

## Perceived work-related stress and early atherosclerotic changes in healthy employees

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### Abstract

**Objective** This study was conducted to investigate the relationship between perceived work-related stress and pre-clinical atherosclerosis.

**Methods** A total of 100 managers and 50 office workers aged 35–65 participated in a questionnaire study. Individual, family and work-related stress risk factors and coping were evaluated in all the studied individuals. Serum levels of biochemical (total cholesterol, LDL, HDL, TG, glucose) and serological risk factors of atherosclerosis (anticardiolipin, anti- $\beta_2$  GPI, anti-oxLDL, anti-HSP and anti-hsCRP antibodies) were evaluated. A computer analysis of B-mode ultrasound images was used to assess carotid artery intima-media

thickness (IMT) and atherosclerotic plaque in carotid arteries. Statistical analysis was conducted with SPSS v. 11.5.

**Results** The studied individuals showed average ranges of both the global stress level and of coping results. In 71% no changes were found in the ultrasound image and in 29% of individuals (43) the presence of plaque was shown. The mean value of the IMT measure was  $0.0618 \pm 0.013$  mm. IMT and plaque correlated negatively with the level of global work-related stress ( $r = -0.26$ ;  $P < 0.01$ ; and  $r = -0.28$ ;  $P < 0.01$ ; respectively). No correlation was found either between work-related stress and coping, or between coping and IMT ( $P > 0.05$ ), or between work-related stress and healthy lifestyle (no smoking, no excessive use of alcohol, high physical activity), or between healthy lifestyle and IMT ( $P > 0.05$ ). Positive correlation between IMT and LDL and smoking did not result from higher stress reaction in the studied individuals.

**Conclusions** The explanation of the negative correlation between perceived work-related stress and preclinical atherosclerosis was not confirmed either by the subjects under high stress undertaking healthy protective activities or by their escaping into unhealthy behaviour. The most probable interpretation of the results is that in individuals with a low level of perceived work-related stress, somatization of stress takes place.

**Keywords** Work-related stress · Early atherosclerosis · Carotid arteries

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### Introduction

Stress can no longer be recognized as a problem of an individual only. Due to its versatile presence in every human's life, often resulting in health complications, stress has

become a social problem and the role of work-related stress in this puzzle should not be underestimated. Coronary heart disease (CHD) is on the list of stress-related health problems.

Atherosclerosis, the basis of CHD, develops in a long-lasting, multifactorial and complex process. In the etiopathogenesis of atherosclerosis, apart from traditional factors like lipids, carbohydrate metabolic disorders, hypertension and lifestyle (smoking, alcohol use and limited physical exercise), immunological disorders, as a consequence of reciprocal interactions in the psycho-neuro-immunological system, have been recently brought up (George and Shoenfeld 1997; Bednarska-Makaruk and Pasierski 2000; Kiecolt-Glaser and Glaser 1991; Amengual et al. 2001; Patryka et al. 2001; Jędryka-Góral et al. 2002; Jędryka-Góral 2003; Dinan 2005). Early atherosclerosis can even occur in young healthy people (Pasierski 1999).

For a long time now, occupational medicine has been interested in the relationship between work-related stress and CHD. Studies undertaken in this field have been based on western as well as eastern european populations (Jonsson et al. 1995; Hammer et al. 1998; Bosma et al. 1998, Kristenson et al. 1998; Kivimaki et al. 2002; Smith et al. 2005; Malinauskiene et al. 2005). Although there is a large body of literature on clinically overt CHD and its relation to work-related stress, there have been very few studies on preclinical CHD in those circumstances (Lynch et al. 1997; Nordstrom et al. 2001; Rosvall et al. 2002; Hintsanen et al. 2005).

The current study aimed to fill this gap and to assess the relationship between work-related stress and preclinical atherosclerotic changes in healthy employees. We considered carotid artery intima-media thickening and/or plaque presence as a surrogate of coronary atherosclerosis. To detect these changes “gold-standard” methodology, i.e., B-mode carotid ultrasound examination, was applied. Because of the complex nature of the pathogenesis of CHD, other contributing factors have not been disregarded.

