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Cervical involvement in severe radiographic axial spondyloarthritis

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Introduction

Spondyloarthritis (SpA) is a heterogeneous group of chronic inflammatory rheumatic diseases with axial and/or peripheral involvement that could be associated with extra- musculoskeletal manifestations (e.g., psoriasis, uveitis, and inflammatory bowel disease). Radiographic axial spondyloarthritis (r-axSpA) refers to a subtype of SpA mainly affecting the spine and sacroiliac joints and characterized by structural damage of the sacroiliac joint [1]. Severity in r-axSpA is defined by hip involvement or progressive ossification of the spinal entheses leading to axial ankylosis [1].

Until now, the resolution of inflammation has been recognized as the main hypothesis leading to new bone formation through fat metaplasia [2]. Risk factors for radiographic progression include male sex, early onset of symptoms [3], smoking status [4], HLA-B27- positive genetic background [5], disease activity [6], and presence of syndesmophytes at baseline [7]. Although syndesmophytes are considered the main structural lesion of the spine, Zygapophyseal Joints (ZJs) or posterior ligamentous structures (interspinous ligament, supraspinous ligament, ligamentum flavum) may also be affected [8]. However, these posterior structures are difficult to study with conventional radiography because of their complex anatomy and the superposition of the right and left side for facet joints. The most validated score for assessing spinal structural damage, the

modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS), is mainly dedicated to clinical trials and not used in daily practice. Moreover, the mSASSS does not provide an exhaustive picture of the spine involvement because it does not score thoracic syndesmophytes or posterior structures [9]. In our clinical experience, the main focus is on the search for syndesmophytes, and involvement of the posterior segments is more frequently neglected, which can lead to a diagnosis delay when these structures are independently affected.

Cervical ankylosis is associated with a severe limitation of mobility, leading to significant impairment in daily quality of life [10]. For years, attention has been paid to the dorsal and lumbar spine. However, cervical involvement may be inaugural in 11% of patients with early axSpA [11] and could lead to a diagnosis delay [12]. It is present in 50% to 75% of patients with severe r-axSpA [12-14]. A CT scan may be a good alternative to study the cervical spine, but the cost, radiation, and accessibility of this tool limit its use.

Recently, the literature has focused on differentiating patients with axSpA and those with axial psoriatic arthritis (axPsA). Inconsistent radiographic features have been described in axPsA, including asymmetric sacroiliitis and paramarginal syndesmophytes. In the 1990s, particular attention was paid to cervical involvement, which seemed more frequent and severe in PsA [14-16], but this was not confirmed in a recent work [10].

In our work, we focused on cervical involvement in r-axSpA. We aimed to (1) describe the radiographic features of the cervical spine in patients with a severe form of r-axSpA and (2) compare these patients who have and do not have psoriasis or peripheral arthritis.

Materials and methods

Patients

The Bamboospine initiative is a national cross-sectional study of patients with severe r-axSpA that was initiated in 2015 to identify genetic factors associated with axial structural severity. Bamboospine inclusion criteria were the presence of bridging syndesmophytes and or fusion between 2 consecutive cervical or lumbar vertebrae, or between 3 consecutives thoracic vertebrae, as proposed in the SPINE study [17] and/or extended facet joint ankylosis. Demographic, clinical, radiological, and biological data were recorded in online case report forms.

In April 2021, 458 patients had been included in the national Bamboospine study. To include patients in the study, the local investigator had to send one of the spine region pictures meeting the inclusion criteria for central reading. For this ancillary study, we selected patients with available imaging of the entire spine in our shared Picture Archiving and Communication System (PACS), enabling easy access to the complete set of patient images and thus limiting missing data.

All patients provided written consent for the use of their data. The ethics committee gave its agreement (protocol PP-14040, September 2014).

