# Atherosclerotic disease in axial spondyloarthritis: increased frequency of carotid plaques

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## Abstract

### Objective

*To establish whether subclinical atherosclerosis is increased in patients with axial spondyloarthritis (ax-SpA).*

### Methods

*A set of 149 consecutive patients with no history of cardiovascular disease that fulfilled the Assessment of SpondyloArthritis International Society classification criteria for ax-SpA was studied by carotid ultrasonography. Carotid intima-media thickness (cIMT) and plaques were assessed. A series of 181 community-based controls with no cardiovascular disease were studied for comparison. To establish whether ax-SpA might have a direct effect on the risk of carotid plaques or an indirect effect via its putative influence on hypertension, dyslipidaemia or obesity, we obtained adjusted odds ratios (OR) for each clinical factor by the development of adjusted models.*

### Results

*cIMT was increased in patients (0.621±0.123 mm) when compared to controls (0.607±0.117 mm) but the difference was not significant (p=0.30). Nevertheless, carotid plaques were more commonly observed in patients with ax-SpA than in controls (41.6% vs. 26.4%; p=0.003). Patients with plaques had longer duration of the disease than those without plaques (20.5±11.2 years vs. 12.0±8.6 years; p<0.001). Plaques were more frequent in patients with hip involvement (crude odds ratio 3.15, 95% confidence interval [CI] 1.02–9.75; p=0.05), syndesmophytes (crude OR 4.94, 95% CI 2.14–11.4; p<0.001), in patients with higher functional limitation and mobility index measured by BASFI (crude OR 1.16, 95% CI 1.02–1.33; p=0.03) and BASMI (crude OR 1.45, 95% CI 1.19–1.77; p<0.001), and in those with psoriasis (crude OR 3.94, 95% CI 1.31–11.84; p=0.02. However, except for psoriasis that continued being a strong risk factor for plaques after adjustment, the relationship between other clinical features of ax-SpA and carotid plaques disappeared in the adjusted models.*

### Conclusion

*Our results confirm the presence of subclinical atherosclerosis in patients with ax-SpA.*

**Key words**

axial spondyloarthritis, non-radiographic axial spondyloarthritis cardiovascular disease, carotid ultrasonography, plaque

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## Introduction

Axial spondyloarthritis (ax-SpA) is characterised by inflammatory back back pain. Although radiographic changes characterised by the presence of sacroiliitis are observed in typical cases (1), an elevated number of patients with this condition have normal radiographs. In these cases inflammation in the sacroiliac joints and/or the spine can be observed when a magnetic resonance imaging (MRI) of the back is perfomed (2). The presence of sacroiliitis by MRI or a HLA-B27 positive along with other typical features of spondyloarthritis make it possible to include these patients in the category of axSpA under the term of non-radiographic axial spondyloarthritis (nr-axSpA) (2, 3).

Patients with spondyloarthropathies have a higher risk of cardiovascular (CV) disease than the general population (4). AS has been associated with 1.5–2.0 times increased mortality rate compared to the general population, which is in great part due to CV complications (4). A population-based study from Quebec confirmed an increased risk for all types of CV events in patients with AS (5). In addition, AS patients required hospitalisation because of CV complications more commonly than the general population (5).

An issue of major importance is to determine the presence of CV disease in subclinical stages before the development of CV events. Several validated noninvasive imaging techniques are currently available to determine subclinical atherosclerosis in patients with rheumatic diseases (6). Among these, by the assessment of carotid intima-media wall thickness (cIMT) and the presence of plaques, carotid ultrasonography (US) has become an affordable efficient technique to measure the presence of subclinical atherosclerosis in patients with chronic inflammatory rheumatic diseases. Both cIMT and carotid plaques were found to be good predictors of CV events in low and intermediate risk groups of non-rheumatic individuals (7). Although cIMT and plaques show significant correlation, cIMT's role as a marker of atherosclerosis has been questioned, especially when measurements only include the common carotid artery (8). Whereas cIMT reflects mostly arterial media thickening in response to aging and elevated blood pressure, the presence of carotid plaques indicate intimal pathology and advanced atherosclerosis that links more closely to coronary heart disease risk factors and myocardial infarction (8). Therefore, carotid plaque is considered a more reliable indicator of severe atherosclerosis (8).