## Methods

### Organization of the study

First, all participants took part in a psychological study in which the level of stress and coping were evaluated with relevant questionnaires (see below). Then, the participants consecutively presented themselves for a clinical visit in which a medical examination took place and a blood sample was taken. Tests for biochemical parameters (see below) were performed on the same day as the blood sample was taken, according to routine laboratory procedures. Sera for immunological parameters (see below) were collected and stored according to international laboratory standards, then tested in runs (up to 40 sera per day) to minimize day-to-day variations.

### Participants

One hundred healthy managers and 50 office workers (F:M = 50:50) aged 35–65 were studied. All of them were investigated for the presence of individual (age, obesity, hypertension, diabetes, smoking, alcohol use and low physical activity) and family (obesity, hypertension, diabetes, heart attack and stroke) risk factors for atherosclerosis. The studied individuals' detailed characteristics are presented in Table 1.

### Instruments

*Work-related stress* was operationalized as perceived pressure caused by inappropriate working conditions. It was measured by the “Sources of pressure in your job” scale that is a part of the short version of the Occupational Stress

**Table 1** Characteristics of studied groups

	Managers (n = 100)	Office workers (n = 50)	Total (n = 150)
Number	50 (50%)	25 (50%)	75 (50%)
Females			
Males	50 (50%)	25 (50%)	75 (50%)
Age	47.2 ± 6.8	50.16 ± 6.46	48.68 ± 6.63
Mean (years)			
Minimum	34	35	34.5
Maximum	65	64	64.5
Individual risk factors	26 (26%)	23 (46%)	49 (32%)
Hypertension			
Obesity	19 (19%)	17 (34%)	36 (24%)
Diabetes	1 (1%)	1 (2%)	2 (1.3%)
Alcohol use			
Every day	3 (3%)	0	3 (2%)
2–3 × a week	23 (23%)	2 (4%)	25 (16.7%)
Less	69 (69%)	47 (94%)	116 (77.3%)
Never	5 (5%)	1 (2%)	6 (4%)
Smoking cigarettes	49 (49%)	30 (60%)	79 (52.7%)
Hormone replacement therapy	8 (8%)	4 (8%)	12 (8%)
Physical activity			
2–3 × a week	26 (26%)	12 (24%)	38 (25%)
1 × in 7–10 days	32 (32%)	14 (28%)	46 (30.7%)
Less	42 (42%)	24 (48%)	66 (44%)
Family risk factors	41 (41%)	31 (62%)	72 (48%)
Hypertension			
Obesity	45 (45%)	23 (46%)	68 (45.3%)
Diabetes	31 (31%)	12 (24%)	43 (28.7%)
Heart attack	36 (36%)	21 (42%)	57 (38%)
Stroke	30 (30%)	17 (34%)	47 (31.3%)

Indicator (OSI-2) by Cooper et al. Widerszal-Bazyl's (2001) Polish adaptation of OSI-2 was used in the study. The scale consists of 40 items on potential sources of pressure at work; respondents are required to rate each source on six-point response scales, in which 1 = it is very definitely not a source (of pressure) to 6 = it is very definitely a source. Those 40 items were divided into eight subscales concerning the following stress factors: workload (e.g. "Having to work very long hours", "Taking work home"), relationships (e.g. "Inadequate guidance and backup from superiors", "Feeling isolated"), home-work balance (e.g. "Pursuing a career at the expense of home life"), recognition (e.g. "Underpromotion—working at a level below my level of ability"), organizational climate (e.g. "Characteristics of the organization's structure and design", managerial role (e.g. "Managing or supervising the work of other people"), personal responsibility (e.g. "Having to take risks"), hassle at work (e.g. "Attending meetings"). The scale made it possible to assess the global level of work-related stress (the sum of scores for all items) as well as to assess the level of a given kind of work stress, e.g. workload (the sum of scores for items related to workload). The reliability of the Polish version of the total scale was very high: Cronbach's  $\alpha = 0.95$ . It was also satisfactory for most subscales: workload  $\alpha = 0.95$ , relationships  $\alpha = 0.89$ , home-work balance  $\alpha = 0.81$ , recognition  $\alpha = 0.75$ , organizational climate  $\alpha = 0.63$ , managerial role  $\alpha = 0.57$ , personal responsibility  $\alpha = 0.78$ , hassle at work  $\alpha = 0.54$ . (Widerszal-Bazyl 2001).

