Figure 1 Time to (A) first joint-sacrificing procedure and (B) first non-joint-sacrificing procedure for patients diagnosed before, compared with those diagnosed after, 1990.

A more detailed version of table 1 is available online at <http://www.annrheumdis.com/supplemental>

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Statin therapy might be beneficial for patients with ankylosing spondylitis

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Therapeutic options for patients with the chronic inflammatory disease ankylosing spondylitis (AS) are limited. Treatment was, until recently, mainly based on non-steroidal anti-inflammatory drugs and physical therapy. The efficacy of disease modifying antirheumatic drugs, such as sulfasalazine and methotrexate, is less beneficial in AS than in other rheumatic diseases such as rheumatoid arthritis.¹ Recently, tumour necrosis factor α blocking agents, have been proved to be very effective in a high proportion of patients with AS. However, these agents are expensive and their use is sometimes accompanied by severe adverse events, as opportunistic infections. Moreover, tumour necrosis factor α

blocking agents are not effective in about 30% of patients.² Hence, there is a continuing need for alternative therapeutic options.

There is growing evidence that statins possess anti-inflammatory properties, as indicated by lowering of C reactive protein (CRP) levels, and recently, the clinically beneficial effect of the statin atorvastatin on disease activity was demonstrated in rheumatoid arthritis.^{3,4} Therefore, we conducted an open pilot study to investigate the effect of rosuvastatin on disease activity in patients with AS.

Fifteen unselected consecutive outpatients with AS, according to the modified New York criteria, were treated

Table 1 Clinical and biological variables (median) in 15 patients at baseline, at weeks 6, 12 (with rosuvastatin), and at weeks 18, 24 (without rosuvastatin)

Variable	Baseline	With rosuvastatin		After stopping rosuvastatin	
		At 6 weeks	At 12 weeks	At 18 weeks	At 24 weeks
ESR (mm/1st h)	22.0	20.0	15.0*	18.0	15.0
CRP (log mg/l)	15.0	10.0	10.0*	12.5	12.0
Total cholesterol (mmol/l)	4.8	3.5*	3.6*	5.0**	5.0**
HDL-cholesterol (mmol/l)	1.3	1.3	1.5	1.3	1.2
LDL-cholesterol (mmol/l)	2.8	1.1*	1.8*	3.3**	3.2**
Triglycerides (mmol/l)	1.4	1.2	1.3	1.5	1.8
BASDAI	6.3	5.6	5.8	5.2	5.6
BASFI	4.7	5.4	4.9	5.0	4.9
BASMI	4.4	4.0	3.8	3.6	4.2
General wellbeing according to doctor	4.4	4.5	3.9	4.2	4.0
General wellbeing according to patient	6.4	5.7	5.3	5.6	5.7
Pain score	6.5	6.8	6.2	5.7	5.2

*Significant changes compared with baseline (Wilcoxon's signed ranks test), $p \leq 0.05$; **significant changes compared with 12 weeks (Wilcoxon's signed rank test), $p \leq 0.05$.

with rosuvastatin (20 mg/day) for 12 weeks, followed by an observational phase of 12 weeks. Patients were eligible for inclusion if they had active disease defined as at least four points on the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI, 0–10) and a pain score of at least four on the visual analogue scale (0–10). The local ethics committee approved the study protocol and all patients gave written informed consent. Main exclusion criteria included cardiovascular events within the previous 3 months, current lipid lowering treatment, and current use of biological agents. No patients were allowed to enter the study who would otherwise have qualified for statins on the basis of calculated risk.

Plasma concentrations of CRP, erythrocyte sedimentation rate (ESR), total cholesterol, low density lipoprotein (LDL)-cholesterol, high density lipoprotein (HDL)-cholesterol, triglycerides and the following clinical measures: BASDAI, Bath Ankylosing Spondylitis Functional Index (BASFI, 0–10), Bath Ankylosing Spondylitis Metrology Index (BASMI, 0–10), general wellbeing according to the doctor/patient (GWBD/P), and pain score were determined. Statistical analysis was performed with Wilcoxon's signed rank test. Values of $p < 0.05$ were considered significant.

The patients' mean age was 46 years (range 29–61), nine were men and 14 were HLA-B27 positive. The mean disease duration was 11.5 years (range 2–22). All patients completed the trial. However, the dose of rosuvastatin was reduced in two patients to 10 mg/day after 6 weeks owing to side effects. Clinical measures, such as BASDAI, BASMI, pain score, and GWBD/P, tended to improve during the treatment period. Improvements in the first three variables were sustained, with further improvement, during the observational phase. In addition, treatment with rosuvastatin resulted in significant improvements of CRP and ESR after 12 weeks. Total and LDL-cholesterol were significantly reduced after 6 and 12 weeks and increased during the observational phase (table 1).

The main conclusion is that treatment with rosuvastatin leads to an improvement of disease activity in patients with active AS and is accompanied by significant reduction of acute phase reactants. Moreover, several clinical measures continued to improve during the follow up phase, suggesting that rosuvastatin has longlasting beneficial effects.

Accumulating evidence suggests that statins exert anti-inflammatory properties through modulation of the immune response. The immune response is up regulated in the inflammatory disorder AS and we suggested that suppression of the immune response by statins would lead to clinical improvement accompanied by lower levels of inflammation markers, such as ESR and CRP. The results of our investigation are in line with this hypothesis, but clearly, confirmatory randomised studies are required.

Finally, as AS is associated with an increased cardiovascular risk,⁵ the use of statins might ultimately lead to reduction of this risk by two pathways: one through the lipoprotein metabolism and the other by beneficial effects on the underlying inflammatory process in AS.

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