

## Arterial Age and Shift Work

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### Abstract

**Background:** The relationship between shift work and cardiovascular disease is controversial.

**Objectives:** The present study aimed to assess the relationship between shift work and arterial age and to identify predictors of early arterial aging.

**Methods/Study Design:** A total of 61 workers, 77% working in 2 or more shifts, underwent arteriography. Arterial age (AA), brachial and aortic augmentation index (Aix Brach and Aix Ao) and pulse wave velocity (PWV) were assessed. The participants were questioned about smoking habits, cardiovascular family and personal history, physical work and number of shifts.

**Results/Findings:** Aix Brach was:  $-40 \pm 29\%$ , AixAo:  $16 \pm 1.71\%$ , PWV:  $8.06 \pm 1.44$  m/s, AA:  $41 \pm 15$  years. The number of shifts was significantly associated with Aix Brach ( $p < 0.01$ ) and Aix Ao ( $p < 0.01$ ) (Multiple  $R = 0.875$ ,  $F < 0.01$ ); PWV ( $p < 0.01$ ) and AA ( $p = 0.0001$ ) (Multiple  $R = 0.922$ ,  $F < 0.01$ ). Multiple regression analysis revealed significant associations between arterial age and smoking ( $p = 0.0008$ ), positive cardiovascular family history ( $p = 0.023$ ) and physical work ( $p = 0.0029$ ) (Multiple  $R = 0.758$ ,  $F < 0.01$ ). Early arterial aging was more likely in shift workers compared to the other participants (OR=1.189, 95%CI=0.346-4.089).

**Conclusion:** Shift work, smoking, positive cardiovascular family history and physical work predict early arterial aging.

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**Key words:** Arteriography, early arterial aging, pulse wave velocity, augmentation index, shift work

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## **Introduction**

Shift work impairs physiological rhythms, causes psychological and physical stress and could be linked to cardiovascular morbidity.<sup>1</sup>

Cardiovascular disease is the leading cause of mortality in the general population, and it is linked to atherosclerosis and its complications.<sup>2</sup> Atherosclerosis begins in young people, and arterial stiffness and endothelial dysfunction are early markers of atherosclerosis. Vascular aging is associated with increased arterial stiffness, especially in the presence of cardiovascular risk factors.<sup>3,4</sup> Arterial age was a better predictor of cardiovascular disease compared to the classical risk factors and was associated with longevity.<sup>5</sup>

Arteriography may assess arterial stiffness, endothelial dysfunction and arterial age. Arterial stiffness and endothelial dysfunction can be determined using pulse wave velocity, and, brachial and aortic augmentation index, respectively.

In order to plan future preventive interventions in shift workers, it was the objective of the present study to assess the relationship between shift work and arterial age and to identify predictors of early arterial aging using a noninvasive procedure.

## **Methods**

### **Study population**

A total of 61 workers employed in a car harness manufacturing enterprise underwent arteriography. Additional data about shift work, physical work, smoking habits, personal and family history were obtained.

The investigations conformed to the principles of the Declaration of Helsinki<sup>6</sup> and were approved by the Ethics Committee of the University. A written informed consent was obtained from each participant.

A power analysis was conducted to determine the number of participants needed in the present study and the minimum sample size required for regression analysis was 54.<sup>1</sup>

### **Arteriography**

The 61 participants underwent arteriography using a Medexpert device (TensioMed Ltd, Budapest, Hungary). Systolic and diastolic blood pressure, mean arterial pressure, brachial and aortic augmentation index (Aix Brach and Aix Ao, respectively), pulse wave velocity (PWV), the diastolic reflection area (DRA), diastolic and systolic area index (DAI and SAI), and arterial age were assessed.

Measurements were made after 10 minutes rest, in supine position, in a quiet room, with normal temperature ( $22\pm 1$  °C). The participants were previously asked not to smoke, eat or drink coffee or alcohol 4 hours before arteriography, and they were forbidden to move or speak during the recording.

An upper arm cuff, in 3 different sizes, was used, according to the arm circumferences. Pulse wave velocity  $< 9.7\text{m/s}$  and brachial augmentation index  $< -10\%$  were considered normal. Increased arterial stiffness was associated with a pulse wave velocity  $>9.7\text{m/s}$ , and endothelial dysfunction with a brachial augmentation index  $>-10\%$ . Arterial age was considered increased (early vascular aging) if higher than the biological age. The differences between arterial and biological age were calculated for each participant (Dif AA).