Coping was measured with the "How you cope with the stress you experience" scale that is also part of OSI-2, too. It consists of 10 items on potential coping strategies; respondents are required to rate the extent to which they actually use them as ways of coping with stress. Answers are given on six-point scales, from 1 = I never use it to 6 = I use it very extensively. Some coping strategies included into the scale dealt with coping through control (e.g. "Effective time management"), and some with coping through social support (e.g. "Talk to understanding friends"). The reliability of the Polish version of the total coping scale was Cronbach's  $\alpha = 0.70$ , and reliability of its subscales: 0.70 (for coping through control) and 0.50 (for coping through social support). Therefore, the total index of coping was used in the analysis, as well as the index of coping through control.

Prior to the study, appropriate approval from the Local Ethics Committee was obtained. Participants were provided with detailed written information on the study's objectives and the methods that were going to be used; subsequently they signed their informed consent.

Serum levels of biochemical (total cholesterol, LDL, HDL, TG, glucose) and serological risk factors of atherosclerosis (anticardiolipin, anti- $\beta_2$  GPI, anti-oxLDL, anti-HSP and anti-hsCRP antibodies) were evaluated.

*Anticardiolipin antibodies* Patients' sera were tested with ELISA for the presence of anticardiolipin antibodies, according to the modified Harris method (Luft et al. 1990). The results were presented as OD units. Reference ranges of aCL were established by studying sera from 100 healthy donors. The cut-off value was established as  $OD = x + 4SD$  estimated for sera of healthy blood donors; it was 0.109 for the IgG class and 0.156 for the IgM class.

*Anti- $\beta_2$  glycoprotein I ( $\beta_2$  GPI) antibody levels* were measured with a commercial DIASTAM—FBGP 200 from Axis-Shield (Cat. No. FBG200) test. The results were expressed as OD units. Reference ranges of anti- $\beta_2$  glycoprotein I antibodies were established by studying sera from 152 healthy Caucasian donors (Axis-Shield Diagnostics Ltd. examination). The cut-off value was established as  $OD = 0.195$ .

*Anti-HSP antibody levels* (IgG class) were estimated with non-commercial methodology, after necessary modification, according to Tsoulfa et al. (1989), with the use of McLean reagents. The cut-off value was established as  $x + 4SD$  estimated for sera of healthy blood donors; it was  $OD = 0.423$ . The estimation of IgM and IgA class antibodies was performed in the same manner.

*Anti-oxLDL IgG antibody levels* were measured with ELISA with the use of a commercial test from OLAB (Cat. No. BI-20032). The cut-off value was established as 200 arbitrary units.

*hsCRP* concentration was measured with ELISA with the use of commercial tests from EUCARDIO Laboratory Inc. (Cat. No. ZZ C4011E). The cut-off value was established as 4000 ng/ml.

*Intima-media thickness (IMT) and atherosclerotic plaque* in carotid arteries were searched using a computer analysis of B-mode ultrasound images. Both carotid arteries were measured with a 7.5-MHz linear-array transducer, part of Hewlett Packard Sonos. Plaque was defined as intima-medial thickening larger than 50% in comparison to the surround area (Pignoli et al. 1986)

*Statistical analysis* of data was performed with SPSS v. 11.5. Means comparisons were carried out with a *t* test for independent groups. In bivariate correlation analysis Pearson's *r* coefficients were calculated. The level of significance was set at  $\alpha < 0.05$ .

## Results

### Assessment of work-related stress

The level of work-related stress measured with OSI-2's Sources of pressure scale was as follows: managers—mean = 154 ( $\sigma = 25$ ), for office workers—mean = 145 ( $\sigma = 28$ ), for both groups—mean = 151 ( $\sigma = 25$ ). According

to Polish sten norms, the sten scale (“sten” stands for standard ten) consists of ten units. Each unit equals 0.5 of a standard deviation. It is, assumed that stens five and six means average results, stens seven to ten high results, and stens one to four low results (Canfield 1951). Developed for Polish managers (Widerszal-Bazyl 2001), the managers’ mean falls on sten six, whereas the office workers’ mean falls on sten five (Table 2). As a rule, stens five and six are interpreted as average results.

### Assessment of coping

The level of coping measured with OSI-2’s Coping scale was as follows: managers—mean = 40, office workers—mean = 38, both groups—mean = 40. According to Polish sten norms the managers’ mean falls on sten five for men and on sten six for women. The office workers’ mean falls on sten five (for both genders). Thus, it can be said that the coping results were in the average range.