Imaging of the spine

Antero-posterior and lateral views of the entire spine were used for x-ray assessment. Depending on imaging availability and center practices, spine imaging could be conventional radiography (n=51) or EOS imaging (n=62) (supplementary Figure 1, illustration 1). The EOS system provides digital images of the skeleton with significantly lower radiation than radiography [18]. With its good intermodality agreement (0.97, 95% CI 0.95-0.98), it can replace conventional radiography for structural damage assessment [18]. The primary objective of this study was to describe cervical involvement in r-axSpA patients. Each cervical level from C2-C3 to C6-C7 (5 levels) was assessed independently for the presence (1) or absence (0) of syndesmophytes, presence (1) or absence (0) of ZJ involvement (erosion or fusion, left and/or right side), and presence (1) or absence (0) of ossification of the posterior Ligamentous Structures (PLSs). At the global cervical level, patients were classified as having syndesmophytes or ZJ involvement if at least one level exhibited such features. In contrast, at the thoracic level, only syndesmophytes were evaluated, providing a global score for presence (1) or absence (0). At the lumbar level, syndesmophytes, ZJ involvement, and ossification of the PLSs were collectively rated, based on the presence (1) or absence (0) at the global level.

Two independent readers, a rheumatologist (SC) and a musculoskeletal radiologist (REB), performed imaging reading. After a period of training, SC and REB separately read the whole set of images. Concordance between the musculoskeletal radiologist and the rheumatologist was then estimated with the Cohen kappa coefficient [19]. Agreement was interpreted as poor for values <0.45, fair to good for values 0.45 to 0.75, and excellent for values >0.75 [19]. In case of disagreement, the set was reviewed by both readers until agreement was reached, unless the result was classified as doubtful due to poor-quality imaging. Additional imaging (all available X-rays and CT scans if accessible) could be used in case of disagreement between readers.

Statistical analysis

Continuous variables were compared by chi-squared or Fisher exact test and expressed as mean (SD). Categorical variables were compared by Student t test or Mann-Whitney test according to the distribution of data and were expressed as number (percentage). A biostatistician (CLM) used RStudio 1.4.1106 for statistical analysis. P<0.005 was considered statistically significant. Four structural damages were identified: cervical syndesmophytes (SC+), cervical ZJ involvement (ZJC+), lumbar syndesmophytes (SL+) and lumbar ZJ involvement (ZJL+). Several analyses of clinical and demographic characteristics were conducted according to the presence or absence of the structural damage mentioned above: patients with full cervical involvement including both syndesmophytes and ZJ damage (SC+ and ZJC+), presence of at least one cervical lesion (ZJC+ or SC+), presence of syndesmophytes at both the cervical and lumbar level (SC+ and SL+), and presence of ZJ involvement at both the cervical and lumbar level (ZJC+ and ZJL+). Ossification of PLSs were systematically associated with ZJ damage, so no further analysis was performed on isolated PLSs. We compared patients with and without cervical involvement. We performed an additional analysis comparing the radiographic pattern according to the presence or absence of a history of psoriasis and peripheral arthritis.

Results

From February 2015 to April 2020, 458 patients were included in the Bamboospine initiative; 144 were from 4 Paris rheumatology centers. After excluding patients with missing X-rays (n=25), discordance in the database (n=3) and duplicates (n=3), 113 patients were included in our study.

Clinical features

The clinical characteristics of patients are summarised in Table 1. Patients were predominantly men (89.4%), with mean (SD) age at inclusion 53.6(11) years and mean disease duration 27(13) years. In total, 65 of 112(58%) patients were current (n=33) or past (n=32) smokers. All patients had radiographic sacroiliitis according to modified New York criteria [20] and 32.4% had a history of peripheral arthritis. Among 80 patients with known HLA-B27 status, 70(85.4%) were positive. A history of uveitis was the most frequent extra-musculoskeletal manifestation (36.2%), followed by psoriasis (17.1%) and inflammatory bowel disease (11.5%). Most patients (n=105) had been exposed to non-steroidal anti-inflammatory drugs and 39 had still received these drugs at least once a week in the last 12 months. Overall, 81 of 112 patients (72%) were on biologic disease-modifying anti-rheumatic drugs; 59 were on infliximab, with a mean exposure of 13.4 (12.3) years.

