Cardiovascular risk stratification in axial spondyloarthritis: carotid ultrasound is more sensitive than coronary artery calcification score to detect high-cardiovascular risk axial spondyloarthritis patients

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Abstract

Objective

To determine the ability of Coronary Artery Calcification Score (CACS) and carotid ultrasonography (US) to detect high cardiovascular (CV) risk axial spondyloarthritis (ax-SpA) patients.

Methods

CACS and carotid plaques were assessed in 66 consecutive ax-SpA patients (51 fulfilling criteria for ankylosing spondylitis and 15 for non-radiological ax-SpA) without history of CV events. The Systematic Coronary Risk Evaluation (SCORE) calculated using total cholesterol (TC-SCORE) was assessed in 64 patients without diabetes mellitus or chronic kidney disease.

Results

The mean age of the patients and the median disease duration since the onset of symptoms were 49.3 and 14.5 years. HLA-B27 was positive in 47 (75%) patients. CV risk was categorised according to the TC-SCORE as low (<1%; n=33), moderate (≥1% and<5%; n=30) and high/very high risk (≥5%; n=1). Most patients with low TC-SCORE (27/33; 82%) had normal CACS (zero), and only 1/33 had CACS >100. However, carotid plaques were observed in patients with CACS=0 (12/37; 32%) and CACS 1-100 (10/16; 62%). The sensitivity to detect high/very high CV risk using only the TC-SCORE was very low as the algorithm only detected 1/33 (3%) of patients with high/very high CV risk. Ten of 33 (30%) high/very high CV risk patients were identified using a chart TC-SCORE risk ≥5% plus the presence of CACS ≥100 in patients with moderate TC-SCORE. The replacement of CACS with carotid US identified a higher number of high/very high CV risk patients (22/33; 67%).

Conclusion

Carotid US is more sensitive than CACS for the detection of high CV risk in ax-SpA patients.

Key words

ankylosing spondylitis, axial spondyloarthritis, cardiovascular risk, carotid ultrasonography, coronary tomography, CAC score

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Introduction

Patients with ankylosing spondylitis (AS) have an increased risk of cardiovascular (CV) disease that is associated with accelerated atherosclerosis (1). Population-based studies disclosed an increased prevalence of ischaemic heart disease (2-4), heart failure and cerebrovascular disease in patients with AS (3, 4). These data were confirmed in a meta-analysis of seven longitudinal studies that showed an increased frequency of myocardial infarction (odds ratio (OR) 1.60, 95% confidence interval (CI) 1.32–1.93) and stroke (OR 1.50, 95% CI 1.39–1.62) in AS patients when compared to the general population (5).

Adequate stratification of the CV risk is an issue of major concern in patients with inflammatory arthritis to identify high-CV risk individuals who may benefit from active therapy to prevent CV events. In Europe, the 2016 "European Guidelines on CV disease prevention in clinical practice" recommended using the systematic coronary risk evaluation (SCORE), which predicts the individual's absolute risk for fatal CV events considering age, sex, lipid levels, smoking and blood pressure (6). According to the prediction obtained, the SCORE stratifies the CV risk in low (<1%), moderate (≥1 and <5%), high (≥5 and <10%) and very high (≥10%).

Besides traditional CV risk factors, the degree of the inflammatory burden and the presence of extra-articular manifestations have been implicated in the elevated CV risk observed in AS (7, 8). The compound effect of these factors may explain the reasons why the SCORE and other similar CV risk algorithms designed for the general population underestimate the actual CV risk of AS patients (9). In this regard, a recent study found a 10-year cumulative incidence of CV events three times higher than the predicted based on the Framingham Risk Score (FRS) (9).

It is worth noting that the 2016 European guidelines proposed the use of additional tools, such us carotid ultrasound (US) or coronary tomography (CT), to redefine risk assessment in healthy individuals with moderate risk (6). The presence of carotid plaques and the coronary artery calcification (CAC) Score were found to be good predictors of CV events in intermediate risk groups of non-rheumatic individuals, and the presence of plaques or high CAC Score (CACS) values were considered indicators of very high CV risk (6). In rheumatoid arthritis (RA), the best characterised inflammatory disease, both findings have demonstrated to be good predictors of CV events (10, 11).

