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Association between psychosocial work-related factors at midlife and arterial stiffness at older age in a prospective cohort of 1736 white-collar workers

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ABSTRACT

Objective Arterial stiffness and exposure to psychosocial work-related factors increase the risk of developing cardiovascular disease. However, little is known about the relationship between psychosocial work-related factors and arterial stiffness. We aimed to examine this relationship.

Design Prospective cohort study.

Setting Public organisations in Quebec City, Canada.

Participants The study included 1736 white-collar workers (women 52%) from 19 public organisations.

Primary and secondary outcome measures Association between psychosocial work-related factors from the job strain and effort–reward imbalance (ERI) models assessed at study baseline (1999–2001) with validated instruments and arterial stiffness assessed using carotid–femoral pulse wave velocity at follow-up, on average 16 years later (2015–2018). Generalised estimating equations were used to estimate differences in arterial stiffness between exposed and unexposed participants. Subgroup analyses according to sex, age, blood pressure (BP), cardiovascular risk score and employment status were conducted.

Results Among participants with high diastolic BP (≥90 mm Hg) at baseline, aged 47 on average, those exposed to high job strain had higher arterial stiffness (1.38 m/s (95% CI: 0.57 to 2.19)) at follow-up, 16 years later, following adjustment for a large set of potential confounders. The trend was similar in participants with high systolic BP (≥140 mm Hg) exposed to high job strain (0.84 m/s (95% CI: −0.35 to 2.03)). No association was observed for ERI in the total sample and counterintuitive associations were observed in subgroup analyses.

Conclusions Job strain may have a long-term deleterious effect on arterial stiffness in people with high BP. Interventions at midlife to reduce job strain may mitigate arterial stiffness progression.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study has a long follow-up period of 16 years.
⇒ Arterial stiffness was measured using carotid–femoral pulse wave velocity, the gold standard.
⇒ Psychosocial work-related factors were assessed using validated instruments.
⇒ This study examines the effect of psychosocial work-related factors measured at a single point in time.

INTRODUCTION

Cardiovascular disease (CVD) is a major public health problem. CVD develops over several years across a continuum initiated by one or several risk factors, which can progress to atherosclerosis, cardiovascular events and end-stage organ disease.[1] The main modifiable risk factors for CVD include dyslipidaemia, high blood pressure (BP), smoking, diabetes and adiposity. Additional factors such as psychosocial work-related factors can contribute to increase the risk of CVD.[2] In Organisation for Economic Co-operation and Development countries, 20%–25% of workers are exposed to adverse psychosocial work-related factors.[3]

Arterial stiffness describes the reduced ability of large proximal arteries to dilate and retract. Carotid–femoral pulse wave velocity (cfPWV), the gold standard method for assessing aortic stiffness, is linearly associated with CVD risk.[4] An increase in aortic pulse wave velocity of 1 m/s corresponds to an adjusted risk increase of 14% in fatal or non-fatal cardiovascular events.[4] Adverse psychosocial work-related factors may be associated with high arterial stiffness. Results of prior studies differ according to types of exposure and sex, suggesting deleterious,[5–9] beneficial[10] or no effect[11] of psychosocial work-related factors on arterial stiffness. All prior studies are limited by their cross-sectional design. None used the gold standard measure for arterial stiffness.

The objective of the present study was to examine the association between psychosocial

work-related factors and arterial stiffness in a prospective cohort study of men and women from Quebec City, Canada. Men and women were considered separately since the prevalence of psychosocial work-related factors and their effects differ by sex.[2] Elevated midlife BP is associated with increased arterial stiffness.[12] The relationship between midlife psychosocial work-related factors and arterial stiffness might therefore vary between people with and without elevated BP. This potential effect modification was examined.

METHODS

Population and study design

We used data from a prospective cohort study. This cohort was initiated in 1991–1993 among 9188 white-collar workers (participation proportion: 75%) from 19 public organisations in Quebec City with two subsequent phases of data collection (1999–2001 and 2015–2018).[13] The current study baseline was set in 1999–2001, since effort–reward imbalance (ERI) exposure was first assessed at that time. Arterial stiffness was assessed at follow-up (2015–2018). Among the 9188 participants in the original cohort initiation, 8120 (88.4 %) and 6707 (73 %) participated in 1999–2001 and 2015–2018, respectively. Arterial stiffness was measured in 1/3 of participants randomly selected. For the present study, baseline corresponds to the 1999–2001 period and follow-up time to 2015–2018. The study sample included 1736 participants with employee status at baseline (figure 1).

Data collection

At each wave, workers completed a self-administered questionnaire on risk factors for hypertension and CVD, demographic, occupational and social characteristics. Trained staff measured BP (using the mercury sphygmomanometer at baseline and the automated BP-TRU device (VSM MedTech, Coquitlam, Canada) at follow-up), height, weight and waist circumference. Arterial stiffness was measured at follow-up.

