ELSEVIER

Shift Work and Arteriosclerosis Risk in Professional Bus Drivers

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PURPOSE: Professional bus drivers are at increased risk for cardiovascular disease, but the underlying causes are unclear. Professional bus drivers often follow shift schedules. Especially, an association between shift work and early manifestations of cardiovascular disease has not been elucidated. Thus we investigated the links between shift work and arteriosclerosis risk in professional bus drivers.
METHODS: Questionnaires were administered to 184 bus drivers on demographic characteristics, lifestyle, and occupational history from 5 transportation companies in Taiwan. Brachial-ankle pulse wave velocity (baPWV) was measured using a volume-plethysmographic apparatus. Body mass index, waist circumference, biochemical variables, and blood pressure were also measured.
RESULTS: Arteriosclerotic risk factors (age, weekly driving hours, systolic blood pressure, diastolic blood pressure, and insulin level) differed in part among different groups of drivers. Long-term shift drivers had higher baPWV compared to regular drivers and short-term shift drivers (1594 cm/s vs. 1497 and 1432, $p<0.01$). Our multiple regression model showed that age ($p<0.01$) and diastolic blood pressure ($p<0.01$) were positively associated with baPWV in our professional drivers. After adjusting for all covariates, we observed that baPWV increased by 3.6 cm/s for per 1-year increment in years of shift driving.
CONCLUSIONS: Long-term shift work could increase the risk of arteriosclerosis in professional bus drivers. Larger studies would be necessary to provide further evidence regarding this finding.
Ann Epidemiol 2010;20:60–66.

KEY WORDS: Arteriosclerosis, Professional Drivers, Pulse Wave Velocity, Shift Work.

INTRODUCTION

Although studies report an increased risk of cardiovascular disease (CVD) in professional drivers (1–3), underlying causes are not fully understood. Cigarette smoking (4, 5), physical inactivity during leisure time (6), obesity (7), diabetes (8), and hypertension (5, 8) have been identified as risk factors for CVD. Previous studies have also indicated an association between shift work and CVD (9–11) such that shift workers have a 40% increased risk compared with day workers (12). Peter and colleagues (13) confirmed the direct effect of shift work on CVD and verified that a stressful psychosocial work environment may mediate hypertension and atherogenic lipids. Long working hours may cause irritability, physical and mental fatigue, excessive sleepiness or insomnia, and inattention at work. These symptoms may be worse in shift workers (12). Especially, long-term shift workers have been reported to experience an increased risk of developing CVD than short-term shift workers and non-shift workers (14).

Whether shift work is associated with early manifestations of CVD (15), however, remains unclear. Arterial stiffness is a pathological state characterized by vascular damage closely associated with arteriosclerotic diseases (16). Since understanding the extent of arteriosclerosis may help us better estimate the risk of CVD in a population, several noninvasive methods for assessing arteriosclerosis severity have been developed. The pulse-wave velocity (PWV), calculated as the distance traveled by the pulse between two recording sites, has been shown to reflect arterial wall stiffness (17, 18). Elevated PWV is associated with increased cardiovascular events and mortality (19–21). Increased arterial stiffness, as reflected in increased PWV, aggravates arteriosclerosis via increased stress on the arterial wall.

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This study was supported by Chung Shan Medical Univeristy CSMU 96-OM-B-001, CSMU 96-OM-B-039, Chung Shan Medical University Hospital CSH-2009-B-002, Taiwan.

No conflicts of interest are declared.

Received February 10, 2009; accepted July 1, 2009.

360 Park Avenue South, New York, NY 10010

1047-2797/10/$–see front matter
doi:10.1016/j.annepidem.2009.07.093

Selected Abbreviations and Acronyms

CVD = cardiovascular disease
baPWV = brachial-ankle pulse wave velocity
SBP = systolic blood pressure
DBP = diastolic blood pressure
BMI = body mass index
HDL = high-density lipoprotein
LDL = low-density lipoprotein

Degree of elevated PWV may correspond to the degree of arteriosclerotic change (17, 18), indicating increased arteriosclerotic risk.