To ensure that our sample of 113 patients was similar to the entire population of the Bamboospine initiative, we compared the clinical and demographic characteristics of the two populations after excluding missing data. Both groups were comparable, except for socio- economic features. Our sample more frequently had an education beyond the secondary level (40% vs 23%, p=0.006) and more frequently were working (55% vs 34%) than retired (15% vs 37%, p=0.001) (data not shown).

Radiographic features

Structural lesions were most frequently found in the lumbar spine (84%), including 62% with syndesmophytes, 75% with ZJ involvement and 50% with PLS involvement (Figure 1 and supplementary Figure 1, illustrations 2-4). The cervical spine was affected in 77% of patients, including 64% with syndesmophytes, 66% with ZJ involvement and 19% with PLS involvement (Figure 1 and supplementary Figure 1, illustrations 5-8). Finally, 61% of patients had thoracic syndesmophytes (61%). ZJ and PLS damage could not be assessed at the thoracic level (Figure 1 and supplementary Figure 1, illustration 9).

Most patients had a combination of syndesmophytes and ZJ damage at the lumbar and/or cervical levels (Figure 2). Overall, 10.9% of patients had isolated cervical involvement without thoraco-lumbar involvement, and 22% had isolated lumbar structural lesions (Figure 2). Thoracic lesions were mostly associated with lumbar (n=60) or cervical lesions (n=55) but were found isolated in only 5 patients (data not shown).

For the 87 patients with cervical structural damages, a more detailed analysis was performed for each vertebral level (Figure 3). Among these patients, we frequently observed syndesmophytes (83%) and ZJ involvement (86%), but PLS damage was rare (24%) and always associated with ZJ lesions (data not shown). Most patients had both syndesmophytes and ZJ damage. Overall, 10.3% of patients had isolated ZJ damage without syndesmophytes. All levels were almost equally affected, C2-C3 being the most affected location for syndesmophytes (56.6%) or ZJ damage (58%), followed by C5-C6 (54.4% and 55.8%), respectively. In this population, 35% of patients had extensive cervical damage corresponding to the presence of syndesmophytes and ZJ involvement at all levels from C2 to C6.

Associations between clinical and radiographic features

We compared patients with full cervical involvement including both syndesmophytes and ZJ damage to the remaining patients but found no differences in clinical or demographic characteristics (Table 2). We also compared patients with at least one structural lesion in the cervical spine (ZJC+ or SC+) to those without any cervical involvement and found the Bath Ankylosing Spondylitis Functional Index higher among patients with than without cervical involvement although not significantly (39.7 vs 29.8; p=0.07) (Supplementary Table 1).

In both analyses, disease duration, extra-musculoskeletal manifestations, disease activity (C-reactive protein level and Bath Ankylosing Spondylitis Disease Activity Index), smoking status, or treatment use were not significantly associated with cervical involvement (Table 2, Supplementary Table 1).

Radiographic pattern according to clinical features

Peripheral arthritis and psoriasis have been found more frequent in axPsA than axSpA [21]. Among the 113 patients, we identified 36 with a history of peripheral arthritis and 19 with psoriasis.

First, we compared patients with and without psoriasis. Demographic data and clinical manifestations were similar (supplementary Table 2). The two groups did not differ in spondylitis pattern for the prevalence of cervical (63.2% vs 62.6%, p=0.966) or lumbar syndesmophytes (63.2% vs 60.4%, p=0.825), zygapophyseal cervical damage (63.2% vs 66.3%, p=0.792) and global cervical involvement (52.6% vs 54.3%, p=0.891).

We also compared patients with and without history of peripheral arthritis (supplementary Table 3). As compared with patients without peripheral involvement, those with peripheral involvement were younger (mean age 26.9 vs 33.4 years, p=0.005) and more often had a history of enthesitis (48.6% vs 26.7%, p=0.024), had dactylitis although not significantly (11.8% vs 2.7%, p=0.075), and were exposed to biologic disease-modifying anti- rheumatic drugs (86.1% vs 65.3%, p=0.002). The two groups had similar ZJ damage at the cervical (72.2% vs 62.7%, p=0.321) or the lumbar level (82.4% vs 71.8%, p=0.243).