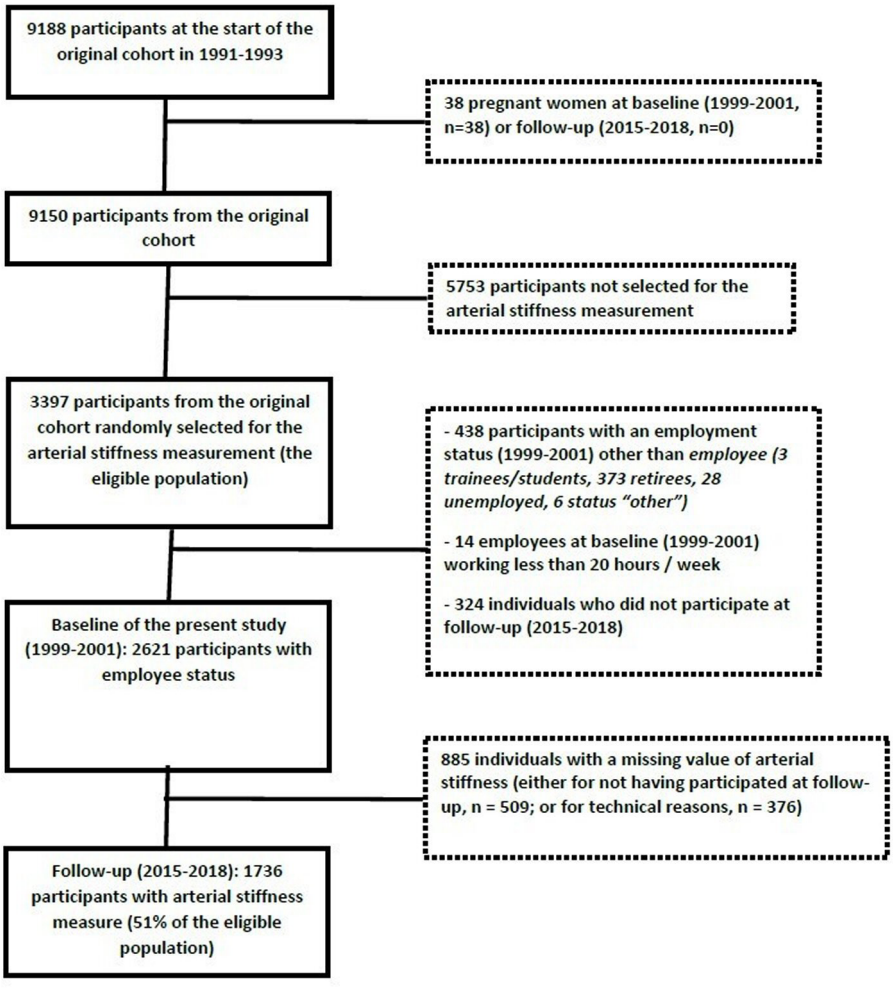

Figure 1 Flow chart. The start of the original cohort: 1991–1993. Baseline: the baseline for the current study in 1999–2001. Follow-up: the follow-up for the current study in 2015–2018. The current study investigates the association between psychosocial work-related factors measured at baseline (1999–2001) and arterial stiffness measured at follow-up (2015–2018), adjusted for covariates measured at follow-up. Covariates measured at the start of the original cohort (1991–1993) were used to compute inverse probability of censoring weights (used in order to minimise potential selection bias due to non-response and lost to follow-up).

Psychosocial work-related factors

Job strain and ERI exposures were assessed at baseline (1999–2001). Components of job strain (psychological demands and job control) were measured using 18 items from the Job Content Questionnaire.[14] Psychological demands include the quantity of work, time constraints and level of intellectual effort. Job control includes opportunities for learning, autonomy and participation in the decision-making process. The theoretical model postulates that the greatest health risk occurs in workers combining high demands and low control. The psychometric properties of the original English[15] and French[16] questionnaires have been demonstrated. We classified workers with demands scores≥24 (the median in the Quebec working population) in the *high demands* group and those with control scores≤72 (the median in the Quebec working population) in the *low control* group. The *low strain* group included workers combining *low demands* and *high control*. The p*assive*, *active* and *high strain* groups included respectively people combining *low demands* and *low control*, *high demands* and *high control* and *high demands* and *low control*.

The ERI model states that efforts should be rewarded with income, respect and esteem, and occupational status control. Workers are in a state of deleterious imbalance when high efforts are accompanied by low reward and are more susceptible to health problems. The modified French version of the questionnaire was used to assess ERI. Reward at work was measured by nine original questions from the French version[17] of the ERI scale. Effort was measured by nine items from the validated French version of the psychological demand scale of the Job Content Questionnaire.[18] The psychometric qualities of this ERI scale version have been demonstrated.[19] Effort and reward scores were computed with the sum of items. A ratio efforts/reward>1 indicated an imbalance. The ratio was also used in its continuous form.

Arterial stiffness as cfPWV (m/s)

Arterial stiffness was measured at follow-up using the Complior Analyse device (Alam Medical, Saint-Quentin-Fallavier, France). The transit time between the carotid and the femoral pulse was measured two times in each participant. cfPWV was calculated by dividing the carotid–femoral transit distance (calculated using the difference in body surface measurements from the suprasternal notch to the femoral and carotid sites) by the carotid–femoral transit time delay. A third measurement was taken if the difference between the two measurements was >0.5 m/s. Interobserver and intraobserver reproducibility of this measurement has been reported as excellent.[20]

Covariates

Potential confounders included the following risk factors for arterial stiffness: demographic characteristics (age, sex, education, household income, marital status and having children); biological factors (BP, body mass index (BMI), waist circumference, diabetes, hypercholesterolaemia and personal history of cardiovascular event), lifestyle factors (daily smoking, alcohol abuse and leisure time physical activity); family history of CVD at ≤60 years of age; psychological distress (Psychiatric Symptom Index); other work factors (hours worked for the organisation, hours worked for another organisation).