Although occupational categories can be surrogate measures for cardiovascular risk (2, 3), the relationship between the job of professional bus driver and severity of arteriosclerosis has not been investigated. In this study, we used an automated device measuring PWV to analyze the relationship of severity of arteriosclerosis in professional bus drivers with probable risk factors. In particular, we tested the hypothesis that long-term shift bus driving is positively associated with severity of arteriosclerosis.

MATERIAL AND METHODS

Study Subjects and Interviews

In Taiwan, professional bus drivers' duties vary by type of vehicle, but may include checking passes, talking to passengers, answering questions about bus routes and making stops at appointed times along a regular route. In addition, bus drivers must be able to drive in all kinds of weather and under all kinds of conditions (e.g., following alternate routes along detours, negotiating heavy traffic) and often work on evenings, weekends, and holidays.

During July–August 2004, five transportation companies in Taichung City in central Taiwan were randomly selected for our study. All professional drivers in these transportation companies were invited to participate. As the number of female bus drivers was small, and the majority of their employment duration was short, they were excluded from the study. All subjects gave written informed consent to participate in this study. A total of 186 male professional bus drivers aged 19–60 years who agreed to participate in our study and underwent detailed questionnaires and our health examination were included in our analysis. Structured questionnaires were administered by trained interviewers who collected demographic characteristics, lifestyle (i.e., cigarette smoking, alcohol consumption, tea and coffee consumption, fruit and vegetable consumption and physical activity), occupational history, and medical history information. Subjects were asked if they had ever worked shift or night work and the number of years and type of job they had while on shift work. The subjects also answered questions discussing the amount, frequency, and duration of smoking. A parameter termed "pack-years" was coined as an indicator of cumulative smoking dose of a subject and was defined as the number of packs of cigarettes smoked daily multiplied by the number of years of active smoking. Because Taiwanese people do not consume much alcohol; habitual drinking was defined as alcohol consumption at least once and as consumption of more than 80 grams of alcohol per week. Participants who reported moderate (⩾10 minutes) vigorous exercise at least once per week in the previous 30 days were defined as "exercisers." Two subjects who self-reported having coronary heart disease or hyperthyroidism were excluded. None of the subjects have self-reported medical history of cerebrovascular disease, peripheral vascular disease, adrenogenital syndrome, or primary aldosteronism. A total of 184 bus drivers were included in the study. Among these, 135 (73.4%) were shift workers who followed irregular schedules, that is, whose driving assignments might start at different times on different days or weeks. The 49 drivers who worked regular (non-shift) schedules were selected as controls. The study design was approved by the institutional review board of the Chung Shan Medical University, Taichung, Taiwan.

Measurement of Brachial-Ankle Pulse Wave Velocity

PWV was measured with a volume-plethysmographic apparatus, the VP-2000 (Colin Co. Ltd., Komaki, Japan), with documented validity and reproducibility (22). As subjects lay supine, pneumatic pressure cuffs were placed snugly around both arms and ankles. Electrocardiographic electrodes were attached to both wrists and a microphone for phonocardiography placed at the second intercostal space at the left margin of the sternum. The device automatically measures blood pressure over the four extremities oscillometrically. Then, it records pulse volume over the right arm and both ankles for 10 seconds while maintaining cuff pressures at 60 mm Hg. The recorded cuff pressure signals, known as the pulse volume traces, correspond to intra-arterial pressure contours (23). Pulse travel distance between arm and ankle was calculated automatically from height according to methods suggested by Yamashina et al. (22). PWV (measured in centimeters per second) is expressed as the ratio of the distance between two sites (in centimeters) over pulse wave transit time (in seconds). In this study, PWV was measured from the brachial artery and ankle (baPWV). Measurement of right and left baPWV was obtained for an average of 10 seconds. Since there was a significant positive correlation between left and right baPWV among our subjects ($r=0.97$, $p<0.001$), we used a mean value between left and right baPWV as the indicator during analysis. For our subjects, the interobserver coefficient of

variation was 2.6% and the intraobserver coefficient of variation was 4.8%.

