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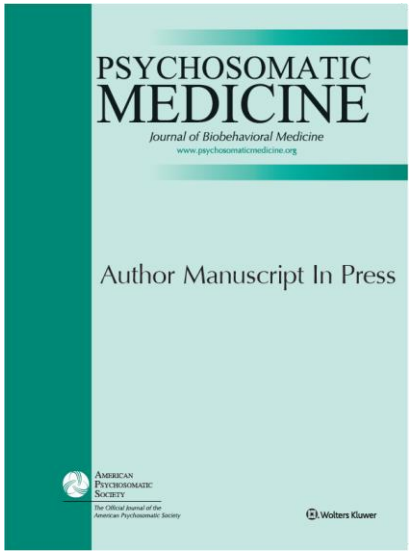

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Pericardial fat, socioeconomic status and biological responses to acute mental stress

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Abstract

Objective

Central adiposity is associated with impaired biological responses to mental stress, and socioeconomic status (SES) might moderate this relationship. However, evidence for associations between pericardial fat, a fat depot implicated in the pathogenesis of cardiovascular disease (CVD), with cardiovascular and inflammatory responses to mental stress is lacking, and moderation by SES is unknown.

Methods

The sample was 473 healthy men and women (mean age 62.8 years) from the Whitehall II study. Cardiovascular and inflammatory responses to laboratory-induced mental stress, consisting of a five minute Stroop task and five minute mirror tracing task, were assessed. Pericardial fat volume was measured using electron bean computed tomography and adjusted for body surface area. SES was defined by grade of employment within the British civil service (higher/intermediate/lower).

Results

Pericardial fat was associated with lower heart rate variability, raised heart rate, plasma interleukin-6, fibrinogen and C-reactive protein at baseline. Furthermore, greater pericardial fat was associated with lower systolic blood pressure reactivity to mental stress, independent of sociodemographics, smoking status, waist to hip ratio and baseline systolic blood pressure. There were no interactions between pericardial fat and SES for any outcome.

Conclusions

Greater pericardial fat was associated with numerous cardiovascular and inflammatory factors implicated in CVD. It was also related to reduced systolic blood pressure reactivity to acute mental stress, independent of central adiposity and baseline systolic blood pressure.

This association did not vary by SES. Reduced systolic blood pressure reactivity to mental stress might contribute to the association between greater pericardial fat and CVD.

Key Words:

Pericardial fat; Socioeconomic status; Cardiovascular disease; Stress reactivity; Stress recovery

Acronyms:

BMI = body mass index

CHD = coronary heart disease

CV = coefficient of variation

CVD = cardiovascular disease

ELISA = enzyme-linked immunosorbent assay

HDL = high-density lipoprotein

IL-6 = interleukin-6

LDL = low-density lipoprotein

RMSSD = root mean square of successive differences

SES = socioeconomic status

TNF- α = tumor necrosis factor- α

Introduction

There is increasing evidence that body fat distribution is more predicative of cardiovascular disease (CVD) than markers of overall adiposity, such as body mass index (BMI) and total body fat (1-3). Pericardial fat is an ectopic fat depot surrounding the heart that has been associated with many CVD risk factors including systolic and diastolic blood pressure, high density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol (4, 5). Furthermore, pericardial fat has been associated with left ventricular remodelling (6), coronary artery calcification (7), coronary heart disease (8, 9) and atrial fibrillation (10). Pericardial fat is hypothesised to be implicated in the pathogenesis of CVD as it is close to the coronary arteries and shares a blood supply with the myocardium (8). Pericardial fat is also highly metabolically active and secretes pro-inflammatory markers such as interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α) (8). In addition, pericardial fat is the anatomical site of ganglionic plexi that can interact with the extrinsic cardiac sympathetic and parasympathetic nervous systems to module autonomic function (11). Dysregulation of the autonomic nervous system, characterised by increased sympathetic and decreased parasympathetic activity, has been associated with increased risk for CVD (12).

Psychological stress is another risk factor for CVD (13). It is hypothesised that impaired cardiovascular and inflammatory responses to stress might be mechanisms linking acute psychological stress and CVD (14). Accordingly, many prospective studies have shown that heightened reactivity to and delayed recovery from laboratory-induced acute mental stress are associated with the development of CVD (15-19). Furthermore, given that low socioeconomic status (SES) is associated with greater risk for CVD (20-22) as well as prolonged elevations in IL-6 (23) and delayed cardiovascular recovery following acute

mental stress (24), it is possible that SES might moderate the association between acute psychological stress and CVD.

Impaired biological responses to stress might mediate the association between greater central adiposity and CVD (25). Several studies have shown that greater central adiposity is associated with greater systolic and diastolic blood pressure and heart rate reactivity to mental stress (26, 27) and delayed systolic and diastolic blood pressure and heart rate recovery following mental stress (28). Furthermore, one study found that low SES interacts with greater central adiposity to predict delayed recovery of systolic and diastolic blood pressure following stress (29). Given that pericardial fat is a close correlate of central adiposity (5), is highly metabolically active (8), can affect autonomic function (11) and is inversely associated with SES (30), it is plausible that impaired cardiovascular and inflammatory responses to stress might also contribute to the association between pericardial fat and CVD, particularly in low SES individuals.

Some studies have found associations between pericardial fat with blunted heart rate recovery following stress (31-33). However, all these studies were conducted in clinical populations, such as individuals with hypertension, metabolic syndrome or obstructive sleep apnoea. Additionally, this work assessed heart rate recovery following exercise, a physical stressor. It can be argued that responses to physical and mental stressors differ, such that responses to physical stressors mainly reflect peripheral physiology (34, 35), whereas responses to psychological stressors such as the Stroop test reflect an interaction between top down processes (interpretation of stressor) and physiological mechanisms (34). To the authors' knowledge, no study has yet examined associations between pericardial fat with cardiovascular and inflammatory responses to acute mental stress in a healthy adult

population, or moderation of these associations by SES. Therefore, the primary aim of this exploratory study was to examine associations between pericardial fat with cardiovascular and inflammatory processes in response to acute mental stress in initially healthy individuals without history or objective signs of coronary heart disease (CHD) from the Whitehall II cohort. A secondary aim was to examine whether associations between pericardial fat with cardiovascular and inflammatory processes at rest and in response to acute mental stress varied by SES.