Information on the prevalence of plaques in patients with ax-SpA is scarce and restricted to two small series of AS with less than 70 patients each. Increased prevalence of plaques was found in AS patients from Northwest Spain when compared to controls (9) whereas no differences were observed in a Brasilian study (10).

To further investigate the presence of subclinical atherosclerosis in patients with ax-SpA, we assessed a large series of patients that fulfilled classification criteria for this entity (2).

## Patients and methods

*Patients*

A set of 149 consecutive patients seen over a 1 year period at Hospital Universitario Marqués de Valdecilla and Hospital de Laredo (Cantabria, Spain) that fulfilled the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for ax-SpA were studied (6). Patients with history of CV events were excluded.

One hundred and fifteen also fulfilled definitions for AS according to the 1984 modified New York criteria as they had definite radiographic sacroiliitis on plain radiographs (grade 2 bilaterally or grade 3–4 unilaterally) (1). Thirty-four patients fulfilled definitions for nr-axSpA as they had active (acute inflammation) on MRI highly suggestive of sacroiliitis associated with SpA plus ≥1 SpA feature or they were HLA-B27 positive and had ≥2 other SpA features (2).

Two clinical indexes of disease activity (Bath Ankylosing Spondylitis Disease Activity Index, BASDAI, and Ankylosing Spondylitis Disease Activity Score, ASDAS), a functional status index (Bath Ankylosing Spondylitis Functional Index, BASFI), a metrologic index (Bath

Ankylosing Spondylitis Metrology Index, BASMI), and an enthesitis index (Maastricht Ankylosing Spondylitis Enthesitis Score -MASES) were evaluated in all patients at the time of carotid US assessment (11-15). Moreover, information on history of hip involvement, synovitis, enthesitis and anterior uveitis, presence of syndesmophytes, HLA-B27 status, psoriasis and disease duration from the first symptoms and from the diagnosis of ax-SpA were assessed. Data on family history of early CV events in first-degree relatives, waist circumference, body max index, blood presure at time of study and history of traditional CV risk factors (smoking, hypertension, diabetes mellitus, dyslipidaemia, and obesity) or chronic kidney disease were also assessed.

Information on C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) at the time of recruitment and at disease diagnosis, and total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides at the time of the study was assessed. Information on therapy including treatment with anti-tumor necrosis factor-α (anti-TNF-α) agents from the disease diagnosis was also reviewed.

*Control group*

The controls (n=181) were community-based, recruited by general practitioners in primary health centres of the Cantabria region. Controls with family history of any inflammatory rheumatic diseases were excluded, as well as those with history of CV disease.

Informed consent was obtained from all cases and controls. The local institutional committee approved the study.

*Carotid US examination*

Carotid US examination included the measurement of cIMT in the common carotid artery and the detection of focal plaques in the extracranial carotid tree. Plaque was defined as a focal protrusion in the lumen at least cIMT>1.5 mm, protrusion at least 50% greater than the surrounding cIMT, or arterial lumen encroaching >0.5 mm (16). Carotid US was performed using a commercially available scanner, Mylab 70, Esaote (Genoa, Italy) equipped with a 7–12 MHz linear transducer and the automated software guided technique radiofrequency - Quality Intima Media Thickness in real-time (QIMT, Esaote, Maastricht, Holland).

**Table I.** Epidemiological and carotid ultrasound differences between 149 patients with axial spondyloarthritis (ax-SpA) and 181 controls.