Discussion

Our study is the first to provide a picture of the clinical and radiographic features of patients with severe r-axSpA. Cervical involvement was frequent (77% of patients) with syndesmophytes (83%) and zygapophyseal damage (86%) mostly evenly distributed at each cervical level. ZJ damage could be isolated (10.8%).

To our knowledge, this study is the largest (n=113) cross-sectional investigation of radiographic features in severe axSpA. Other cross-sectional studies of axSpA patients include a Korean study (n=61) [22], the subgroup with cervical X-rays in the GLAS cohort (n=99) [13] and the SIAS cohort of Stal et al. (n=60) [23]. The OASIS [24], DESIR [7] and GESPIC [5] cohorts include patients with less severe axSpA. In contrast to previous studies, we provided a full set of radiographic and clinical data. The Korean study excluded patients with a history of psoriasis or inflammatory bowel disease, the GLAS and SIAS studies did not report any demographic data (smoking, education), and

Table 1: Characteristics of patients with radiographic axial spondyloarthritis (r-axSpA) (n=113).

Demographics		
Men	101	89.4%
Age at diagnosis (years) (mean, SD)	31.2	11.7
Age at inclusion (years) (mean, SD)	53.6	11
Disease duration (years) (mean, SD)	27	13
Smoking status, n=112		
Never	47	42%
Current	33	29.5%
Ever smoke	65	58%
Education level, n=112		
Elementary school	20	17.7%
High school	43	38.1%
College	40	35.4%
Working status, n=111		
Unemployed	9	8.1%
Working	62	55.8%
Disability	19	17.1%
Retired	21	18.9%

SpA features (ever)#		
Chronic back pain (for >3 months)	109	96.5%
Chest pain	45	40.9%
Buttock pain	78	71.6%
Peripheral arthritis	36	32.4%
Enthesitis	38	33.9%
Dactylitis	6	5.4%
HLA-B27 positivity	70	85.4%
Elevated C-reactive protein level	87	84.5%
X-ray sacroiliitis according to modified New York criteria	112	100%
Personal history of Uveitis, n=113	41	36.3%
Inflammatory bowel disease, n=113	13	11.5%
Reactive arthritis, n=112	2	1.8%
Psoriasis, n=111	19	17.1%
Family history of Spondyloarthritis, n=107	35	32.7%
Psoriasis, n=102	14	13.7%
Uveitis, n=98	9	9.2%
Reactive arthritis, n=99	1	1.0%
Inflammatory bowel disease, n=101	6	5.9%
Surgical history Hip replacement (n=113)	12	10.6%
Replacement other than hip (n=113)	3	2.7%
Arthrodesis (n=113)	2	1.8%
Vertebrotomy (n=112)	1	0.9%
BASDAI, 0-100 (median, SD)	28	22.4
BASFI, 0-100 (median, SD)	36	25.3
Treatment exposure (history of treatment)		
NSAIDs (n=112)	105	93.8%
Duration of exposure (years) (mean, SD)	18.1	12.2
csDMARDs* (n=113)	51	45.1%
bDMARDs (n=112)	81	72%
Including infliximab (n=81)	59	
Duration of exposure (years) (mean, SD)	13.4	12.3

BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; NSAIDs: Non-Steroidal Anti-Inflammatory Drugs; csDMARDs: conventional synthetic Disease-Modifying Anti-Rheumatic Drugs; bDMARDs: biologic Disease- Modifying Anti-Rheumatic Drugs.

refers to a history of all SpA features, but not mandatory at the time of assessment.

*csDMARDs were methotrexate, leflunomide, sulfasalazine and hydroxychloroquine.