Methods

Participants

We recruited a sample of participants from the Heart Scan Study, a sub-study of the Whitehall II epidemiological cohort study of British civil servants (36). The Heart Scan study was a psychophysiological study that assessed biological responses to acute mental stress and risk factors for CVD (29, 37). The original sample consisted of 543 healthy white European men (n = 294) and women (n = 249) aged 53-76 years. Participants were included if they had no history or objective signs of CHD, previous diagnosis or treatment for hypertension, diabetes, inflammatory diseases, or allergies. Sampling for this study was stratified to recruit participants from higher, intermediate and lower grades of employment within the British civil service. Grade of employment acted as a proxy for SES, and therefore, this stratified sampling method ensured a broad range of SES were represented. Analyses in the present study were conducted on 473 participants who had complete data on pericardial fat volume adjusted for body surface area. All participants provided full informed consent and ethical approval was obtained from the National Research Ethics Service (ref 97/0356).

Procedures

Mental stress testing sessions took place individually either in the morning (9:30 am) or afternoon (1:00 pm) in a light and temperature controlled laboratory between 2006-2008. Participants were instructed not to take any anti-inflammatory or anti-histamine medication in the seven days prior to the testing day and to not have consumed alcohol or participated in excessive exercise from the previous evening. Participants were also instructed not to have eaten within four hours of testing, and not to have drunk tea, coffee or caffeinated beverages or to have smoked for at least 2 hours before the study. Individuals who reported colds or infections on the day of testing had their tests rescheduled for another day.

Prior to the stress testing session, participants completed questionnaires and anthropometric measurements were taken. Waist circumference was measured using a metal tape halfway between the bottom rib and iliac crest, and hip circumference was measured at the level of the great trochanters. Measurements were taken twice to ensure accuracy. Waist to hip ratio was calculated as waist circumference divided by hip circumference. Thereafter, participants were seated, and a venous cannula was inserted into the lower arm for the collection of blood samples. Systolic and diastolic blood pressure were assessed continuously from the finger using a Finometer (Finapres Medical Systems, Amsterdam). Heart rate and heart rate variability were measured continuously using an ActiHeart monitoring device (Cambridge Neurotechnology, UK) attached to the participant's chest with electrocardiogram (ECG) electrodes. The raw data were reduced and analysed using the Heart Rate Variability Analysis Software (Biomedical Signal Analysis Group, University of Kuopio, Finland) (38). The data were cleaned by a different person from the one who undertook the analysis. Participants spent a thirty minute rest period sitting quietly. The last five minutes of this rest period were used to measure baseline systolic and diastolic blood pressure, heart rate and heart rate

variability (baseline trial). Following this, a blood sample was drawn into EDTA and citrated tubes.

Two 5-minute behavioural tasks that have been described previously were then administered in a counter-balanced order (39). These tasks included an adapted version of the Stroop colour-word interference task and a mirror tracing task. In the Stroop colour-word interference task, participants were presented target words at the centre of the screen that indicated colours (e.g., red, blue, etc.) and were printed in a colour incongruent to the word itself (e.g., the word "red" printed in the colour blue). Four possible response options (names of colours) written in incongruent colours were presented at the bottom of the screen. Participants had to choose one out of the four possible response options that matched the colour of the target word displayed at the centre of the screen. The rate of administration of the Stroop colour-word interference task varied with performance. In the mirror tracing task, participants had to trace a star that could only be seen in a mirror image using a mental stylus. Each time participants made an error (i.e., their stylus went outside the borders of the star), the device emitted a loud beep. Participants were told that most people trace the star five times during the allocated five-minute period. The mirror tracing task was not titrated.

Blood samples were taken immediately after the tasks and 45 and 75 minutes after task completion (recovery period). Systolic and diastolic blood pressure, heart rate and heart rate variability were measured continuously during the tasks and throughout the 75 minute recovery period.

Blood measures

Immediately after blood samples were drawn, they were centrifuged at 2500 rpm for 10 minutes at room temperature and the separated plasma was aliquoted into 0.5 ml portions stored at −80 °C until further analysis. Plasma IL-6 was assayed using a Quantikine high sensitivity two-site enzyme-linked immunosorbent assay (ELISA) from R&D Systems (Oxford, UK). The sensitivity of the assay ranged from 0.016 to 0.110 pg/mol. The intra assay coefficient of variation (CV) was 7.3% and the inter assay CV was 7.7%. Fibrinogen was measured from citrated blood using an automated Clauss assay in a MDA-180 coagulometer (Oragon Teknika, Cambridge, UK). The intra and inter assay CVs were 8%. High sensitivity C-reactive protein was assayed in duplicate using a high sensitivity enzyme immunoassay test kit (BioCheck, CA, USA). The intra and inter assay CVs were 4.5%.

Pericardial fat

Pericardial fat was measured using noncontrast coronary artery calcium scans acquired using electron beam computed tomography (GE-Imatron C-150; GE-Imatron, San Francisco, CA). The methods by which pericardial fat was assessed have been described previously (40). Forty contiguous 3-mm slices were taken during a single breath-hold starting at the carina and proceeding to the level of the diaphragm. Scan time was 100 ms/slice, synchronized to 40% of the R—R interval. Two experienced investigators blinded to any psychophysiological and clinical data calculated volume of pericardial fat (in cm^3) on a Siemens multimodality workstation (Siemens, Forchheim, Germany). For the present study, we adjusted pericardial fat volume for body surface area using the formula derived by Dubois and Dubois (body surface area (m^2) = weight $(kg)^{0.425}$ × height $(cm)^{0.725}$ × 0.007184) (41) to correct for differences in heart size (giving values in cm^3/m^2) (42).

Depressive symptoms

Depressive symptoms were measured using the Centre for Epidemiological Studies Depression Scale (CES-D), a 20-item scale which assesses the frequency of depressive symptoms during the past week (43). Responses are given on a four-point Likert scale ranging from 'less than once a week' to '5–7 days a week'. The total CES-D score ranges from 0-60, and higher scores indicate greater depression (Cronbach's $\alpha = 0.86$).

Physical activity

Physical activity was assessed using a self-report question asking participants the number of hours per week they spend in mildly energetic (e.g., walking)/moderately energetic (e.g., cycling)/vigorous (e.g., running) activities. Duration of moderately energetic and vigorous activities was combined to calculate number of hours of moderate-vigorous physical activity per week. The cohort was divided into quartiles based on their responses (<1 hour/1-4 hours/5-7 hours/>7 hours).

