Lipoproteins and their subfractions in psoriatic arthritis: identification of an atherogenic profile with active joint disease

S M Jones, C P D Harris, J Lloyd, C A Stirling, J P D Reckless, N J McHugh

Abstract

Objectives—(a) To characterise the lipid profile in psoriatic arthritis and investigate whether there are similarities to the dyslipoproteinaemia reported in rheumatoid arthritis and other inflammatory forms of joint disease; (b) to investigate whether there is an atherogenic lipid profile in psoriatic arthritis, which may have a bearing on mortality.

Methods—Fasting lipids, lipoproteins, and their subfractions were measured in 50 patients with psoriatic arthritis and their age and sex matched controls.

Results—High density lipoprotein cholesterol (HDL cholesterol) and its third subfraction, HDL, cholesterol, were significantly reduced and the most dense subfraction of low density lipoprotein (LDL), LDL2, was significantly increased in the patients with psoriatic arthritis. Twenty patients with active synovitis had significantly lower total cholesterol, LDL cholesterol, and HDL cholesterol than their controls. 25% of the patients with psoriatic arthritis had raised Lp(a) lipoprotein levels (>300 mg/l) compared with 19% of controls, but this was not statistically significant.

Conclusion—Raised levels of LDL, and low levels of HDL cholesterol are associated with coronary artery disease. Such an atherogenic profile in a chronic inflammatory form of arthritis is reported, which may be associated with accelerated mortality.

Patients with rheumatoid arthritis (RA) have an accelerated mortality compared with the general population, which may be attributed in part to an increased risk of cardiovascular disease. Active RA is associated with an abnormal lipid profile (dyslipidaemia), though the relative contribution of this to the increased mortality is uncertain. Altered concentrations of serum transthyretin and synovial lipids and lipoproteins may occur, including reduced serum cholesterol, decreased serum triglycerides, and altered apoprotein concentrations. In addition, decreased cholesterol in low density lipoprotein (LDL), and cholesterol in high density lipoprotein (HDL) have been found, especially in association with active disease. The causes of mortality in patients with psoriatic arthritis are less well documented, though there is evidence that mortality may be increased. A pattern of dyslipoproteinaemia, similar to that seen in RA, has previously been reported in psoriatic arthritis, which normalises with a reduction in disease activity.

Routine plasma lipid measurement, which does not take account of lipoprotein composition, may not identify patients with risk factors for atherosclerosis. For instance, a reduction in HDL cholesterol contributes to a risk of atheroma, whereas a concomitant reduction in total LDL cholesterol may be protective. In population studies a low HDL cholesterol associated with a high LDL cholesterol has been associated with an increased risk of atherosclerosis. Increased knowledge of lipoprotein composition, and the identification of lipoprotein subfractions, have added to our understanding of the mechanisms of metabolic disturbance in lipid disorders. It is now well established that the smallest, most dense component of LDL (LDL3 in our study), is the most important factor in contributing to atheroma.

Lp(a) lipoprotein has emerged as an important and independent contributing factor to the risk of atherosclerosis. It is a high density lipoprotein in which apoprotein B 100, the protein moiety of LDL, is linked to apoprotein(a) by one or two disulphide bridges. Increased levels of Lp(a) lipoprotein have been found in RA, but have not previously been measured in psoriatic arthritis. In this study we performed a detailed analysis of lipoprotein composition in psoriatic arthritis and found changes that may lead to increased atherosclerosis and shortened survival.

Patients and methods

PATIENTS AND CONTROLS

Fifty patients attending the psoriatic arthritis clinic at the Royal National Hospital for Rheumatic Diseases were studied. Twenty of these patients had active joint disease, and LDL and very low density lipoprotein (VLDL) subfraction data were obtained for 13 of these. All patients had psoriasis, an inflammatory arthropathy, and were seronegative for rheumatoid factor. Age and sex matched controls were obtained from a concurrent local population survey. Table 1 shows demographic details for both patients and controls. The exclusion criteria for patients and controls were diabetes, hypothyroidism, renal disease, excess alcohol intake, current treatment with a lipid lowering agent, admission to hospital with a severe illness within the previous three months, pregnancy, and breast feeding. Excess alcohol intake was defined as an intake of greater than the recommended upper limit for alcohol consumption for men and women (28 units for
Lipoproteins in psoriatic arthritis

905

measured in these subfractions by cholesterol respectively. Cholesterol and triglyceride were
manganese chloride, and dextran sulphate
tation with sodium dodecyl sulphate, heparin-
trifugation were analysed immediately.