Statistical analyses

Continuous data were expressed as the mean along with the SD. Categorical data were expressed as number and percentages. Generalised estimating equations were used to estimate differences in arterial stiffness means between the exposed and unexposed groups, with their 95% CI.[21] Regression models accounted for the correlation between employees of the same organisation. The models were sequentially adjusted for sets of covariates given that biological factors, psychological distress and lifestyle factors potentially mediate the associations (figure 2). As job strain and ERI models

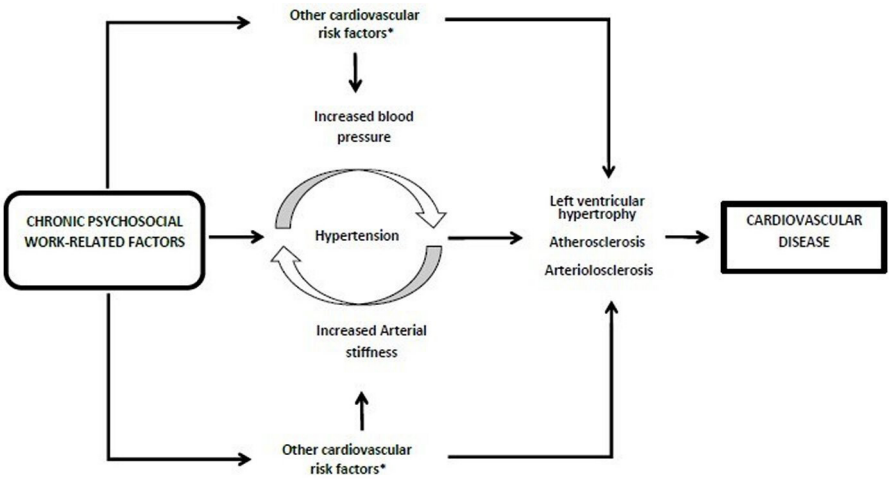

Figure 2 Possible sequences of events between chronic exposure to psychosocial work-related factors and the development of arterial stiffness, hypertension and cardiovascular diseases, based on the cardiovascular continuum. *Adiposity, smoking, alcohol abuse, excessive salt intake, physical inactivity, dyslipidaemia, diabetes, mental health, chronic inflammation.

Table 1 Population characteristics at baseline (1999–2001) (unless otherwise stated) by sex

	Missing	All 1736 (100.0%)	Missing	Men 839 (48.3%)	Missing	Women 897 (51.7%)
Age, year, mean (SD), cohort initiation (1991–1993)	0	37.3 (6.6)	0	38.6 (6.9)		36.2 (6.1)
Age, year, mean (SD), baseline (1999–2001)	0	44.9 (6.7)	0	46.2 (7.0)	0	43.8 (6.2)
Age, year, mean (SD), follow-up (2015–2018)	0	61.7 (6.1)	0	63.0 (6.4)		60.6 (5.6)
Job strain	16		7		9	
Low strain		298 (17.3)		174 (20.9)		124 (14.0)
Passive		592 (34.4)		237 (28.5)		355 (40.0)
Active		486 (28.3)		280 (33.7)		206 (23.2)
High strain		344 (20.0)		141 (17.0)		203 (22.9)
Effort–reward imbalance	47		24		23	
Yes		408 (24.2)		197 (24.2)		211 (24.1)
No		1281 (75.8)		618 (75.8)		663 (75.9)
Completed education	12		3		9	
Secondary or less		334 (19.4)		67 (8.0)		267 (30.1)
College		530 (30.7)		238 (28.5)		292 (32.9)
University		860 (49.9)		531 (63.5)		329 (37.1)
Household income $C*	11		4		7	
0–49 999		426 (24.7)		144 (17.3)		282 (31.7)
50 000–79 999		681 (39.5)		362 (43.4)		319 (35.8)
≥80 000		618 (35.8)		329 (39.4)		289 (32.5)
Marital status	4		2		2	
Partnered		1328 (76.7)		695 (83.0)		633 (70.7)
Unpartnered		404 (23.3)		142 (17.0)		262 (29.3)
Having children			2		1	
One or more				652 (77.9)		625 (69.8)
No				185 (22.1)		271 (30.3)
Diabetes†	0		0		0	
Yes		34 (2.0)		16 (1.9)		18 (2.0)
No		1702 (98.0)		823 (98.1)		879 (98.0)
Hypercholesterolaemia‡	1		1		0	
Yes		493 (28.4)		320 (38.2)		173 (19.3))
No		1242 (71.6)		518 (61.8)		724 (80.7)
Systolic blood pressure, mm Hg, mean (SD)	48	118.2 (13.7)	16	123.4 (12.9)	32	113.2 (12.6))
Systolic blood pressure≥140 mm Hg	48		16		32	
Yes		111 (6.6)		89 (10.8)		22 (2.5)
No		1577 (93.4)		734 (89.2)		843 (97.5)
Diastolic blood pressure, mm Hg, mean (SD)	48	76.7 (9.5)	16	80.1 (9.0)	32	73.4 (8.8)
Diastolic blood pressure≥90 mm Hg	48		16		32	
Yes		169 (10.0)		122 (14.8)		47 (5.4)
No		1519 (90.0)		701 (85.2)		818 (94.6)
Hypertension status§	22		13		9	
Yes		298 (17.4)		206 (24.9)		92 (10.4)
No		1416 (82.6)		620 (75.1)		796 (89.6)
Pulse pressure, mm Hg, mean (SD)	48	41.5 (8.7)	16	43.3 (9.2)	32	39.8 (7.8)
Pulse pressure≥60 mm Hg	48		16		32	
Yes		46 (2.7)		34 (4.1)		12 (1.4)
No		1642 (97.3)		789 (95.9)		853 (98.6)
Waist circumference, cm, mean (SD)	50	84.4 (12.3)	17	92.2 (9.5)	33	76.9 (9.6)
High waist circumference¶	50		17		33	