Covariates

Covariates included age, sex, SES, current smoking status (smoker/non-smoker) and waist to hip ratio. SES, defined by current or most recent grade of employment within the British civil service (higher, intermediate and lower), was adjusted for as lower SES is associated with impaired recovery of cardiovascular responses to stress (29). The 12 possible employment grades of the British civil service were categorised as follows: administrative assistant, administrative officer and executive office (lower), higher executive office and senior executive office (intermediate), and grades 7 to 1 (higher). Waist to hip ratio was adjusted for as pericardial fat is positively correlated with central adiposity (5). In sensitivity analyses, we additionally adjusted for depressive symptoms as greater depressive symptoms have been

associated with lower blood pressure and heart rate reactivity to mental stress (44-46), as well as greater pericardial fat (47). We also ran a sensitivity analysis additionally adjusting for moderate-vigorous physical activity, as greater moderate-vigorous physical activity has been associated with lower pericardial fat, independently of BMI (40).

Statistical analysis

Descriptive statistics were calculated for the sample. Cardiovascular data were averaged across four time points: at baseline, the two behavioural tasks, and 40-45 and 70-75 minutes after tasks. Heart rate variability was modelled as the root mean square of successive differences (RMSSD) over these four time periods and was log transformed prior to analysis due to negative skew. Plasma IL-6 was sampled at baseline, immediately after tasks, and 45 and 75 minutes after tasks, and was also log transformed prior to analysis due to positive skew. Plasma fibrinogen was assessed at three time points (baseline, immediately after tasks and 45 minutes after tasks) as levels return to baseline quickly after stress (48). Plasma C-reactive protein was only measured at baseline, and was log transformed due to positive skew.

Multiple linear regression analyses were used to examine associations between pericardial fat with cardiovascular and inflammatory measures. We first assessed associations between pericardial fat with cardiovascular and inflammatory measures at baseline. In this analysis, the model was adjusted for age, sex, SES, smoking status and waist to hip ratio. We then examined associations between pericardial fat with stress reactivity operationalised as difference scores between baseline and task values (higher scores = greater reactivity), and stress recovery operationalised as difference scores between task and recovery trials (higher scores = greater recovery). In these analyses, the model was the same as described above but

to account for ceiling effects and within-person changes, we additionally controlled for baseline levels when examining task reactivity as an outcome, or baseline and task levels when examining recovery as an outcome. Time of testing was not adjusted for in analyses as it did not relate to outcomes. Finally, we examined whether the associations between pericardial fat with cardiovascular and inflammatory measures at baseline and in response to stress differed by SES. We centred pericardial fat values by the mean and then computed mean centred pericardial fat * SES interaction terms for each of the SES dummy variables (reference group = low SES) and added these terms to the fully adjusted models. Multicollinearity was not present in any analyses as variance inflation factors were less than 10 and tolerance values were greater than 0.2. Results are presented as unstandardised regression coefficients (*B*) with corresponding 95% confidence intervals (CIs), standard errors (SEs) and *p* values. Bonferroni correction was used to correct for multiple testing (a total of seven baseline tests, $p < 0.007$; four cardiovascular reactivity tests, $p < 0.0125$; two inflammatory reactivity tests, $p < 0.025$; eight cardiovascular recovery tests, $p < 0.00625$; three inflammatory recovery tests, $p < 0.0167$).

Five sensitivity analyses were conducted. First, we reran analyses using a categorical outcome of complete post-stress recovery ("complete recovery" value = 0/"incomplete recovery" value = 1), defined previously as the failure of physiological measures to return to baseline, or fall below baseline, by 45 minutes and 75 minutes after mental stress tasks (24). Second, we reran analyses using raw values of pericardial fat volume rather than pericardial fat volume adjusted for body surface area. Third, we reran all analyses with depressive symptoms as an additional covariate. Fourth, we reran all analyses with moderate-vigorous physical activity as an additional covariate. Fifth, we tested whether sex acted as a moderator in associations by including interaction terms between sex and pericardial fat in models and

stratifying analyses by sex. Analyses in the present study were conducted using SPSS version 27.

Results

Table 1 displays participant characteristics at baseline. Inter-correlations between the main study variables are shown in Table S1, Supplemental Digital Content (SDC), http://links.lww.com/PSYMED/A899. There were 186 higher (39.3%), 189 intermediate (40%), and 98 lower (20.7%) SES participants. The sample had a mean age of 62.8 years and were mostly male (60.3%) and non-smokers (94.7%). Mean waist circumference was 87 cm (92 cm in men; 80 cm in women) and mean hip circumference was 98 cm (same in both men and women). The mean volume of pericardial fat adjusted for body surface area was 62 cm^3/m^2, and the mean CES-D score was 6.58. Approximately 23% of participants were in the lowest quartile for hours of moderate-vigorous physical activity per week (<1 hour), 33% were in the second quartile (1-4 hours), 22% were in the third quartile (5-7 hours), and 22% were in the highest quartile (>7 hours). The complete case sample (n = 473) were more likely to be male ($\chi2(1) = 55.170$, $p < 0.001$), had a higher grade of employment ($\chi2(2) = 6.445$, $p = 0.040$), had a higher waist circumference ($t(535) = -3.442$, $p = 0.001$) and had a higher waist to hip ratio ($t(535) = -5.310$, $p < 0.001$) than individuals without complete data on pericardial fat volume adjusted for body surface area (n = 70). There were no significant differences in age, smoking status, BMI, hip circumference, depression scores, physical activity, systolic blood pressure, diastolic blood pressure, heart rate, heart rate variability, IL-6 levels, fibrinogen levels and CRP levels between complete and incomplete cases ($p > 0.05$).

A summary of participants' cardiovascular and inflammatory measures at baseline and in response to the stress tasks is shown in Table 2. On average, systolic blood pressure increased by 30 mmHg from baseline to tasks, decreased by 21.5 mmHg from tasks to 45 minutes after tasks, and then increased by 2.3 mmHg from 45 to 75 minutes after tasks. A similar pattern emerged for diastolic blood pressure, such that diastolic blood pressure increased by 13.9 mmHg from baseline to tasks, decreased by 9.2 mmHg from tasks to 45 minutes after tasks, and increased by 1.4 mmHg from 45 to 75 minutes after tasks. With regards to heart rate, there was a mean increase of 8.7 bpm from baseline to tasks, a mean decrease of 10.7 bpm from tasks to 45 minutes after tasks and no change from 45 to 75 minutes after tasks. RMSSD showed the reverse pattern, decreasing by 0.3 ln rms from baseline to stress tasks, increased by 0.4 ln rms from tasks to 45 minutes after tasks and did not change from 45 to 75 minutes after tasks. With regards to IL-6, concentrations increased by 0.01 ln pg/ml from baseline to tasks, increased further by 0.07 ln pg/ml from tasks to 45 minutes after tasks, and increased again by 0.04 ln pg/ml from 45 to 75 minutes after tasks. Finally, fibrinogen concentration increased by 0.16 g/L from baseline to tasks and decreased by 0.08 g/L from tasks to 45 minutes after tasks.

