

Research Article

Association between Life Stressors and Arterial Stiffness: The Finnish Retirement and Aging Study

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ARTICLE INFO

Article History

Received 12 November 2020

Accepted 22 May 2021

Keywords

Ageing
blood pressure
cardiovascular disease
occupational health
stress
pulse wave velocity

ABSTRACT

Objective: Besides traditional risk factors, other factors such as life stressors are linked with incident cardiovascular disease. However, the underlying mechanisms for this association remain mostly unknown. We studied the relation of life stressors (job strain, sleep loss due to worry, illness or death in family, financial difficulties and caregiving) and their accumulation with arterial stiffness, an independent predictor of cardiovascular disease.

Methods: 258 participants (mean age 62.4 years, 82% women) from the Finnish Retirement and Aging Study underwent measurements for carotid-femoral Pulse Wave Velocity (PWV), a standard criterion for assessing arterial stiffness and responded to a survey inquiring life stressors. Using analysis of covariance, we estimated group means adjusted for age, gender, occupation, lifestyle factors and hypertension.

Results: Participants with recent illness or death in family (8.04 m/s; 95% CI, 7.40–8.73 vs. 7.52 m/s; 95% CI, 7.03–8.05) and financial difficulties (8.65 m/s; 95% CI, 7.62–9.81 vs. 7.71 m/s; 95% CI, 7.21–8.24) had increased PWV compared to those who did not have exposed to these stressors independent of lifestyle factors, diabetes and systolic blood pressure. In addition, increasing number of life stressors demonstrated an association towards increased PWV (≥ 2 stressors: 8.04 m/s; 95% CI, 7.42–8.72 vs. 0 stressors 7.74 m/s; 95% CI, 7.23–8.28; p for trend 0.27) but the association attenuated after adjusting for lifestyle factors, diabetes and systolic blood pressure.

Conclusion: Life stress was found to associate with higher arterial stiffness. Increased arterial stiffness could explain some of the increased cardiovascular disease risk related to life stressors.

HIGHLIGHTS

- Arterial stiffness was assessed as carotid-femoral pulse wave velocity.
- Illness or death in the family were associated with an increased arterial stiffness.
- Financial difficulties were associated with an increased arterial stiffness.
- A trend toward increasing number of stressors and higher arterial stiffness exists.

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1. INTRODUCTION

Cardiovascular Disease (CVD) is a leading cause of mortality worldwide. Conventional risk factors, e.g., smoking, hypercholesterolemia and high blood pressure has been shown to partially

explain the increased risk [1]. However, other CVD risk factors have also been identified, including exposure to stressors in private life or at work, such as stressful events and job strain [2]. Chronic stress resulting from occupational stressors has been associated with higher blood pressure in some studies, but the association between other life stressors and blood pressure is more complicated [3,4].

The exact mechanisms through which mental strain and stress increase CVD risk remain obscure [5]. Increased arterial stiffness, most commonly measured using carotid-femoral Pulse Wave Velocity (PWV), is a strong predictor of future CVD events [6]. A few studies have examined the association of stressful life events, life stress and job strain with arterial stiffness [7–13]. However,

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Peer review under responsibility of the Association for Research into Arterial Structure and Physiology

Data availability statement: Anonymized partial datasets of the Finnish Retirement and Aging Study are available by application with bona fide researchers with an established scientific record and bona fide organizations. For more information, please contact prof. Sari Stenholm (sari.stenholm@utu.fi).

since these studies have provided conflicting findings, were based on study samples that consisted mainly of young Asians, and have used non-standard methods for measuring PWV, further research on this topic is warranted.

The aim of this study was to examine the association of life stressors related to work and private life and their accumulation, with arterial stiffness, among late middle-aged persons.

