SUPPLEMENTAL DATA

Supplemental Methods

Study population

AS patients were included at the out-patient clinics of the Academic Medical Center (AMC) and the Amsterdam Rheumatology & Immunology Center. They were selected based on stable use of medication for more than 6 weeks. Exclusion criteria for all subjects were a history of diabetes mellitus, hypertension or cardiovascular events, use of systemic medication including cardiovascular drugs such as antihypertensive medication or statins, and use of methotrexate or biological based medications.

Biometric and Biochemical Measurements

Presence of cardiovascular risk factors and use of medication were assessed by questionnaire. Date of onset of AS, Human Leukocyte Antigen (HLA)-B27 status and disease activity (Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) (1)) were extracted from medical history. Brachial artery blood pressure was measured using an oscillometric blood pressure device. Weight and height were measured to calculate body mass index (BMI). Fasting EDTA blood was obtained through venous blood samples to measure total cholesterol (TChol), high-density lipoprotein cholesterol (HDL), triglycerides (TG), C-reactive protein (CRP), glucose, leukocyte counts and differentiation using commercially available methods. Low-density lipoprotein cholesterol (LDL) levels were calculated using the Friedewald equation. 10-Year CVD risk was assessed using the Framingham Risk (FHR) Score (2) (http://cvdrisk.nhlbi.nih.gov/).

^{18}F-FDG PET/CT imaging and analysis

^{18}F-FDG PET/CT scans were performed on a PET/CT scanner (Philips, Best, the Netherlands). Subjects fasted for at least 6 hours prior to infusion of 200 MBq of ^{18}F-FDG

(5.5 mCi). PET imaging was initiated with a low-dose, non-contrast enhanced CT for attenuation correction and anatomic co-registration (slice thickness 3 mm), 90 minutes after intravenous administration of ^{18}F-FDG. Images were analyzed using dedicated software (OsiriX, Geneva, Switzerland; http://www.osirix-viewer.com/). In the carotid arteries, ^{18}F-FDG uptake was assessed in at least 5 regions of interest (ROI). From each ROI, the mean and maximum standardized uptake values (SUVs) were obtained. The SUV represents the ^{18}F-FDG activity in the ROI (in kBq/ml), adjusted for the administered ^{18}F-FDG dose corrected for decay (in MBq) and divided by body weight (in kg). Mean and maximum SUVs were averaged for each arterial segment (SUV_{mean} and SUV_{max}). Background ^{18}F-FDG activity was measured in the venous blood pool as an average of at least 5 ROIs. Target to background ratio (TBR) values were derived as: $TBR_{mean\ or\ max} = SUV_{target\ (mean\ or\ max)} / SUV_{Background\ Venous\ Activity}$. In addition, most diseased segment TBR (TBR_{mds}) was recorded as the mean of 3 adjacent slices with the highest arterial wall value of SUV_{max}.

Linear regression

Unadjusted and adjusted (for age, gender, current smoking and NSAID use) linear regression analysis with the difference in TBR_{max} before and after statin treatment (ΔTBR) as the dependent variable were applied to asses i) if ΔTBR could be predicted by baseline values and ii) if ΔTBR was correlated to changes in these parameters.

References

1. Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. *J Rheumatol* 1994;21:2286–91.

2. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* 2002;106:3143–421.

Supplemental Tables

Supplemental table S1: Clinical characteristics for the whole AS statin cohort

Characteristic	AS patients (n=24)	P-value vs controls
Age, y	44 ± 10	0.071
Gender, %male (n)	75% (18)	0.396
BMI, kg/m^2	26 ± 4	0.926
FHR score	1.5 [0.3-3]	0.365
SBP, mmHg	124 ± 10	0.150
DBP, mmHg	73 ± 4	0.201
Smoking,%active(n)	12.5% (3)	0.173
TChol, mmol/L	5.32 ± 1.17	0.919
LDL, mmol/L	3.41 ± 1.07	0.558
HDL, mmol/L	1.30 ± 0.39	**0.001**
TG, mmol/L	1.08 [0.73-1.85]	0.080
Glucose, mmol/L	4.85 ± 0.32	0.927
Leukocytes, 10^9/L	7.53 ± 2.23	0.026
Neutrophils, 10^9/L	4.60 ± 1.78	0.058
Lymphocytes, 10^9/L	2.16 ± 0.68	0.184
Monocytes, 10^9/L	0.56 ± 0.20	**0.001**
CRP, mg/L	3.80 [1.45-8.7]	**0.002**