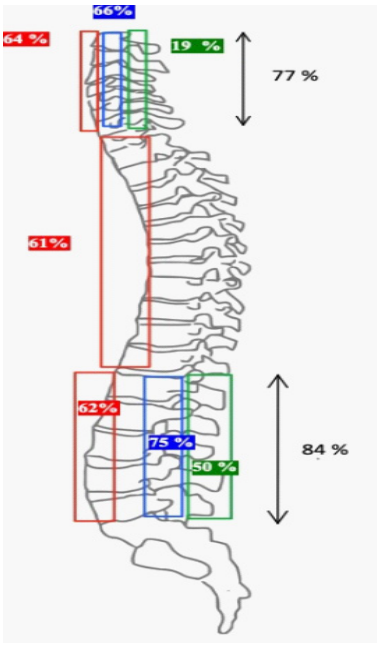

Figure 1: Distribution of cervical involvement by structural region in patients with axial spondyloarthritis (n=113).
This diagram excludes 7 patients with doubtful lesions and 5 without cervical and lumbar lesions. For each spinal segment, frequencies of syndesmophytes (red), zygapophyseal joints (blue) and posterior ligamentous structures (green) are depicted.

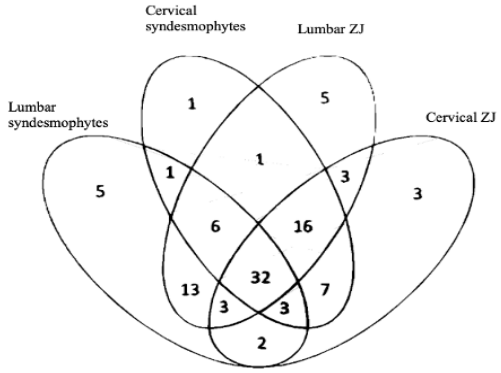

Figure 2: Distribution of structural lesions in axial spondyloarthritis patients (n=113).

Table 2: Patient characteristics according to the presence or absence of cervical involvement.

	SC+ & ZJC+ N = 61	SC- or ZJC- N = 52	p-value
Demographics			
Men	55 (90.2%)	46 (88.5%)	0.771
Age diagnosis (mean, SD)	31.4 (11.9)	30.8 (11.5)	0.170
Disease duration (mean, SD)	28.0 (12.4)	25.8 (13.7)	0.378
Education level Elementary High school College	 13/56 (23.2%) 24/56 (42.9%) 19/56 (33.9%)	 7/47 (14.9%) 19/47 (40.4%) 21/47 (44.7%)	0.426
Working status Unemployed Working disability retired	 5/59 (8.5%) 33/59 (55.9%) 10/59 (16.9%) 11/59 (18.6%)	 4 (7.7%) 29 (55.8%) 9 (17.3%) 10 (19.2%)	1.000
Smoking Never Current Past >3 y Past <3 y	*N = 60* 22 (36.7%) 21 (35.0%) 13. (21.7%) 4 (6.7%)	 25 (48.1%) 12 (23.1%) 9 (17.3%) 6 (11.5%)	0.358
Smoking ever	38 (63.3%)	27 (51.9%)	0.222
SpA features (ever)			
Chronic back pain (>3 months)	59 (96.7%)	50 (96.2%)	0.849
Chest pain	21/60 (35.0%)	24/50 (48.0%)	0.167
Buttock pain	41/58 (70.7%)	37/51 (72.5%)	0.830
Arthritis	22/60 (36.7%)	14/51 (27.5%)	0.301
Enthesitis	19 (31.1%)	19/51 (37.3%)	0.497
Dactylitis	2/60 (3.3%)	4/51 (7.8%)	0.411
Elevated C-reactive protein level	1.3 (0.6)	1.3 (0.6)	0.730
HLA-B27 positivity	39/44 (88.6%)	31/38 (81.6%)	0.367
X-ray sacroiliitis according to modified New York criteria	61 (100%)	51/51 (100%)	1.000
Personal history of			
Uveitis	24 (39.3%)	17 (32.7%)	0.464
Crohn's disease	8 (13.1%)	5 (9.6%)	0.561
Psoriasis	10/60 (16.7%)	9/51 (17.6%)	0.891
Family history of			
SpA	16/55 (29.1%)	19 (36.5%)	0.412
Psoriasis	7/55 (12.7%)	7/47 (14.9%)	0.751
Uveitis	6/51 (11.8%)	3/47 (6.4%)	0.490
Inflammatory bowel disease	5/54 (9.3%)	1/47 (2.1%)	0.212
Surgical history of			
Hip replacement	3 (4.9%)	2 (3.8%)	0.188
Arthrodesis	1 (1,6%)	0	0.711
BASDAI (mean, SD)	32.2 (22.5)	32.2 (21.0)	0.989
BASFI (mean, SD)	40.4 (25.2)	35.9 (24.4)	0.334
Treatment exposure (history of treatment)			
bDMARDs ever	43 (70.5%)	38 (73.1%)	0.761
Total time under bDMARDs (years) (mean, SD)	20.0 (27.2)	20.5 (33.9)	0.801

