Relationship between C-reactive protein and intima-media thickness in the carotid and femoral arteries and to antibodies against oxidized low-density lipoprotein in healthy men: the Atherosclerosis and Insulin Resistance (AIR) study

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ABSTRACT

Results from several recent reports have linked high serum C-reactive protein (CRP) levels to atherosclerotic disease and its complications. The aims of the present study were to investigate the relationship between CRP levels and subclinical atherosclerosis, as measured by ultrasound in the carotid and femoral arteries; and also to examine whether CRP levels are associated with antibodies to oxidized low-density lipoprotein (Ox-LDL). The study group (n = 391) consisted of clinically healthy 58-year-old men recruited from the general population. CRP and antibody titres to Ox-LDL were measured by ELISA. The results showed an association between CRP and ultrasound-assessed subclinical atherosclerosis in the femoral artery (r = 0.14, P = 0.010), and also between CRP and systolic blood pressure, diastolic blood pressure, heart rate, triglycerides, high-density lipoprotein, body mass index, waist-to-hip ratio (WHR), blood glucose, cigarette-years and antibody titres to ox-LDL (r = 0.19, P < 0.001). In this clinically healthy population of 58-year-old men, CRP levels were associated with both intima-media thickness and plaque occurrence in the femoral artery. The association between CRP and femoral atherosclerosis was not independent of smoking, serum LDL cholesterol, or systolic blood pressure. CRP levels were independently related to abdominal obesity measured as WHR, smoking and antibody titres to Ox-LDL.

INTRODUCTION

C-reactive protein (CRP), an acute-phase protein, is a sensitive marker of inflammation and infection [1]. Inflammation has also been postulated to play an important role in atherosclerosis development [2]. Results from several recent reports have linked high serum CRP to atherosclerotic disease and its complications, as summarized in two overviews [3,4]. For example, elevated levels of CRP have been found among subjects with stable and unstable angina who are at risk of future myocardial infarction or sudden death [5], and in subjects at high risk of coronary death [6]. CRP has also been found to have a predictive value for coronary heart disease in initially healthy men [6,7]. The production of CRP is regulated by cytokines, including interleukins 1 and 6 and tumour necrosis factor-α [8]. Although reportedly expressed by some mono-
nuclear populations, these cells do not secrete CRP [9,10]. CRP is exclusively produced by hepatocytes, but the stimuli responsible for the generally modest elevations in plasma CRP associated with coronary events are not known. CRP has been shown to be associated with other measures of unspecific inflammation, such as white cell count, fibrinogen and albumin [11]. However, to our knowledge no previous population-based study has investigated the relationship between CRP, as a marker of unspecific inflammation, and the immune response to oxidized low-density lipoprotein (Ox-LDL), a proposed antigen for atherosclerosis development [12].

Measurement of intima-media thickness (IMT) is used in pathophysiological studies of the atherosclerotic process, e.g. in studies of the factors regulating the early development of atherosclerosis in the carotid and femoral arteries. An increased IMT is also used as an index of generalized atherosclerosis, including coronary atherosclerosis [13,14], and carotid artery IMT has also been shown to be associated with coronary atherosclerosis, as measured by coronary angiography in several studies [15,16].

Accordingly, the aim of the present study was to investigate the relationship between CRP levels and subclinical atherosclerosis in clinically healthy men, as measured by ultrasound of the carotid and femoral arteries. The aim was also to examine the association between CRP levels, risk factors for atherosclerotic disease and antibodies to Ox-LDL, as an indicator of the immune response in the atherosclerotic process.

METHODS

Study subjects

The study criteria was 58-year-old men of Swedish ancestry. Exclusion criteria were cardiovascular disease (i.e. a history of myocardial infarction, angina pectoris, heart failure, stroke, intermittent claudication, treatment for hypertension or hyperlipidaemia), or other clinically overt disease, treatment with cardiovascular drugs that might disturb the measurements performed in the study, or unwillingness to participate. The subjects were randomly selected among men in the County Council register of Göteborg, Sweden, and were invited to a screening examination.