−20

trifuged within two hours of collection, and kept

measured by cholesterol and triglyceride were

determination of the severity and activity of skin

>1.72 mPa), and/or CRP (>10 mg/l). The

a raised ESR (>20 mm/1st h) and/or viscosity

measured in all patients. Active disease was defined as at least

13 patients (nine female, four male) with

polyarthritis, thiazides, β blockers, oral contraceptives,
and hormone replacement therapy. Five of the
control group were taking oral contraceptives and hormone replacement therapy. Five of the
control group were taking oral contraceptives and seven hormone replacement therapy. None
of the controls for the 13 patients on whom LDL and VLDL subfractions were measured were taking hormone replacement therapy.

All patients and controls were eating a normal Western diet. Body mass indices (kg/m²) were
calculated for all patients. Blood samples were taken from all patients after a 14 hour fast, cen-
trifuged within two hours of collection, and kept at −20°C until analysis. Samples for ultracen-
trifugation were analysed immediately.

ASSESSMENT OF DISEASE ACTIVITY

The inflammatory markers, plasma viscosity, erythrocyte sedimentation rate (ESR), and C
reactive protein (CRP) were measured in all patients. Active disease was defined as at least
one clinically inflamed joint in association with a raised ESR (>20 mm/1st h) and/or viscosity
(>1.72 mPa), and/or CRP (>10 mg/l). The psoriasis area and severity index (PASI) were used to record the severity and activity of skin
disease.16

MEASUREMENT OF LIPOPROTEINS

Automated measurements were performed using an Abbott VP supersystem autoanalyzer
(Abbott Diagnostic Division, Maidenhead, UK). Lipids and lipoproteins were measured by
standard precipitation techniques. Briefly, VLDL, total HDL, and its third, most dense sub-
fraction (HDL3) were prepared by precipitation techniques. Briefly, plasma was adjusted to a density of
1.118 g/ml by adding solid sodium chloride (NaCl). Density adjusted plasma (2 ml) was
layered onto the surface of 0.5 ml of a NaCl/sodium bromide solution (density 1.182
mg/ml) in an ultracentrifuge tube. Solutions with the following densities were layered onto the
surface of the plasma: 1 ml of 1.0988 g/ml followed by 1 ml of 1.086 g/ml, 2 ml of 1.079
mg/ml, 2 ml of 1.0722 g/ml, 1.5 ml of 1.0641 g/ml, and, finally, 1.5 ml of 1.0588 g/ml. Ultra-
tracentrifugation was carried out in an SW41 Ti

°C. Seven consecutive runs were

performed, calculated to float lipoproteins of the following flotation rates (Sf = Svedberg flo-

tation units) to the top of the tube: chylo-

microns (Sf>400), three subfractions of

VLDL: VLDL1, Sf 100–400; VLDL2, Sf 60–100; VLDL3, Sf 20–60; and three subfrac-
tions of LDL: LDL1, Sf 12–20; LDL2, Sf 6–12;

LDL3, Sf 3–6. After each run, chylomicrons,
VLDL1, VLDL2, and VLDL3 were aspirated from the top 0.5 ml of the tube and LDL1,
LDL2, and LDL3 were aspirated from the top
1.0 ml of the tube, and the tube refilled with the same amount of solution of density
1.0588 g/ml. The cholesterol and triglyceride components of these subfractions were mea-
ured by the enzymatic calorimetric methods described above and automated measurements
were made using the Abbott VP supersym system autoanalyzer.