| Variable | ax-SpA (n=149) | Controls (n=181) | *p*-value |
|---|---|---|---|
| Men/Women, n | 88/61 | 92/89 | 0.14 |
| Age (years), mean±SD | 46.2±11.9 | 45.3±12.5 | 0.47 |
| History of classic cardiovascular risk factors, n (%) | | | |
| Non-smokers | 71(47.7) | 110 (60.8) | 0.03 |
| Current smokers | 42(28.2) | 32 (17.7) | |
| Ex-smokers | 36(24.2) | 39 (21.6) | |
| Obesity | 33(22.2) | 25 (13.7) | 0.05 |
| Dyslipidaemia | 32(21.5) | 26 (14.3) | 0.09 |
| Hypertension | 25(16.8) | 21 (11.5) | 0.17 |
| Diabetes mellitus | 6(4.0) | 4 (2.2) | 0.33 |
| Chronic kidney disease | 2(1.3) | 2 (1.1) | 0.84 |
| Family history of early cardiovascular events, n (%) | 18(12.1) | 19 (10.7) | 0.70 |
| Body mass index, mean±SD (kg/m2) | 26.4±4.6 | 26.1±4.4 | 0.55 |
| Blood pressure, mean±SD (mm Hg) | | | |
| Systolic | 130±14 | 125±15 | 0.003 |
| Diastolic | 79±10 | 78±9 | 0.21 |
| Waist circumference (cm), mean±SD | 94.7±13.3 | 90.6±14.5 | 0.01 |
| Cholesterol or triglycerides (mg/dl), mean±SD | | | |
| Total cholesterol | 194±34 | 199±34 | 0.24 |
| HDL cholesterol | 56±18 | 59±175 | 0.26 |
| LDL cholesterol | 119±30 | 119±31 | 0.86 |
| Triglycerides | 101±59 | 103±55 | 0.72 |
| CRP (mg/l), mean±SD | 6.7±13.3 | 2.2±5.1 | <0.001 |
| ESR (mm/1st hour), mean±SD | 12.3±14.4 | 6.6±7.0 | <0.001 |
| Carotid IMT (mm), mean±SD | 0.621±0.123 | 0.607±0.117 | 0.30 |
| Carotid plaques, n (%) | 62 (41.6) | 48 (26.4) | 0.003 |

*Statistical analysis*

Continuous data were expressed as mean±standard deviation (SD) and categorical variables as percentages. Continuous variables were compared by Student *t*-test or Mann-Whitney U-test. Proportions were compared by chi-square test or Fisher exact test. Logistic regression models were perfomed to estimate the relationship between the different variables and carotid plaque. To establish whether clinical features of axial-SpA may have a direct effect on the risk of carotid plaques (model 1) or an indirect effect via its putative influence on hypertension, dyslipidaemia or obesity (model 2), we obtained adjusted odds ratios (OR) for each clinical factor: In model 1, we adjusted for age at the time of the study, sex, obesity, hypertension, dyslipidemia, diabetes mellitus and smoking; if this model reached significant results, it would be interpreted as a direct effect of inflammation on carotid plaque risk. In model 2, we only adjusted for age at the time of the study, sex, and smoking; if this model reached significant results, it would be interpreted as an indirect effect: ax-SpA, as a chronic disease, would increase the risk for metabolic syndrome features, eventually increasing the risk of carotid plaques. Logistic regression results were expressed as OR with 95% confidence intervals (CI). Two-sided *p*-values ≤0.05 were considered statistically significant. The study was performed using Stata 12/SE (StataCorp, College Station, TX).

## Results

*Characteristics of ax-SpA patients and controls*

The main epidemiologic and clinical features of 149 patients with ax-SpA and 181 controls are summarised in Table I.

cIMT was increased in patients when compared to controls (0.621±0.123 mm *vs*. 0.607±0.117 mm) but the difference was not significant (*p*=0.30). Nevertheless, carotid plaques were more commonly observed in ax-SpA patients than in controls (41.6% *vs*. 26.4%; *p*=0.003). This difference re-

mained statistically significant after adjustment for sex, traditional CV risk factors (smoking, dyslipdaemia, hypertension, obesity and diabetes mellitus) and chronic kidney disease ($p$=0.003).

*Differences between ax-SpA patients with and without plaques*

Since plaque is the paradigm of atherosclerotic disease, we aimed to determine whether there were some differences between ax-SpA patients with and without carotid plaques (Table II). As expected, patients with plaques were older and more commonly men. They also had longer disease duration than those without plaques (duration of the disease since the first symptoms 20.5±11.2 years in patients with plaques *vs*. 12.0±8.6 years in those without plaques; $p$<0.001). Patients with hip involvement (16.1% *vs*. 5.8%; $p$=0.04) had plaques more commonly. It was also the case for the presence of syndesmophytes (50% *vs*. 23%; $p$<0.001). Consequently, the degree of functional limitation and the mobility index were higher in patients with plaques (BASFI 4.7±2.6 *vs*. 3.8±2.4, $p$=0.03 and BASMI 3.9±1.7 *vs*. 2.7±1.8, $p$<0.001, respectively). cIMT values were higher in patients with plaques (0.690±0.115 mm *vs*. 0.572±0.104 mm in those without plaques; $p$<0.001).

*Relationship between carotid plaques and the main clinical features of patients with ax-SpA.*

As observed in the general population, the levels of cholesterol were associated with the presence of plaques in patients with ax-SpA (Table III).