A power calculation indicated that it was necessary to recruit at least 300 men in the study (alpha = 0.05 and beta = 0.20), with the main objective to examine the relationship between insulin sensitivity and ultrasound-assessed atherosclerosis. This calculation was based on data from the Atherosclerosis Risk in Communities (ARIC) study [17], and the S. D. (0.015 mm) for our data from the Atherosclerosis Risk in Communities (ARIC) study [17], and the S. D. (0.015 mm) for our measurement was based on data from the Atherosclerosis Risk in Communities (ARIC) study [17], and the S. D. (0.015 mm) for our method to measure IMT.

The present report is a substudy in that project [18]. The subjects received both written and oral information before they gave their consent to participate. The study was approved by the Ethics Committee at Sahlgrenska University Hospital, Gothenburg, Sweden.

Measurements

All measurements were performed in the morning. Venous blood samples were drawn after a fasting period of 10–12 h, serum was separated and frozen within 4 h at −70 °C. Body weight, height, waist and hip circumference were measured, and body mass index (BMI) and waist-to-hip ratio (WHR) were calculated.

Information on general health and smoking habits were obtained by a self-administered questionnaire. The total number of years of smoking was multiplied by the number of cigarettes smoked daily. The product was called ‘cigarette-years’.

Antibody titres to modified lipoproteins

Antibody titres were determined with a solid-phase ELISA (96-well plates) developed at the Wallenberg Laboratory, Gothenburg, Sweden, as described earlier [19]. Antibody titre was defined as: titre = absorbance (subject serum-postcoat)/(internal antibody titre standard serum-postcoat).

For IgG, the post-coated wells gave no absorbance, therefore this correction was made only for IgM. On each plate two different internal standard serum samples were repeatedly performed. The absorbances for these two samples, named internal control sample (ICS) and internal standard sample (ISS), respectively, were used to calculate the ratio of ICS/ISS which was used as internal antibody titre standard. When using the following pre-defined criteria, the variability has earlier been shown to be satisfactory [19]; if the absorbance of ISS was outside the 90% confidence interval, calculated on the basis of all readings of the internal standard (n = 25) in the experiment, the whole plate should be re-analysed. The plate should also be re-analysed if the ICS/ISS ratio was outside the 90% confidence interval for this ratio.

When using these pre-specified criteria, S. D.s for the mean value of the ICS/ISS ratio (i.e. internal antibody titre standard used) from all plates were 0.07 and 0.03 for IgG titres against Ox-LDL (IgG–Ox-LDL Ab; where Ab is antibody) and malondialdehyde (MDA)-LDL (IgG–MDA-LDL Ab), respectively; and 0.06 and 0.06 for IgM titres against Ox-LDL (IgM–Ox-LDL Ab) and MDA-LDL (IgM–MDA-LDL Ab) respectively.

Ultrasoundography

IMT

Examination was performed with an ultrasound scanner (Acuson 128; Acuson Corp., Mountain View, CA, U.S.A.) with a 7 MHz linear transducer aperture of 38 mm. The electrocardiographic signal (lead II) was simultaneously recorded to synchronize the image cap-
ture of the top of the R wave to minimize variability during the cardiac cycle. Both the left and right carotid arteries were scanned at the level of the bifurcation and images for IMT measurements were recorded from the far wall in the common carotid artery and the carotid artery bulb, and from the right femoral artery. The software program gives the average thickness of the intima-media complex. Measurements in the common femoral artery were made in a similar way as for the carotid artery, but along a 15 mm long section proximal to the bifurcation [20]. IMT was defined as the distance from the leading edge of the lumen–intima interface to the leading edge of the media–adventitia interface of the far wall. At the position of the thickest part of the wall (visually judged), a frozen longitudinal image was captured and recorded on videotape. A short sequence of real-time images was also recorded on videotape to assist in the interpretation of the frozen images. The images were measured in an automated analysing system [21], based on automatic detection of the echo structures in the ultrasound image, but with the option to make manual corrections by the operator. The inter-observer variations for IMT have been shown to be satisfactory [22].