DATA ANALYSIS

Data were entered onto an Apple Macintosh computer and analysis was performed using
paired t tests for continuous variables following normality testing and the χ² test for comparing
proportions. Before the analysis the non-

normally distributed data, including all triglyc-

eride fractions and ratios and the VLDL

cholesterol:apolipoprotein B ratio, were loga-

Table 1 Clinical details of 50 patients and controls with specific reference to factors known to affect lipids

<table>
<thead>
<tr>
<th>Factor</th>
<th>Patient</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years, range)</td>
<td>44.8 (20–72)</td>
<td>44.8 (20–72)</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>21/29</td>
<td>21/29</td>
</tr>
<tr>
<td>Mean body mass index (SD)</td>
<td>25.8 (5.6)</td>
<td>24.6 (4.7)</td>
</tr>
<tr>
<td>PASI* score (mean, range)</td>
<td>3.3 (0–8.7)</td>
<td>0</td>
</tr>
<tr>
<td>Subgroup of joint disease (number of patients)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oligoarthritis</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Polyarthritis</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Mutilans</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Spondylitis</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>History of gout</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Topical doxavex</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>NSAIDs*</td>
<td>48</td>
<td>0</td>
</tr>
<tr>
<td>Oral contraceptive</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hormone replacement therapy</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Antihypertensive drugs</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>β Blockers</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Thiazides</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

No patient or control had concurrent infection, malignancy, ischaemic heart disease, liver disease or was taking cortico-

steroids or retinoids.

*PASI = psoriasis area and severity index; NSAIDs = non-steroidal anti-inflammatory drugs.

men and 21 units for women). Any other concurrent or previous illness known to affect the

lipid profile (infection, malignancy, gout, ischaemic heart disease, or liver disease) was

recorded. Four patients in the control group had a history of gout but were not hyperurica-

eemic at the time of the study.

Present and previous drugs were noted for all patients, particularly oral corticosteroids, retin-

oids, thiazides, β blockers, oral contraceptives, and hormone replacement therapy. Five of the

control group were taking oral contraceptives and seven hormone replacement therapy. None

of the controls for the 13 patients on whom LDL and VLDL subfractions were measured were taking hormone replacement therapy.

In 13 patients (nine female, four male) with active psoriatic arthritis randomly selected from the total patient group and 13 age and sex matched healthy volunteers, blood samples were fractionated by cumulative flotation ultracentrifugation as described by Lindgren et al. Briefly, plasma was adjusted to a density of

1.118 g/ml by adding solid sodium chloride (NaCl). Density adjusted plasma (2 ml) was

layered onto the surface of 0.5 ml of a NaCl/sodium bromide solution (density 1.182

mg/ml) in an ultracentrifuge tube. Solutions with the following densities were layered onto the

surface of the plasma: 1 ml of 1.0988 g/ml followed by 1 ml of 1.086 g/ml, 2 ml of 1.079

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proportions. Before the analysis the non-

normally distributed data, including all triglyc-

eride fractions and ratios and the VLDL

cholesterol:apolipoprotein B ratio, were loga-
Table 2 Lipid and lipoprotein concentrations in 50 patients with psoriatic arthritis and 20 patients with active disease and their age and sex matched controls. Results are expressed as means (SEM). Statistics: t test