Patients with inflammatory conditions in general and specifically with AS may benefit from the use of imaging techniques to identify patients at high-risk who would otherwise go unnoticed. We have recently confirmed this point in RA patients with moderate CV risk according to the SCORE since they are often found to have subclinical carotid and coronary atherosclerosis (12). In keeping with these results, our group has recently demonstrated that carotid US is very useful to redefine the CV risk in AS. Up to 61% and 20% of our AS patients with moderate and low CV risk respectively had carotid plaques (13). Nevertheless, to the best of our knowledge, the potential value of CT for this purpose has not been studied in patients with AS.

CACS assessed by the multi-detector CT (MDCT) scan is useful in the assessment of the extension and severity of atherosclerosis in vascular beds. However MDCT can only detect the atherosclerotic disease in its later stages since, unlike carotid US, it is unable to identify non-calcified 'unstable' plaques. The aim of the present study was to determine the ability of CACS to detect subclinical atherosclerosis in a series of axial spondyloarthritis (ax-SpA) patients, most of them fulfilling criteria for AS. We also sought to compare CACS and carotid US to establish the best tool to improve the stratification of the CV risk in ax-SpA patients without clinically evident CV disease.

Patients and methods

Patients

A set of 66 consecutive patients seen over a 1-year period at Hospital Universitario Marqués de Valdecilla and Hospital de Laredo (Cantabria, Northern Spain) that fulfilled the Assessment of Spondyloarthritis international So-

ciety (ASAS) classification criteria for ax- SpA were recruited (14). Patients with history of CV events (ischaemic heart disease, cerebrovascular accident, peripheral arterial disease or heart failure) were excluded. Fifty-one fulfilled definitions for AS according to the 1984 modified New York criteria because besides clinical criteria they also had definite radiographic sacroiliitis on plain radiographs (grade 2 bilaterally or grade 3–4 unilaterally) (15). Fifteen patients fulfilled definitions for non-radiologic (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 (14).

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 the carotid US assessment (16-20).

Information on history of hip involvement, synovitis, enthesitis, extra-articular manifestations (anterior uveitis, psoriasis and inflammatory bowel disease), syndesmophytes, HLA-B27 status, 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 pressure at the time of study and history of traditional CV risk factors (smoking, hypertension, diabetes mellitus, dyslipidaemia, and obesity) or chronic kidney disease were also assessed.

Data on C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) at the time of recruitment and at disease diagnosis, CRP serum levels higher than 3 mg/L at the time of diagnosis, and total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides at the time of the study were assessed. Information on therapy including treatment with anti- tumour necrosis factor (TNF)-α agents from the disease diagnosis was also reviewed.

The SCORE system estimates the 10-year risk of a first fatal atherosclerotic event, whether heart attack, stroke or other occlusive arterial disease, including sudden cardiac death. Risk estimates have been produced as charts for high and low risk regions in Europe (6). Spain was included in the low risk region of Europe. The risk factors incorporated in the SCORE are the following: age, gender, smoking, cholesterol and systolic blood pressure. Subjects with SCORE <1% are included in the category of low risk. Those with a SCORE ≥1% and <5% are in the category of moderate risk. When the chart SCORE result is ≥5% and <10% they are classified as having high risk. Finally, those patients with SCORE results ≥10% are included in the category of very high CV risk.

To compensate for the underestimation of the CV risk in patients with inflammatory arthritis, the task force of the European League Against Rheumatism (EULAR) has proposed to adapt the CV risk management calculated in RA patients according to the SCORE function by the application of a multiplier factor of 1.5 (modified(m)SCORE) (21). In the present study we calculated the mSCORE as well as the TC-SCORE to compare their ability to detect high-risk patients. Sixty-four of 66 patients were assessed. Two of the 66 patients were excluded because they were included in the category of high/very high CV risk because of the presence of type 2 diabetes mellitus (n=1) and chronic kidney disease (n=1) respectively (6).