Assessment of plaque occurrence
The carotid and femoral arteries were scanned both longitudinally and transversely to assess the occurrence of plaques [20]. A plaque was defined as a distinct area with an IMT more than 50% thicker as compared with neighbouring sites (visually judged). A semi-quantitative subjective scale was used to grade the size of plaques into grade 1, one or more small plaques (less than approx. 10 mm²); grade 2, moderate-to-large plaques (the differentiation between grades 1 and 2 was made subjectively in most cases, and quantitative measurements were made in the computerized system [23] only when the correct classification was not obvious to the observer); grade 3, plaques giving flow disturbances [20]. In the present study, no plaque of grade 3 was found in the femoral artery and three subjects had plaques of grade 3 in the carotid artery. Therefore plaques of grade 2 and 3 were merged into one group of moderate-to-large plaques. This analysis included plaques in the near wall as well as the far wall of the vessel. Analyses of plaques were performed in both the right and left carotid artery. The largest plaque in either artery was used in the present analysis. In a re-reading reproducibility study (n = 45) of plaque size, there were high correlation coefficients for the right and left carotid arteries (rFL = 0.96 and rSL = 0.96 respectively), and also for the right femoral artery (rFL = 0.86).

Biochemical analysis
Cholesterol and triglyceride levels were determined by fully enzymic techniques [24,25]. High-density lipoprotein (HDL) was determined after precipitation of apolipoprotein B-containing lipoproteins with manganese chloride and dextran sulphate [26]. LDL cholesterol was calculated as described by Friedewald et al. [27]. Blood glucose was measured with the glucose oxidase technique. Plasma insulin was determined in all subjects by RIA (Pharmacia insulin RIA; Pharmacia Diagnostics, Uppsala, Sweden). All lipid analyses were performed at the Wallenberg Laboratory. CRP was measured by commercially available ELISA kits (Medix Biochemica, Kauniainen, Finland). Frozen serum samples from 36 healthy men obtained at the same occasion were evaluated twice on different days, and the correlation coefficient was 0.99 (no systematic difference).

Statistical analysis
All statistics were analysed using SPSS for Windows 8.0 (Chicago, IL, U.S.A.). The subject group was divided into tertiles for CRP when describing the characteristics of the studied men and in order to analyse trends in characteristics by CRP tertile. A total of 13 subjects had CRP concentrations above the upper reference level (10.0 mg/l; see Figure 1) and were excluded from the analyses in the present paper. Furthermore, 11 subjects had no serum samples available. The total number of subjects included was, therefore, 367.

Mantel’s test for linear association was used to test the relationship between tertiles of CRP and the variables displayed in Tables 1, 2 and 4. The chi-square test was used to investigate the relationship between tertiles of CRP and plaque occurrence. Non-parametric Spearman’s rank correlation test was used in the correlation analysis, with the relationship illustrated by Pearson’s correlation coefficient (r). A forward stepwise multiple-regression model was used to study the determinants of log CRP and log femoral IMT. CRP was log-transformed before statistical testing to improve skewness. P < 0.05 (two-sided) was regarded as statistically significant.

RESULTS
Characteristics of the subjects by tertiles of logCRP
The distribution of CRP in the study group is shown in Figure 1. A total of 13 subjects had CRP concentrations above the upper reference level (10.0 mg/l), indicative of an acute inflammatory response, and were therefore excluded from all analyses in the present paper. No significant differences were found between subjects with CRP levels above 10 mg/l and subjects with CRP levels below 10 mg/l for blood pressure, pulse pressure, total cholesterol, LDL cholesterol, triglycerides, body-mass index, waist-hip ratio, fasting blood glucose, antibody titres to Ox-LDL or IMT. However, subjects with elevated CRP levels had significantly lower HDL levels

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Figure 1 Distribution of serum concentrations of CRP in 380 clinically healthy 58-year-old men