We designed two models (model 1 and model 2) to analyse whether clinical features of axial-SpA were directly (model 1) or indirectly (model 2) associated with carotid plaques. Total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides and cIMT are well known risk factors for carotid plaques and they are not clinical features of axial-SpA, so we did not consider them in models 1 and 2. We confirmed the potential association of these variables with plaques adjusting for age and sex just to confirm that they act as risk factors for plaques, as occurs in the general population.

**Table II.** Axial spondyloarthritis: differences according to the presence or absence or carotid plaques.

| Variable | with plaques (n=62) | without plaques (n=87) | $p$-value |
|---|---|---|---|
| Age (years), mean ±SD | 54.3 ± 10.8 | 40.4 ± 8.8 | <0.001 |
| Men/Women | 45/17 | 43/44 | 0.005 |
| Disease duration (yr), mean ±SD | | | |
| Since first symptoms | 20.5 ± 11.2 | 12.0 ± 8.6 | <0.001 |
| Since diagnosis of ax-SpA | 11.3 ± 11.1 | 6.5 ± 7.1 | 0.002 |
| BASDAI, mean±SD | 3.8 ± 2.2 | 4.0 ± 2.3 | 0.66 |
| ASDAS, mean±SD | 2.5 ± 1.1 | 2.3 ± 1.0 | 0.36 |
| BASFI, mean±SD | 4.7 ± 2.6 | 3.8 ± 2.4 | 0.03 |
| BASMI, mean±SD | 3.9 ± 1.7 | 2.7 ± 1.8 | <0.001 |
| Anterior uveitis, n (%) | 13 (21.0) | 14 (16.1) | 0.45 |
| Synovitis and or enthesitis, n (%) | 22 (35.5) | 36 (41.4) | 0.47 |
| Hip involvement, n (%) | 10 (16.1) | 5 (5.8) | 0.04 |
| MASES | 2.0 ± 2.5 | 2.4 ± 2.6 | 0.44 |
| Anti-TNF-α from the disease diagnosis, n (%) | 26 (41.9) | 35 (40.2) | 0.84 |
| HLA-B27 positive, n (%) | 43 (69.4) | 65 (74.7) | 0.47 |
| CRP (mg/l), mean±SD | | | |
| At the time of the study | 8.4 ± 16.0 | 5.6 ± 10.9 | 0.20 |
| At time of disease diagnosis | 15.9 ± 28.3 | 13.5 ± 28.3 | 0.66 |
| ESR (mm/1st hour), mean±SD | | | |
| At the time of the study | 14.7 ± 17.2 | 10.5 ± 11.8 | 0.08 |
| At time of disease diagnosis | 19.2 ± 19.3 | 17.4 ± 22.1 | 0.64 |
| Syndesmophytes, n (%) | 31 (50.0) | 20 (23.0) | <0.001 |
| Psoriasis, n (%) | 12 (19.4) | 5 (5.8) | 0.01 |
| Cholesterol or triglycerides (mg/dl), mean±SD | | | |
| Total cholesterol, | 202 ± 34 | 188 ± 32 | 0.01 |
| HDL-cholesterol | 54 ± 15 | 58 ± 19 | 0.12 |
| LDL-cholesterol | 126 ± 32 | 113 ± 27 | 0.02 |
| Triglycerides | 108 ± 50 | 95 ± 64 | 0.19 |
| Patients fulfilling definitions for AS, n (%) | 52 (83.9) | 63 (72.4) | 0.10 |
| Carotid IMT, mean±SD | 0.690 ± 0.115 | 0.572 ± 0.104 | <0.001 |

**Table III.** Classic cardiovascular risk factors and their relationship with carotid plaques in 149 patients with axial spondyloarthritis. Odds ratios (OR) adjusted for sex and age at study.

| Variable | OR (95% CI) | $p$-value |
|---|---|---|
| Total cholesterol | 1.01 (1.00–1.02) | <0.001 |
| HDL-cholesterol | 0.98 (0.96–1.00) | 0.01 |
| LDL-cholesterol | 1.01 (1.00–1.03) | <0.001 |
| Triglycerides | 1.00 (1.00–1.01) | 0.03 |
| Current smoker (ref.: never) | 1.42 (0.70–2.87) | 0.33 |
| Former smoker (ref.: never) | 0.87 (0.42–1.78) | 0.70 |
| Obesity (ref.: No) | 0.56 (0.26–1.23) | 0.15 |
| Diabetes mellitus (ref.: No) | 2.60 (0.51–13.4) | 0.25 |
| Carotid IMT (each 0.1 mm) | 2.73 (1.86–4.00) | <0.001 |