Continued

Table 1 Continued

	Missing	All 1736 (100.0%)	Missing	Men 839 (48.3%)	Missing	Women 897 (51.7%)
Yes		229 (13.6)		124 (15.1)		105 (12.2)
No		1457 (86.4)		698 (84.9)		759 (87.9)
Body mass index, kg/m^2, mean (SD)	18	25.3 (3.9)	8	26.2 (3.4)	10	24.4 (4.2)
Body mass index≥25 kg/m^2	18		8		10	
Yes		843 (49.1)		520 (62.6)		323 (36.4)
No		875 (50.9)		311 (37.4)		564 (63.6)
Alcohol abuse**	4		1		3	
Yes		106 (6.1)		61 (7.3)		45 (5.0)
No		1626 (93.9)		777 (92.7)		849 (95.0)
Daily smoking	4		1		3	
Yes		200 (11.6)		91 (10.9)		109 (12.2)
No		1532 (88.5)		747 (89.1)		785 (87.8)
Physical activity††	4		1		3	
Yes		898 (51.9)		465 (55.5)		433 (48.4)
No		834 (48.2)		373 (44.5)		461 (51.6)
Psychological distress score, mean (STD)			6	15.3 (11.4)	7	19.0 (12.5)
High psychological distress score‡‡	13		6		7	
Yes		381 (22.1)		143 (17.2)		238 (26.7)
No		1342 (77.9)		690 (82.8)		652 (73.3)
Hours worked per week for the organisation	24		13		11	
≤40		1601 (93.5)		748 (90.6)		853 (96.3)
>40		111 (6.5)		78 (9.4)		33 (3.7)
Hours worked per week for another organisation	30		10		20	
0		1477 (86.6)		698 (84.2)		779 (88.8)
≥1		229 (13.4)		131 (15.8)		98 (11.2)
Employee status, follow-up (2015–2018)	2		1		1	
Yes		507 (29.2)		230 (27.5)		277 (30.9)
No		1222 (70.5)		606 (72.3)		616 (68.8)
Imprecise		5 (0.3)		2 (0.24)		3 (0.33)
Personal history of cardiovascular disease§§	8		1		7	
Yes		101 (5.8)		54 (6.4)		47 (5.3)
No		1627 (94.2)		784 (93.6)		843 (94.7)
Family history of cardiovascular disease¶¶	34		15		19	
Yes		784 (46.1)		356 (43.2)		428 (48.8)
No		897 (52.7)		460 (55.8)		437 (49.8)
Don't know		21 (1.23)		8 (1.0)		13 (1.5)
Gaziano's predicted cardiovascular risk score	53		18		35	
Low		1453 (86.3)		639 (77.8)		814 (94.4)
Moderate or high		230 (13.7)		182 (22.2)		48 (5.6)

*Canadian dollars.
†Diabetes was measured by the item 'has a doctor ever told you that you have diabetes?'.
‡Hypercholesterolaemia was measured by the item 'has a doctor, nurse or other healthcare professional ever told you that your cholesterol level is too high?'.
§Hypertension status refers to participants who had high blood pressure or those who reported taking medication to lower their blood pressure.
¶High waist circumference≥88 cm (in women) or ≥102 cm (in men).
**10 or more drinks a week in women or 15 or more drinks a week in men.
††Performed leisure physical activity for 20–30 min per session at least two times per week.
‡‡Psychological distress score greater than or equal to the highest quintile (score>26.19).
§§Personal history of angina pectoris, unstable angina, acute myocardial infarction, coronary bypass surgery, percutaneous coronary intervention, stroke.
¶¶A member of the immediate family (father, mother, brother or sister) has had a cardiac medical problem (angina, myocardial infarction, coronary bypass) or a stroke (paralysis, embolism, haemorrhage, thrombosis) under the age of 60 years.

Table 2 Arterial stiffness at follow-up (2015–2018) in men and women according to main cardiovascular diseases risk factors and psychosocial work-related factor at baseline (1999–2001)

