Subclinical atherosclerosis is not increased in patients with non-radiographic axial spondyloarthritis

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Mortality rate in patients with ankylosing spondylitis (AS) is 1.5–2.0 times increased as compared to the general population. This is mainly due to cardiovascular (CV) disease (1). Subclinical atherosclerosis manifested by the presence of carotid plaques is more commonly observed in AS patients than in matched controls (2).

Axial (ax) spondyloarthritis (SpA) is characterized by chronic back pain with an onset before the age of 45 years. It encompasses both patients with radiographic evidence of sacroiliitis, who fulfill the 1984 Modified New York criteria for AS (3), and some others without radiographically definite sacroiliitis. In this regard, the presence of sacroiliitis by magnetic resonance imaging or an HLA-B27 positive testing along with other typical features of SpA make it possible to include some patients in the category of ax-SpA under the term of non-radiographic (nr)-axSpA (4).

We have recently confirmed that carotid plaques are more common in patients with ax-SpA than in healthy controls (5). However, our sample included mostly patients who fulfilled the 1984 Modified New York criteria for AS (5).

In the present study we aimed to establish if the atherosclerotic burden is also increased in nr-axSpA. For this purpose, a series of 51 consecutive patients without history of CV disease who fulfilled the Assessment of SpondyloArthritis international Society classification criteria for nr-axSpA was studied by carotid ultrasonography (US). A series of 51 community-based age and sex and traditional CV risk factors-matched controls without CV disease were studied for comparison. Carotid US was performed as previously described (6) using a Mylab 70, Esaote (Genoa, Italy) equipped with 7–12 MHz linear transducer and the automated software guided technique radiofrequency - Quality Intima Media Thickness (IMT) in real-time (Esaote, Maastricht, Holland). Plaque was defined as a focal protrusion in the lumen at least carotid (c)IMT >1.5 mm, protrusion at least 50% greater than the surrounding cIMT, or arterial lumen encroaching >0.5 mm (6).

There were no differences between patients and controls in the frequency of carotid plaques (25.5% *vs*. 21.6%; p=0.61) and cIMT (0.571±0.11 mm *vs*. 0.574±0.089 mm; p=0.90).

Since plaque is the paradigm of atherosclerotic disease, we aimed to determine whether there could be some differences between nr-axSpA patients with and without carotid plaques (Table I). Patients with plaques were older (50.46±8.52 years *vs*. 38.28±8.07 years; p<0.001) and had higher cIMT values (0.639±0.117 mm *vs*. 0.548±0.101 mm; p=0.01) than those without plaques. They had a longer duration of the disease since the first symptoms (12.61±7.39 years in patients with plaques *vs*. 6.26±6.01 years in those without plaques; p<0.001), and a higher degree of functional limitation (BASFI 5.12±1.99 *vs*. 3.60±2.37; p=0.05). However, after adjusting for age, sex, and traditional CV risk factors, only a marginally significant association between the presence carotid plaques and extra-articular manifestations was found (odds ratio 6.47; 95% confidence interval 0.94–44.24; p=0.05). No other clinical variables were associated with the presence of plaques in nr-axSpA patients.

Table I. Non-radiographic axial spondyloarthritis: differences according to the presence or absence or carotid plaques.

Variable	With plaques (n=13)	Without plaques (n=38)	p-value
Age (years), mean±SD	50.46 ± 8.52	38.28 ± 8.07	<0.001
Men/Women	5/8	14/24	0.91
Disease duration (years), mean ±SD			
Since the first symptoms	12.61 ± 7.39	6.26 ± 6.01	0.003
Since diagnosis of ax-SpA	3.15 ± 3.46	1.31 ± 2.23	0.03
BASDAI, mean±SD	4.7 ± 1.84	4.55 ± 2.34	0.83
ASDAS, mean±SD	2.6 ± 0.75	2.38 ± 1.02	0.51
BASFI, mean±SD	5.12 ± 1.99	3.60 ± 2.37	0.05
BASMI, mean±SD	2.6 ± 1.33	2.17 ± 1.66	0.42
Extra-articular manifestations n (%)	7 (53.8)	5 (13.2)	0.003
Anterior uveitis, n (%)	2 (15.4)	4 (10.5)	0.63
Enthesitis, n (%)	6 (46.2)	16 (42.1)	0.79
Hip involvement n (%)	0	0	-
Syndesmophytes, n (%)	1 (7.7)	2 (5.3)	0.21
Psoriasis, n (%)	4 (30.8)	0	<0.001
Anti-TNF-α from the disease diagnosis, n (%)	2 (15.4)	8 (21.1)	0.65
HLA-B27 positive, n (%)	5 (38.5)	17 (44.7)	0.69
CRP (mg/l), mean±SD			
At the time of the study	2.83 ± 2.4	3.96 ± 6.73	0.55
At time of disease diagnosis	6.99 ± 12.31	5.54 ± 10.29	0.68
ESR (mm/1st hour), mean±SD			
At the time of the study	8.92 ± 5.37	7.62 ± 9.53	0.64
At time of disease diagnosis	13.69 ± 14.44	9.08 ± 8.82	0.18
Cholesterol or triglycerides (mg/dl), mean±SD			
Total colesterol,	202.0 ± 32.9	188.3 ± 34.1	0.20
HDL-cholesterol	57.7 ± 13.5	62.0 ± 21.8	0.52
LDL-cholesterol	127.0 ± 16.1	108.0 ± 26.5	0.04
Triglycerides	103.61 ± 42,9	97 ± 67.36	0.77
Carotid IMT, mean±SD	0.639 ± 0.117	0.548 ± 0.101	0.01

ax-SpA: axial spondyloarthritis; SD: Standard deviation; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate; IMT intima-media thickness.

There are a number of potential explanations for our findings. When compared with AS, patients with nr-axSpA are characterized by shorter disease duration (7, 8). Patients with nr-axSpA patients often experience a less severe inflammatory process with lower CRP levels than those with AS (7, 9). Moreover, although data indicates that nr-axSpA will evolve into AS over time, the natural evolution of disease is still undetermined since a proportion of cases do not progress (10). Therefore; a subgroup of patients with nr-axSpA will not develop radiographic sacroiliitis and, in consequence, will not fulfill definitions for AS.

In conclusion, unlike in patients with AS, our results do not confirm an association between nr-axSpA and an increased risk of atherosclerosis. Further research is required to confirm our observations.

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