The earliest age at which the CV risk scores should be used in the general population has not been rigorously established. Both European (6) and North American (22) guidelines recommend their application in individuals over 40 years old. However, this cut off is not uniform and varies across the different CV risk scores: 30 years old in the FRS (23), 40 years old in the SCORE (4) and 45 years old in the Reynolds Risk Score (24), which can only be applied from this age onwards. In Spain, the Framingham-based REGICOR adapted function, a CV risk function validated in the Spanish population (25), established its use at an intermediate point of 35 years old. Since patients with spondyloarthritis have early accelerated atherosclerosis, and we observed carotid plaques in patients under 40, we included in the analysis all patients who were 35 years old and older.

Carotid US examination

Carotid US examination included the measurement of the carotid intima-media thickness (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 (26). The cIMT was determined as the average of three measurements in each common carotid artery. The final cIMT was the largest average cIMT (left or right). Carotid US was performed using a commercially available scanner, Mylab 70, Esaote (Genoa, Italy) equipped with 7–12 MHz linear transducer and the automated software guided technique radiofrequency -Quality Intima Media Thickness in real-time (QIMT, Esaote, Maastricht, Holland). Patients with carotid plaques and/or cIMT greater than 0.90 mm were considered as having very high CV risk.

The reproducibility of the cIMT measurements was evaluated in 20 patients within 1 week of the first US examination. The correlation coefficient for cIMT was 0.97.

MDCT imaging assessment

To determine CACS, all subjects underwent CT imaging of coronary arteries using a 32-slice multi-detector computed tomography (MDCT) scanner (Lightspeed, Pro 32, GE Healthcare, USA). It was performed following current guidelines on the screening for CAC for cardiac risk assessment (27). Patient's score was calculated as the sum of calcium score in the left main coronary artery, left anterior descending artery, left circumflex coronary artery, right coronary artery and posterior descending artery. Patients were further stratified into

four groups according to their range of CACS: CACS=0, CACS=1–100, CACS=101– 400 and CACS >400.

In general, the higher the score the more likely the patient is going to have coronary heart disease. CACS >100 indicates a high probability of coronary artery disease. Based on CACS results, a CACS 0 is normal; CACS 1–10 indicates low CV risk; CACS 11–100 moderate CV risk; CACS 101–400 moderate to high CV risk; and CAC >400 high CV risk (28). For the purpose of estimation of high/very high CV risk we used as cut-off a CACS >100 (29).

Analysis of all the scans and interpretation of calcium scores was performed by a radiologist (JAP), who was blind to the clinical information. The intraobserver variability correlation coefficient of CAC score measurements was 0.94.

The subject's written consent was obtained in all the cases. The study was approved by the local ethics committee

Statistical analysis

Categorical variables were described as percentages and quantitative variables as mean ± standard deviation (SD) or median (interquartile range- IQR). The relationship among SCORE and CACS was studied using the Goodman-Kruskal γ test with its 95% CI. Sensitivities for each CV-risk model were estimated as number of positive findings divided by number of positive results applying the gold standard procedure.

Results

Characteristics of ax-SpA patients

A set of 66 patients fulfilling ASAS criteria for ax-SpA was recruited in the present study, 51 of them fulfilling criteria for AS and the remaining 15 patients meeting criteria for non-radiological ax-SpA. Their main features are summarised in Table I. Most patients were men (56%), and the mean ± SD age at time of study and at time of disease diagnosis were 49.3±7.1 and 41.7±9.8 years, respectively. The median (IQR) disease duration since the onset of symptoms and since the disease diagnosis were 14.5 (9–23) and 5 (2–12) years respectively. Twenty-six ax-SpA patients (39%) had extra-articular manifestations (6 psoriasis,

Table I. Main clinical, epidemiologic and carotid ultrasound features of a series of 66 axial spondyloarthritis (Ax-SpA) patients without cardiovascular events.