SC: Cervical Syndesmophytes; ZJC: Cervical Zygapophyseal Joint involvement; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; bDMARDs: biologic Disease-Modifying Anti-Rheumatic Drugs; SpA: Spondyloarthritis.

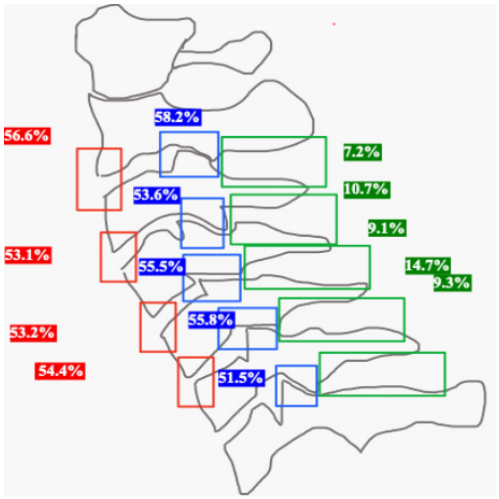

Figure 3: Distribution of cervical involvement by structural region in patients with axial spondyloarthritis in the Bamboospine population study.
This diagram excludes 7 patients with doubtful lesions and 5 without cervical and lumbar lesions. For each spinal segment, frequencies of syndesmophytes (red), zygapophyseal joints (blue) and posterior ligamentous structures (green) are depicted.

Stal et al. [23] did not report the duration of symptoms or time since diagnosis. Finally, none of these studies gave an idea of the heterogeneity of the spondyloarthritis phenotype because it was diluted in the scores [3,22]. They ignored possible lumbar involvement [13] or did not provide a correlation between radiographic and clinical features [23].

In our study, patients were predominantly men (89%), were HLA-B27 carriers (85%) and had long disease duration (mean 27 years), which are known risk factors for severity [25] and were expected because inclusion criteria was bridging syndesmophytes or ZJ fusion. Regarding extra-musculoskeletal manifestations [26], our results are as expected for uveitis (36%) for patients with a long disease duration. The prevalence of psoriasis (past or present) was 17% in our study, which allowed a specific analysis of the radiographic characteristics associated with this specific phenotype.

Regarding the radiographic features, we chose a simple and reproducible criterion (presence or absence of lesions), as in clinical practice. When doubtful, we tended to assess the result as normal. Good to excellent agreement on cervical radiographs reflects the feasibility of such imaging for assessing cervical involvement. The study by Stal et al. supports our choice because although the authors used a three-stage classification (normal, irregularity, ankylosis), they also simplified it for data analysis (presence, absence) [23].

Our findings are consistent with the available data on radiographic damage distribution. All included patients had radiographic sacroiliitis, although this was not an inclusion criterion. We found 60.9% of patients with thoracic syndesmophytes, which is consistent with the literature for severe spondylarthritis [14,30,31]. Lumbar syndesmophytes were slightly more frequent (61.6%) than thoracic syndesmophytes (60.9%), unlike in a previous CT study [31] because X-rays tend to underestimate the thoracic involvement [31]. In all cases, thoracic involvement is difficult to assess because of bony superimpositions. Thoracic syndesmophytes were not accounted for in the statistical analysis. We found broad radiographic heterogeneity in terms of the extent and localization of structural damage. Overall, 10.9% of patients in this severe axSpA population had isolated cervical involvement without thoraco-lumbar involvement. This is a strong argument against the so-called linear progression from thoraco- lumbar localization to cervical localization.