	All, 1736		Men, 839		Women, 897	
	N*	8.1 (1.7)	N*	8.6 (1.9)	N*	7.7 (1.4)
Age, years						
<55	1602	8.0 (1.5)	750	8.4 (1.7)	852	7.7 (1.3)
≥55	134	9.7 (2.3)	89	10.0 (2.6)	45	9.1 (1.5)
Systolic blood pressure, mm Hg						
<140	1625	8.1 (1.6)	750	8.5 (1.8)	875	7.7 (1.4)
≥140	111	9.2 (1.9)	89	9.4 (1.9)	22	8.7 (1.7)
Diastolic blood pressure mm Hg						
<90	1567	8.1 (1.7)	717	8.5 (1.9)	850	7.7 (1.4)
≥90	169	8.9 (1.7)	122	9.1 (1.7)	47	8.4 (1.5)
Hypertension status†						
Yes	298	8.9 (1.9)	206	9.2 (2.0)	92	8.4 (1.6)
No	1416	8.0 (1.6)	620	8.4 (1.8)	796	7.7 (1.3)
High pulse pressure‡ (>60 mm Hg)						
Yes	46	9.4 (2.3)	34	9.43 (2.4)	12	9.2 (2.0)
No	1642	8.1 (1.7)	789	8.5 (1.8)	853	7.7 (1.4)
Diabetes§						
Yes	34	9.7 (3.0)	16	11.3 (3.5)	18	8.3 (1.6)
No	1702	8.1 (1.6)	823	8.5 (1.8)	879	7.7 (1.4)
Hypercholesterolaemia¶						
Yes	493	8.5 (1.8)	320	8.8 (1.9)	173	7.9 (1.4)
No	1242	8.0 (1.6)	518	8.4 (1.8)	724	7.7 (1.4)
High waist circumference**						
Yes	229	8.6 (1.8)	124	9.0 (2.1)	105	8.0 (1.3)
No	1457	8.1 (1.7)	715	8.5 (1.8)	792	7.7 (1.4)
Body mass index, kg/m^2, mean (SD)						
<25	893	7.9 (1.5)	319	8.4 (1.7)	574	7.7 (1.4)
≥25	843	8.4 (1.8)	520	8.7 (1.9)	323	7.9 (1.4)
Daily smoking						
Yes	200	8.3 (1.7)	91	8.7 (1.9)	109	7.9 (1.4)
No	1532	8.1 (1.7)	747	8.5 (1.8)	785	7.7 (1.4)
Physical activity††						
Yes	898	8.1 (1.7)	465	8.5 (1.8)	433	7.6 (1.4)
No	834	8.2 (1.7)	373	8.7 (1.9)	461	7.8 (1.4)
Gaziano's predicted cardiovascular risk score						
Low	1453	7.9 (1.5)	639	8.3 (1.6)	814	7.7 (1.3)
Moderate or high	230	9.5 (2.1)	182	9.6 (2.2)	48	9.1 (1.6)
Number of accumulated cardiovascular risk factors						
0–1	1489	8.0 (1.6)	690	8.4 (1.7)	799	7.7 (1.4)
2+	194	9.1 (2.1)	131	9.4 (2.3)	63	8.4 (1.6)
Family history of cardiovascular disease‡‡						
Yes	784	8.2 (1.7)	356	8.6 (1.9)	428	7.8 (1.4)
No	897	8.1 (1.6)	460	8.5 (1.8)	437	7.6 (1.3)
Don't know	21	7.7 (1.8)	8	8.4 (2.5)	13	7.3 (1.2)

Continued

Table 2 Continued

	All, 1736		Men, 839		Women, 897	
Job strain						
Low strain	298	8.3 (1.8)	174	8.7 (1.9)	124	7.8 (1.4)
Passive	592	8.1 (1.7)	237	8.6 (1.8)	355	7.7 (1.5)
Active	486	8.2 (1.8)	280	8.4 (2.0)	206	7.8 (1.4)
High strain	344	8.0 (1.4)	141	8.5 (1.6)	203	7.6 (1.2)
Effort–reward imbalance						
Yes	408	8.2 (1.7)	197	8.6 (1.9)	211	7.8 (1.4)
No	1281	8.1 (1.7)	618	8.6 (1.9)	663	7.7 (1.4)

Arterial stiffness (m/s) in different subgroups are presented as mean and SD.
*The number of observations used.
†Hypertension status refers to participants who had high blood pressure or those who reported taking medication to lower their blood pressure.
‡Pulse pressure = systolic blood pressure – diastolic blood pressure.
§Diabetes was measured by the item 'has a doctor ever told you that you have diabetes?'.
¶Hypercholesterolaemia was measured by the item 'has a doctor, nurse or other health care professional ever told you that your cholesterol level is too high?'.
**High waist circumference: ≥88 cm (in women) or ≥102 cm (in men).
††Performed leisure physical activity for 20–30 min per session at least two times per week
‡‡A member of the immediate family (father, mother, brother or sister) has had a cardiac medical problem (angina, myocardial infarction, coronary bypass) or a stroke (paralysis, embolism, haemorrhage, thrombosis) under the age of 60 years.

provide distinct information, we assessed the independent effect of job strain and ERI by adjusting for job strain when measuring the association with ERI and vice versa. In order to assess effect modification, we conducted subgroup analyses by sex and BP (systolic, diastolic and pulse pressure) at baseline. Sensitivity analyses were also conducted (1) with and without individuals with personal history of CVD since they may have increased arterial stiffness; (2) according to risk factors for arterial stiffness at baseline (age and Gaziano's cardiovascular risk score[22]) since they may increase the deleterious effects of psychosocial work-related factors[23] ; (3) according to job status at follow-up since retirement may attenuate the effects of psychosocial work-related factors.[24] Multiple imputations[25] and inverse probability weighting[26] were performed to minimise potential selection bias due to non-response and/or loss to follow-up. Covariates measured at the initiation of the original cohort (in 1991–1993) were used in the calculation of the weights that were used for inverse probability weighting in order to minimise the potential selection bias resulting from losses to follow-up between cohort initiation and subsequent time points.

Analyses were performed with SAS V.9.4 software. The level of statistical significance was set at 0.05.

Participant and public involvement

Participants or the public were not involved in the study design, conduct, reporting or dissemination plans.

RESULTS

The mean follow-up time between exposure (baseline) and arterial stiffness assessment (follow-up) was 16.8 (SD: 1.3) years. At baseline, participants were on average 45 years old. More women (23%) than men (17%) were exposed to high job strain. As many men as women were exposed to ERI (24%). At follow-up, participants were on average 62 years old (table 1).