### Laboratory findings

The abnormality most frequently disclosed in biochemical findings were elevated levels of total cholesterol, LDL and triglycerides (in 52, 39 and 22% of the studied individuals, respectively). Decreased levels of HDL and increased levels of glucose were less frequent and were found in 12% of cases each.

Of the immunological parameters studied, oxLDL antibodies were most frequently found (in 26% of cases), followed by an elevated level of hsCRP (in 11% of cases). In a few cases antibodies to  $\beta_2$  GPI and HSP-65 (IgG class) were found (in 1% and 3% of studied cases, respectively). None of the studied individuals was positive for aCl. For six sera which were borderline or positive for HSP-65 IgG class, IgM and IgA class antibodies were searched. Only in three cases were the results weakly positive (two in IgM and one in IgA class).

### Ultrasound examination of carotid arteries

Changes in the ultrasound examination of carotid arteries confirming the presence of early atherosclerosis are shown in Table 3. Plaque was found in 43 (29%) cases: in 26 man-

**Table 2** Results of psychological examination

Studied groups	Work-related stress		Coping			
	Mean	Stens	Mean	Stens		
Managers	154	6	6	40	5	6
Office workers	145	5	5	38	5	5
Total	151	6	5	40	5	6

**Table 3** Results of ultrasound examination of carotid arteries in studied groups

	Managers ( <i>n</i> = 100)	Office workers ( <i>n</i> = 50)	Total ( <i>n</i> = 150)
Number of individuals without changes	74 (74%)	33 (66%)	107 (71%)
Number of individuals with plaque	26 (26%)	17 (34%)	43 (29%)
Intima-media measurement values	0.0620 ± 0.014	0.0610 ± 0.012	0.0618 ± 0.013

agers (26%) and in 17 office workers (34%); groups did not differ statistically. The distribution of the mean values of the IMT measure was slightly skewed to the right. The mean values of IMT in managers and office workers were 0.0620 ± 0.014 and 0.0610 ± 0.012 mm, respectively; groups did not differ statistically.

### Correlation between IMT and the presence of plaque in carotid arteries with atherosclerosis risk factors

Positive correlation was found between IMT and age ( $r = 0.42$ ;  $P < 0.001$ ), diastolic blood pressure ( $r = 0.20$ ;  $P < 0.05$ ), LDL ( $r = 0.28$ ;  $P = 0.001$ ), anti-HSP antibodies ( $r = 0.24$ ;  $P < 0.05$ ), whereas negative correlation was revealed with aCl—IgG ( $r = -0.20$ ;  $P < 0.05$ ) and global work-related stress level ( $r = -0.26$ ;  $P < 0.01$ ). Among the stressors studied, statistical significance was shown for interpersonal relations ( $r = -0.23$ ;  $P < 0.00$ ), work–home balance ( $r = -0.19$ ;  $P < 0.05$ ), managerial role ( $r = -0.24$ ;  $P < 0.01$ ) and organization climate ( $r = -0.22$ ;  $P < 0.01$ ). The presence of plaque correlated positively with age ( $r = 0.42$ ;  $P < 0.001$ ), smoking ( $r = 0.18$ ;  $P < 0.05$ ), LDL ( $r = 0.30$ ;  $P < 0.01$ ) and negatively with global work-related stress level ( $r = -0.28$ ;  $P < 0.01$ ). Statistical significance was shown for the following stressors: work load ( $r = -0.24$ ;  $P < 0.01$ ), interpersonal relations ( $r = -0.18$ ;  $P < 0.05$ ), work–home balance ( $r = -0.33$ ;  $P < 0.01$ ) and responsibility ( $r = -0.25$ ;  $P < 0.01$ ) (see Table 4).

### Correlation between LDL/smoking and global stress level

Pearson’s analysis showed a negative relation between LDL and global stress level ( $r = -0.17$ ;  $P < 0.05$ ), and between smoking and global stress level ( $r = -0.17$ ;  $P < 0.05$ ).