Blood Pressure, Anthropometric Data, and Laboratory Assay

Blood pressure and baPWV were measured simultaneously using an automatic waveform analyzer. The average systolic BP (SBP) and average diastolic BP (DBP) were determined for each subject. Abnormal blood pressure was defined as average SBP $\geq$ 140 mm Hg, or average DBP $\geq$ 90 mm Hg. Anthropometric measures of body mass index (BMI) and waist circumference were taken with indoor clothing without shoes during the physical examination. Fasting venous blood samples were tested for fasting plasma glucose, insulin, total cholesterol, triglyceride, high-density lipoprotein (HDL)-cholesterol and low-density lipoprotein (LDL)-cholesterol. Plasma glucose was determined by the glucose-oxidase method. Insulin was determined by monoclonal antibody-based immunofluorimetric assay. Total cholesterol, triglyceride, HDL-cholesterol and LDL-cholesterol were measured using enzymatic methods by an automatic analyzer (Hitachi 7250; Hitachi Medical Corp., Hitachi, Japan).

Statistical Analysis

Professional bus drivers were categorized by driving assignment as regular (non-shift) drivers or shift drivers. The median time of shift work at this occupation for subjects was 60 months (5 years). Adverse effects on the cardiovascular system commences sometime between 5 and 10 years of shift work (24). Therefore, shift drivers were further classified into those driving <10 years (short-term shift drivers) and those driving $\geq$ 10 years (long-term shift drivers). Because of the normal distribution of years of shift driving and baPWV, data transformation for these two variables had not been performed. Comparisons between driver groups were made taking into account age, educational level, cigarette smoking status, alcohol consumption, physical exercise, tea and coffee consumption, vegetable and fruit intake, amount of sleep per day (greater or less than 420 minutes or 7 hours), waist circumference, blood pressure, BMI, total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol, plasma glucose, and insulin. Comparisons were made using analysis of variance (ANOVA) for continuous variables and the χ^2 test for discrete variables. Subsequently, ANOVA was used to compare difference in baPWV according to driving status and a Student t test was used to test the association between baPWV and other factors. Association between years of shift driving and baPWV was further assessed using a general linear model. All data were analyzed with SAS 9.1 software (SAS Institute, Cary, NC). Statistical tests were two sided with $p<0.05$ considered statistically significant.

RESULTS

In total, 184 professional bus drivers were studied. The average cumulative years of rotating shift work for long-term shift drivers and short-term shift drivers were 11.5 and 2.6 years, respectively. The mean age of all drivers was 42.2 years (Table 1). Long-term shift drivers were significantly older (49.3 years vs. 42.3 and 39.7; ANOVA, $p<0.001$) and drove for fewer hours per week (53 vs. 69 and 63, $p=0.001$) than either non-shift drivers or short-term shift drivers, respectively. However, no statistically significant differences were found between groups in education level, cigarette smoking, alcohol consumption, frequency of weekly exercise, tea and coffee consumption, vegetable and fruit intake (data not shown), and amount of average daily sleep. Long-term shift drivers had also higher SBP ($p=0.02$), higher DBP ($p=0.001$) and lower insulin level ($p=0.04$) compared to non-shift drivers and short-term shift drivers, but the groups did not differ significantly in waist circumference, BMI, total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol, or fasting glucose.

In current study, we considered that a confounding factor must be a risk factor of the disease, and a confounding factor must be associated with the exposure under study in our study population. Since the distribution of age, weekly driving hours, SBP, DBP, and insulin level differed between the three driver groups, these risk factors were considered as confounding factors in our study. Subsequently, we also evaluated the association of baPWV with these confounding factors (Table 2). Compared with short-term shift and regular drivers, long-term shift drivers had a significantly higher baPWV (1594 cm/s vs. 1497 and 1432, $p<0.01$). Short-term shift (1583 cm/s vs. 1468 and 1371, $p<0.01$) and regular drivers (1643 cm/s vs. 1534 and 1352, $p<0.01$) older than 50 years had higher baPWV than those 40 – 49 years of age or those younger than 40 years, but this age distinction did not hold true for long-term shift drivers; all of these had elevated baPWV, whatever their age. Higher baPWV was also seen in all drivers with high SBP ($\geq$140 mm Hg) and DBP ($\geq$90 mm Hg). However, number of hours driven per week and insulin level were not associated with elevated baPWV.

