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Depression and Inflammation in Patients With Coronary Heart Disease: Findings from the Heart and Soul Study

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Abstract

Background—Depression and inflammation independently predict adverse cardiovascular outcomes in patients with coronary heart disease (CHD). Depression has been associated with elevated levels of inflammation in otherwise healthy patients without known CHD. However, studies investigating the link between depression and inflammation in patients with established CHD have produced inconclusive results.

Methods—We sought to examine the association of major depression with inflammation in 984 outpatients with established CHD from the Heart and Soul Study. We assessed current major depression with the Computerized Diagnostic Interview Schedule and collected venous blood samples for measurement of five inflammatory biomarkers (white blood cell count, CD40 ligand, C-reactive protein [CRP], fibrinogen, and interleukin-6 [IL-6]). We used multivariate analysis of variance to examine the association of current depression with inflammatory markers, adjusted for potential confounding variables.

Results—Of the 984 participants, 217 (22%) had current major depression. Depression was not associated with increased levels of any inflammatory marker. Contrary to our hypothesis, depression was associated with lower levels of CRP ($p = .09$), fibrinogen ($p = .006$), and IL-6 ($p = .007$) in both unadjusted and adjusted models.

Conclusions—We found no evidence that current depression is associated with greater inflammation in outpatients with CHD. Inflammation is unlikely to explain the adverse cardiovascular outcomes associated with depression in patients with established CHD.

Keywords

Epidemiology; heart disease; inflammation; major depressive disorder

Depression is associated with adverse cardiovascular outcomes among patients with coronary heart disease (CHD) (Barth *et al.* 2004; Evans *et al.* 2005; Lett *et al.* 2004; Raison *et al.* 2006; Stewart *et al.* 2003; van Melle *et al.* 2004). Several biological factors have been proposed as potential mechanisms by which depression might lead to CHD events, including increased sympathetic tone (Carney *et al.* 2001; Gehi *et al.* 2003), increased catecholamine levels (Otte *et al.* 2005), increased cortisol (Otte *et al.* 2004), and greater inflammation (Lesperance *et al.* 2004). Of these, inflammation has generated particular interest as a risk factor for CHD events that might be modifiable in depressed patients.

Depression has been associated with markers of inflammation in otherwise healthy patients without known CHD (Dentino *et al.* 1999; Empana *et al.* 2005; Folsom *et al.* 1993; Kop *et al.* 2002; Ladwig *et al.* 2005; Lahlou-Laforet *et al.* 2006; Maes *et al.* 1997; Miller *et al.* 2002; Panagiotakos *et al.* 2004; Penninx *et al.* 2003; Sluzewska *et al.* 1996; Suarez 2004; Tiemeier *et al.* 2003). However, recent studies of depression and inflammation in patients with established CHD have yielded mixed results (Janszky *et al.* 2005; Lesperance *et al.* 2004; Miller *et al.* 2005; Schins *et al.* 2005). Miller *et al.* (2005) found higher levels of C-reactive protein (CRP) associated with depression after acute coronary syndrome. Lesperance *et al.* (2004) found that depression was associated with increased levels of CRP in non-users but not in users of statins. Conversely, two studies found no evidence of a relationship between depression and inflammatory markers in patients between 0 and 17 months after myocardial infarction (MI) or coronary revascularization (Janszky *et al.* 2005; Schins *et al.* 2005).

Whether depression is associated with inflammation in patients with stable CHD is unknown. Because acute coronary syndromes are themselves pro-inflammatory states, the association of depression with inflammation after hospitalization for acute coronary syndrome might be different than in outpatients with stable CHD. Likewise, the relation between depression and inflammation in patients with stable CHD might be different than in otherwise healthy individuals who have lower baseline levels of inflammation. We sought to examine the association of current depression with five inflammatory biomarkers in a cross-sectional study of 984 outpatients with stable CHD.

Methods and Materials

Participants

The Heart and Soul Study is a prospective cohort study of psychosocial factors and health outcomes in patients with CHD. Methods have been described previously (Beattie *et al.* 2003; Lubbock *et al.* 2005; Ruo *et al.* 2003). Patients with CHD were recruited with administrative databases from two Department of Veterans Affairs Medical Centers (San Francisco, California, and Palo Alto, California), one university medical center (University of California, San Francisco), and nine public health clinics in the Community Health Network of San Francisco. Patients were eligible to participate if at any point in their adulthood they had an MI, angiographic evidence of $\geq 50\%$ stenosis in one or more coronary vessels, evidence of exercise-induced ischemia by treadmill or nuclear testing, or coronary revascularization. Patients were not eligible if they had an acute coronary syndrome within the past 6 months, could not walk one block, or were planning to move out of the local area within 3 years.