2. MATERIALS AND METHODS

2.1. Study Sample

The study sample consisted of participants from the Finnish Retirement and Aging Study (FIREA). Details of the design and implementation of the FIREA study have been reported elsewhere [14]. The eligible population for the FIREA study cohort included all public sector employees with an estimated retirement date between 2014 and 2019 who worked in 2012 in Southwest Finland or in the nine selected cities or five hospital districts around Finland and who responded to at least one of the FIREA questionnaires ($N = 6679$). Participants were first contacted 18 months prior to their estimated retirement date by sending a questionnaire. After responding to the questionnaire, Finnish speaking participants, with estimated retirement date between 2017 and 2019, who lived in the Southwest Finland and were still working, were invited to participate in the clinical substudy ($n = 773$). Of them, 291 participated in the study between September 2015 and May 2018. We excluded 31 persons for not undergoing PWV measurements (due to refusal, cardiac arrhythmia, pacemaker, failed measurement or

unknown reasons) and two persons for not answering the stressor questions, resulting on a final sample of 258 participants. The participants who took part in the PWV measurements reported less job strain, were physically more active, less often smokers, had lower body mass index as well as reported less hypertension and diabetes than survey participants indicating a healthier study population (Table 1).

The FIREA study was conducted in accordance with the Helsinki declaration and was approved by the Ethics Committee of Hospital District of Southwest Finland (ETMK: 84/1801/2014). All participants gave written informed consent.

2.2. Assessment of Life Stressors

Job strain was assessed with nine items measuring job control and five items measuring job demands derived from the Job Content Questionnaire [15]. The presence of job strain was defined as having high demands (above the median score of 3.2) and a low control (below the median score of 3.8) based on the FIREA surveys cut-off points. Sleep loss due to worry was obtained from the single question of General Health Questionnaire [16] in which participants were asked “Have you recently lost much sleep due to worry?” Participants were categorized into no (“Not at all” and “No more than usual”) and yes (“Rather more than usual” and “Much more than usual”). Severe life events within the past 12 months (yes vs. no) were measured by the occurrence of severe illness or death in the family (spouse, child, parent or other) and severe financial difficulties were based on a question of having had severe financial problems within the past 12 months [yes vs. no (earlier or

Table 1 | The selection of survey participants

	Survey participants ($n = 4649$)		Participants who underwent PWV measurement ($n = 258$)		<i>p</i> -value
	Mean (SD)	<i>N</i> (%)	Mean (SD)	<i>N</i> (%)	
Age	62.5 (1.2)		62.4 (1.0)		0.03
Female		3797 (82)		212 (82)	0.84
Life stressors					
Job strain		1127 (29)		55 (22)	0.02
Sleep loss because of worries		733 (16)		40 (16)	0.89
Illness or death in the family		768 (18)		44 (18)	0.99
Financial difficulties		165 (4)		11 (4)	0.58
Caregiving		710 (16)		43 (17)	0.53
Sum of life stressors					0.92
0 points		2207 (47)		123 (48)	
1 point		1614 (35)		87 (34)	
2 or more points		828 (18)		48 (19)	
Occupational status					0.08
Higher non-manual		1483 (32)		95 (37)	
Lower non-manual		1395 (30)		84 (33)	
Manual		1729 (38)		79 (30)	
Self-reported body mass index					0.04
Normal weight		1767 (39)		109 (43)	
Overweight		1818 (40)		106 (42)	
Obese		972 (21)		37 (15)	
Low physical activity		1815 (39)		64 (25)	<0.0001
Heavy alcohol use		388 (8)		29 (11)	0.11
Current smokers		496 (11)		13 (5)	0.004
Self-reported hypertension		1660 (39)		62 (25)	<0.0001
Self-reported diabetes		428 (10)		13 (5)	0.02

not at all]). Caregiving was assessed with the following question: “Do you provide care to a family member or relative, who is unable to take care of himself or herself because of age, illness or disability?” (giving a care for health children was discounted) (yes vs. no).

Based on these five life stressors (job strain, sleep loss due to worry, illness or death in family, financial difficulties and caregiving), the cumulative sum score was calculated by giving one point to each stressor, maximum points being 5. Participants were then categorized into three groups: 0, 1 and 2 or more points.