Next, we adjusted for the effects of potential confounders by multiple regression (Table 3). We excluded SBP in our model because the variables of SBP and DBP had high collinearity. Multivariate analysis verified a dose-dependent association between cumulated years of shift driving and elevated baPWV after adjusting for age (Model 1; regression coefficient = 5.7, $p=0.01$). The relation of cumulated years

TABLE 1. Demographic characteristics, lifestyle, dietary habits, driving patterns, physical measurements, and biochemical parameters of professional drivers

	Regular drivers $N=49$	Short-term shift drivers $N=99$	Long-term shift drivers $N=36$	Total $N=184$
Age, yr	42.3±1.4	39.7±0.8	49.3 ±0.7*	42.2±0.6
Education level				
≤Junior high school	13 (26.5%)	25 (25.3%)	15 (41.7%)	53 (28.8%)
Senior high school	24 (49.0%)	60 (60.6%)	19 (52.8%)	103 (56.0%)
≥University	12 (24.5%)	14 (14.1%)	2 (5.5%)	28 (15.2%)
Cigarette smoking				
Yes	29 (59.2%)	63 (63.6%)	17 (47.2%)	109 (59.2%)
No	20 (40.8%)	36 (36.4%)	19 (52.8%)	75 (40.8%)
Pack-years smoked	13.9±3.9	13.1±1.4	10.5±2.7	12.8±1.4
Alcohol consumption†				
Yes	7 (14.3%)	10 (10.3%)	3 (8.3%)	20 (11.0%)
No	42 (85.7%)	87 (89.7%)	33 (91.7%)	162 (89.0%)
Frequency of exercise				
<1 time/wk	35 (71.4%)	68 (68.7%)	20 (55.6%)	123 (66.8%)
≥1 time/wk	14 (28.6%)	31 (31.3%)	16 (44.4%)	61 (33.2%)
Average daily sleep (min)	409±12	425±10	406±18	417±7
Weekly driving hours	69±2.8	63±1.9	53±3.8*	63±1.5
Waist circumference (cm)	91.7±2.3	89.9±1.0	92.9±1.4	90.9±0.8
Systolic BP (mm Hg)	134.0±2.5	131.3±1.5	140.9±3.6‡	133.9±1.3
Diastolic BP (mm Hg)	83.6±1.7	80.5±1.0	89.1±2.3*	83.0±0.9
BMI (kg/m^2)	26.4±0.6	26.0±0.4	26.6±0.6	26.2±0.3
Total cholesterol (mg/dL)	201.7±5.7	195.9±3.8	191.5±6.1	196.6±2.8
Triglycerides (mg/dL)	253.9±32.3	242.4±20.5	257.3±59.8	248.3±18.1
HDL-C (mg/dL)	46.1±1.2	44.9±0.9	42.3±1.4	44.7±0.7
LDL-C (mg/dL)	127.8±5.0	123.1±3.7	118.6±4.9	123.5±2.6
Fasting glucose (mg/dL)	103.7±5.8	99.6±4.7	104.2±10.1	101.6±3.5
Insulin (μU/mL)	24.8±4.6	18.5±2.2	11.5±2.3*	18.8±1.8

BP=Blood pressure; BMI=body mass index; HDL-C=high-density lipoprotein cholesterol; LDL-C=low-density lipoprotein cholesterol.
Data represent number of individuals or mean ± standard error for continuous variables and comparison between driver groups.
*$p<0.01$; ANOVA, long-term shift drivers significantly differed from short-term shift and regular driver groups.
†Two subjects had unknown alcohol consumption.
‡$0.01<p<0.05$.

of shift driving and elevated baPWV remained stable when weekly driving hours were included in the model (Model 2; regression coefficient = 5.6, $p=0.02$). Finally, we performed a multiple linear regression model for baPWV as a function of accumulated years of shift driving, age, weekly driving hours, DBP, and insulin (Model 3). Age ($p<0.01$) and DBP ($p<0.01$) were positively associated with baPWV in our professional drivers. After adjusting for all covariates, we observed that baPWV increased by 3.6 cm/s per 1-year increment in years of shift driving (Model 3, $p=0.08$).