Between September 2000 and December 2002, a total of 1024 participants enrolled and completed a daylong study protocol at the San Francisco Veterans Affairs Medical Center. Of these, 39 patients were excluded owing to incomplete serum samples, and 1 owing to an incomplete depression interview, leaving 984 participants for this cross-sectional analysis. The Heart and Soul Study protocol was approved by the appropriate institutional review boards, and all participants provided written, informed consent.

Major Depression

Because inflammatory markers are acute phase reactants that typically change within hours of a stimulus, we evaluated current (past month) major depression for our primary analysis. We assessed current major depression with the Computerized Diagnostic Interview Schedule (CDIS-IV), a highly structured interview designed to yield psychiatric diagnoses (Robins *et al.* 1981) according to DSM-IV criteria (American Psychiatric Association 2000). The DIS has been used extensively to study the epidemiology of depression (Wells *et al.* 1989). Trained research assistants administered the interview during the daylong study appointment.

Participants found to have current depression were informed of this diagnosis, instructed to discuss their symptoms with their primary care provider, and provided a list of local resources available for further evaluation and treatment.

We also performed secondary analysis examining the association of inflammation with past year depression, lifetime depression, age at first onset of depression, and number of prior episodes of depression. To assess severity of depression, we administered the 9-item Patient Health Questionnaire (PHQ), a self-report inventory of depressive symptoms (Spitzer *et al.* 1999). To rule out the possibility of depression misclassification, we compared inflammation in patients with depression by both instruments (CDIS positive and PHQ ≥ 10) vs. those without depression by either instrument (CDIS negative and PHQ < 4) according to validated cut points (Kroenke *et al.* 2001; McManus *et al.* 2005). For this sensitivity analysis, we excluded any participant who could possibly have been misclassified in the primary analysis (CDIS positive and PHQ < 10 , or CDIS negative and PHQ > 4).

Inflammatory Biomarkers

Participants were instructed to fast for 12 hours (except for medication, which they were able to take with water), not to take aspirin for 1 week, and not to smoke for 5 hours before their study appointment. Venous blood samples were obtained for measurement of white blood cell count (WBC) (Panagiotakos *et al.* 2004). Plasma and serum samples were stored at -70°C for measurement of CD40 ligand (Schins *et al.* 2005), CRP (Miller *et al.* 2005), fibrinogen (Kop *et al.* 2002), and interleukin-6 (IL-6) (Empana *et al.* 2005). The laboratory technicians who assayed the inflammatory markers were blinded to the results of the depression interview.

White blood cells (also called leukocytes) are responsible for maintaining the immune system's response to foreign substances and infection (Dorland's Illustrated Medical Dictionary 2003). They have a number of roles in the immune system, including antibody production, attacking and destroying invading microorganisms, and producing substances that kill cancer cells. The WBC measures the number of WBC/volume of blood. We used the Beckman Coulter LH 750 to measure WBC. The interassay coefficient of variation was $\leq 1.7\%$.

Fibrinogen is a protein in the blood plasma that is essential for the coagulation of blood and is converted to fibrin by the action of thrombin. It is involved in clotting and increases in quantity during the acute phase of inflammation (O'Toole 2003). Serum fibrinogen concentrations were determined by the Clauss assay. Dilutions of plasma standard (of known concentrations) are clotted with a high concentration of thrombin, with the resultant clotting time being proportional to the fibrinogen concentration. The clotting time of the participant's plasma was used to read the fibrinogen concentration from the standard curves. The standard assay range is from 60 to 10,000 mg/dL and the interassay and intraassay coefficients of variation are both $< 3\%$.

Inflammation is a normal response to many physical states, including fever, injury, and infection, and CRP is a protein that the body releases in response to inflammation (Kuo *et al.* 2005; Ridker 2003). We used the Roche Integra high-sensitivity assay to measure CRP in the first 229 participants and (owing to a change in the laboratory) the Beckman Extended Range assay to measure CRP in the remaining 755 samples. Results from these two assays were highly correlated ($r = .99$ in 185 participants). The Roche Integra high-sensitivity CRP assay has an interassay coefficient of variation of 3.2%, and the lowest detectable measurement of this assay is .25 mg/L. The Beckman Extended Range high-sensitivity CRP assay has an interassay coefficient of variation of $\leq 6.7\%$, an intraassay coefficient of variation of $< 6.2\%$, and a reportable range of .20–1140 mg/L.