Data are expressed as mean±SD, percentage (number) or median[IQR]. *BMI* body mass index; *FHR* Framingham risk; *SBP* systolic blood pressure; *DBP* diastolic blood pressure; *TChol* total cholesterol; *LDL* low-density lipoprotein cholesterol; *HDL* high-density lipoprotein cholesterol; *TG* triglycerides. *CRP* C-reactive protein

Supplemental table S2: AS disease specific characteristics for the whole cohort

Characteristic	AS Patients (n=24)
Disease duration, years	7 [5-9]
HLA-B27 positivity, n (%)	22 (91)[#]
BASDAI	1.9[0.8-3.0]
CRP > ULN, n (%)	14 (58)
NSAID use, n (%)	18 (75)
- Diclofenac	7 (29)
- Etoricoxib	3 (13)
- Meloxicam	2 (8)
- Ibuprofen	3 (13)
- Fenylbutazon	1 (4)
- Arthrotec	1 (4)
- Piroxicam	1 (4)

Data are median (IQR) or n (%). *HLA* indicates Human Leukocyte Antigen; *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index*; CRP* c-reactive protein; *ULN* upper limit of normal; *NSAID* non-steroidal anti-inflammatory drugs. # for 2 patients, HLA-B27 status was not available.

Supplemental table S3: Carotid ^{18}F-FDG uptake in the whole AS cohort and controls

Carotid ^{18}F-FDG uptake	Control subjects (n=20)	AS patients (n=24)	P-value$^{\alpha}$
TBR$_{mean}$	1.37±0.15	1.50±0.14	**0.003**
TBR$_{max}$	1.54±0.18	1.87±0.26	**<0.001**
TBR$_{mds}$	1.61±0.16	1.94±0.27	**<0.001**

Data are mean±SD. *TBR* target to background ratio; *mds* most diseased segment.

$^{\alpha}$ANCOVA analysis adjusted for age, gender and smoking status

Table S4: Adjusted$^{\alpha}$ linear regression analysis for baseline TBR$_{max}$ in AS patients

Variable	β (95% CI)	P value
CRP	0.322(-0.010-0.046)	0.199
BASDAI	-0.034(-0.178-0.163)	0.924
Leukocytes	-0.083(-0.065-0.046)	0.732
Neutrofils	-0.018(-0.073-0.067)	0.940
Lymphocytes	-0.198(-0.256-0.111)	0.418
Monocytes	-0.179(01.848-0.390)	0.448
TChol	-0.050(-0.117-0.096)	0.639
HDL	-0.426(-0.594-0.029)	0.073
LDL	0.101(-0.668-0.093)	0.668

Data are standardized coefficient (β) with 95% confidence intervals (CI). *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index; *CRP* c-reactive protein; *TChol* total cholesterol; *LDL* low density lipoprotein cholesterol; *HDL* high density lipoprotein cholesterol; *TG* triglycerides; $^{\alpha}$Data are adjusted for age, gender and smoking status

Table S5: Unadjusted and adjusted linear regression analysis with ΔTBR Max as the dependent variable

Characteristic		Unadjusted analyses		Adjusted analyses[α]	
		β (95% CI)	P value	β (95% CI)	P value
Age		0.108(-0.008-0.12)	0.682	-	
Gender		0.095(-0.009-0.012)	0.735	-	
Smoking		-0.086(-0.397-0.293)	0.752	-	
NSAID use		0.153(-0.131-0.227)	0.573	-	
HDL	Baseline	-0.006(-0.223-0.219)	0.984	0.132(-0.294-0.388)	0.765
	Change	-0.397(-0.672-0.108)	0.143	-0.573(-0.888-0.063)	0.208
Leukocytes	Baseline	-0.161(-0.047-0.027)	0.567	-0.193(-0.056-0.032)	0.560
	Change	-0.128(-0.052-0.034)	0.649	0.093(-0.041-0.053)	0.782
Neutrofils	Baseline	-0.192(-0.061-0.031)	0.494	-0.185(-0.071-0.042)	0.570
	Change	-0.306 (-0.078-0.024)	0.268	-0.216(-0.081-0.042)	0.504
Monocytes	Baseline	-0.034(-0.637-0.568)	0.903	-0.255(-0.972-0.479)	0.466
	Change	-0.074(-0.309-0.241)	0.794	0.152(-0.255-0.389)	0.635

Data are standardized coefficient (β) with 95% confidence intervals (CI). *NSAID* non-steroidal anti-inflammatory drugs; *HDL* high density lipoprotein cholesterol; [α]Adjusted for age, gender, current smoking and NSAID use.