### Work-related stress, coping, lifestyle and IMT

Pearson’s analysis was performed in two triangles: (a) work-related stress–coping–IMT, and (b) work-related stress–healthy lifestyle–IMT. No statistically significant

**Table 4** Correlations between IMT and the presence of plaque in carotid arteries and atherosclerosis risk factors (Pearson's *r*)

Risk factor	IMT	Plaque
Age	0.42**	0.43**
BMI	0.12	0.04
Systolic blood pressure	0.13	0.06
Diastolic blood pressure	0.20*	0.10
Cigarette smoking	0.13	0.18*
Physical activity	−0.02	0.07
LDL	0.28**	0.30**
HDL	−0.16	−0.05
Triglycerides	0.04	0.05
Glucose	0.08	0.02
hsCRP	0.05	0.02
Anti-HSP	0.16	0.19
aCl-IgG	−0.20*	−0.10
aCl-IgM	−0.14	−0.15
Anti-oxLDL	−0.10	−0.17
Workload	−0.15	−0.24**
Relationships	−0.23**	−0.18*
Home–work balance	−0.19*	−0.33**
Managerial role	−0.24*	−0.14
Personal responsibility	−0.14	−0.25**
Hassle at work	−0.11	−0.14
Recognition	−0.25**	−0.15
Organizational climate	−0.22**	−0.15
Total index of coping	−0.12	−0.01
Coping through control	−0.05	0.02
Global level of stress	−0.26**	−0.28**

\* Correlation is significant at 0.01 (2-tailed)

\*\* Correlation is significant at 0.05 (2-tailed)

relations were shown either between work-related stress and coping, or between coping and IMT ( $P > 0.05$ ), or between work-related stress and healthy lifestyle (no smoking, no excessive use of alcohol, high physical activity), or between healthy lifestyle and IMT ( $P > 0.05$ ).

## Discussion

A multidisciplinary approach to assessing risk factors for atherosclerosis was considered by us in an earlier study (Jędryka-Góral et al. 2006). On the basis of a deep multi-level analysis we were able to show that in healthy individuals, as in CHD patients, individual and biochemical risk factors were likely to play a leading role in the development of early atherosclerosis. Psychosocial stress should also be considered; however, inflammatory-immunological factors have not been found to be an independent predictor.

As inflammatory-immunological factors, antibodies to oxLDL and HSP-65, hsCRP as well as anticardiolipin and anti- $\beta_2$  GPI antibodies were considered. In the extensive literature of the subject, these parameters are recognized as directly involved in the pathogenesis of atherosclerosis (George and Shoenfeld 1997; Kiecolt-Glaser, Glaser 1991; Amengual et al. 2001; Patryka et al. 2001; Jędryka-Góral et al. 2002; Jędryka-Góral 2003).

The present study was undertaken to extend the investigation of psychosocial stress and atherosclerosis. We looked in depth for correlation between preclinical atherosclerosis and work-related stress; correlations with other risk factors of CHD were done in parallel.

As expected, we found correlation between IMT and age, diastolic blood pressure, LDL and anti-HSP antibodies, and correlation between plaque and age, smoking and LDL.

Surprisingly, our results revealed that early atherosclerotic changes negatively correlated with the level of global job strain and some of its components (interpersonal relations, work–home balance, managerial role, organization climate—for IMT; work load, interpersonal relations, work–home balance, responsibility—for plaque).

Ambiguous results have been previously reported in other, although very few, studies where work, psychosocial factors and carotid atherosclerosis were studied with ultrasound. Rosvall et al.'s (2002) hypothesis that work-related stress characterized by high psychological demands and low decision latitude was associated with increased carotid atherosclerosis could not be confirmed either for women or for men. On the other hand, Lynch et al.'s (1997) prospective study showed that men who experienced work-related stress (demanding work and low economic rewards) had significantly greater progression of carotid atherosclerosis than more advantaged men. Hintsanen et al. (2005) provided data that job strain (a joint effect of job demands and job control) was associated with increased IMT in men but not in women. Similarly, Nordstrom et al. (2001) showed that in men with greater work-related stress (workplace demands and intrusion of work concerns into home life) the risk of focal lesions or intima-media thickness in coronary artery increased, whereas in women stress was not related to the prevalence of early atherosclerosis. Hlatky et al. (1995) disclosed that job strain (high psychological demands and low decision latitude) did not correlate with the presence of coronary disease in angiography, either for men or for women.