Table 2 presents mean arterial stiffness at follow-up in men and women according to main risk factors for CVDs and psychosocial work-related factor at baseline. Arterial stiffness (mean:8.1±1.7 m/s) was higher in men, in older participants and among those with high BP, diabetes, hypercholesterolaemia, high waist circumference, high BMI and moderate or high cardiovascular risk score.

Table 3 presents the association between psychosocial work-related factors at baseline and arterial stiffness at follow-up. In men, arterial stiffness was slightly higher in those with passive jobs. In women, arterial stiffness was higher in participants exposed to ERI. All differences were modest and not statistically significant, with CIs including the null value.

Table 4 presents the association between psychosocial work-related factors and arterial stiffness according to BP at baseline. The high job strain group had higher arterial stiffness (1.38 m/s (95% CI: 0.57 to 2.19)) among participants with high diastolic BP (DBP) (≥90 mm Hg) and lower arterial stiffness (−0.25 (95% CI: −0.48 to −0.02)) among those with lower DBP (<90 mm Hg). The same trend was observed for systolic BP. The high job strain group had higher arterial stiffness (0.84 m/s (95% CI: −0.35 to 2.03), p=0.17) among those with systolic BP≥140 mm Hg. Arterial stiffness was also higher in the high job strain (3.00 (95% CI: 1.18 to 4.76)) and

Table 3 Arterial stiffness (m/s) mean differences at follow-up (2015–2018) and 95% CIs according to psychosocial work-related factors at baseline (1999–2001) in men and women

	Modele I	Modele II	Modele III	Modele IV
Job strain in men				
Missing values/785 observations read	6	28	55	79
Low strain	Ref.	Ref.	Ref.	Ref.
Passive	0.04 (–0.26 to 0.33)	0.11 (–0.19 to 0.41)	0.16 (–0.15 to 0.47)	0.19 (–0.13 to 0.51)
Active	0.11 (–0.51 to 0.29)	0.14 (–0.50 to 0.23)	0.14 (–0.51 to 0.23)	0.05 (–0.42 to 0.31)
High job strain	0.07 (–0.68 to 0.53)	0.04 (–0.50 to 0.58)	0.05 (–0.61 to 0.51)	0.02 (–0.55 to 0.50)
Job strain in women				
Missing values/850 observations read	9	44	86	110
Low strain	Ref.	Ref.	Ref.	Ref.
Passive	0.09 (–0.35 to 0.18)	0.21 (–0.44 to 0.02)	0.20 (–0.42 to 0.03)	0.23 (–0.47 to 0.00)
Active	0.03 (–0.31 to 0.24)	0.06 (–0.31 to 0.18)	0.03 (–0.30 to 0.24)	0.11 (–0.39 to 0.16)
High job strain	0.14 (–0.47 to 0.20)	0.25 (–0.54 to 0.03)	0.20 (–0.53 to 0.13)	0.27 (–0.59 to 0.06)
ERI in men				
Missing values/785 observations read	22	44	68	79
ERI (categorical variable)				
No	Ref.	Ref.	Ref.	Ref.
Yes	0.13 (–0.22 to 0.47)	0.02 (–0.27 to 0.31)	0.07 (–0.39 to 0.24)	0.04 (–0.35 to 0.28)
ERI (continuous variable)	0.21 (–0.75 to 1.17)	0.06 (–0.89 to 0.76)	0.27 (–1.19 to 0.66)	0.16 (–1.20 to 0.89)
ERI in women				
Missing values/850 observations read	21	53	94	110
ERI				
No	Ref.	Ref.	Ref.	Ref.
Yes	0.13 (–0.14 to 0.39)	0.05 (–0.16 to 0.27)	0.13 (–0.10 to 0.36)	0.18 (–0.08 to 0.43)
ERI (continuous form)	0.17 (–0.36 to 0.69)	0.04 (–0.46 to 0.38)	0.12 (–0.25 to 0.49)	0.18 (–0.28 to 0.64)

Model I: unadjusted.
Model II: I+age, education, income, marital status, children, familial history of cardiovascular disease at baseline.
Model III: II+systolic blood pressure (mm Hg), diastolic blood pressure (mm Hg), diabetes, hypercholesterolaemia, body mass index (kg/m^2), waist circumference (cm), lifestyle (alcohol abuse, daily smoking, physical activity), psychological distress score at baseline.
Model IV: III+hours worked per week for the organisation, hours worked per week for another organisation, effort–reward imbalance (when studying the effect of job strain) or job strain (when studying the effect of effort–reward imbalance) at baseline.
Models are restricted to people with no personal history of cardiovascular disease at baseline.
ERI, effort–reward imbalance.

the passive (2.06 (95% CI: 0.69 to 3.44)) groups among participants with pulse pressure>60 mm Hg. However, only 43 participants had high pulse pressure. ERI was associated with lower arterial stiffness in participants with systolic BP≥140 mm Hg (–1.17 (95% CI: –2.12 to –0.22)), in those with DBP≥90 mm Hg (–0.48 (95% CI: –1.10 to 0.14)) and with pulse pressure>60 mm Hg (–2.06 (95% CI: –3.33 to –0.79)) (table 4).