Table 1 Study group characteristics by tertiles of logCRP

<table>
<thead>
<tr>
<th>Tertile</th>
<th>CRP (mg/l)</th>
<th>BMI (kg/m²)</th>
<th>WHR</th>
<th>SBP (mmHg)</th>
<th>DBP (mmHg)</th>
<th>HR (beats/min)</th>
<th>Total cholesterol (mmol/l)</th>
<th>LDL cholesterol (mmol/l)</th>
<th>Triglycerides (mmol/l)</th>
<th>HDL cholesterol (mmol/l)</th>
<th>Fasting blood glucose (mmol/l)</th>
<th>Cigarette-years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lowest tertile (n = 122)</td>
<td>0.40 (0.03–0.69)</td>
<td>24.8 ± 3.8</td>
<td>0.92 ± 0.06</td>
<td>120 ± 14</td>
<td>70 ± 10</td>
<td>59 ± 9</td>
<td>5.92 ± 1.06</td>
<td>3.95 ± 0.96</td>
<td>1.16 (0.53–4.31)</td>
<td>1.37 ± 0.37</td>
<td>4.84 ± 1.18</td>
<td>210 ± 320</td>
</tr>
<tr>
<td>Middle tertile (n = 123)</td>
<td>1.10 (0.69–1.89)</td>
<td>26.5 ± 4.5</td>
<td>0.95 ± 0.07</td>
<td>125 ± 18</td>
<td>73 ± 11</td>
<td>61 ± 9</td>
<td>6.06 ± 1.08</td>
<td>4.15 ± 0.95</td>
<td>1.34 (0.41–6.00)</td>
<td>1.25 ± 0.36</td>
<td>4.80 ± 0.99</td>
<td>296 ± 390</td>
</tr>
<tr>
<td>Highest tertile (n = 122)</td>
<td>3.35 (1.92–9.69)</td>
<td>27.8 ± 4.3</td>
<td>0.97 ± 0.06</td>
<td>125 ± 17</td>
<td>73 ± 10</td>
<td>61 ± 7</td>
<td>6.07 ± 1.07</td>
<td>4.07 ± 0.94</td>
<td>1.47 (0.47–9.89)</td>
<td>1.24 ± 0.40</td>
<td>5.05 ± 1.39</td>
<td>467 ± 467</td>
</tr>
</tbody>
</table>

Table 2 Antibody titres to modified LDL by tertiles of logCRP

<table>
<thead>
<tr>
<th>Ab type</th>
<th>CRP (mg/l)</th>
<th>IgG-titres</th>
<th>IgM-titres</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Ox-LDL</td>
<td>MDA-LDL</td>
</tr>
<tr>
<td>Lowest tertile</td>
<td>0.40 (0.03–0.69)</td>
<td>1.06 ± 0.37</td>
<td>1.08 ± 0.16</td>
</tr>
<tr>
<td>Middle tertile</td>
<td>1.10 (0.69–1.89)</td>
<td>1.26 ± 0.51</td>
<td>1.12 ± 0.17</td>
</tr>
<tr>
<td>Highest tertile</td>
<td>3.35 (1.92–9.69)</td>
<td>1.14 ± 0.31</td>
<td>1.24 ± 0.40</td>
</tr>
</tbody>
</table>

Antibodies to modified LDL by tertiles of logCRP

There was a positive trend in IgG–Ox-LDL Ab and IgG–MDA-LDL Ab respectively by tertiles of CRP (Table 2). There was no statistically significant trend in IgM titres to modified LDL by CRP tertiles (Table 2).

Correlations between logCRP, cardiovascular risk factors and antibody titres to modified LDL

CRP showed statistically significant associations with systolic blood pressure (r = 0.15, P = 0.029), diastolic blood pressure (r = 0.14, P = 0.016), heart rate (r = 0.14, P = 0.007), triglycerides (r = 0.19, P < 0.001), HDL (r = −0.18, P < 0.001), BMI (r = 0.29, P < 0.001), WHR (r = 0.35, P < 0.001), blood glucose (r = 0.10, P = 0.021), IgG–Ox-LDL Ab (r = 0.19, P < 0.001), IgG–MDA-LDL Ab (r = 0.20, P < 0.001) and cigarette-years (r = 0.28, P < 0.001).
375C-reactive protein, oxidized low-density lipoprotein antibodies and intima-media thickness

Table 3  Stepwise multiple-regression analyses showing contributions to the variance of logCRP
The model also included systolic blood pressure, heart rate, triglycerides, HDL, BMI, and fasting blood glucose, which did not make a statistically significant contribution to the variance in log CRP. ** P < 0.001.

