interaction $P = 0.198$ (Table 4). There is evidence in the literature showing smoking to be a strong risk factor for changes in the retinal vasculature.[34] We stratified by smoking status. After stratification by smoking status (never vs current and former smokers), a significant association was observed between shiftwork and CRVE among current and former smokers only; age-adjusted $P = 0.034$. After further adjustment for sex, race/ethnicity, metabolic syndrome, hypertension status, vitamin D3 levels, and WBC count, the association remained weakly significant ($P = 0.040$). Pairwise comparisons showed that, among officers who were current or former smokers, those who worked the night shift had a significantly wider mean CRVE ($230.0 \pm 4.5 \, \mu m$) compared with those who worked the day shift ($215.1 \pm 3.5 \, \mu m$); $P = 0.014$. The sample sizes for either current or former smokers were too small across the categories of shiftwork status, hence our reason for combining both groups into one category.

TABLE 5. Prevalence and Prevalence Ratios (95% CI) of Wider CRVE (ie, >Median) Across Shiftwork, Stratified by Smoking Status

	N	No. Cases	Prevalence	Model 1: PR (95% CI)	Model 2: PR (95% CI)	Model 3: PR (95% CI)
Never smokers						
Day	57	31	54.4	Referent	Referent	Referent
Afternoon	44	20	45.5	0.84 (0.56–1.25)	0.82 (0.55–1.24)	0.91 (0.58–1.44)
Night	22	10	45.5	0.84 (0.50–1.40)	0.80 (0.46–1.39)	0.83 (0.50–1.38)
Current and former smokers						
Day	30	11	36.7	Referent	Referent	Referent
Afternoon	28	14	50.0	1.36 (0.75–2.48)	1.32 (0.70–2.48)	1.75 (0.88–3.48)
Night	17	13	76.5	**2.09 (1.22–3.58)**	**2.06 (1.20–3.55)**	**2.35 (1.26–4.37)**

Model 1: Unadjusted.
Model 2: Adjusted for age.
Model 3: Adjusted for age, sex, race/ethnicity, metabolic syndrome, hypertension, vitamin D3, and WBC.
CI, confidence intervals.

The prevalence ratios (PR) and 95% confidence intervals (CI) for wider versus narrower CRVE across shiftwork status are presented in Table 5. After adjustment for all confounders and risk factors, officers who worked the night shift were 135% more likely to have a CRVE that was wider than the median compared with those officers who worked the day shift; PR = 2.35 (1.26 to 4.37).

DISCUSSION

In this occupational cohort, we examined associations between shiftwork status and retinal vasculature diameters in police officers. We did not find significant associations between shiftwork and CRAE. However, we found a significant association between shiftwork and CRVE among a subset of the officers.

We stratified by smoking status and a significant association was seen between shiftwork and CRVE, but only among current or former smokers. Our results showed that among current or former smokers, officers who worked the night shift had a significantly wider mean CRVE compared with those who worked the day shift, independent of confounders and traditional CVD risk factors. In addition, officers who worked the night shift were 135% more likely to have a CRVE that was wider (than the median) compared with those officers who worked the day shift, although this may be a chance finding. Liew et al[36] observed that retinal arteriolar and venular caliber size are highly correlated and individuals with narrower arterioles are more likely to have narrower venules. Therefore, we initially adjusted for CRAE and CRVE in the analyses of venular and arteriolar diameters based on their research.[36] However, we decided to remove this variable from our final models since it did not influence the means and *P* values.

A thorough search of the literature failed to identify studies that investigated associations between shiftwork and retinal vasculature diameters. Research has shown that wider venules may be related, in part, to cumulative structural damage to the microvasculature (eg, from inflammation or endothelial dysfunction) and indicate problems with the oxygen supply to the brain.[37,38]

The association between shiftwork and CRAE was not statistically significant and no variable significantly modified the association. Arterioles have a similar structure to small arteries but less elastic and muscular fibers.[39] In previous studies, arteriolar narrowing was positively and independently associated with older age and elevated blood pressure.[19,20] Retinal arteriolar narrowing may be an early indicator of microvascular structural and/or physiologic changes resulting from aging, hypertension, and other processes. It may also reflect intimal thickening and medial hyperplasia, hyalinization, and sclerosis.[33]

Shiftwork has been observed to increase the risk of CVD.[6–9] Oxidative stress and inflammation are known to play a role in cardiac and vascular abnormalities in CVD.[26,40] Shiftwork may be associated with retinal venular changes via increased oxidative stress. Among employees in a Finnish airline company, those working on afternoon and night shifts were shown to have increased levels of systemic inflammation as measured by high sensitivity CRP and WBC count.[25] Oxidative stress and chronic inflammation were found to be associated with atherosclerosis in the retinal arterioles among adults in the general population in Japan.[27] It is possible that increased inflammation from smoking status and night-shift work might have a synergistic effect on the retinal microvessel diameter.

Experimental and observational studies provide evidence that disease begins in the microvasculature and then progresses in the macrovasculature before manifesting as clinical disease.[41–44] In an experimental study, it has been shown that microvascular endothelial dysfunction occurred earlier than macrovascular endothelial dysfunction in rats with adjuvant-induced arthritis.[43] In a prospective cohort study, microvascular disease was observed to be a predictor for the development of major peripheral artery disease during a 5-year follow-up in patients with type 2 diabetes.[42] Another study reported that an unhealthy retinal microvascular profile, namely, narrower retinal arterioles and wider venules were associated with more severe coronary artery disease among women.[44] Changes in the retinal venular (but not arteriolar) caliber appear to predict future cerebrovascular events.[41] The study by van Hecke et al[45] showed contradictory results. In their study, retinal microvascular disease was not independently associated with impaired brachial reactivity flow-mediated dilation (FMD) or increased carotid intima media thickness (IMT).

Limitations and Strengths

One limitation of our study is the cross-sectional study design which precluded us from making causal inferences. Police officers with a low tolerance for night-shift work may leave that shift or occupation for one with a normal schedule. If that was the case in our study, our results are most likely underestimated, that is, the actual findings are even stronger than what was observed. In addition, our study had a poor participation rate and a relatively small sample size which may have affected the outcome of interest and our ability to detect significance in stratified analyses. Approximately 28% of the eligible cohort participated which limits generalization of the findings. However, our use of objective shiftwork data, which is rarely seen in studies of shiftwork, is a strength of the study. To the best of our knowledge, this is the first study to investigate associations between shiftwork and retinal diameters.

CONCLUSIONS

In summary, our results showed that there was no relationship of shiftwork with retinal vessel diameters. However, we found that officers who were current or former smokers and who worked the night shift had a significantly (though weak) wider mean venular diameter compared with those who worked the day shift. Future epidemiological studies to detect the causal relationship between shiftwork, smoking status, and retinal vasculature diameters are warranted. It is important to replicate these findings and if replicated, to identify factors that explain these findings.

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