DISCUSSION

The occupation of driving is closely linked to the practice of shift work and shift work has been reported to be associated with CVD (9–13). However, an association between shift work and early manifestations of CVD is unclear. In our analysis, Taiwanese professional bus drivers who worked shift schedules for longer than 10 years (long-term shift drivers) had a higher baPWV compared to those who worked regular hours and followed shift-schedules for less than 10 years (short-term shift drivers). In particular, baPWV increased with number of years of shift driving, even after adjustment for confounding factors.

Several pathways may account for the association between shift drivers and increased baPWV. First, groups of drivers may differ by level of cardiovascular risk. Several studies have shown that unfavorable cardiovascular risk profiles are more prevalent among shift workers than among regular workers (9, 25, 26). However, in the present study, cardiovascular risk factor profiles were similar among the three groups of drivers, except for age, number of hours driving, blood pressure, and insulin level. Furthermore, long-term shift drivers older than 50 years did not have higher levels of baPWV than younger drivers in this cohort. Number of hours driving per week and insulin level were also not associated with elevated baPWV in our study. The effect of shift work on baPWV remained even after adjusting for these potential confounding factors. In addition, shift work influences the circadian rhythms and physiologic functions in humans, such as blood pressure, heart rate, and levels of hormones including catecholamines (25, 27, 28). However, we did not account the interaction between

TABLE 2. Brachial-ankle pulse wave velocity of professional drivers stratified by potential confounders and driving pattern

	Regular drivers		Short-term shift drivers		Long-term shift drivers	
	N	baPWV (cm/s)	*N*	baPWV (cm/s)	*N*	baPWV (cm/s)
Total	49	1497±39	99	1432±22	36	1594±43*
Age, yr						
≥50	15	1643±86†	10	1583±85†	19	1614±49
40–49	15	1534±62	40	1468±41	16	1589±77
<40	19	1352±39	49	1371±20	1	1250
Hours driven per week						
≥40	44	1506±42	91	1436±22	28	1561±48
<40	5	1421±115	8	1380±109	8	1709±90
Systolic BP, mm Hg						
≥140	16	1709±80‡	24	1597±61‡	14	1805±65‡
<140	33	1394±31	75	1379±18	22	1459±34
Diastolic BP, mm Hg						
≥90	12	1803±91§	15	1658±83§	14	1805±65§
<90	37	1398±28	84	1391±18	22	1459±34
Insulin, μU/mL						
≥20	16	1498±53	30	1516±54¶	5	1699±72
<20	33	1497±53	69	1395±20	31	1576±48

baPWV = brachial-ankle pulse wave velocity; BP = blood pressure.
Data represent number of individuals or mean ± standard error for continuous variables.
*$p<0.01$; ANOVA, long-term shift drivers differed significantly from short-term shift and regular drivers.
†$p<0.01$; ANOVA, compared with short-term shift drivers and regular drivers 40–49 years old and <40 years, respectively.
‡$p<0.01$; *t* test, compared with regular drivers, short-term shift drivers, and long-term shift drivers with systolic BP<140 mm Hg, respectively.
§$p<0.01$; *t* test, compared with regular drivers, short-term shift drivers, and long-term shift drivers with diastolic BP<90 mm Hg, respectively.
¶$p<0.01$; *t* test, compared with short-term shift drivers whose insulin level was less than 20 μU/mL.

physiologic functions (blood pressure especially) and shift work on baPWV in current study.

Insufficient sleep is a common feature of shift work. Long-term shift drivers in this study averaged less sleep than did drivers in other groups (406 min/d vs. 409 and 425), but the difference was not significant. Nonetheless, misalignment of the biological clock with work schedules can substantially weaken the quality of sleep (29), particularly for those who work at night. The sleep abnormality of shift workers may be causally linked to CVD (29), and working shifts over time has previously been associated with an increased risk of CVD (11). Thus shift drivers with irregular sleep patterns and longer working hours could be at increased risk of developing arteriosclerosis. While the exact pathophysiology of shift work needs further elucidation, several important cardiovascular associations with shift work may be noted.