Pericardial fat and baseline levels of cardiovascular and inflammatory measures

Multiple linear regression analyses showed that pericardial fat was not associated with baseline levels of systolic blood pressure (B = 0.006; SE = 0.032; 95% CI: -0.057, 0.069; p = 0.852) or diastolic blood pressure (B = 0.038; SE = 0.021; 95% CI: -0.004, 0.080; p = 0.073) (Table 3). However, there was a significant association between pericardial fat and increased resting heart rate (B = 0.082; SE = 0.021; 95% CI: 0.042, 0.123; p < 0.001), lower heart rate variability (B = -0.004; SE = 0.001; 95% CI: -0.006, -0.002; p = 0.001), greater plasma IL-6 (B = 0.002; SE = 0.001; 95% CI: 0.001, 0.003; p < 0.001), greater plasma fibrinogen (B =

0.003; SE = 0.001; 95% CI: 0.002, 0.004; $p < 0.001$) and greater plasma C-reactive protein (B = 0.002; SE = 0.001; 95% CI: 0.001, 0.003; $p < 0.001$). These results all held under Bonferroni correction. All interactions between pericardial fat and SES for baseline levels of cardiovascular and inflammatory measures were non-significant.

Pericardial fat and cardiovascular responses to stress

Analysis showed that even after applying Bonferroni correction, pericardial fat was associated with lower systolic blood pressure reactivity to acute mental stress after adjustment for age, sex, SES, smoking status, waist to hip ratio and baseline systolic blood pressure (B = -0.087; SE = 0.034; 95% CI: -0.154, -0.020; p = 0.011). There were no associations between pericardial fat with systolic blood pressure recovery levels at 45 and 75 minutes after stress tasks after adjustment for age, sex, SES, smoking status, waist to hip ratio, and baseline and task levels of systolic blood pressure. There were also no significant associations between pericardial fat with diastolic blood pressure reactivity to stress or recovery levels at 45 and 75 minutes post-stress after adjustment for covariates. Interactions between pericardial fat and SES for systolic and diastolic blood pressure reactivity and recovery levels were all non-significant.

With regards to heart rate, pericardial fat was not significantly associated with heart rate reactivity (p = 0.123), recovery levels 45 minutes after stress (p = 0.932), or recovery levels 75 minutes after stress after adjustment for covariates (p = 0.553). The analysis of heart rate variability also found that pericardial fat was not significantly associated with heart rate variability reactivity (p = 0.075), recovery levels 45 minutes after stress (p = 0.219) or recovery levels 75 minutes after stress after adjustment for covariates (p = 0.216). All

interactions between pericardial fat and SES for heart rate and heart rate variability reactivity and recovery levels were non-significant.

Pericardial fat and inflammatory responses to stress

Pericardial fat was not associated with IL-6 stress reactivity after adjustment for age, sex, SES, smoking status, waist to hip ratio and baseline IL-6 (p = 0.175). There were also no significant associations between pericardial fat and IL-6 recovery levels at 45 and 75 minutes after stress after adjustment for age, sex, SES, smoking status, waist to hip ratio, and baseline and task levels of IL-6. The results further showed that pericardial fat was not associated with fibrinogen reactivity (p = 0.613) or recovery levels at 45 minutes after stress after adjustment for covariates (p = 0.966). All interactions between pericardial fat and SES for IL-6 and fibrinogen reactivity and recovery levels were non-significant.

Sensitivity analyses

The first sensitivity analysis examined associations between pericardial fat and complete or incomplete post-stress recovery of cardiovascular and inflammatory measures. There were no significant associations between pericardial fat and complete post-stress recovery for any of the cardiovascular and inflammatory measures tested (SDC, Table S2). All interactions between pericardial fat and SES for the cardiovascular and inflammatory measures during tasks and 45 and 75 minutes after tasks were non-significant.

The second sensitivity analysis examined associations between raw values of pericardial fat (not adjusted for body surface area) and cardiovascular and inflammatory measures at baseline or in response to acute mental stress. The findings were largely consistent with the main analyses (Table S3). Greater pericardial fat was associated with reduced heart rate

reactivity after adjustment for age, sex, SES, smoking status, waist to hip ratio and baseline heart rate, but not under Bonferroni correction (*B* = -0.017; SE = 0.008; 95% CI: -0.034, -0.001; *p* = 0.035).

The third sensitivity analysis examined the association between pericardial fat and cardiovascular and inflammatory measures at baseline or in response to stress, additionally adjusting for depressive symptoms in all models. The findings were identical to the main analyses (Table S4).

The fourth sensitivity analysis examined the association between pericardial fat and cardiovascular and inflammatory measures at baseline or in response to stress, additionally adjusting for weekly hours of moderate-vigorous physical activity in all models. The findings were identical to the main analyses (Table S5).

The fifth sensitivity analysis examined whether sex moderated associations between pericardial fat and cardiovascular and inflammatory measures at baseline or in response to stress. We found evidence that sex moderated the association between pericardial fat and fibrinogen at baseline (interaction term *p* = 0.001). Subgroup analyses showed that there was a statistically significant association between pericardial fat and fibrinogen at baseline in men, adjusting for age, SES, smoking status and waist to hip ratio (*B* = 0.009; SE = 0.004; 95% CI: 0.001, 0.016; *p* = 0.026). However, this association did not hold under Bonferroni correction. There was no association between pericardial fat and fibrinogen at baseline in women after adjustment for the same covariates (*p* = 0.538).

Discussion

This exploratory study showed that pericardial fat was associated with greater baseline heart rate, lower baseline heart rate variability, greater baseline plasma IL-6, greater baseline plasma fibrinogen and greater baseline plasma CRP. We also found that greater pericardial fat was associated with lower systolic blood pressure reactivity to acute mental stress in a cohort of middle-aged and older men and women without prior history of CHD. This association was independent of sociodemographic factors, waist to hip ratio and baseline systolic blood pressure. Sensitivity analyses showed that the association remained significant after additional adjustment for depressive symptoms and physical activity. There was no evidence that SES moderated any of the associations between pericardial fat and cardiovascular or inflammatory measures at baseline or in response to acute mental stress.