Variable	Ax-SpA (n=66)
Men/Women, n	37/29
AS/non rx Ax-SpA, n	51/15
Age at the time of study (years), mean ± SD	49.3 ± 7.1
Age at the time of diagnosis (years), mean ± SD	41.7 ± 9.8
Delay to diagnosis (years), median (IQR)	6 2-12)
Disease duration (years), median (IQR)	
Since first symptoms	14.5 (9-23)
Since the diagnosis of Ax-SpA	5 (2-12)
BASDAI, mean ±SD	3.9 ± 2.0
ASDAS, mean ±SD	2.4 ± 1.0
BASFI, mean ±SD	4.5 ± 2.2
BASMI, mean ±SD	3.4 ± 1.7
MASES, median (IQR)	2 (0-5)
Extra-articular manifestations, n (%)	26 (39)
Psoriasis, n (%)	6 (9)
Inflammatory bowel disease, n (%)	4 (6)
Uveitis, n (%)	16 (24)
History of synovitis or enthesitis, n (%)	26 (39)
History of hip involvement, n (%)	5 (8)
Syndesmophytes, n (%)	24 (36)
Therapy, n (%)	
Anti-TNF	24 (36)
DMARDs	41 (62)
NSAIDs	60 (91)
Corticosteroids	12 (18)
HLA-B27 positive, n (%)	47 (75)
CRP (mg/l), median (IQR)	
At the time of study	3 (0.5 – 9)
At the time of disease diagnosis	5 (2 – 12)
CRP > 3 mg/L at disease diagnosis, n (%)	39 (61)
ESR (mm/1st hour), median (IQR)	
At the time of study	6.5 (3 – 18)
At the time of disease diagnosis	13 (6 – 19)
History of classic cardiovascular risk factors, n (%)	44 (67)
Current smokers	19 (29)
Had ever smoked	16 (24)
Obesity	21 (32)
Dyslipidaemia	21 (32)
Hypertension	15 (23)
Blood pressure (mm Hg), mean ± SD	
Systolic	131 ± 14
Diastolic	80 ± 10
Diabetes mellitus, n (%)	1 (2)
Chronic kidney disease, n (%)	1 (2)
Cholesterol or triglycerides (mg/dl), mean ±SD	
Total cholesterol	204 ± 36
HDL cholesterol	59 ± 21
LDL cholesterol	122 ± 32
Triglycerides	101 ± 54
Carotid IMT (mm), mean ±SD	0.652 ± 0.128
Carotid IMT (mm) >0.90, n (%)	0 (0)
Carotid plaques, n (%)	33 (50)
CACS >100, n (%)	13 (20)
TC-SCORE, mean ±SD	0.89 ± 1.22
TC-SCORE ≥5, n (%)	1 (2)
mSCORE, mean ±SD	1.34 ± 1.83
mSCORE ≥5, n (%)	2 (6)

TC-SCORE: Systematic Coronary Risk Evaluation calculated using total cholesterol; mSCORE: modified SCORE, calculated by the application of a multiplier factor of 1.5.

4 inflammatory bowel disease and 16 uveitis), and 24 (36%) were found to have syndesmophytes. HLA-B27 was positive in 47 (75%) of them. Twenty-four (36%) and 41 (62%) patients had been treated with TNF-α inhibitors and synthetic disease modifying anti-rheumatic drugs, respectively. A value of CRP higher than 3 mg/L at the time of disease diagnosis, considered as a predictive factor of CV events, was observed in 61% of patients.

With respect to the CV risk assessment, only one patient had a SCORE ≥5%, indicator of high or very high CV risk, by using the TC-SCORE. The mSCORE, calculated by the application of a multiplier factor of 1.5, only identified 2 patients with high/very high CV risk. In contrast, the imaging techniques showed findings of high CV risk in several patients: 13 (20%) were found to have CACS >100, and 33 patients (50%) exhibited carotid plaques. There were no patients with cIMT >0.90 mm.

TC-SCORE risk and CACS results

As previously discussed, two patients with type 2 diabetes mellitus and chronic kidney disease were not included in the analysis since they fulfilled definitions for high/very high CV risk independently of the SCORE prediction, as indicated in the 2016 European guidelines (6). The remaining 64 ax-SpA patients were stratified in different CV risk groups according to the SCORE (Table II). We did not use of the mSCORE because this algorithm did not increase the sensitivity of the TC-SCORE (Table I).