<table>
<thead>
<tr>
<th>Lipid/lipoprotein concentration (units)</th>
<th>Patients with psoriatic arthritis (n=50)</th>
<th>Controls</th>
<th>Patients with active disease (n=20)</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years, range)</td>
<td>44.8 (20–72)</td>
<td>44.8 (20–72)</td>
<td>42.5 (20–72)</td>
<td>42.5 (20–72)</td>
</tr>
<tr>
<td>Total cholesterol (mmol/l)</td>
<td>5.43 (0.2)</td>
<td>5.82 (0.13)</td>
<td>4.99 (0.24)***</td>
<td>6.08 (0.22)***</td>
</tr>
<tr>
<td>VLDL cholesterol (mmol/l)</td>
<td>0.51 (0.05)</td>
<td>0.49 (0.04)</td>
<td>0.51 (0.05)</td>
<td>0.51 (0.04)</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/l)</td>
<td>3.67 (0.19)</td>
<td>4.0 (0.1)</td>
<td>3.3 (0.25)*</td>
<td>4.12 (0.25)*</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/l)</td>
<td>1.12 (0.05)*</td>
<td>1.29 (0.1)*</td>
<td>1.09 (0.05)</td>
<td>1.33 (0.1)</td>
</tr>
<tr>
<td>HDL-3 cholesterol (mmol/l)</td>
<td>0.62 (0.04)**</td>
<td>0.75 (0.04)**</td>
<td>0.61 (0.1)**</td>
<td>0.77 (0.09)**</td>
</tr>
<tr>
<td>HDL-2 cholesterol (mmol/l)</td>
<td>0.52 (0.03)</td>
<td>0.57 (0.04)</td>
<td>0.49 (0.16)</td>
<td>0.56 (0.17)</td>
</tr>
<tr>
<td>Total cholesterol: HDL cholesterol</td>
<td>5.40 (0.34)</td>
<td>5.14 (0.47)</td>
<td>5.30 (0.65)</td>
<td>4.86 (0.33)</td>
</tr>
<tr>
<td>Total triglyceride (mmol/l)</td>
<td>1.15 (1.09)</td>
<td>1.13 (1.07)</td>
<td>0.99 (1.14)</td>
<td>1.35 (1.1)</td>
</tr>
<tr>
<td>VLDL triglyceride (mmol/l)</td>
<td>0.30 (1.15)</td>
<td>0.32 (1.13)</td>
<td>0.25 (1.22)</td>
<td>0.35 (1.27)</td>
</tr>
<tr>
<td>LDL triglyceride (mmol/l)</td>
<td>0.63 (1.1)</td>
<td>0.52 (1.1)</td>
<td>0.53 (1.16)</td>
<td>0.59 (1.13)</td>
</tr>
<tr>
<td>HDL triglyceride (mmol/l)</td>
<td>0.23 (1.03)</td>
<td>0.25 (1.15)</td>
<td>0.21 (1.06)</td>
<td>0.24 (1.11)</td>
</tr>
<tr>
<td>Total cholesterol: total triglyceride</td>
<td>4.57 (1.07)</td>
<td>5.00 (1.07)</td>
<td>4.95 (1.65)</td>
<td>4.44 (1.51)</td>
</tr>
<tr>
<td>VLDL cholesterol: VLDL triglyceride</td>
<td>1.35 (1.17)</td>
<td>1.36 (1.07)</td>
<td>1.36 (1.65)</td>
<td>1.23 (1.84)</td>
</tr>
<tr>
<td>LDL cholesterol: LDL triglyceride</td>
<td>5.47 (2.23)**</td>
<td>7.40 (1.07)**</td>
<td>5.75 (1.86)</td>
<td>6.69 (1.49)</td>
</tr>
<tr>
<td>HDL cholesterol: HDL triglyceride</td>
<td>4.76 (1.05)</td>
<td>4.95 (1.20)</td>
<td>4.71 (1.54)</td>
<td>5.26 (1.55)</td>
</tr>
<tr>
<td>Apolipoprotein A I (mg/l)</td>
<td>1370 (42.2)</td>
<td>1370 (48.8)</td>
<td>1340 (42.2)</td>
<td>1450 (48.8)</td>
</tr>
<tr>
<td>Apolipoprotein B (mg/l)</td>
<td>800 (36.8)</td>
<td>780 (58.6)</td>
<td>710 (36.8)</td>
<td>830 (58.6)</td>
</tr>
<tr>
<td>Apolipoprotein A I: HDL cholesterol</td>
<td>132 (6.8)</td>
<td>115 (6.2)</td>
<td>138 (16.7)</td>
<td>111 (14.6)</td>
</tr>
<tr>
<td>Apolipoprotein B: LDL cholesterol</td>
<td>24 (2.2)</td>
<td>19.9 (0.92)</td>
<td>25 (4.08)</td>
<td>21 (1.12)</td>
</tr>
</tbody>
</table>

Significant results for patients with psoriatic arthritis v controls: *p<0.05; **p<0.01; ***p<0.005. 
VLDL = very low density lipoprotein; LDL = low density lipoprotein; HDL = high density lipoprotein.

Rithmically transformed for data analysis, and are given in the text and tables as antilogs. Values are presented as means (SEM) for normally distributed data or as antilogs (means (SEM)) for non-normally distributed data. The Mann-Whitney U test was used for the non-parametric Lp(a) lipoprotein data. Pearson’s coefficient of correlation was used for correlation analysis.

Results

CLINICAL CHARACTERISTICS

Fifty patients with psoriatic arthritis were recruited, 20 of whom met the criteria for clinically active peripheral joint disease. The patients spanned a spectrum of disease subgroups. All patients had mild skin disease only, at the time of the study, and no patient had a PASI score greater than 8.7 (table 1). There were no significant correlations between PASI scores and any lipid parameter.