Many studies have examined associations between measures of adiposity and cardiovascular reactivity to mental stress. For instance, a study of older men found that those with overweight or obesity had reduced systolic blood pressure reactivity to mental stress compared to those without (49). Furthermore, another study of healthy men and women found that greater visceral fat was associated with blunted systolic blood pressure responses to mental stress (50). However, some studies have shown no association between central adiposity (indexed by waist to hip ratio) and cardiovascular reactivity to mental stress (29). Our study found an association between pericardial fat, a fat depot surrounding the heart, and reduced systolic blood pressure reactivity to mental stress. The association found in this study was independent of baseline systolic blood pressure, suggesting that the association was not simply due to lower resting levels of systolic blood pressure. Furthermore, sensitivity analyses showed that the association between pericardial fat and reduced systolic blood pressure reactivity to stress was independent of depressive symptoms and physical activity,

suggesting that depression and physical activity are unlikely to account for the observed association. This is in spite of evidence showing that patients with depression have greater pericardial fat (51, 52) and show lower cardiovascular responses to stress than those without depression (44-46), as well as evidence showing that greater physical activity is associated with lower pericardial fat (40) and lower cardiovascular responses to stress (53). Reduced cardiovascular reactivity to acute mental stress might therefore be an independent mechanism linking pericardial fat and CVD, since blunted cardiovascular reactivity to stress is associated with many CVD risk factors (54).

One possible explanation of the association between greater pericardial fat and lower systolic blood pressure reactivity to mental stress is that the association might reflect exposure to early life adversity. Evidence suggests that early life adversity is linked to blunted cardiovascular reactivity to stress (55, 56) and further evidence shows that there is a dose-response relationship between the two (57). Furthermore, early life adversity is linked with a greater risk of visceral fat deposition (58). However, most of the work conducted on the association between early life adversity and blunted cardiovascular reactivity to stress has found associations with blunted heart rate reactivity, not blood pressure (34). Furthermore, recent evidence suggests that depression mediates the link between early life adversity and blunted cardiovascular reactivity (59), but our findings were independent of depressive symptoms. Therefore, it is unlikely that early life adversity can explain our findings. Another possible explanation of the association between pericardial fat and systolic blood pressure reactivity found in this study is allostatic load. It has been argued that chronic stress in adulthood might contribute to allostatic load, and therefore, cause a blunted biological response to stress (34, 60). For instance, evidence shows that individuals exposed to early life adversity combined with distress in adulthood have blunted cortisol reactivity compared to

those exposed to early life adversity with less distress in adulthood (61). Studies have also shown that abdominal obesity interacts with chronic stress to predict reduced systolic blood pressure reactivity to mental stress (62). Further, greater chronic stress burden is associated with the accumulation of visceral fat (25, 63). Future research could examine whether an interaction between early life adversity and chronic stress in adulthood exists in terms of the association between pericardial fat and systolic blood pressure reactivity to stress.

We did not find any relationships between pericardial fat and diastolic blood pressure or heart rate reactivity to acute mental stress, as well as cardiovascular or inflammatory recovery from stress. However, our sensitivity analyses showed that pericardial fat not adjusted for body surface area was associated with lower heart rate reactivity to stress, although not under Bonferroni correction. Despite the fact that pericardial fat volume is often adjusted for by body surface area to account for differences in heart size by body size (42, 64, 65), this method might be limited and unreliable, particularly in individuals with obesity (66). Nevertheless, evidence suggests that pericardial fat volume and pericardial fat volume adjusted for body surface area have similar predictive value in predicting coronary artery disease (67). Future studies are needed to compare the predictive value of these methods of pericardial fat assessment for other cardiovascular outcomes.

Greater pericardial fat was associated with greater resting values of plasma IL-6, plasma fibrinogen and plasma C-reactive protein in the present study, independent of sociodemographic factors, waist to hip ratio and depressive symptoms. Several large-scale epidemiological studies conducted in community samples have also found positive associations between pericardial fat with C-reactive protein, IL-6 and fibrinogen, even after adjusting for many covariates including central adiposity (68-70). Furthermore, individuals

with coronary artery disease have been shown to have greater levels of IL-6 expressed in their pericardial adipose tissue compared to controls without coronary artery disease (71). Given that inflammatory processes are implicated in the development of CVD, inflammation might therefore underly associations between pericardial fat with CVD (8). However, unlike some prior studies (71), the present study measured systemic rather than local inflammatory marker concentrations. Local adipose tissue expression of inflammatory markers has been shown not to correlate with systemic concentrations (68). Consequently, the present study does not provide information on associations between pericardial fat with inflammatory markers that might act locally to contribute to coronary vascular inflammation and atherosclerosis development.

We also examined associations between pericardial fat with other measures of autonomic function at rest. We found no association between pericardial fat and resting levels of systolic or diastolic blood pressure, contrary to evidence which has found positive associations between these variables (33, 72). One reason for these discrepant findings is differences in statistical covariates. Specifically, Iacobellis et al. only adjusted for gender in their analyses and Kim et al. did not adjust for any covariates at all, whereas we adjusted for multiple potential confounders known to correlate with both pericardial fat and blood pressure including age, SES and central adiposity (5, 30, 73). Therefore, associations found in prior studies might have been confounded by sociodemographic factors or central adiposity. Nevertheless, we did find an association between greater pericardial fat and lower heart rate variability at rest, independent of multiple covariates. This finding is in line with another cross-sectional study which found that pericardial fat thickness was inversely associated with heart rate variability at rest (74). Additionally, a prospective study in hypercholesteremic Ossabaw mini-pigs showed that increases in pericardial fat volume were associated with

decreased heart rate variability (75). Low heart rate variability is associated with greater risk for CVD (76) and might therefore help explain how pericardial fat is associated with CVD.

Interestingly, SES did not moderate any relationship between pericardial fat with cardiovascular and inflammatory measures at baseline or in response to mental stress in the present study. This finding contrasts with evidence showing an interaction between SES and waist to hip ratio for systolic and diastolic blood pressure recovery from acute mental stress, such that blood pressure recovery was impaired in individuals with a lower SES and large waist to hip ratio (29). Furthermore, low SES is generally associated with poorer cardiovascular recovery from acute mental stress (77), and one small-scale, cross-sectional study has found an inverse association between pericardial fat and SES (30). Therefore, it is possible that SES only interacts with central adiposity when predicting cardiovascular responses to stress and has less of an effect on the relationship between pericardial fat and cardiovascular responses to stress.

There are some other limitations of the present study. All participants were of White European ethnicity, which might impact the generalisability of the findings to other ethnicities given that there are ethnic differences in volume of pericardial fat and its association with CVD (69), as well as in autonomic responses to stress (78). Furthermore, the study was observational and cross-sectional meaning that causality and the direction of causality cannot be concluded. However, we did adjust statistically for a broad range of potential confounders, and to reduce the risk of reverse causality, we adjusted statistically for baseline and/or task levels of cardiovascular and inflammatory markers where appropriate. Nevertheless, residual confounding by unmeasured factors is a potential problem.