<table>
<thead>
<tr>
<th>Variable</th>
<th>β-coefficient (S.E.M.)</th>
<th>P</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP</td>
<td>0.17***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>2.10 (0.39)</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>Cigarette-years</td>
<td>0.0002 (0.00)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>IgG–Ox-LDL Ab</td>
<td>0.13 (0.05)</td>
<td>0.010</td>
<td></td>
</tr>
</tbody>
</table>

In a multiple-regression model with log CRP as dependent variable and the above mentioned variables as co-variates, the following variables turned out to be independent predictors of log femoral IMT: cigarette-years (β coefficient = 0.0002 ± 0.00, P < 0.001; F-value = 43), LDL cholesterol (β coefficient = 0.03 ± 0.01, P < 0.001; F-value = 43) and systolic blood pressure (β coefficient = 0.002 ± 0.000, P = 0.001; F-value = 35). These variables explained 23% of the variability in femoral IMT (P < 0.001). Hence, no independent association between CRP and femoral IMT was observed.

**DISCUSSION**

To our knowledge this is the first study to demonstrate an association between CRP, a biochemical marker of inflammation, and antibody titres to Ox-LDL, a suggested major antigenic factor in the atherosclerotic process in a population sample of healthy men. Furthermore, a univariate association was found between CRP and ultrasound-assessed atherosclerosis in the femoral artery.

These observations were made in a group of 58-year-old clinically healthy men, chosen from the general population. A confounding factor in the present study may have been elevations of CRP caused by diseases unrelated to the mechanisms under study. Therefore the 13 subjects with elevated CRP levels were excluded from the analyses.

We observed an association between serum CRP levels and sub-clinical atherosclerosis in the common femoral artery, either measured as plaque occurrence or increased IMT. The relationship was, however, not independent of other risk factors. The independent co-variates to IMT in the femoral artery turned out to be smoking, LDL

Table 4  IMT and plaque occurrence on the basis of tertiles of logCRP

<table>
<thead>
<tr>
<th>CRP</th>
<th>Lowest tertile (n = 122)</th>
<th>Middle tertile (n = 123)</th>
<th>Highest tertile (n = 122)</th>
<th>P value for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMT (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carotis communis</td>
<td>0.79 ± 0.13</td>
<td>0.81 ± 0.12</td>
<td>0.81 ± 0.14</td>
<td>0.098</td>
</tr>
<tr>
<td>Carotis bulb</td>
<td>0.96 ± 0.23</td>
<td>1.03 ± 0.30</td>
<td>0.99 ± 0.25</td>
<td>0.300</td>
</tr>
<tr>
<td>Femoralis communis</td>
<td>1.00 ± 0.43</td>
<td>1.03 ± 0.49</td>
<td>1.13 ± 0.48</td>
<td>0.029</td>
</tr>
<tr>
<td>Carotid plaque occurrence</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No plaques (%)</td>
<td>62</td>
<td>50</td>
<td>57</td>
<td>0.296</td>
</tr>
<tr>
<td>Moderate to large plaques (%)</td>
<td>18</td>
<td>31</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Femoral plaque occurrence</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No plaques (%)</td>
<td>68</td>
<td>67</td>
<td>54</td>
<td>0.001</td>
</tr>
<tr>
<td>Moderate-to-large plaques (%)</td>
<td>17</td>
<td>20</td>
<td>39</td>
<td></td>
</tr>
</tbody>
</table>

C-reactive protein, oxidized low-density lipoprotein antibodies and intima-media thickness

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cholesterol and systolic blood pressure. These variables explained 23% of the variability in femoral IMT. Smoking was the variable that also showed the strongest association with CRP. The fact that there was no similar significant association between sub-clinical atherosclerosis in the carotid artery and CRP levels raises the question of whether there is a true difference between the carotid and femoral artery territories regarding accompanying inflammation as measured by CRP. In a previous study of patients who had suffered from an acute myocardial infarction [28], plasma CRP concentrations did not differ between patients with vessel wall thickening or non-stenosing plaques in the carotid artery and those without any such changes. Another study [11] provided results which showed no relation between common carotid IMT and CRP in healthy elderly subjects. Hak et al. [29] did find a statistically significant association between common carotid IMT and CRP levels in healthy middle-aged women, but the association was weak and limited to ever-smokers. Taken together, available data do not consistently demonstrate an association between carotid artery atherosclerosis and circulating CRP concentrations.