We then calculated the CACS in each group of risk. We observed a good correlation between CACS and TC-SCORE (Goodman-Kruskal γ test=0.7095 (0.5488–0.8702), $p<0.001$). This was especially true in the group of low CV risk, where most patients (27/33, 82%) had CACS=0. However 5/33 (15%) and 1/33 (3%) of low-risk patients had findings of low-moderate (CACS 1–100) and moderate-high (CACS >100–400) CV risk respectively.

The percentage of ax-SpA patients reclassified using this surrogate marker of atherosclerosis was higher in the group of moderate TC-SCORE. In this group 5/30 (17%) and 4/30 (13%) had a CACS >100–400 and >400 respectively. However, CACS=0 was found in a third of the patients with moderate TC-SCORE. Finally, the only patient included in the high-risk group according to TC-SCORE also had MDCT findings of high CV risk (CACS>400).

TC-SCORE risk and severe atherosclerotic disease by using carotid US and CACS

As shown in Table III, carotid US showed higher ability to detect high-CV risk patients compared to the MTCD. Only 1/33 ax-SpA patient (3%) with low TC-SCORE was found to have CACS >100 while 9/33 patients with low TC-SCORE (27%) exhibited carotid plaques. Similar findings were observed in the group of moderate CV risk, where carotid US detected plaques in most patients (21/30, 70%) but only 9/30 patients (30%) had a CACS >100.

Correlation between CACS and carotid US

Table IV shows the presence of carotid plaques in ax-SpA stratified according to CACS.

Table II. Cardiovascular risk stratification according to the TC-SCORE risk in 64 axial spondyloarthritis patients without cardiovascular events, chronic kidney disease or diabetes mellitus.

TC-SCORE		Coronary Artery Calcification Score (CACS)			
		Normal (CACS 0) n=37 (58%)	Low-moderate (CACS 1–100) n=16 (25%)	Moderate-high (CACS >100–400) n=6 (9%)	High (CACS >400) n=5 (8%)
Low (<1%)	n=33	27/33 (82%)	5/33 (15%)	1/33 (3%)	0
Moderate (≥1% and <5%)	n=30	10/30 (33%)	11/30 (37%)	5/30 (17%)	4/30 (13%)
High (≥5% and <10%)	n=1	0	0	0	1/1 (100%)
Very high (≥10%)	n=0	0	0	0	0

TC-SCORE: Systematic Coronary Risk Evaluation calculated using total cholesterol.

Table III. Cardiovascular risk stratification according to the TC-SCORE risk in 64 axial spondyloarthritis patients without cardiovascular events, chronic kidney disease or diabetes mellitus.

		Coronary Artery Calcification Score (CACS)	Carotid ultrasonography
TC-SCORE		CACS > 100 n=11 (17%)	Carotid plaques n=31 (48%)
Low (<1%)	n= 33	1/33 (3%)	9/33 (27%)
Moderate (≥1% and <5%)	n=30	9/30 (30%)	21/30 (70%)
High (≥5% and <10%)	n=1	1/1 (100%)	1/1 (100%)
Very high (≥10%)	n=0	0 (0%)	0 (0%)

TC-SCORE: Systematic Coronary Risk Evaluation calculated using total cholesterol.

Table IV. Correlation between the Coronary Artery Calcification Score (CACS) and the presence of unilateral or bilateral carotid plaques in 64 patients with axial spondyloarthritis without cardiovascular events, chronic kidney disease or diabetes mellitus.