Notwithstanding these limitations, the present study has several notable strengths. First, the study was conducted in a well-characterised sample of large size particularly when compared to other studies of biological stress responses. The sample included a broad range of SES and had no history of CHD, so poor health is unlikely to confound our findings. In addition, the stress tasks were chosen based on pilot work showing that these tasks induce stress and task engagement ratings that do not differ by SES (24), and elicit cardiovascular and inflammatory responses that do not habituate in response to repeat testing (79). Finally, all the significant associations detailed in Table 2 survived Bonferroni correction for multiple testing.

To conclude, the present study has shown that greater pericardial fat is associated with reduced systolic blood pressure reactivity to acute mental stress. This association is independent of sociodemographic factors, waist to hip ratio and baseline systolic blood pressure.

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Table 1. Participant characteristics at baseline (N = 473)

	Mean (SD)/Frequency (%)
Age, *N* = 473	62.83 (5.71)
Sex, *N* = 473	
Male	285 (60.3)
Female	188 (39.7)
Grade of employment, *N* = 473	
Lower	98 (20.7)
Intermediate	189 (40.0)
Higher	186 (39.3)
Smoking status, *N* = 473	
Smoker	25 (5.3)
Non-smoker	448 (94.7)
Waist circumference (cm), *N* = 467	87.47 (12.55)
Hip circumference (cm), *N* = 467	98.37 (7.74)
Waist to hip ratio, *N* = 467	0.89 (0.10)
Body mass index, *N* = 473	25.88 (3.89)
Pericardial fat adjusted for body surface area (cm^3/m^2), *N* = 473	62.08 (22.99)
Depressive symptoms score, *N* = 472	6.58 (6.29)
Moderate-vigorous activity (hours/week), *N* = 473	
<1 hour	107 (22.6)
1-4 hours	157 (33.2)
5-7 hours	103 (21.8)
>7 hours	106 (22.4)

Note. SD = standard deviation.

Values are presented as means (SD) for continuous variables and *n* (%) for categorical variables.

Table 2. Summary of cardiovascular and inflammatory measures at baseline and in response to acute mental stress during tasks and recovery periods

	Mean (SD)
Systolic blood pressure (mmHg)	
Baseline, *N* = 473	125.87 (14.60)
Tasks, *N* = 460	155.89 (21.85)
45 min recovery, *N* = 457	134.35 (17.34)
75 min recovery, *N* = 457	136.68 (18.07)
Diastolic blood pressure (mmHg)	
Baseline, *N* = 473	74.30 (9.67)
Tasks, *N* = 459	88.24 (12.35)
45 min recovery, *N* = 456	79.04 (11.24)
75 min recovery, *N* = 456	80.39 (11.31)
Heart rate (bpm)	
Baseline, *N* = 473	66.60 (9.15)
Tasks, *N* = 424	75.32 (11.01)
45 min recovery, *N* = 421	64.59 (8.34)
75 min recovery, *N* = 415	64.78 (8.33)
Heart rate variability (rms, ln)	
Baseline, *N* = 473	3.06 (0.47)
Tasks, *N* = 391	2.79 (0.51)
45 min recovery, *N* = 390	3.18 (0.45)
75 min recovery, *N* = 390	3.18 (0.47)
Plasma interleukin-6 (pg/ml, ln)	
Baseline, *N* = 473	0.06 (0.23)
Tasks, *N* = 453	0.07 (0.24)
45 min recovery, *N* = 448	0.14 (0.24)
75 min recovery, *N* = 446	0.18 (0.24)
Plasma fibrinogen (g/L)	

Baseline, $N = 473$	3.12 (0.62)
Tasks, $N = 448$	3.28 (0.65)
45 min recovery, $N = 448$	3.20 (0.64)
Plasma C-reactive protein (mg/L, ln)	
Baseline, $N = 457$	0.35 (0.23)

Note. SD = standard deviation.

Table 3. Associations between pericardial fat adjusted for body surface area and cardiovascular and inflammatory measures at baseline and in response to stress

	B (95% CI)	SE	*p*
Systolic blood pressure, *N* = 450			
Baseline	0.006 (-0.057, 0.069)	0.032	0.852
Task reactivity	-0.087 (-0.154, -0.020)	0.034	0.011*
45 min recovery	0.003 (-0.043, 0.048)	0.023	0.904
75 min recovery	-0.004 (-0.051, 0.043)	0.024	0.858
Diastolic blood pressure, *N* = 449			
Baseline	0.038 (-0.004, 0.080)	0.021	0.073
Task reactivity	-0.023 (-0.055, 0.009)	0.016	0.154
45 min recovery	-0.013 (-0.040, 0.015)	0.014	0.362
75 min recovery	-0.012 (-0.039, 0.015)	0.014	0.382
Heart rate, *N* = 407			
Baseline	0.082 (0.042, 0.123)	0.021	<0.001***
Task reactivity	-0.027 (-0.061, 0.007)	0.017	0.123
45 min recovery	-0.001 (-0.017, 0.015)	0.008	0.932
75 min recovery	-0.005 (-0.021, 0.011)	0.008	0.553
Heart rate variability, *N* = 384			
Baseline	-0.004 (-0.006, -0.002)	0.001	0.001**
Task reactivity	0.002 (0.000, 0.004)	0.001	0.075
45 min recovery	-0.001 (-0.002, 0.000)	0.001	0.219
75 min recovery	0.001 (-0.001, 0.002)	0.001	0.216
Plasma interleukin-6, *N* = 440			
Baseline	0.002 (0.001, 0.003)	0.001	<0.001***
Task reactivity	0.000 (0.000, 0.000)	0.000	0.175

45 min recovery	0.000 (-0.001, 0.000)	0.000	0.333
75 min recovery	-0.001 (-0.001, 0.000)	0.000	0.052
Plasma fibrinogen, *N* = 440			
Baseline	0.003 (0.002, 0.004)	0.001	<0.001***
Task reactivity	0.000 (-0.001, 0.000)	0.000	0.613
45 min recovery	0.000 (-0.001, 0.001)	0.000	0.966
Plasma C-reactive protein, *N* = 451			
Baseline	0.002 (0.001, 0.003)	0.001	<0.001***

For baseline values: Models included age, sex, socioeconomic status, smoking status, waist to hip ratio and pericardial fat.
For task reactivity values: Models included age, sex, socioeconomic status, smoking status, waist to hip ratio, pericardial fat and either baseline levels of cardiovascular measures (in cardiovascular measure analyses) or baseline levels of inflammatory measures (in inflammatory marker analyses).
For recovery at 45 and 75 mins: Models included age, sex, socioeconomic status, smoking status, waist to hip ratio, pericardial fat and either baseline and task levels of cardiovascular measures (in cardiovascular measure analyses) or baseline and task levels of inflammatory measures (in inflammatory marker analyses).
CI, confidence interval.