Participants in which pulse wave velocity, augmentation indices and arterial age could not be determined, were excluded from the study.

### **Additional data**

Family history was considered positive if cardiovascular diseases or diabetes mellitus were mentioned.

Smoking habits were also self-reported. Data about the number of cigarettes and smoking period were collected. Participants who quitted smoking 10 years before were considered nonsmokers.

### **Statistical methods**

Categorical data are given as numbers and percentages, continuous data are given as means  $\pm$  standard deviation. Linear and multiple regression analysis, Bravais-Pearson correlations and odds ratio were used as statistical methods.

## **Results**

The characteristics of the study population are shown in table 1. Most of the participants (77%) were shift workers, with a shift career of 10-120 months. Early arterial aging, endothelial dysfunction and arterial stiffness were detected in 70%, 10% and 15%, respectively.

### **Bravais-Pearson correlations**

The correlations between the number of shifts and arteriography parameters were weak: 0.14 and -0.12 (with the differences between arterial and biological age, and Aix Brach, respectively). The only significant correlation was obtained between Dif AA and pulse wave velocity ( $r=0.716$ ) (Figure 1).

### **Regression analysis**

Linear regression analysis revealed significant associations between shift work and early arterial aging (more than 10 years difference between arterial and biological age) (Table 2).

Multiple regression analysis showed significant associations between shift work, pulse wave velocity, arterial age and augmentation indices (Table 2). Positive cardiovascular family history, smoking and physical work were significantly associated with arterial age (Table 2).

### **Odds ratio**

Early arterial aging was more likely in shift workers compared to the other workers (OR=1.189; 95%CI: 0.346-4.089), but not endothelial dysfunction, arterial stiffness or impaired diastolic filling.

### **Discussion**

The most important finding of the present study is the influence of shift work, smoking, positive cardiovascular family history and physical work on early arterial aging.

Early arterial aging was detected in 70% of the participants, and only 10% and 15% had endothelial dysfunction and increased arterial stiffness, respectively. Pulse wave velocity correlated with Dif AA, suggesting a strong connection between arterial stiffness and early arterial aging. Several other factors also contribute to early vascular aging, besides endothelial dysfunction, arterial stiffness and impaired diastolic perfusion.

Despite the significant associations between the number of shifts and pulse wave velocity and endothelial dysfunction, arterial stiffness and endothelial dysfunction were not more prevalent in shift workers compared to the other participants.

Endothelial function was previously assessed in shift workers after night work, and reduced flow-mediated dilation of the brachial artery was found, independent of shift-work history<sup>7</sup>.

High job strain causes cardiovascular and cerebrovascular disease through the progression of atherosclerosis, demonstrated by subclinical markers of atherosclerosis in the aorta, cerebral and carotid artery in male Japanese factory workers.<sup>8</sup> An association between high job strain and elevated pulse wave velocity was observed in several studies.<sup>8,9</sup>

A positive association was previously found between brachial pulse wave velocity and physiological variables including age, heart rate, body mass index, and total serum cholesterol, fasting glucose and noradrenaline, and a negative association with job strain, in Japanese male workers.<sup>10</sup>

Detection of subjects with preclinical atherosclerosis and increased arterial age could represent an effective primary prevention method for cardiovascular disease. Further large, follow up

studies are needed in order to demonstrate the usefulness of endothelial dysfunction and arterial stiffness as biomarker of shift work stress. Unhealthy behaviors, including smoking, require further interventions, considering that healthy lifestyle is the best therapy for blood vessels.

### **Study limitations**

No data about other unhealthy lifestyle factors (alcohol intake, unhealthy diets), sleep schedule, job strain, overtime work and lipid profile were available. Although overtime work, lifestyle factors, such as ethanol consumption, and lipid profile are known predictors of atherosclerosis, they were not included in the present analysis, requiring further investigation in future studies.

A large number of studies have reported that both long and short sleep durations are independently associated with cardiovascular disease.<sup>11</sup> Night shifts cause sleep deprivation, mental stress and impair coronary microcirculation,<sup>12</sup> but no data were available about the sleep schedule of the shift workers.

Several data, including smoking status and family history of cardiovascular disease are self-reported, which could cause over- or underestimations.

The results of the present study can not be extrapolated to other types of professional exposure.

### **Conclusion**

The present study demonstrates the link between early arterial aging and shift work, smoking status, cardiovascular family history and physical work. Arterial stiffness and endothelial dysfunction are not more prevalent in shift workers compared to non shift workers.