CAC		Carotid plaques		
		No, n (%)	Yes, n (%)	
0 (normal)	n=37	25/37 (68%)	12/37 (32%)	Unilateral: 6/37 (16%) Bilateral: 6/37 (16%)
1-100 (low-moderate)	n=16	6/16 (38%)	10/16 (62%)	Unilateral: 5/16 (31%) Bilateral: 5/16 (31%)
101-400 (moderate-high)	n=6	2/6 (33%)	4/6 (67%)	Unilateral: 1/6 (17%) Bilateral: 3/6 (50%)
>400 (high)	n=5	0/5 (0%)	5/5 (100%)	Unilateral: 1/5 (20%) Bilateral: 4/5 (80%)

Most patients with any degree of coronary atherosclerosis had carotid plaques (19/27 [70%] of those with CACS ≥1 and 9/11 [82%] of patients with a CACS >100). In addition, more than 50% of patients with a CACS >100 had bilateral plaques that indicated the presence of severe atherosclerotic disease. Remarkably, we also observed carotid plaques in patients with CACS=0 (12/37 [32%)]) or CACS 1–100 (10/16 [62%]). These patients would not have been classified as having very high CV risk if they had only undergone a MDCT.

Model to establish the presence of high/very high CV risk in patients with ax-SpA

Considering the high number of patients with subclinical atherosclerosis according to imaging techniques that had been included in the categories of low and moderate CV risk when the TC-SCORE was used, we set up a predictive model that may help us to disclose ax-SpA patients with high/very high CV risk (Table V).

As considered in the 2016 European guidelines, we classified patients as having high/very high CV risk if they had a SCORE ≥5 (6). For this purpose we applied the TC-SCORE, commonly used in the Spanish general population. We also included in these categories those patients with carotid plaques or a CACS >100.

Based on that, the gold standard for high/very high CV risk was a TC-SCORE ≥5% or TC-SCORE <5% plus one of the following: severe carotid ultrasound findings (carotid plaques) or a CACS >100. Following this approach 33 of 64 patients fulfilled definitions of high/very high CV risk. As shown in Table V, the sensitivity to detect high or very high CV risk using only the TC-SCORE was very low (3%) as the charts only detected 1 of the 33 patients with high risk (Model 1). Only 2 (6%) patients were detected by applying the mSCORE instead of the TC-SCORE (Model 2).

Using a chart TC-SCORE risk ≥5% plus the presence of a CACS ≥100 in patients with moderate TC-SCORE (≥1% and <5%), the sensitivity of the model increased up to 30% (10 of the 33 patients; Model 5). The replacement of CACS with carotid US allowed us to identify a higher number of ax-SpA patients with high/very high CV risk (22 of 33; 67%) (Model 6).

We have previously reported that AS patients with low CV risk and CRP at diagnosis >3 mg/L plus syndesmophytes or extra-articular manifestations have an increased risk having subclinical atherosclerosis (13). Because of that, we added to models 5 and 6 respectively those patients with low TC-SCORE and CRP at diagnosis >3 mg/L plus syndesmophytes or extra-articular manifestations and the presence of CACS >100 (Model 7) or carotid plaques (Model 8). As shown in table 5, the use of MDCT in these selected ax-SpA patients did not improve the detection of high-CV risk patients (Model 7). Nevertheless, the carotid US use allowed us to identify four additional patients, reaching a sensitivity of 79% (26 of 33 patients; Model 8).

Table V. Sensitivity to establish the presence of high/very high cardiovascular risk in 64 axial spondyloarthritis patients without cardiovascular events, chronic kidney disease or diabetes mellitus older than 35 years using the TC-SCORE, severe carotid ultrasound findings (carotid plaques) or a Coronary Artery Calcification Score (CACS) >100 .

Model	Sensitivity
Gold standard*	n=33/64
1. TC-SCORE ≥5%	n=1/33 (3%)
2. mSCORE ≥5%	n=2/33(6%)
3. CACS≥100	n=11/33 (33%)
4. Carotid plaques	n=31/33 (94%)
5. TC-SCORE ≥5% or TC-SCORE ≥1% and <5% plus CACS >100	n=10/33 (30%)
6. TC-SCORE ≥5% or TC-SCORE ≥1% and <5% plus carotid plaques	n=22/33 (67%)
7. TC-SCORE ≥5% or TC-SCORE ≥1% and <5% plus CACS >100 or TC-SCORE <1% % and CRP>3 mg/L at the time of disease diagnosis + syndesmophytes/extraarticular manifestations plus CACS>100	n=10/33 (30%)
8. TC-SCORE ≥5% or TC-SCORE ≥1% and <5% plus carotid plaques or TC-SCORE <1 % and CRP >3 mg/L at the time of disease diagnosis + syndesmophytes/extraarticular manifestations plus carotid plaques	n=26/33 (79%)

*Gold standard for high/very high cardiovascular risk: TC-SCORE≥5% or TC-SCORE <5% plus one of the following: severe carotid ultrasound findings (carotid plaques) or a CACS >100. TC- SCORE: Systematic Coronary Risk Evaluation calculated using total cholesterol. mSCORE: modified SCORE, calculated by the application of a multiplier factor of 1.5.