Supplementary Table S1. Inter-correlations among main study variables, $N = 393$.

	Age	Sex	Socioeconomic status	Smoking status	Waist to hip ratio	Pericardial fat	SBP reactivity	DBP reactivity	HR reactivity	IL-6 reactivity
Age	-	0.164**	0.094	-0.105*	-0.106*	0.094	0.100*	0.076	0.044	0.227**
Sex	0.164**	-	0.090	-0.033	-0.656**	-0.235**	-0.049	-0.009	0.055	-0.039
Socioeconomic status	0.094	0.090	-	-0.001	-0.023	0.058	-0.090	-0.083	-0.142**	0.145**
Smoking status	-0.105*	-0.033	-0.001	-	0.058	0.069	-0.133**	-0.102*	-0.066	0.088
Waist to hip ratio	-0.106*	-0.656**	-0.023	0.058	-	0.449**	0.035	0.052	-0.057	0.159**
Pericardial fat	0.094	-0.235**	0.058	0.069	0.449**	-	-0.083	-0.026	-0.126*	0.290**
SBP reactivity	0.100*	-0.049	-0.090	-0.133**	0.035	-0.083	-	0.869**	0.418**	-0.153**
DBP reactivity	0.076	-0.009	-0.083	-0.102*	0.052	-0.026	0.869**	-	0.373**	-0.082
HR reactivity	0.044	0.055	-0.142**	-0.066	-0.057	-0.126*	0.418**	0.373**	-	-0.073
IL-6 reactivity	0.227**	-0.039	0.145**	0.088	0.159**	0.290**	-0.153**	-0.082	-0.073	-

*$p < 0.05$, **$p < 0.01$
DBP = diastolic blood pressure; IL-6 = interleukin-6; HR = heart rate; SBP = systolic blood pressure

Pearson correlation coefficients calculated between continuous variables, Point-biserial correlation coefficients between continuous and dichotomous variables, Phi correlation coefficients between two dichotomous variables, and Cramer's V between two nominal variables where the contingency is greater than 2x2.
Sex: male (0), female (1)
Socioeconomic status: higher (1), intermediate (2), lower (3)
Smoking status: non-smoker (0), smoker (1)

Supplementary Table S2. Associations between pericardial fat and complete post-stress recovery (sensitivity analysis).

		OR (95% CI)	SE	*p*
Systolic blood pressure, *N* = 450				
45 min	Incomplete	Ref		
	Complete	1.008 (0.996, 1.019)	0.006	0.194
75 min	Incomplete	Ref		
	Complete	1.006 (0.993, 1.020)	0.007	0.340
Diastolic blood pressure, *N* = 449				
45 min	Incomplete	Ref		
	Complete	1.001 (0.989, 1.014)	0.006	0.848
75 min	Incomplete	Ref		
	Complete	1.002 (0.988, 1.016)	0.007	0.750
Heart rate, *N* = 407				
45 min	Incomplete	Ref		
	Complete	1.006 (0.994, 1.018)	0.006	0.309
75 min	Incomplete	Ref		
	Complete	1.001 (0.990, 1.012)	0.005	0.876
Heart rate variability, *N* = 384				
45 min	Incomplete	Ref		
	Complete	1.003 (0.991, 1.014)	0.006	0.645
75 min	Incomplete	Ref		
	Complete	0.996 (0.985, 1.007)	0.006	0.517
Plasma interleukin-6, *N* = 440				

45 min	Incomplete	Ref		
	Complete	1.005 (0.994, 1.016)	0.006	0.352
75 min	Incomplete	Ref		
	Complete	0.998 (0.986, 1.009)	0.006	0.669
Plasma fibrinogen, *N* = 440				
45 min	Incomplete	Ref		
	Complete	1.006 (0.997, 1.016)	0.005	0.192

Models included age, sex, socioeconomic status, smoking status, waist to hip ratio and pericardial fat.
CI, confidence interval; OR, odds ratio.

Supplementary Table S3. Associations between raw values of pericardial fat (not adjusted for body surface area) and cardiovascular and inflammatory measures at baseline and in response to stress (sensitivity analysis).

	B (95% CI)	SE	*p*
Systolic blood pressure, *N* = 450			
Baseline	0.011 (-0.019, 0.041)	0.016	0.479
Task reactivity	-0.046 (-0.078, -0.013)	0.016	0.006**
45 min recovery	-0.001 (-0.023, 0.021)	0.011	0.926
75 min recovery	-0.005 (-0.028, 0.017)	0.012	0.644
Diastolic blood pressure, *N* = 449			
Baseline	0.020 (-0.000, 0.040)	0.010	0.052
Task reactivity	-0.011 (-0.026, 0.004)	0.008	0.156
45 min recovery	-0.007 (-0.020, 0.006)	0.007	0.285
75 min recovery	-0.008 (-0.021, 0.005)	0.007	0.254
Heart rate, *N* = 407			
Baseline	0.040 (0.020, 0.059)	0.010	<0.001***
Task reactivity	-0.017 (-0.034, -0.001)	0.008	0.035*
45 min recovery	0.000 (-0.008, 0.008)	0.004	0.966
75 min recovery	-0.001 (-0.009, 0.006)	0.004	0.729
Heart rate variability, *N* = 384			
Baseline	-0.002 (-0.003, -0.001)	0.001	<0.001***
Task reactivity	0.001 (-0.000, 0.002)	0.000	0.080
45 min recovery	0.000 (-0.001, 0.000)	0.000	0.241
75 min recovery	0.000 (-0.000, 0.001)	0.000	0.300

Plasma interleukin-6, $N = 440$			
Baseline	0.001 (0.001, 0.002)	0.000	<0.001***
45 min recovery	0.000 (-0.000, 0.000)	0.000	0.552
75 min recovery	0.000 (-0.001, 0.000)	0.000	0.077
Plasma fibrinogen, $N = 440$			
Baseline	0.001 (0.001, 0.002)	0.000	<0.001***
Task reactivity	0.000 (-0.001, 0.000)	0.000	0.613
45 min recovery	0.000 (-0.000, 0.000)	0.000	0.966
Plasma C-reactive protein, $N = 451$			
Baseline	0.001 (0.001, 0.002)	0.000	<0.001***

For baseline values: Models included age, sex, socioeconomic status, smoking status, waist to hip ratio and pericardial fat.
For task reactivity values: Models included age, sex, socioeconomic status, smoking status, waist to hip ratio, pericardial fat and either baseline levels of cardiovascular measures (in cardiovascular measure analyses) or baseline levels of inflammatory measures (in inflammatory marker analyses).
For recovery at 45 and 75 mins: Models included age, sex, socioeconomic status, smoking status, waist to hip ratio, pericardial fat and either baseline and task levels of cardiovascular measures (in cardiovascular measure analyses) or baseline and task levels of inflammatory measures (in inflammatory marker analyses).
CI, confidence interval.