By searching for a relationship between work-related stress and atherosclerosis, we wanted to prove that the correlation found between early atherosclerotic changes and LDL and smoking is, at least partly, caused by a higher stress reaction in the studied individuals. It was assumed that individuals with a level of high stress undertook

unhealthy behaviour: smoking or excessive food intake. However, for both LDL and smoking the correlation with stress was negative. One should keep in mind that only 39% of the studied individuals had elevated levels of LDL and 47% reported smoking. Therefore, these results should be interpreted causally.

We explored in depth the negative correlation we found between IMT and the presence of plaque, and the level of work-related stress. Being aware that OSI-2 measured perceived stress, another hypothesis was formulated; persons with a high level of work-related stress (conscious stress) undertake preventive activities at the level of coping or healthy lifestyle.

Perceived work-related stress as a risk factor for a clinically overt CHD has been investigated in multiple studies. Some prospective studies showed an association of work-related stress with an incidence of CHD (Bosma et al. 1998; Kivimaki et al. 2002; Kivimaki et al. 2005); whereas others did not (De Bacquer et al. 2005; Rosvall et al. 2002; Eaker et al. 2004). The largest INTERHEART study covering 11 119 cases and 13 648 controls from 52 different countries all over the world confirmed this association with regard to work, home, financial and major life stress (Rosengren et al. 2004). There are studies which, indicated that perceived work-related stress had profound impact on internal organs, sensual organs, the locomotor system and skin health problems (Cheng et al. 2001; Lindgren et al. 2002).

In the literature of the subject, coping is closely linked to stress. The most common meaning of coping is, an effort to solve problems and to seek reduction of tolerance to stress. The CATS theory (cognitive activation theory of stress) offered a new approach to coping (Ursin, Eriksen 2004; Eriksen et al. 2005). This theory assumed two cognitive reformulations of the learning theory (stimulus–stimulus learning = classical conditioning and response learning = instrumental conditioning). Both reformulations are essential to understanding the relationship between learning, activation and relations between stress and health. The stress response (an alarm in the homeostatic system) results in behaviors that aim to cope with a situation. The level of alarm depends on what outcome of a stimulus is expected and the specific responses available for coping. Response outcome expectancy might be positive (coping), negative (hopelessness) or none (helplessness). Hence, coping defined as acquired positive outcome expectancy has some predictive value for stress and health.

According to Weidner and Cain (2003) research on how people cope with stress situations disclosed avoidant mechanisms (denial, distraction, excessive alcohol consumption) in men, whereas more cardioprotective strategies (depression, asking for help)—in females.

Stress management goes far beyond coping strategies. Toobert et al.'s (2002) results disclosed success of a

complex intervention program to reduce CHD risk, which included improvement of diet, stress management, social support, smoking and physical activity.

In our study on preclinical atherosclerosis and work-related stress, we were not able to confirm the hypothesis about the above-mentioned prophylactic activities. An analysis of correlation showed no significant relations between work-related stress and coping, between coping and IMT, between work-related stress and healthy lifestyle, or between healthy lifestyle and IMT.

A relatively novel conception was presented by de Lange et al. (2005), who claimed that the relationship between stressful work and psychological well-being may be reciprocal. Their results showed that mental health might influence employees' perceived work characteristics. It is likely that the employees in our study had been recruited from that part of working society who felt fit to undertake ambitious tasks of managers and office workers and who developed job adaptive mechanisms over time.

The most probable interpretation of the negative correlation between perceived work-related stress and preclinical atherosclerosis is that in the case of individuals with a low level of perceived work-related stress, somatization of stress took place, i.e., stress is not perceived at the conscious level but it leads to somatic effects (e.g., IMT).

We are aware of some limitations of our study. Firstly, the results regarding work-related stress were based on self-reported data, which per se could always be a matter of some bias. Secondly, the number of employees studied was limited to 150. Voluntary participation of employees and fully unselected method of recruitment can guarantee the objectivity of the results. Thirdly, it was a cross-sectional study. A prospective type of research on risk assessment is preferable nowadays. However, our study did not aim to assess risk of CHD but to find correlation between work-related stress and early atherosclerosis, so we believe the measure taken for this purpose was appropriate.

We are more than convinced that to achieve full understanding of negative correlation between work-related stress and early atherosclerosis requires further interdisciplinary studies and we would be happy to continue exploration into this intriguing field.

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