Interleukin-6 is a lymphokine produced by T cells, fibroblasts, macrophages, and various other cells. One of its main functions is to synthesize plasma proteins that are involved in acute phase responses. We used the R&D Systems Quantikine HS IL-6 Immunoassay (R&D Systems, Minneapolis, Minnesota) to determine the concentration of IL-6 from ethylenediaminetetraacetic acid (EDTA) plasma. The interassay coefficient of variation is 6.5%–9.6%, and the intraassay coefficient of variation is 6.9%–7.8%. The reportable range for IL-6 in EDTA plasma is .428–8.87 pg/mL.

The CD40 ligand is an immunoregulatory protein that mediates contact-dependent signals between immune cells (Matthies *et al.* 2006). We used the R&D Systems Quantikine HS CD40 Ligand Immunoassay to measure serum CD40 ligand with the quantitative sandwich enzyme immunoassay technique. The interassay coefficient of variation for this assay was 4.5%–5.4%, and the intrassay coefficient of variation was 6.0%–6.4%, with a reportable range of non-detectable to 11,451 pg/mL.

Other Participant Characteristics

Age, gender, ethnicity, medical history, smoking status, and alcohol consumption were determined by self-reported questionnaire. We measured height and weight and calculated body mass index (weight in kilograms divided by the square of height in meters). Physical activity was determined with the multiple-choice question, “Which of the following statements best describes how physically active you have been during the past month, that is, done activities such as 15–20 minutes of brisk walking, swimming, general conditioning, or recreational sports?” Participants who answered fairly, quite, very, or extremely active (vs. not at all or a little active) were considered physically active.

We assessed left ventricular ejection fraction with a resting echocardiogram. To measure ischemia, we performed a symptom-limited, graded exercise treadmill test according to a standard Bruce protocol and defined ischemia as the presence of a new echocardiographic wall motion abnormality at peak exercise that was not present at rest. We measured systolic and diastolic blood pressure and assayed fasting total cholesterol, high-density lipoprotein cholesterol, and triglycerides with an enzymatic assay. Low-density lipoprotein cholesterol was calculated as (total cholesterol) – (high-density lipoprotein cholesterol) – (triglycerides/5).

Participants were instructed to bring all of their medication bottles to the study appointment, and trained research assistants recorded all current medications. We collected 24-hour urine for measurement of creatinine clearance.

Statistical Analysis

The goal of this study was to examine the association of depression with inflammatory markers in outpatients with stable CHD. Differences in characteristics between participants with and without current depression (by CDIS) were compared with Student *t* test for continuous variables and χ^2 test for dichotomous variables. We used multivariate analysis of variance to compare mean levels of inflammatory markers in depressed and non-depressed participants, adjusted for potential confounding variables (listed in Table 1). We also used multivariate analysis of variance to evaluate the association of PHQ depression score with inflammatory markers as continuous variables. For these analyses, we log transformed CRP and IL-6, because they were not normally distributed, and verified that log transformation resulted in normal distribution. All other biomarkers were normally distributed.

To further evaluate the association between depression and inflammatory markers, we used logistic regression with current depression as the predictor and inflammation as a dichotomous

outcome variable. With the exception of CRP, where we defined inflammation with the established cut point of > 3 mg/L (Pearson *et al.* 2003), we defined inflammation *a priori* as having a biomarker level in the highest quartile. To obtain adjusted risk estimates, we entered all variables from Table 1 into logistic regression models. These results are reported as odds ratios with 95% confidence intervals. We also tested for interactions of depression with gender, smoking, obesity, statin use, β -blocker use, antidepressant use, prior MI, history of congestive heart failure, left ventricular ejection fraction, and inducible ischemia (Albert *et al.* 2001; Danner *et al.* 2003; Ford and Erlinger 2004; Ladwig *et al.* 2005; Lesperance *et al.* 2004). We calculated p values for each of these interaction terms and performed stratified analyses for any interaction with a p value $< .1$. Analyses were performed with SAS 9.1 (SAS Institute, Cary, North Carolina).