Supplementary analyses showed that arterial stiffness tended to be higher in participants exposed to job strain who were≥55 years old or had a moderate or high CVD risk score. The ERI group had higher arterial stiffness in the 55+ age stratum (0.52 (95% CI: –0.67 to 1.71) (online supplemental table S1). Psychosocial work-related factors were not associated with arterial stiffness when stratifying according to employment status and duration of retirement (online supplemental table S2a and S2b). The findings were similar with and without participants with history of CVD (online supplemental table S3) and before and after multiple imputation and inverse probability weighting (online supplemental table S4).

DISCUSSION

In the present study, arterial stiffness was not significantly higher in men and women exposed to high job strain and ERI overall. However, among participants with higher DBP at midlife, high job strain was associated with higher

Table 4 Arterial stiffness (m/s) mean differences at follow-up (2015–2018) and 95% CIs according to psychosocial work-related factors at baseline (1999–2001) stratified by blood pressure at the time of exposure

	Systolic blood pressure, mm Hg		Diastolic blood pressure, mm Hg		Pulse pressure, mm Hg	
	<140	≥140	<90	≥90	≤60	>60
Missing/observations read	174/1529	15/106	166/1476	23/159	139/1546	4/43
Job strain						
Low strain	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Passive	0.02 (–0.23 to 0.19)	0.27 (–1.28 to 0.74)	0.05 (–0.28 to 0.18)	0.03 (–0.72 to 0.79)	0.06 (–0.27 to 0.14)	1.54 (–0.47 to 3.55)
Active	0.05 (–0.28 to 0.18)	0.13 (–1.05 to 0.80)	0.08 (–0.33 to 0.16)	0.43 (–0.18 to 1.04)	0.09 (–0.31 to 0.13)	2.06 (0.69 to 3.44)
High job strain	0.17 (–0.40 to 0.07)	0.84 (–0.35 to 2.03)	0.25 (–0.48 to –0.02)	1.38 (0.57 to 2.19)	0.16 (–0.40 to 0.08)	3.00 (1.18 to 4.76)
Missing/observations read	174/1529	15/106	166/1476	23/159	139/1546	4/43
ERI						
No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Yes	0.13 (–0.08 to 0.34)	1.17 (–2.12 to –0.22)	0.11 (–0.12 to 0.35)	0.48 (–1.10 to 0.14)	0.08 (–0.10 to 0.27)	2.06 (–3.33 to –0.79)
ERI (continuous form)	0.02 (–0.55 to 0.50)	0.66 (–1.44 to 2.77)	0.04 (–0.57 to 0.50)	0.34 (–1.99 to 1.31)	0.04 (–0.56 to 0.48)	0.43 (–4.69 to 5.55)

Models are adjusted for sex and covariates at baseline (age, education, income, marital status, children, systolic blood pressure (mm Hg), diastolic blood pressure (mm Hg), diabetes, hypercholesterolaemia, body mass index (kg/m^2), waist circumference (cm), alcohol abuse, daily smoking, physical activity, familial history of cardiovascular disease, psychological distress, hours worked per week for the organisation, hours worked per week for another organisation, ERI (when studying the effect of job strain) or job strain (when studying the effect of ERI).
Models are restricted to people with no personal history of cardiovascular disease at baseline.
Pulse pressure = systolic blood pressure – diastolic blood pressure.
ERI, effort–reward imbalance.

arterial stiffness 16 years later. This association was robust to adjustment for sociodemographics, lifestyle-related risk factors, CVD risk factors and other factors from the work environment.

Prior studies assessing the relationship between psychosocial work-related factors and arterial stiffness were cross-sectional.[5–11] Most suggest a deleterious effect.[5–9] Studies suggesting a protective[10] or no effect[11] involved relatively young participants (≤40 years). Studies showing deleterious associations included people aged over 40 years on average,[5–7 9] a high proportion of smokers (>40%)[5 6] or targeted workers in professions at higher risk of developing CVD such as firefighters.[9] Given their cross-sectional design, previous studies do not inform on different aspects of the temporal relationship between psychosocial work-related factors and arterial stiffness, including the optimal time window and follow-up period. The time required between exposure to psychosocial work-related factors and arterial stiffness may vary according to the position of individuals on the cardiovascular continuum. A longer follow-up time could be required for participants who are at an earlier stage than for those who are at a more advanced stage of progression. In the present study, high job strain was associated with increased arterial stiffness 16 years later (1.38 m/s), in participants with high DBP at time of exposure assessment (baseline). The mean age of participants with high DBP at baseline was 47 years old. Given that diastolic hypertension predominates in relatively young individuals, at a relatively early stage of the cardiovascular continuum and that CVD develops over at least a decade, it is reasonable to postulate that the follow-up period used in the present study was appropriate for measuring the association between midlife work-related factors and arterial stiffness in participants with high DBP at midlife.[12 27]

Increased arterial stiffness was also observed among participants with high systolic BP. This association was however of smaller magnitude and did not reach statistical significance. This is consistent with the natural history of systolic/DBP progression and its link with CVD diseases onset.[27] On the contrary, high job strain was associated with reduced arterial stiffness in participants who did not have high BP. Measuring the association between midlife stressors and arterial stiffness among people who do not have high BP may require a longer follow-up, which could explain the presence of this counterintuitive protective association. This is consistent with a previous cross-sectional study which showed a protective association between job strain index and brachial–ankle PWV (–1.38 m/s, p<0.01). This previous study included young participants (median age: 31 years) with diastolic (median: 79 mm Hg) and systolic (median: 110 mm Hg) BP in the normal range.[10] Further studies are needed to confirm these results.