In a further step, when adjusting for confounding factors, a significant association between the age at the time of the study and presence of carotid plaques was observed (Table IV). It was noteworthy that women had lower risk of carotid plaques than men when adjusting for age and smoking (OR 0.36, 95% CI 0.15–0.87; $p$=0.02). However, this association did not remain statistically significant after additional adjustment for obesity, hypertension, diabetes mellitus and dyslipidaemia (OR 0.44, 95% CI 0.18–1.13; $p$=0.09).

Patients with hip involvement (crude OR 3.15, 95% CI 1.02–9.75; $p$=0.05), syndesmophytes (crude OR 4.94, 95% CI 2.14–11.4; $p$<0.001) or psoriasis (crude OR 3.94, 95% CI 1.31–11.84; $p$=0.02) had increased risk of having plaques. In keeping with that, there was a significant association between the presence of plaques and the degree of functional limitation and mobility index measured by BASFI (crude OR 1.16, 95% CI 1.02–1.33; $p$=0.03) and BASMI (crude OR 1.45, 95% CI 1.19–1.77; $p$<0.001), respectively. However, as

**Table IV.** Axial spondyloarthritis: association between carotid plaques and the main clinical features.

| | Model 1* | | Model 2** | |
|---|---|---|---|---|
| Variable | OR (95% CI) | *p*-value | OR (95% CI) | *p*-value |
| Age (years)*** | 1.16 (1.09–1.22) | <0.001 | 1.16 (1.10-1.22) | <0.001 |
| Women**** | 0.44 (0.18–1.13) | 0.09 | 0.36 (0.15-0.87) | 0.02 |
| Disease duration (years) | | | | |
| Since the first symptoms | 1.02 (0.96–1.07) | 0.54 | 1.00 (0.95-1.05) | 0.91 |
| Since the diagnosis of ax-SpA | 0.98 (0.92–1.04) | 0.51 | 0.97 (0.92-1.03) | 0.32 |
| BASDAI | 1.00 (0.81–1.22) | 0.98 | 0.95 (0.78-1.17) | 0.65 |
| ASDAS | 0.87 (0.56–1.34) | 0.53 | 0.81 (0.53-1.25) | 0.35 |
| BASFI | 0.97 (0.80–1.18) | 0.79 | 0.94 (0.77-1.13) | 0.50 |
| BASMI | 0.91 (0.67–1.24) | 0.54 | 0.85 (0.63-1.15) | 0.63 |
| Anterior uveitis | 1.66 (0.56–5.00) | 0.36 | 1.52 (0.55-4.26) | 0.42 |
| Synovitis and or enthesitis | 0.76 (0.31–1.86) | 0.55 | 0.74 (0.31-1.78) | 0.51 |
| Psoriasis | 5.20 (1.18 – 22.9) | 0.03 | 4.90 (1.15 – 20.9) | 0.03 |
| Hip involvement | 0.81 (0.19–3.41) | 0.78 | 0.91 (0.22-3.75) | 0.90 |
| MASES | 0.96 (0.79–1.17) | 0.69 | 0.95 (0.79-1.14) | 0.59 |
| Anti-TNF-α from the disease diagnosis | 0.88 (0.35–2.17) | 0.78 | 0.79 (0.33-1.86) | 0.58 |
| HLA-B27 positive | 0.94 (0.35–2.52) | 0.90 | 0.72 (0.28-1.84) | 0.49 |
| CRP (mg/l) | | | | |
| At the time of the study | 0.98 (0.95–1.17) | 0.20 | 0.97 (0.94-1.01) | 0.11 |
| At the time of disease diagnosis | 1.00 (0.98–1.02) | 0.95 | 1.00 (0.98-1.01) | 0.79 |
| ESR (mm/1st hour) | | | | |
| At the time of the study | 0.99 (0.95–1.02) | 0.49 | 0.99 (0.95-1.02) | 0.49 |
| At the time of disease diagnosis | 0.99 (0.97–1.02) | 0.68 | 0.99 (0.96-1.02) | 0.37 |
| Syndesmophytes | 1.09 (0.39–3.05) | 0.87 | 1.12 (0.42-2.99) | 0.82 |
| Patients fulfilling definitions for AS | 1.61 (0.53–4.85) | 0.40 | 1.47 (0.51-4.21) | 0.48 |