Supplementary Table S4. Associations between pericardial fat adjusted for body surface area and cardiovascular and inflammatory measures at baseline and in response to stress, additionally controlling for depressive symptoms (sensitivity analysis).

	B (95% CI)	SE	*p*
Systolic blood pressure, *N* = 449			
Baseline	0.007 (-0.057, 0.071)	0.032	0.828
Task reactivity	-0.079 (-0.146, -0.012)	0.034	0.021*
45 min recovery	0.002 (-0.044, 0.048)	0.023	0.944
75 min recovery	-0.002 (-0.050, 0.045)	0.024	0.918
Diastolic blood pressure, *N* = 448			
Baseline	0.038 (-0.004, 0.080)	0.021	0.078
Task reactivity	-0.020 (-0.051, 0.012)	0.016	0.221
45 min recovery	-0.014 (-0.041, 0.014)	0.014	0.322
75 min recovery	-0.012 (-0.039, 0.016)	0.014	0.398
Heart rate, *N* = 406			
Baseline	0.083 (0.042, 0.125)	0.021	<0.001***
Task reactivity	-0.025 (-0.060, 0.009)	0.017	0.148
45 min recovery	0.000 (-0.017, 0.016)	0.008	0.969
75 min recovery	-0.004 (-0.020, 0.013)	0.008	0.674
Heart rate variability, *N* = 383			
Baseline	-0.004 (-0.006, -0.002)	0.001	0.001**
Task reactivity	0.002 (-0.000, 0.004)	0.001	0.060
45 min recovery	-0.001 (-0.002, 0.001)	0.001	0.244
75 min recovery	0.001 (-0.001, 0.002)	0.001	0.202
Plasma interleukin-6, *N* = 439			
Baseline	0.002 (0.001, 0.003)	0.001	<0.001***
Task reactivity	0.000 (0.000, 0.000)	0.000	0.146

45 min recovery	0.000 (-0.001, 0.000)	0.000	0.390
75 min recovery	-0.001 (-0.001, 0.000)	0.000	0.064
Plasma fibrinogen, *N* = 439			
Baseline	0.005 (0.002, 0.008)	0.001	<0.001***
Task reactivity	0.000 (-0.001, 0.001)	0.001	0.458
45 min recovery	0.000 (-0.001, 0.001)	0.000	0.761
Plasma C-reactive protein, *N* = 450			
Baseline	0.002 (0.001, 0.003)	0.001	<0.001***

For baseline values: Models included age, sex, socioeconomic status, smoking status, waist to hip ratio, depressive symptoms and pericardial fat.
For task reactivity values: Models included age, sex, socioeconomic status, smoking status, waist to hip ratio, pericardial fat and either baseline levels of cardiovascular measures (in cardiovascular measure analyses) or baseline levels of inflammatory measures (in inflammatory marker analyses).
For recovery at 45 and 75 mins: Models included age, sex, socioeconomic status, smoking status, waist to hip ratio, pericardial fat and either baseline and task levels of cardiovascular measures (in cardiovascular measure analyses) or baseline and task levels of inflammatory measures (in inflammatory marker analyses).
CI, confidence interval.

Supplementary Table S5. Associations between pericardial fat adjusted for body surface area and cardiovascular and inflammatory measures at baseline and in response to stress, additionally controlling for physical activity (sensitivity analysis).

	B (95% CI)	SE	*p*
Systolic blood pressure, *N* = 450			
Baseline	0.010 (-0.053, 0.074)	0.032	0.755
Task reactivity	-0.082 (-0.149, -0.015)	0.034	0.016*
45 min recovery	0.005 (-0.041, 0.051)	0.023	0.825
75 min recovery	-0.003 (-0.050, 0.044)	0.024	0.896
Diastolic blood pressure, *N* = 449			
Baseline	0.043 (-0.053, 0.140)	0.049	0.377
Task reactivity	-0.023 (-0.055, 0.009)	0.016	0.160
45 min recovery	-0.012 (-0.040, 0.015)	0.014	0.381
75 min recovery	-0.011 (-0.039, 0.016)	0.014	0.411
Heart rate, *N* = 407			
Baseline	0.077 (0.036, 0.117)	0.021	<0.001***
Task reactivity	-0.026 (-0.060, 0.008)	0.017	0.137
45 min recovery	-0.001 (-0.017, 0.016)	0.008	0.939
75 min recovery	-0.004 (-0.021, 0.012)	0.008	0.601
Heart rate variability, *N* = 384			
Baseline	-0.004 (-0.006, -0.002)	0.001	0.001**
Task reactivity	0.002 (0.000, 0.004)	0.001	0.059
45 min recovery	-0.001 (-0.002, 0.001)	0.001	0.230
75 min recovery	0.001 (-0.001, 0.002)	0.001	0.200
Plasma interleukin-6, *N* = 440			
Baseline	0.002 (0.001, 0.003)	0.001	<0.001***
Task reactivity	0.000 (0.000, 0.000)	0.000	0.177

45 min recovery	0.000 (-0.001, 0.000)	0.000	0.341
75 min recovery	-0.001 (-0.001, 0.000)	0.000	0.041
Plasma fibrinogen, *N* = 440			
Baseline	0.005 (0.002, 0.008)	0.001	<0.001***
Task reactivity	0.000 (-0.001, 0.001)	0.001	0.496
45 min recovery	0.000 (-0.001, 0.001)	0.000	0.855
Plasma C-reactive protein, *N* = 451			
Baseline	0.002 (0.001, 0.003)	0.001	<0.001***

For baseline values: Models included age, sex, socioeconomic status, smoking status, waist to hip ratio, physical activity and pericardial fat.
For task reactivity values: Models included age, sex, socioeconomic status, smoking status, waist to hip ratio, pericardial fat and either baseline levels of cardiovascular measures (in cardiovascular measure analyses) or baseline levels of inflammatory measures (in inflammatory marker analyses).
For recovery at 45 and 75 mins: Models included age, sex, socioeconomic status, smoking status, waist to hip ratio, pericardial fat and either baseline and task levels of cardiovascular measures (in cardiovascular measure analyses) or baseline and task levels of inflammatory measures (in inflammatory marker analyses).
CI, confidence interval.