2.3. Carotid-femoral Pulse Wave Velocity

Arterial stiffness was assessed using carotid-femoral PWV measurements (SphygmoCor PVx with MM3 electronics module and Millar tonometer), as previously described [17]. Briefly, three electrodes were attached to the body to record timing of cardiac R-wave (time of pulse wave departure from the heart). The pulse wave measurements were made at the right femoral artery and right common carotid artery (time of pulse wave arrival at the distal arteries). Distance between manubrium sternum and registration points was measured to give a straight distance between registration points. Transit time was acquired from the time delay between the feet of two waveforms in relation to the R-wave of the simultaneously recorded electrocardiogram (ECG). PWV was then calculated by dividing the distance by the transit time (m/s). PWV measurements were performed twice and averaged for statistical analyses. Participants were asked to avoid food, caffeine drinks and tobacco use for 3 h and alcohol for 24 h before the measurement. The PWV measurement happened in the different study visit than the blood pressure measurement.

2.4. Covariates

Occupational titles were obtained from the pension insurance institute for the municipal sector in Finland (Keva; based in Helsinki, Finland). To measure occupational status, occupational titles, coded according to the International Standard Classification of Occupation, were categorized to three groups: higher-grade non-manual workers (e.g. teachers, physicians), lower-grade non-manual workers (e.g. registered nurses, technicians) and manual workers (e.g. cleaners, maintenance workers). Body Mass Index (BMI) was calculated from measured weight and height and categorised into normal weight (<25.0 kg/m²), overweight (25 to <30 kg/m²) and obese (≥30 kg/m²). Physical activity was defined as average weekly hours of leisure-time physical activity and dichotomized into low (<14 metabolic equivalent) and high groups based on the self-reported and pre-defined criteria [14]. Alcohol consumption was categorized according to the habitual frequencies of drinking beer, wine and spirits; heavy alcohol use (yes vs. no) was defined as >16 drinks/week for women and >24 drinks/week for men. Smoking status was categorized as non-smokers (never and former) and current smokers. A nurse who stayed in the room during the measurements measured blood pressure twice with a digital blood pressure monitor (Microlife WatchBP Office Central) from right arm in the sitting position. Diabetes was based on self-reported doctor diagnosed condition. In addition, participants were asked to list all their medication. We defined hypertension as the use of

antihypertensive medication, systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg.

2.5. Statistical Analyses

Characteristics of the participants are provided as percentages for categorical variables and as mean values for continuous variables. We compared adjusted mean log-transformed PWV values between groups using analysis of covariance. Model 1 was performed using age and gender as covariates. Model 2 was additionally adjusted for occupational status, BMI, physical activity, alcohol consumption, diabetes and smoking. Model 3 was further adjusted for systolic blood pressure. Statistical analysis were performed with SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA).

3. RESULTS

The study sample characteristics are shown in Table 2. The majority of the participants were women ($N = 212$; 82%) and mean age was 62.4 ± 1.0 years. Mean PWV was 7.8 ± 1.3 m/s. 22% of the participants had job strain, 16% reported sleep loss due to worry, 18% had recent illness or death in the family, 4% had recent financial difficulties and 17% reported caregiving. 48% had none life stressors while 19% had two or more.

Table 3 shows the association between individual and cumulative life stressors and PWV. In the age and gender adjusted model (Model 1), PWV was higher among participants with recent

Table 2 | Characteristics of the study participants ($n = 258$)

	<i>n</i> (%)	Mean (SD)
Age, years		62.4 (1.0)
Women	212 (82)	
PWV, m/s		7.8 (1.3)
Blood pressure from the right hand		137.9 (17.7)
Life stressors		
Job strain	55 (22)	
Sleep loss due to worry	40 (16)	
Illness or death in the family	44 (18)	
Financial difficulties	11 (4)	
Caregiving	43 (17)	
Sum of life stressors		
0 points	123 (48)	
1 point	87 (34)	
2 or more points	48 (19)	
Occupational status		
Higher non-manual	95 (37)	
Lower non-manual	84 (33)	
Manual	79 (31)	
Body mass index		
Normal weight (<25 kg/m ²)	106 (41)	
Overweight (25 to <30 kg/m ²)	110 (43)	
Obese (≥30 kg/m ²)	42 (16)	
Low physical activity	64 (25)	
Heavy alcohol use	29 (11)	
Current smokers	13 (5)	
Hypertension	116 (45)	
Self-reported diabetes	13 (5)	