Results

Of the 984 participants, 217 (22%) had current depression. Compared with those who were not depressed, depressed participants were younger, less likely to be male, less likely to use statins, and more likely to use antidepressant drugs (Table 1). Depressed participants were also more likely to smoke and to be physically inactive. They had higher creatinine clearance and ejection fraction and were less likely to have inducible ischemia than participants who were not depressed. The ranges of values in our sample were 2.5–18.5 k/cmm for WBC, 255–23,169 pg/mL for CD40 ligand, .06–132 mg/L for CRP (–2.81 to 4.88 mg/L for log CRP), 120–820 mg/dL for fibrinogen, and .24–15.9 pg/mL for IL-6 (–1.45 to 2.76 pg/mL for log IL-6).

Current depression was not associated with increased mean levels of any inflammatory marker in unadjusted or adjusted analyses (Table 2). Likewise, we found no evidence of greater inflammation associated with past year depression, lifetime depression, age of first onset, or number of prior episodes (data not shown). When PHQ score was entered as a continuous variable, we observed no evidence for a linear or non-linear association of depressive symptoms with greater inflammation. In contrast, PHQ score seemed to be negatively associated with fibrinogen ($p = .007$), log IL-6 ($p = .03$), and log CRP ($p = .1$) after adjustment for Table 1 variables.

When we examined the inflammatory markers as dichotomous variables, we also found no evidence of greater inflammation in participants with current depression (Table 3, Figure 1). In contrast, current depression was inversely associated with log CRP ($p = .09$), fibrinogen ($p = .006$), and log IL-6 ($p = .007$) (Table 2). Similarly, the presence of severe depressive symptoms was inversely associated with log CRP ($p = .08$), fibrinogen ($p = .002$), and log IL-6 ($p = .02$) (Table 4).

We found no consistent evidence for interactions of depression with smoking, use of β blockers, use of antidepressant drugs, history of MI, congestive heart failure, left ventricular ejection fraction, or inducible ischemia (p values for interaction $> .10$). However, the inverse association of depression with CRP, IL-6, and fibrinogen seemed to differ by gender, use of statins, and presence of obesity (p values for interaction $< .10$). Depression seemed to be associated with lower CRP, fibrinogen, and IL-6 in men, statin users, and non-obese participants but not in their respective counterparts (Table 5). There was no association of depression with WBC or CD40 ligand in any subgroup stratified by gender, statin use, or obesity (all p values $> .10$).

Discussion

In a sample of 984 outpatients with stable CHD, we found no evidence that depression is associated with increased inflammation. Specifically, we found that depression was not associated with increased WBC, CD40 ligand, CRP, fibrinogen, or IL-6. To the contrary, mean

levels of CRP, fibrinogen, and IL-6 appeared lower in depressed as compared with nondepressed participants. Our results suggest that inflammation is unlikely to be responsible for the adverse cardiovascular outcomes associated with depression in patients with established CHD.

Many studies have found that depression is associated with greater inflammation in otherwise healthy patients without known CHD (Dentino *et al.* 1999; Empana *et al.* 2005; Folsom *et al.* 1993; Kop *et al.* 2002; Ladwig *et al.* 2005; Lahlou-Laforet *et al.* 2006; Maes *et al.* 1997; Miller *et al.* 2002; Panagiotakos *et al.* 2004; Penninx *et al.* 2003; Sluzewska *et al.* 1996; Suarez 2004; Tiemeier *et al.* 2003). Whether depression is associated with inflammation in patients with stable CHD is less clear. Because chronic CHD is itself a pro-inflammatory state (Schins *et al.* 2005), one potential explanation for our observed lack of association between depression and increased inflammation is a ceiling effect in which the presence of depression cannot further increase inflammation in patients with CHD. Participants in our sample were older and more likely to have comorbid medical illnesses than those in other studies after acute coronary syndrome. These factors might contribute to a more chronically elevated state of inflammation in patients with stable CHD. Alternatively, there might be other differences in methodologies that account for the varied results across studies.

We were surprised to find that depression was associated with lower CRP, IL-6, and fibrinogen. This unexpected inverse association should be considered only as hypothesis-generating, unless confirmed by future studies. However, there is some prior evidence that monocytes are decreased in depressed patients (McAdams and Leonard 1993; Rothermundt *et al.* 2001). Because monocytes secrete IL-6 as one of their byproducts, a decreased level of monocytes might result in lower levels of IL-6. Margaglione *et al.* (1996) showed that IL-6 affects the production of plasma fibrinogen via a mechanism involving protein kinase C. Thus, it is possible that decreased levels of IL-6 in depressed individuals lead to lower levels of plasma fibrinogen via this mechanism. Depression is associated with elevated levels of cortisol in patients with CHD (Otte *et al.* 2004), and cortisol is known to have anti-inflammatory properties. It is possible that the increased cortisol in depressed CHD patients contributes to lower levels of inflammation.