**Conflict of Interest:** None declared.

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**Table 1:** Characteristics of the study population

Variable	Reference range (Means±SD)
Biological age	33±8 years
Gender (Male)	28 (46%)
Positive cardiovascular history	17 (28%)
Current smokers	29 (48%)
Physical work	32 (52%)
Shift workers	47 (77%)
Body mass index (kg/m <sup>2</sup> )	25±6
Systolic blood pressure (mmHg)	123±11.2
Diastolic blood pressure (mmHg)	72±9.28
High normal blood pressure and hypertension (%)	15 (25%)
Pulse pressure (mmHg)	51±10
Mean arterial pressure (mmHg)	89±10
Heart rate (beats/minute)	74±11
Brachial augmentation index Aix Brach (%)	-40±29%
Aix Brach > -10%	6 (10%)
Aortic augmentation index Aix Ao (%)	16±1.71%
Pulse wave velocity (PWV) (m/s)	8.06±1.44
DRA (diastolic reflection area)	53±11
DAI (diastolic area index)(%)	52±4.9
PWV>9.7 m/s	9 (15%)
Arterial age (years)	41±15
Difference between arterial and biological age (Dif AA) (years)	10.44±1.23
Early arterial aging (%)	43 (70%)

**Table 2:** Linear and multiple regression analysis. Factors significantly associated with shift work, number of shifts and arterial age

Variable	Associated variables	Multiple R	R square	Adjusted R	Significance F
Shift work	EAA (p<0.01)	0.756	0.571	0.555	<0.01
Shift work	AAD (p<0.01)	0.568	0.324	0.307	<0.01
Number of shifts	PWV (p<0.01) AA (p = 0.00011) EAA (p = 0.0033)	0.922	0.851	0.828	<0.01
Number of shifts	Aix Brach (p<0.01) Aix Ao (p<0.01)	0.875	0.765	0.744	<0.01

<b>Arterial age</b>	<b>Smokers</b> (p = 0.0008) <b>Positive cardiovascular family history</b> (p = 0.023) <b>Physical work</b> (p = 0.0029)	0.758	0.574	0.542	<0.01
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Multiple R = multiple correlation coefficient

R square = coefficient of determination

Adjusted R = the coefficient of determination adjusted for the number of independent variables in the regression model

AA = arterial age

EAA = early arterial aging (AA > biological age) (dichotomous variable)

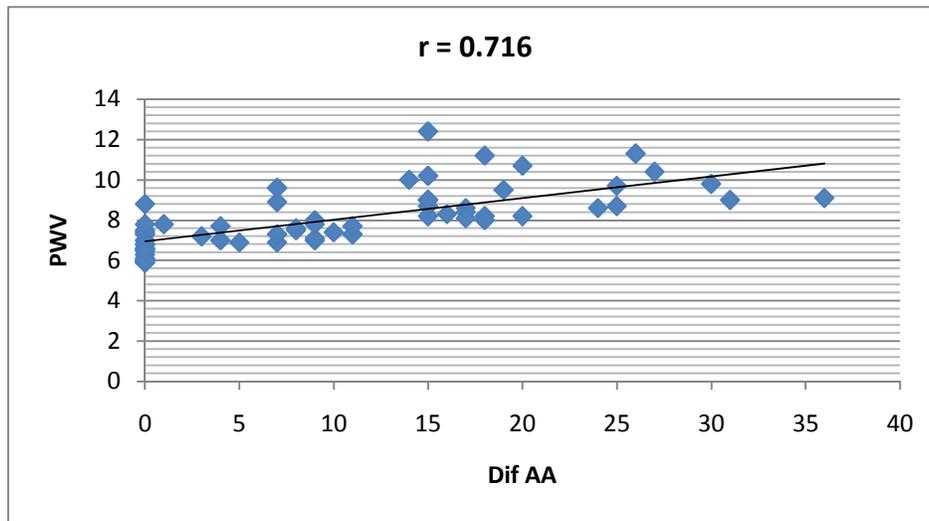
Shift work = 2 or more shifts (dichotomous variable)

AAD = differences between AA and biological age >10 years, with higher AA (dichotomous variable)

Aix Brach = brachial augmentation index

Aix Ao = aortic augmentation index

PWV = pulse wave velocity



**Figure 1:** The correlation between the differences between arterial and biological age (Dif AA) and pulse wave velocity (PWV); r = 0.716