*Model 1: Odds ratios adjusted for age at the time of the study, sex, obesity, hypertension, dyslipidaemia, diabetes mellitus and smoking but not for the remaining variables included in the table.
**Model 2: Odds ratios adjusted for age at the time of the study, sex, and smoking but not for the remaining variables included in the table.
***Age at study was not included in the adjustments.
****Sex was not included in the adjustments.

shown in Table IV, except for psoriasis that continued being a strong risk factor for plaques after adjustment, the relationship between other clinical features of ax-SpA and carotid plaques disappeared in the adjusted models 1 and 2.

## Discussion

Our study confirms the presence of severe atherosclerotic disease in patients fulfilling the ASAS criteria for ax-SpA (2).

Carotid plaque is considered a more reliable indicator of severe atherosclerosis than increased cIMT (8). Studies performed in small series of AS patients showed contradictory results in terms of cIMT (9, 17-19). Our study which included a large series of patients with ax-SpA did not confirm significant differences in cIMT between patients and controls. Nevertheless, the high prevalence of carotid plaques observed in our series supports the claim of increased subclinical atherosclerosis in ax-SpA. Of note, 41% of the patients from this series that included middle-aged individuals with long-standing ax-SpA had plaques. This finding has clinical relevance as carotid plaques are recognised to represent very high CV risk (20).

Therefore, our results support the existence of subclinical atherosclerosis in patients with ax-SpA.

Interestingly, patients with psoriasis and psoriatic arthritis have been associated with increased risk of carotid plaques (21, 22). Hypertension and diabetes significantly enhance the risk of cardiovascular disease in patients with psoriatic arthritis (23). Nevertheless, in our series, we found that the presence of psoriasis was a specific clinical feature of ax-SpA independently associated with the risk of atherosclerosis in patients with ax-SpA. However, except for psoriasis, results on the potential association of other clinical features of ax-SpA with carotid plaques were so far from significance that they would hardly be due to lack of statistical power. Therefore, our interpretation is that apart from psoriasis none of the clinical data assessed in the present study were related to carotid plaques. It is possible that still unidentified CV risk factors may be operative in patients with ax-SpA. A good example of this has been found in rheumatoid arthritis where a genetic component appears to influence the presence of subclinical atherosclerosis and the risk of CV events (24, 25). Taking all these considerations together, individuals with ax-SpA should be included within the category of people with high CV risk.

## References


1. VAN DER LINDEN S, VALKENBURG HA, CATS A: Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. *Arthritis Rheum* 1984; 27: 361-8.
2. RUDWALEIT M, VAN DER HEIJDE D, LANDEWÉ R *et al*.: The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. *Ann Rheum Dis* 2009; 68: 777-83.
3. RUDWALEIT M, LANDEWÉ R, VAN DER HEIJDE D *et al*.: The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part I): classification of paper patients by expert opinion including uncertainty appraisal. *Ann Rheum Dis* 2009; 68: 770-6.
4. PETERS MJ, VAN DER HORST-BRUINSMA IE, DIJKMANS BA, NURMOHAMED MT: Cardiovascular risk profile of patients with spondylarthropathies, particularly ankylosing spondylitis and psoriatic arthritis. *Semin Arthritis Rheum* 2004; 34: 585-92.
5. SZABO SM, LEVY AR, RAO SR *et al*.: Increased risk of cardiovascular and cerebrovascular diseases in individuals with ankylosing spondylitis: a population-based study. *Arthritis Rheum* 2011; 63: 3294-304.
6. KEREKES G, SOLTÉSZ P, NURMOHAMED MT *et al*.: Validated methods for assessment of subclinical atherosclerosis in rheumatology. *Nat Rev Rheumatol* 2012; 8: 224-34.
7. NAMBI V, CHAMBLESS L, FOLSOM AR *et al*.: Carotid intima-media thickness and presence or absence of plaque improves prediction of coronary heart disease risk: the ARIC (Atherosclerosis Risk In Communities) study. *J Am Coll Cardiol* 2010; 55: 1600-7.
8. JOHNSEN SH, MATHIESEN EB: Carotid plaque compared with intima-media thickness as a predictor of coronary and cerebrovascular disease. *Curr Cardiol Rep* 2009; 11: 21-7.
9. GONZALEZ-JUANATEY C, VAZQUEZ-RODRIGUEZ TR, MIRANDA-FILLOY JA *et al*.: The high prevalence of subclinical athero-

sclerosis in patients with ankylosing spondylitis without clinically evident cardiovascular disease. *Medicine* (Baltimore) 2009; 88: 358-65.