Prior work has suggested that the association of depression with inflammation might vary by gender (Danner *et al.* 2003; Ford and Erlinger 2004), statin use (Lesperance *et al.* 2004), and obesity (Ladwig *et al.* 2005). Two studies of young adults without known CHD have reported an association of depression with increased CRP in men but not in women (Danner *et al.* 2003; Ford and Erlinger 2004). In contrast, we found that depression was associated with lower inflammation in men. However, the lack of association we observed between depression and CRP in women is similar to the findings of these two studies. One group of authors suggested that menstrual fluctuations in CRP might render the relationship between depression and CRP more difficult to detect in women (Ford and Erlinger 2004), but the vast majority of women in our sample were post-menopausal, making a menstrual effect unlikely.

A study of patients hospitalized for acute coronary syndrome found that depression was associated with increased CRP in nonusers but not in users of statins (Lesperance *et al.* 2004), suggesting that the absence of association in users might have been due to the anti-inflammatory properties of statins (Albert *et al.* 2001). We found no evidence for an association of depression with greater inflammation in users or nonusers of statins. Conversely, we found that depression was associated with decreased fibrinogen and IL-6 in statin users and no evidence of an association in statin nonusers.

A study of middle-age healthy men demonstrated that depression was associated with elevated CRP in obese but not in non-obese patients (Ladwig *et al.* 2005). We found no evidence of

elevated CRP in obese patients. In contrast, we found that depression was associated with lower CRP, fibrinogen, and IL-6 in non-obese patients. These inconsistencies across studies increase the likelihood that the inverse association we observed between depression and inflammation might be due to chance. However, the absolute lack of association we observed between depression and increased inflammation remains a robust finding.

Strengths of our study include its large sample of outpatients with stable CHD, comprehensive measurement of potential confounding variables, and standardized measurement of inflammatory markers after fasting for 12 hours, abstaining from smoking for 5 hours, and not taking aspirin for a week. However, several limitations must be considered in interpreting our results. First, because our study population consisted of mostly older men, our results might not generalize to all populations. Second, it is possible that the CDIS resulted in some misclassification of depression, because use of a standardized instrument cannot replace the diagnosis of depression by a clinician. Finally, owing to the cross-sectional study design, we are not able to determine the causal direction of any relation (or lack of relation) between depression and inflammatory markers.

In summary, we found no evidence that depression is associated with elevated levels of inflammation in patients with stable CHD. We observed an inverse association of depression with CRP, fibrinogen, and IL-6 that needs confirmation in future studies. In the meantime, our results indicate that greater inflammation is unlikely to explain the adverse cardiovascular outcomes associated with depression in patients with CHD.

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Figure 1. Proportion with inflammation by depression status (all *p* values NS). WBC, white blood cell count; CRP, C-reactive protein; IL-6, interleukin-6.

Table 1

Characteristics of 984 Participants, Divided by the Presence of Depression

Variables	Current Depression n = 217	No Current Depression n = 767	p Value
Demographic:			
Age (years)	62 ± 11	68 ± 11	< .0001
Male	149 (69%)	652 (85%)	< .0001
White	131 (60%)	464 (61%)	.96
Medical history:			
Myocardial infarction	107 (50%)	420 (55%)	.17
Congestive heart failure	40 (19%)	133 (17%)	.71
Diabetes mellitus	68 (31%)	192 (25%)	.07
Medication use:			
Statin	126 (58%)	506 (66%)	.03
Beta blocker	119 (55%)	446 (58%)	.38
Hormone replacement therapy	14 (6%)	32 (4%)	.16
Aspirin	168 (77%)	593 (77%)	.97
Antidepressant	102 (47%)	79 (10%)	< .0001
Other characteristics:			
Regular alcohol use	66 (31%)	219 (29%)	.61
Current smoking	63 (29%)	132 (17%)	.0001
Body Mass Index (kg/m ²)	29 ± 5.6	28 ± 5.3	.06
Physically active	114 (53%)	508 (66%)	.0002
Creatinine clearance (mL/min)	87.4 ± 30.2	79.4 ± 28	.0009
Cardiac function:			
Resting left ventricular ejection fraction	.63 ± .08	.61 ± .10	.009
Systolic blood pressure (mm Hg)	133 ± 22	133 ± 21	.96
Diastolic blood pressure (mm Hg)	75 ± 12	74 ± 11	.26
Low-density lipoprotein (mg/dL)	107 ± 37	104 ± 33	.24
High-density lipoprotein (mg/dL)	45 ± 15	46 ± 14	.79
Inducible ischemia	35 (18%)	182 (26%)	.04