Differences in eating habits and socioeconomic status between shift workers and regular workers may explain part of our observed association (30, 31). In particular, unfavorable nutrition patterns have been reported for shift workers (31, 32). However, no statistically significant differences were found in cigarette smoking, alcohol consumption, tea and coffee consumption, or vegetable and fruit intake between our groups of shift drivers. In Taiwan, high unemployment forces vulnerable populations (e.g., unskilled young men and elderly men) to accept unfavorable working conditions which may evoke a feeling of job insecurity even in those who actually hold a job. Nearly all shift drivers cite financial need as their most important reason

TABLE 3. Multiple linear regression model of the association between years of shift driving and brachial-ankle pulse wave velocity in professional drivers

	Model 1		Model 2		Model 3	
Variables	Regression coefficient (SE)	*p* Value	Regression coefficient (SE)	*p* Value	Regression coefficient (SE)	*p* Value
Intercept	1140.8 (66.1)	<0.01	1083.5 (79.8)	<0.01	428.9 (93.6)	<0.01
Years of shift driving per 1-year increment	5.7 (2.5)	0.02	5.6 (2.5)	0.02	3.6 (2.0)	0.08
Age per 1-year increment	6.7 (1.6)	<0.01	7.2 (1.6)	<0.01	4.4 (1.3)	<0.01
Weekly driving hours per 1-hour increment			0.6 (0.6)	0.32	0.5 (0.5)	0.34
Diastolic BP per 1-mm Hg increment					9.4 (1.0)	<0.01
Insulin per 1-μU/mL increment					0.7 (0.4)	0.10

BP = blood pressure.

to work long-term shifts, indicating that the association between shift work and arteriosclerosis risk in our study may reflect the emotional burden of being marginally employed.

Aging and blood pressure are important determinants of PWV (33, 34). Aging induces degeneration of elastic fibers and is associated with progressive stiffening of the arterial wall (33, 34). Furthermore, as arteries stiffen, changes in the dynamics of the cardiovascular system may increase cardiovascular events because the elevation in blood pressure raises left ventricular afterload (33). A recent cohort study showed that middle-aged Japanese men have an increased risk of arterial stiffening in the presence of raised blood pressure (35). In the present cross-sectional study, we confirmed that age and raised blood pressure were associated with baPWV in professional drivers. Multivariate analysis also confirmed an independent and significant effect of cumulated years of shift driving on baPWV after adjusting for age, blood pressure, and other confounding effects.

Our study had some limitations. In general, Taiwanese shift drivers often follow irregular schedules, which means their driving assignments might start at different times. Ideally, a group of drivers should be selected on the basis that they share a particular shift rotation. This has the advantage that drivers can be measured during the normal course of their work, which improves the ecological validity of the study. Unfortunately, the heterogeneous nature of work practices in the transport industry makes it difficult to recruit a sufficient sample of drivers working in a particular regime. In addition, the drivers who worked regular (non-shift) schedules were selected as our controls. Their biological clock should not be affected by their work. Exposure to motor exhaust (36) and noise (37) have been proposed as possible risk factors for CVD for drivers, but in this case such information was not available. Since baPWV is measured as a surrogate of arteriosclerosis, the underlying mechanisms of shift work and their link to the process of arteriosclerosis still need further study. Future studies should explore the relationship between baPWV and subclinical arteriosclerosis by measuring such validated markers such as intimal-medial thickness. In our cross-sectional study, baPWV is a single measure taken on one occasion. Future studies should be longitudinal in order to trace alterations in baPWV over time. In addition, the healthy-worker effect (selection bias) may have biased results, either through workplace hiring procedures that screen out less healthy applicants, or through workers' estimates of their own ability to tolerate irregular working hours (i.e., less healthy drivers give up shift work because of health concerns). However, both of these biases would tend to attenuate any association between shift work and baPWV. A substantial survival bias (33, 34) is unlikely, since all of our participants were younger than 60 years of age. Another limitation is that estimates of fruit and vegetable consumption derived from questionnaires can never be free of error. Lastly, our small sample size limited the statistical ability to detect small increases in risk, especially in the analysis of subgroups.

In summary, our results suggest an association between long-term shift work and arteriosclerosis risk in professional drivers.

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