Due to limited statistical power, caution should be exercised in interpreting the trends of increased arterial stiffness among participants exposed to job strain in moderate to high cardiovascular risk score and older

participants' strata. These results should be regarded as hypothesis generating. In our study, the participants who remained actively employed at follow-up were relatively young (on average 39 years old) and had a low cardiovascular risk score (98%) at baseline. Younger age combined with low cardiovascular risk score may contribute to the absence of observed association. Indeed, among this younger subgroup, the timeframe for arterial stiffness assessment could have been suboptimal. ERI was associated with lower arterial stiffness in participants with high systolic BP, DBP and high pulse pressure. This is counterintuitive and needs to be replicated.

In normotensive people without additional cardiovascular risk factors aged 60–69, the reference value for arterial stiffness is on average 10.3 m/s.[28 29] In the present study, the average value (8.3 m/s) of participants in this age group (n=930) is lower. The attrition due to non-response and loss to follow-up may have contributed to these finding given the loss of individuals who may be sicker than those who participated, as demonstrated in this cohort.[30] As expected, participants at higher risk of CVD (men, older age, high BP, diabetes, hypercholesterolaemia, high waist circumference, high BMI, moderate or high cardiovascular risk score) generally had higher arterial stiffness than those at lower risk. The observed association between psychosocial work-related factors and cfPWV can be translated into vascular age. For example, among participants with elevated DBP, those exposed to job strain (mean age: 63.1) had a mean cfPWV of 9.4 m/s, which is compatible with a vascular age of 50–59 years.[28 29] However, participants with elevated DBP in the low strain category (mean age: 64.9) had a mean cfPWV=7.9 m/s, which is compatible with a vascular age of 30–39 years.[28 29] The observed difference in cfPWV among participants exposed to job strain within this subgroup is therefore compatible with a decade discrepancy in vascular age.

Chronic stress accelerates ageing of arteries by incompletely understood mechanisms. Chronic stress can on one hand activate the sympathetic nervous system interconnected with the renin-angiotensin-aldosterone system and endothelin-1 activity and on the other hand promote risky lifestyle.[31 32] This leads to changes in vascular cell phenotypes and to thickening of the arterial innermost and intermediate layers, stiffness and increase in systolic and pulse pressure later on.[31] Increased arterial stiffness causes excessive transmission of pulse pressure that can damage the microcirculation of target organs, which increases the risk of cardiovascular events.[33] Older subjects or those with cardiovascular risk factors could have decreased endothelial regeneration capacity due to a reduced number of circulating progenitor endothelial cells.[31 34] A reduced regenerative capacity could explain a deleterious effect of job strain in people with an increased risk of developing a cardiovascular event given their age, cardiovascular risk score or high BP. Al Mheid *et al* observed significant interactions (p≤0.005) between age and the burden of cardiovascular risk factors (smoking, diabetes mellitus, hypertension or hyperlipidemia), such that for younger subjects (<40 years), cardiovascular risk factors were associated with increased progenitor cells counts, whereas for older subjects (>60 years), cardiovascular risk factors and CVD were associated with lower progenitor cells counts.[34]

Our study has several strengths. To our knowledge, this is the first study to examine the association between psychosocial work-related factors assessed at midlife and arterial stiffness assessed at older age, using a prospective cohort. The 16-year follow-up allowed exploration of long-term effects. Other strengths are the use of a gold standard arterial stiffness measurement and validated psychosocial work-related factors models, sequential adjustment by several potentially confounding factors, inverse probability weighting to minimise the potential for selection bias and subgroup analyses based on a priori evidence.

Our study also has limitations. First, the potential for selection bias due to a high proportion of missing values (40% (approximately 1048) out of 2621 participants) and losses to follow-up (19% (approximately 500) out of 2621) may underestimate associations.[30] However, the associations were similar before and after accounting for potential selection bias using multiple imputations and inverse probability weighting, suggesting that this potential bias could not have explained our results. Second, the use of a single measure of exposure limits the capacity to capture fluctuations in exposure and can lead to non-differential misclassification of exposure that may underestimate the association. Third, measuring arterial stiffness in 1/3 of participants combined with attrition reduced statistical power. Fourth, the study population was entirely composed of white-collar workers. Caution is therefore advised in generalising to other types of occupations. The fact that our sample is composed exclusively of white-collar employees limits potential confounding by occupational physical burden (repetitive movements, lifting heavy loads, long walking distance …). Fifth, arterial stiffness was measured at a single time point (at follow-up only). Therefore, stiffness progression over time could not be assessed limiting the possibility to draw causal inferences. However, data on several other major cardiovascular risk factors (age, BP, cholesterol, smoking, etc) were controlled for, which minimised the possibility for participants in compared group to substantially differ regarding their overall cardiovascular profile at baseline.

CONCLUSION

Job strain exposure combined with high BP at midlife may have long-term deleterious effects on arterial stiffness. Interventions at midlife to reduce job strain may be considered as a potential way to manage CVD risk.

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Contributors VKM conceptualised and designed the study, performed the statistical analysis, drafted, reviewed and edited the manuscript. CB was responsible for the study concept, supervised the data collection and the methodological aspects, reviewed and edited the manuscript. DT supervised the analytical approach, revised the statistical analysis program, reviewed and edited the manuscript. AM supervised aspects related to arterial stiffness, blood pressure and other cardiovascular risk factors, reviewed and edited the manuscript. XT supervised the methodological aspects, reviewed and edited the manuscript and isresponsible for the overall content as the guarantor. MV, CED, BM, MG-O, GRD and NP reviewed and edited the manuscript.

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