The major differences in treatment between patients and controls were in the use of hormone replacement therapy (HRT) in seven of the controls, and non-steroidal anti-inflammatory drugs (NSAIDs) in all but two of the patients, which will be discussed. None of the nine female controls used in the ultracentrifuge study were taking HRT or oral contraceptives.

LIPID AND LIPOPROTEIN CONCENTRATIONS

Table 2 shows the lipid and lipoprotein results for 50 patients with psoriatic arthritis, including 20 patients with active joint disease, and their age and sex matched controls. HDL cholesterol was significantly reduced in the patients with psoriatic arthritis and the difference was related to cholesterol in HDL3. There was no difference in the mean cholesterol in HDL, between the total group of 50 patients and those with active disease, so the significance of the difference between patients and controls was greater for the total group. Reduced total cholesterol levels were even more pronounced in the 20 patients with active synovitis who were analysed separately. Patients with active arthritis had significantly lower total cholesterol and LDL cholesterol than their controls. The relative overall influence of LDL cholesterol and HDL cholesterol was expressed by calculating the ratio of serum total cholesterol concentration to that of HDL cholesterol (table 2). The ratio tended to be higher for patients than controls in both the total patient group and those with active disease, but did not reach statistical significance.

To assess any proportional changes in cholesterol and triglyceride in patients versus controls, the ratios of total cholesterol to triglyceride and their relative proportions in each lipoprotein were analysed (table 2). For the total group of 50 patients, the cholesterol:triglyceride ratio in LDL was significantly less than in the control subjects, indicating a relative depletion of cholesterol compared with triglyceride in this lipoprotein. There was a similar trend in patients with active arthritis, though the difference did not reach significance. The total cholesterol:total triglyceride ratio and proportions of cholesterol and triglyceride in HDL tended to be lower in the patient group, but the differences were not significant. The VLDL cholesterol:VLDL triglyceride ratio was similar for patients and controls.

APOLIPOPROTEINS

For the total group there were no significant differences in the apolipoproteins A I and B in the patients with psoriatic arthritis compared with controls (table 2). In the 20 patients with active disease, both apolipoproteins tended to slightly lower, but this was not significant. Apolipoprotein A I is the predominant protein in HDL and apolipoprotein B the predominant protein in LDL. Therefore the apolipoprotein A I:LDL cholesterol and apolipoprotein B:LDL cholesterol ratios were calculated and compared for patients and controls. Both ratios
Significant results for patients with psoriatic arthritis: tended to be greater for patients than controls, but in no case was this significant.

**LIPOPROTEIN SUBFRACTION COMPOSITION**

Thirteen patients with active joint disease, randomly selected from the group of 20 patients, were further studied to determine their lipoprotein subfraction composition. Their initial profiles were similar to the 20 patients with active disease (data not shown). Their mean age was 37 years (range 20–59). HDL cholesterol was again significantly reduced in the patients compared with controls, and there was a trend for an increase in the percentage of triglyceride in VLDL1.

The chylomicron phospholipid concentration was significantly less in psoriatic arthritis than controls (table 3), which was reflected in a significant decrease in the percentage composition of phospholipid in chylomicrons.

**LP(a) LIPOPROTEIN**

There were no significant differences in Lp(a) lipoprotein levels in patients with psoriatic arthritis and controls (median 174 mg/l (range 10–800) vs 157 mg/l (range 10–800)). When the patients with active synovitis were analysed separately, Lp(a) lipoprotein levels were found to be increased (median 187 mg/l vs 88 mg/l), but this did not reach statistical significance (Mann–Whitney U test). Also, 25% of patients with psoriatic arthritis had Lp(a) lipoprotein levels greater than 300 mg/l compared with 19% of the controls, though the difference in the proportion was not significantly different. A power calculation indicates that 360 patients and controls would be required to gain a significant difference in the proportion of patients and controls with an Lp(a) lipoprotein of greater than 300 mg/l. There were weak positive correlations between Lp(a) lipoprotein levels and ESR (Pearson’s r=0.27, p=0.098), plasma viscosity (r=0.27), and CRP (r=0.18).