Table 3 | Adjusted mean levels of pulse wave velocity (m/s) in groups by individual and cumulative life stressors

Life stressor	n (%)	Model 1	Model 2	Model 3
		Mean (95% CI)	Mean (95% CI)	Mean (95% CI)
Job strain				
No	197 (78)	7.70 (7.48–7.92)	7.78 (7.25–8.34)	7.78 (7.26–8.34)
Yes	55 (22)	7.82 (7.48–8.19)	7.80 (7.16–8.48)	7.82 (7.19–8.50)
<i>p</i> -value		0.50	0.94	0.86
Sleep loss due to worry				
No	218 (85)	7.69 (7.49–7.90)	7.78 (7.28–8.33)	7.79 (7.29–8.33)
Yes	40 (16)	7.76 (7.37–8.18)	7.77 (7.13–8.46)	7.76 (7.13–8.45)
<i>p</i> -value		0.74	0.94	0.91
Illness or death in family				
No	200 (82)	7.63 (7.43–7.82)	7.48 (6.99–8.01)	7.52 (7.03–8.05)
Yes	44 (18)	8.09 (7.69–8.51)	7.93 (7.29–8.62)	8.04 (7.40–8.73)
<i>p</i> -value		0.02	0.042	0.02
Financial difficulties				
No	243 (96)	7.68 (7.49–7.88)	7.70 (7.20–8.24)	7.71 (7.21–8.24)
Yes	11 (4)	8.39 (7.61–9.24)	8.66 (7.61–9.84)	8.65 (7.62–9.81)
<i>p</i> -value		0.07	0.056	0.06
Caregiver				
No	209 (83)	7.69 (7.49–7.90)	7.75 (7.23–8.32)	7.78 (7.26–8.33)
Yes	43 (17)	7.74 (7.35–8.16)	7.70 (7.07–8.39)	7.62 (7.01–8.29)
<i>p</i> -value		0.80	0.82	0.50
Stress sum				
0	123 (48)	7.61 (7.38–7.85)	7.73 (7.22–8.29)	7.74 (7.23–8.28)
1	87 (34)	7.71 (7.42–8.00)	7.75 (7.18–8.36)	7.74 (7.18–8.34)
>1	48 (19)	8.03 (7.64–8.44)	8.01 (7.38–8.70)	8.04 (7.42–8.72)
<i>p</i> for trend		0.06	0.30	0.27

Model 1: adjusted for age and gender. Model 2: Model 1 and additionally adjusted for occupational status, BMI, physical activity, alcohol consumption, smoking and diabetes. Model 3: Model 2 and additionally adjusted for systolic blood pressure.

illness or death in the family and borderline higher among participants with recent financial difficulties compared to those without these events, 8.09 (95% CI 7.69–8.51) vs. 7.63 (95% CI 7.43–7.82); 8.39 (95% CI 7.61–9.24) vs. 7.68 (95% CI 7.49–7.88). No significant associations were observed for job strain, sleep loss due to worry, or caregiving with PWV. In the lifestyle factors and diabetes adjusted model (Model 2), PWV both in participants with recent illness or death in family and recent financial difficulties proved to be borderline significant higher compared to those without these risks, 7.93 (95% CI 7.29–8.62) vs. 7.48 (95% CI 6.99–8.01); 8.66 (95% CI 7.61–9.84) vs. 7.70 (95% CI 7.20–8.24). Moreover, in the Model 3, additionally adjusted for systolic blood pressure, participants with recent illness or death in family had significantly higher PWV compared to those without this risk, 8.04 (95% CI 7.40–8.73) vs. 7.52 (95% CI 7.03–8.05). Again, participants with recent financial difficulties showed borderline significantly higher PWV values compared to participants without recent financial difficulties, 8.65 (95% CI 7.62–9.81) vs. 7.71 (95% CI 7.21–8.24). A trend toward higher PWVs with increasing number of stressors was observed, but adjustment for lifestyle factors, diabetes and systolic blood pressure attenuated the association.