10. VALENTE RL, VALENTE JM, DE CASTRO GR, ZIMMERMANN AF, FIALHO SC, PEREIRA IA: Subclinical atherosclerosis in ankylosing spondylitis: is there a role for inflammation? *Rev Bras Reumatol* 2013; 53: 377-81.
11. 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.
12. LUKAS C, LANDEWÉ R, SIEPER J *et al*.: Development of an ASAS-endorsed disease activity score (ASDAS) in patients with ankylosing spondylitis. *Ann Rheum Dis* 2009; 68: 18-24.
13. CALIN A, GARRETT S, WHITELOCK H *et al*.: A new approach to defining functional ability in ankylosing spondylitis: the development of the Bath Ankylosing Spondylitis Functional Index. *J Rheumatol* 1994; 21: 2281-5
14. CALIN A, GARRETT S, WHITELOCK H *et al*.: Defining spinal mobility in ankylosing spondylitis (AS). The Bath AS Metrology Index. *J Rheumatol* 1994; 21: 1694-8.
15. HEUFT-DORENBOSCH L, SPOORENBERG A, VAN TUBERGEN A *et al*.: Assessment of enthesitis in ankylosing spondylitis. *Ann Rheum Dis* 2003; 62: 127-32.
16. CORRALES A, GONZÁLEZ-JUANATEY C, PEIRÓ ME, BLANCO R, LLORCA J, GONZÁLEZ-GAY MA: Carotid ultrasound is useful for the cardiovascular risk stratification of patients with rheumatoid arthritis: results of a population-based study. *Ann Rheum Dis* 2014; 73: 722-7.
17. PETERS MJ, VAN EIJK IC, SMULDERS YM *et al*.: Signs of accelerated preclinical atherosclerosis in patients with ankylosing spondylitis. *J Rheumatol* 2010; 37: 161-6 .
18. BODNÁR N, KEREKES G, SERES I *et al*.: Assessment of subclinical vascular disease associated with ankylosing spondylitis. *J Rheumatol* 2011; 38: 723-9.
19. HAMDI W, CHELLI BOUAZIZ M, ZOUCH I *et al*.: Assessment of preclinical atherosclerosis in patients with ankylosing spondylitis. *J Rheumatol* 2012; 39: 322-6.
20. DESSEIN PH, SEMB AG: Could cardiovascular disease risk stratification and management in rheumatoid arthritis be enhanced? *Ann Rheum Dis* 2013; 72: 1743-6.
21. EL-MONGY S, FATHY H, ABDELAZIZ A *et al*.: Subclinical atherosclerosis in patients with chronic psoriasis: a potential association. *J Eur Acad Dermatol Venereol* 2010; 24: 661-6.
22. GONZALEZ-JUANATEY C, LLORCA J, AMIGO-DIAZ E, DIERSSEN T, MARTIN J, GONZALEZ-GAY MA: High prevalence of subclinical atherosclerosis in psoriatic arthritis patients without clinically evident cardiovascular disease or classic atherosclerosis risk factors. *Arthritis Rheum* 2007; 57: 1074-80.
23. FAVARATO MH, MEASE P, GONÇALVES CR, GONÇALVES SAAD C, SAMPAIO-BARROS PD, GOLDENSTEIN-SCHAINBERG C: Hypertension and diabetes significantly enhance the risk of cardiovascular disease in patients with psoriatic arthritis. *Clin Exp Rheumatol* 2014; 32: 182-7.
24. LÓPEZ-MEJÍAS R, GENRE F, GARCÍA-BERMÚDEZ M *et al*.: The ZC3HC1 rs11556924 polymorphism is associated with increased carotid intima-media thickness in patients with rheumatoid arthritis. *Arthritis Res Ther* 2013; 15: R152.
25. RODRÍGUEZ-RODRÍGUEZ L, GONZÁLEZ-JUANATEY C, PALOMINO-MORALES R *et al*.: TNFA -308 (rs1800629) polymorphism is associated with a higher risk of cardiovascular disease in patients with rheumatoid arthritis. *Atherosclerosis* 2011; 216: 125-30.