Our observation of a relation between CRP and femoral artery atherosclerosis is supported both by a previously reported cross-sectional study in patients who had suffered from a myocardial infarction [28], and a prospective study demonstrating that plasma CRP elevation predicts future peripheral artery disease among apparently healthy men [30].

A possible explanation to this consistent finding of an association between femoral artery disease and CRP could be the fact that smoking might be a more important risk factor for atherosclerotic disease in the femoral than the carotid artery [31,32]. Smoking is also one of the strongest determinants of raised CRP levels and may be a confounder that is difficult to adjust for in the multivariate analyses.

It is unknown whether CRP exerts a direct effect on the atherosclerotic process or if serum CRP elevation is a phenomenon secondary to the impact of other factors. In the first place, CRP has been found to bind to lipoproteins and to activate complement [33]. Immunohistochemical studies of human coronary arteries have revealed that CRP is deposited in early atherosclerotic lesions and that the grade of CRP immunoreactivity is associated with relative intimal thickness [33,34].

Secondly, previous studies have shown a relationship between CRP and traditional risk factors for cardiovascular disease, e.g. BMI, WHR, low HDL cholesterol, triglycerides and smoking [11,29]. Similar observations were made in the present study in which circulating CRP concentrations were associated with blood pressure, heart rate, triglycerides, HDL, BMI, WHR and smoking. In a stepwise multiple-regression model WHR, cigarette-years and IgG–Ox-LDL Ab turned out to be independently predictive of CRP levels and explained 17% of the variability.

The observation that CRP was independently associated with WHR, as a measure of central or abdominal obesity may be explained by a regulatory link between adipose tissue and the hepatic production of CRP [35,36]. There is experimental evidence showing that adipocytes produce tumour necrosis factor-α [36], which, in turn, induces interleukin-6 synthesis [37]. Interleukin-6 is a prime regulator of CRP synthesis in the liver [8,39]. This hypothesis is also supported by studies showing that central obesity is associated with elevated serum tumour necrosis factor-α concentrations [40] and that subjects with high BMI, WHR and insulin resistance have high CRP levels [41].

The second independent co-variate to CRP was the number of cigarette-years. The relationship between smoking and biochemical markers of inflammation such as fibrinogen or serum CRP levels is well established [11,29,30,42]. The mechanisms by which tobacco use causes an inflammatory response are not clarified, although the observation that only smoking and not smokeless tobacco is associated with biochemical markers of inflammation indicates that the inhalation of tobacco smoke is of more importance than nicotine in itself [42].

The third independent predictor of CRP levels was IgG–Ox-LDL Ab. This finding is very interesting, since several lines of evidence support the concept that Ox-LDL may be a key antigen in atherosclerosis. T-cell clones responsive to Ox-LDL have been isolated from human lesions [43]. Immune responses to Ox-LDL have also been observed in apolipoprotein E knockout mice, an animal model for atherosclerosis development [44]. Antibodies against epitopes of Ox-LDL have been found in several studies in both human [45,46] and rabbit [45–47] plasma, and in atherosclerotic lesions. Furthermore, there are case-control studies suggesting an elevated antibody titre against Ox-LDL in patients with various manifestations of atherosclerotic disease [48–52]. High titres of antibodies have also been found to be independent predictors of progression of carotid atherosclerosis [53]. Any mechanisms by which Ox-LDL might cause an increased hepatic production of CRP have not yet been established. On the contrary, macrophages which have internalized Ox-LDL have a suppressed production of tumour necrosis factor-α [54].

We conclude that in this healthy population of 58-year-old men with a high prevalence of sub-clinical atherosclerotic plaques in the femoral and carotid arteries, serum CRP levels were associated with both increased femoral artery IMT and plaque occurrence; that this association between CRP and femoral atherosclerosis was not independent of smoking, serum LDL cholesterol, and systolic blood pressure; and that CRP was independently related to abdominal obesity...
measured as WHR, smoking and antibody titres to Ox-LDL. This study was not designed to examine whether CRP had a direct effect on the atherosclerotic process.

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