Discussion

This is the first study aimed to evaluate the usefulness of the MDCT in assessing CV risk in patients with ax-SpA. This is an issue of major importance since the detection of subclinical coronary atherosclerosis may allow us to identify patients with high risk of experiencing fatal CV events who will benefit from aggressive preventive treatment (6). A recent study showing that statins, the cornerstone of the primary CV prevention, were capable of decreasing all-cause mortality by 32% in 2904 patients with AS or psoriatic arthritis, supports the critical importance of an adequate CV risk management in ax-SpA (30).

In the present study 30% of our ax-SpA patients with moderate TC-SCORE exhibited severe findings of coronary atherosclerosis (CACS >100). This ob-

servation confirms the claim that the SCORE underestimates the CV risk in ax-SpA, as we had already reported in AS by using carotid US (13). It is also in keeping with our observations in a recent study in RA, which showed that 24% of 66 patients with moderate mSCORE exhibited CACS >100 (12).

Also, we have compared for first time the ability of CACS and carotid US to detect ax-SpA patients with high CV risk. Our results suggest that carotid US may be a more sensitive test than CACS. Up to 32% and 62% of patients with MDCT findings of low (CACS=0) and low-intermediate (CACS 1–100) risk exhibited carotid plaques, which often were bilateral. This observation is of particular relevance since the presence of severe carotid US findings is considered a reliable predictor of CV events (31), and is also capable of identifying high-CV risk patients (6).

The discrepancy between CACS and carotid plaques has previously been reported. In a series of 89 healthy individuals with low CV risk and a CACS=0, carotid plaques were found in 34% of the cases (32). The percentage was even higher in another study that included 136 asymptomatic subjects, most of them with low risk, in which 52% of individuals with CACS=0 had carotid plaques (33). We have also reported similar results in a series of 104 RA patients without CV events. In our series 23 of 40 (57%) patients without coronary atherosclerosis had carotid plaques (12). A possible explanation for this finding may be the limitation of the MDCT to detect non-calcified plaques, which are present in the early stages of the atherosclerotic disease.

The superiority shown by carotid US over MDCT was reflected in the different predictive models that we designed to identify high-CV risk patients. The combination of a TC-SCORE ≥5 plus the use of carotid US in patients with moderate TC-SCORE was able to detect 67% of ax-SpA patients with high CV risk. However, the use of MDCT instead of carotid US in that model resulted in a decrease in the sensitivity to 30%.

Besides being cheaper, we feel that carotid US may have advantages when compared with MDCT as it can be performed at the out-patient rheumatology clinics. In contrast, MDCT has a limited availability and exposes patients to a considerable amount of radiation.

In our search for a strategy to improve the CV risk assessment in ax-SpA, we also analysed the ability of the mSCORE to increase the recognition of high-CV risk patients (21). However, the application of a multiplication factor of 1.5 did not significantly increase the sensitivity of the TC-SCORE. We were not surprised at seeing that finding as we previously described that the mSCORE only allowed us to reclassify as having high-CV risk a few patients with RA (34).

Finally, it is important to highlight that 36% of patients from our series were undergoing treatment with anti-TNF-α agents. These drugs have been reported to have a beneficial effect on preventing the progression of subclinical atherosclerosis in patients with inflammatory arthritis including spondyloarthritis (35). Therefore, it is possible that the use of these biologic agents may have reduced the atherosclerotic burden in our patients.

In conclusion, our results support the claim of using non-invasive tools to detect high/very high CV risk ax-SpA patients and highlight the value of carotid US as the imaging technique of choice for this purpose.

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