Table 2

Mean Levels of Inflammatory Markers by Depression Status

	Unadjusted Mean ($\pm$ SE)			Mean ($\pm$ SE), Adjusted for Table 1 Variables		
	Current Depression n = 217	No Current Depression n = 767	p Value	Current Depression n = 217	No Current Depression n = 767	p Value
WBC (K/cmm)	6.8 $\pm$.13	6.5 $\pm$.07	.08	7.1 $\pm$.23	7.1 $\pm$.21	.65
CD40 Ligand (pg/mL)	5933 $\pm$ 212	5851 $\pm$ 112	.73	5760 $\pm$ 390	5918 $\pm$ 351	.60
Log CRP	.74 $\pm$.09	.70 $\pm$.05	.65	1.4 $\pm$.15	1.6 $\pm$.13	.09
Fibrinogen (mg/dL)	374 $\pm$ 6	397 $\pm$ 3	.001	400 $\pm$ 10.5	423 $\pm$ 9.5	.006
Log IL-6	.86 $\pm$.05	.98 $\pm$.03	.03	1.05 $\pm$.08	1.2 $\pm$.07	.007

Table 3

Association of Current Depression with Inflammation

	Unadjusted OR (95% CI)	<i>p</i> Value	Adjusted OR* (95% CI)	<i>p</i> Value
WBC (> 7.5 K/cmm)	1.2 (.82–1.6)	.41	1.0 (.62–1.6)	.97
CD40 Ligand (> 7531 pg/mL)	1.3 (.95–1.9)	.10	1.3 (.85–2.0)	.22
CRP (> 3.0 mg/L)	.95 (.70–1.3)	.75	.66 (.43–1.0)	.07
Fibrinogen (> 443 mg/dL)	.69 (.47–1.0)	.05	.59 (.35–1.0)	.05
IL-6 (> 4.19 pg/mL)	.94 (.66–1.3)	.74	.71 (.43–1.2)	.19

* Adjusted for all Table 1 variables.

Table 5

Mean $\pm$ Standard Error Levels of Inflammatory Markers by Depression Status, Adjusted for Table 1 Variables, Stratified by Gender, Statin Use, and Obesity

	Current Depression n = 217	No Current Depression n = 767	p Value
Women (n = 183)			
Log CRP	1.7 $\pm$.27	1.8 $\pm$.24	.54
Fibrinogen (mg/dL)	415 $\pm$ 18.2	403 $\pm$ 16.4	.46
Log IL-6	1.1 $\pm$.17	1.1 $\pm$.16	.96
Men (n = 801)			
Log CRP	.87 $\pm$.13	1.1 $\pm$.11	.07
Fibrinogen (mg/dL)	398 $\pm$ 9.7	429 $\pm$ 7.8	.001
Log IL-6	1.0 $\pm$.07	1.2 $\pm$.06	.002
Statin non-users (n = 352)			
Log CRP	1.8 $\pm$.24	1.8 $\pm$.21	.64
Fibrinogen (mg/dL)	419 $\pm$ 17.9	433 $\pm$ 15.5	.36
Log IL-6	1.1 $\pm$.13	1.1 $\pm$.11	.95
Statin users (n = 632)			
Log CRP	1.0 $\pm$.20	1.3 $\pm$.19	.12
Fibrinogen (mg/dL)	388 $\pm$ 14.2	417 $\pm$ 13.2	.006
Log IL-6	1.0 $\pm$.11	1.3 $\pm$.10	.0007
Obese (body mass index $\geq$ 30 kg/m ²) (n = 317)			
Log CRP	1.7 $\pm$.23	1.7 $\pm$.22	.99
Fibrinogen (mg/dL)	429 $\pm$ 17.4	434 $\pm$ 16.2	.72
Log IL-6	1.2 $\pm$.13	1.2 $\pm$.12	.82
Not obese (body mass index < 30 kg/m ²) (n = 667)			
Log CRP	1.2 $\pm$.20	1.5 $\pm$.17	.04
Fibrinogen (mg/dL)	390 $\pm$ 13.6	420 $\pm$ 11.9	.003
Log IL-6	.94 $\pm$.10	1.2 $\pm$.09	.002