**Discussion**

A pattern of dyslipidaemia similar to that found in RA has been reported in patients with psoriatic arthritis. Lazaroviec et al studied 40 patients with psoriatic arthritis and found decreased concentrations of total lipids, total cholesterol, cholesterol in LDL, and cholesterol in HDL, which normalised with a reduction in disease activity.1 In our study we also found significantly reduced total cholesterol, LDL cholesterol, and HDL cholesterol, and a generalised suppression of total cholesterol, LDL and HDL cholesterol was most apparent in those patients with active joint disease. In addition, LDL total mass and its cholesterol and triglyceride components were...
significantly raised, and there was a tendency for Lp(a) lipoprotein to be increased. Neither of the lipid particles LDL, or Lp(a)lipoprotein have been previously studied in psoriatic arthritis.

Psoriasis alone may affect serum lipid levels, though usually only when severe, which was not the case in the current study.17 The effect of hormone replacement therapy, taken by seven of the controls, and NSAIDs, taken by 48 of the patients, requires discussion. Oestrogens tend to increase HDL cholesterol, reduce LDL cholesterol, especially small dense LDL (LDL₃) in this study) and may reduce Lp(a) lipoprotein; progesterones tend to have the opposite effect. This might have had a small impact on the comparative data for the total group of 50 patients; however, we found a similar pattern with the controls for the 13 patients included in the ultracentrifuge study, in whom hormone replacement therapy was not a confounding factor. NSAIDs are not reported to affect lipid or lipoprotein levels but may have a minor effect on the acute phase response.

The decrease in total LDL cholesterol seen in our study group may imply protection from atherosclerosis. However, patients with active psoriatic arthritis had a significant shift in distribution towards the smallest, most dense particles of LDL (LDL₃), with normal or low levels of LDL₁ and LDL₂. LDL₃, constituted 24.8% of the total LDL for the patients compared with 15% for the controls. These findings are clinically relevant because high levels of LDL₃, in comparison with the levels of LDL₁ and LDL₂, are strongly associated with atherosclerosis in population studies.18 A similar pattern has been reported in non-insulin dependent diabetes mellitus, in which LDL cholesterol may be normal or reduced in association with excess small dense LDL, and low HDL cholesterol.19 20 The shift in LDL composition is much more marked in diabetes mellitus, where the percentage of LDL₃, in total LDL may reach 40%. In diabetes the shift is associated with hypertriglyceridaemia and increased VLDL. High levels of VLDL may be more slowly catabolised, particularly if there is reduced lipoprotein lipase activity. High levels of VLDL encourage increased neutral lipid transfer of cholesterol ester from HDL and LDL to VLDL, in exchange for triglyceride, leading to small dense LDL (LDL₃). In the current study there were no significant differences in the total triglyceride levels or the concentration of VLDL subfractions compared with controls; however, there was a trend for a slightly greater proportion of VLDL in relation to VLDL and VLDL₃, which suggests that the postulated mechanism in diabetes may be operating to some extent in active psoriatic arthritis. Small dense LDL has also been linked to increased hepatic triglyceride lipase and it would be of value to measure this in a further study.21

The combination of a low HDL cholesterol and a high LDL₃, found in the current study, is strongly associated with an increased risk of atherosclerosis in population studies.22 Both subfractions of HDL were reduced compared with controls in this study, but only the depression of HDL₃, reached statistical significance. HDL₃ is thought to be less “athero-protective” than HDL₁, so its increased suppression in relation to HDL₃ has less relevance to the cardiovascular risk.

There are a number of mechanisms whereby increased LDL₃ may cause atherosclerosis. LDL₃ becomes rapidly oxidised and has an enhanced ability to cross cell surfaces, where it may be directly toxic to endothelium. The clearance of LDL₃ from the circulation by the LDL receptor mechanism may also be impaired, making more LDL₃ available for removal by the atherogenic scavenger pathway.23 In the arterial wall, the resulting lipid-rich macrophages become foam cells that accumulate in early atheromatous lesions. An association between the susceptibility of LDL to oxidation in vitro and the extent of atherosclerosis of coronary vessels has been demonstrated.24 Lp(a) lipoprotein is an independent risk factor for atherosclerosis and thrombosis, with values above 300 mg/l associated with a twofold increased risk of myocardial infarction25 and an accelerated progression of coronary atheroma.26 Its mode of action is thought to be related to homology with plasminogen, resulting in inhibition of fibrinolytic activity and increasing the likelihood of thrombosis. Increased levels of Lp(a) lipoprotein have been reported in RA, where it may behave as an acute phase protein.27 NSAIIDs may have a modest effect of reducing the Lp(a) lipoprotein by reducing the acute phase response. Our results show a similar pattern to that reported in RA, with a slight increase in Lp(a) lipoprotein levels and weak positive correlations with inflammatory markers. A power calculation indicates that 360 patients and controls would be needed to produce a significant proportional increase in Lp(a) lipoprotein in patients compared with controls.