4. DISCUSSION

We observed an increased arterial stiffness among the individuals who reported occurrence of a recent illness or death in the family or financial difficulties within the past 12 months. Other studied

life stressors, such as job strain, sleep loss due to worry and caregiving were not associated with arterial stiffness. We observed a borderline association between increasing number of life stressors with higher PWV, which was however attenuated after taking into account lifestyle factors, diabetes and systolic blood pressure.

To the best of our knowledge, the association between recent death or illness in family and greater arterial stiffness has not been previously reported. However, this finding is in line with the earlier finding on the increased risk of myocardial infarct in parents that had faced a death of a child [18]. We also observed equivocal evidence of an association between higher PVW and multiple life stressors and so far very little research on the combined impact of multiple stressors on CVD risk has been conducted [19]. These findings are plausible, since it has been debated that stress can result in cardiovascular diseases via dysregulation of the hypothalamic–pituitary axis, inflammation and sympathetic nervous system activation [20].

From clinical point of view, it has been earlier concluded that a change of 1 m/s in carotid-femoral PWV corresponds to 12% increased risk to cardiovascular events [21]. Moreover, the mortality to cardiovascular diseases increases by 9% while carotid-femoral PWV increases by 1 m/s [21]. While in our study between group differences did not reach that level it can be assumed that the higher PWV values can lead to unfavourable consequences. However, it has to be regarded that the PWV values were overall at a good level in this study population consisting of relatively healthy aging workers.

The strengths of our study include having a relatively large number of participants with varying occupational backgrounds as earlier studies have concluded that manual workers may be more vulnerable to job strain induced high blood pressure [22], a strong correlate of arterial stiffness. Moreover, we used carotid-femoral PWV, the noninvasive gold standard for measuring PWV [23], in contrast to previous studies that used a wide scale of non-conventional methods for assessing arterial stiffness (augmentation index, brachial-ankle pulse wave velocity and finger photoplethysmogram) [7,8,10–12].

The present study has also limitations. First, aging workers are a selected group of individuals that may be somewhat healthier than the general population. This was also expressed by the relatively low mean PWV of the study sample (7.8 m/s). Moreover, the participation rate was relatively low leading to healthier study population compared to the FIREA survey participants. This may have distorted the association between life stressors and PWV. Despite we were able to control for the role of blood pressure and lifestyle factors in the association between stressors and PWV, residual confounding due to unmeasured confounders remains an issue in an observational study. Finally, as an observational study this study is primarily hypothesis-generating and risk of false positive findings also remains.

5. CONCLUSION

Recent death or illness in family and recent financial difficulties associate with increased PWV even after controlling for systolic blood pressure. Moreover, the PWV showed an elevating trend toward increasing stressors. Increased arterial stiffness could explain some of the cardiovascular disease risk related to life stressors. Future studies are warranted to examine the association of different stressors and arterial stiffness in more general populations.

CONFLICTS OF INTEREST

The authors declare they have no conflicts of interest.

AUTHORS' CONTRIBUTION

SK, TJN and SS conceived and designed the work. SS contributed to data acquisition. SK, TJN and SS analyzed, and interpreted the data. SK, TJN and SS drafted the manuscript. JV and OJH revised the manuscript critically for important intellectual content.

FUNDING

The funders had no role in the study design, the collection, analysis and interpretation of the data, the writing of the report, or the decision to submit the paper for publication.

ACKNOWLEDGMENTS

This work was supported by grants from the Urmas Pekkala Foundation and Turku University Foundation (for SK), the

Hospital District of Southwest Finland (for TJN), the Academy of Finland (grant number 286294, 294154, 332030 and 319246 for SS; and 321351 for TJN), the Emil Aaltonen Foundation (for TJN), the Finnish Medical Foundation (for TJN), the Finnish Foundation for Cardiovascular Research (for TJN) and the Paavo Nurmi Foundation (for TJN).

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