Lipoproteins exist as packages containing predominantly cholesterol, triglyceride, and apolipoproteins. The synthesis and catabolism of each constituent can proceed independently of the other contents of the package, though a certain amount of covariance exists. LDL cholesterol and triglyceride may be high or low, without any change or with an opposing change in apolipoprotein concentration. Apolipoprotein A I is the predominant apolipoprotein in HDL, comprising 60% of the protein mass, and apolipoprotein B is the predominant apolipoprotein in LDL and VLDL, comprising 90% of the protein mass of LDL and VLDL. LDL and VLDL have one apolipoprotein per lipoprotein package, so apolipoprotein concentration is an indication of the number of particles present. Lower apolipoprotein A I and high apolipoprotein B have been found in association with coronary artery disease. The apolipoproteins A I and B in the patients with psoriatic arthritis were not significantly different from those in controls, though they tended to be lower in the active group, perhaps partly reflecting the generalised reduction in cholesterol and cholesterol associated lipids. This notion is supported by the apolipoprotein A I:LDL cholesterol and apolipoprotein B:LDL cholesterol ratios, which tended to be greater in the patients than controls, reflecting a
greater relative suppression of HDL cholesterol than apolipoprotein A I and of LDL cholesterol than apolipoprotein B.

There are a number of reasons why dyslipidaemia may be associated with an active inflammatory arthritis. An increased production of acute phase proteins by the liver in inflammation may occur at the expense of lipoprotein production, thereby tending to reduce lipoprotein levels. Enhanced reticuloendothelial system uptake of lipoproteins in chronic inflammation may occur, which is compatible with an accelerated atherosclerotic process at the vessel wall. Mediators of inflammation, such as the interferons (α, β, γ), CRP, and the proinflammatory cytokines, interleukin 1 and tumour necrosis factor α, produced by macrophages have been shown to suppress lipoprotein lipase activity and increase oxidative metabolism. Reduced levels of the antioxidant selenium have also been found in psoriatic arthritis.

It is likely that a combination of factors related to the systemic inflammatory response may operate in psoriatic arthritis to produce the observed pattern of dyslipoproteinaemia. A reported increase in occlusive vascular disease in psoriasis has led to various studies of lipids and lipoproteins, with conflicting results. Hypercholesterolaemia or hypertriglyceridaemia, or both, may occur, which contrasts with the findings in psoriatic arthropathy. Apolipoprotein B has been reported to be low, unchanged, or increased in different studies.

However, an increased prevalence of hypertension, diabetes mellitus, impaired glucose tolerance, and hyperuricaemia, all of which are known to be associated with dyslipoproteinaemia, is associated with psoriasis and may not have been adequately controlled in some studies. In addition the severity of psoriasis may affect the results. None of our patients had severe skin disease (defined as a PASI score of greater than 30) at the time of the study, making it unlikely that psoriasis itself contributed to our findings.

To conclude, this is the first report documenting high levels of LDL in relation to total LDL in an inflammatory form of arthritis. Lipoprotein subfractions and Lp(a) lipoprotein warrant further investigation in a larger group of patients with psoriatic arthritis, with the inclusion of hepatic triglyceride lipase measurement, and longitudinal data. Lipoprotein composition also warrants investigation in RA, where the increased mortality from atherosclerosis is more clearly established. In patients with a pattern of low HDL, high LDL, and high Lp(a) lipoprotein, long term follow up is needed to determine the predictive risk of macrovascular disease.

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Lipoproteins and their subfractions in psoriatic arthritis: identification of an atherogenic profile with active joint disease
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