Our study is the first to give details of the different types of cervical damage, namely damage to the vertebral corners, posterior joints, and posterior ligamentous structures. All cervical levels were almost equally affected, C2-C3 and C5-C6 being the most affected. The frequency of radiographic cervical involvement of all types that we report (77%) is broadly similar to that reported by Lee et al. with a cervical Bath Ankylosing Spondylitis Radiology Index >0 (81%) [22]. The studies by Stal et al. [23] and Maas et al. [13] did not allow for evaluating this overall prevalence.

We report a higher prevalence of cervical ZJ ankylosis (66%) than the 47% for Lee et al. [22] and 7% to 25% by CT scan for Stal et al. [23] and Maas et al. [13]. The main explanation for this difference is the disease duration [13]. This is an important result because ZJ damage is clinically relevant and important. At the cervical spine, posterior joint impairment is responsible for a significant loss of cervical rotation independent of disease activity and vertebral involvement [13]. In a recent prospective study, low-dose CT scans revealing ZJ ankylosis were associated with restricted spinal motion and functional decline [32].

In our study, psoriasis was not associated with cervical involvement of any type. Our result is consistent with a recent study that compared psoriatic PsA and r-axSpA without psoriasis [10]. In this study, 29 of 118 (24.6%) of the PsA patients and 60 of 157 (38.2%) of the r-axSpA patients had cervical facet-joint damage (odds ratio 1.48; p=0.2 after multivariate logistic regression) [10].

ZJ damage was highly prevalent in our study. The inclusion of patients with more severe disease in our study might be an explanation. In addition, because ZJs are synovial joints, we wondered whether arthritis history was associated with ZJ damage [33] but found no significant associations.

The Bamboospine study helped gather sufficient patients with significant structural damage to be able to describe such radiographic findings. Additionally, extreme phenotypes offer valuable insights into the disease. These findings are present in severe axSpA and may not reflect all axSpA patients. Despite potential for selection bias and over-representation of cervical involvement due to imaging preferences for symptomatic patients, we mitigated missing images by using our centralized PACS and proactive search for spine images. Also, more than half of the patients were recruited in our center, where cervical spine radiography was routine.

Conclusion

Cervical spine involvement in severe r-axSpA is frequent (77% of our population) and disabling. Among patients with cervical spine damage, 86% had ZJ ankylosis, and 10.9% had ZJ involvement without syndesmophytes. Classical radiographic classifications overlook ZJ involvement. Our results strongly suggest that cervical, especially ZJ, involvement should be systematically assessed by cervical radiography at the first evaluation and with cervical symptoms (pain, decreased mobility). This is crucial because cervical involvement can be profoundly disabling and may manifest independently of structural lesions in the thoraco- lumbar region, thus emphasizing its clinical significance in r-axSpA management.

Declarations

Conflicts of interest: None

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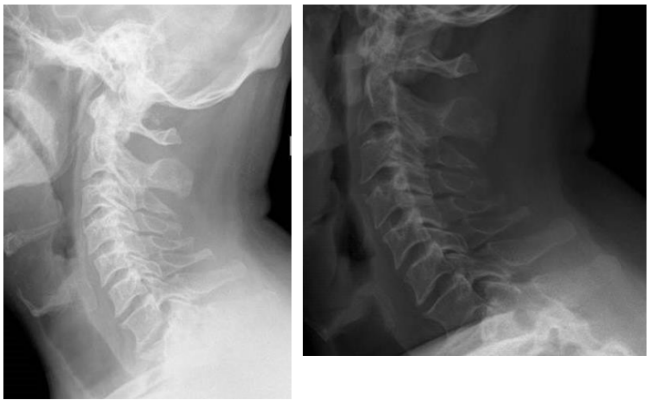


X-rays of the cervical spine (2010) EOS image of the cervical spine (2016) same patient

Illustration 1: Cervical spine of the same patient using different imaging modalities.

Illustration 2: Lumbar syndesmophytes.

Illustration 3: Lumbar zygapophyseal joint ankylosis.

Ossification of supra-spinous and interspinous posterior ligament

Illustration 4: Lumbar posterior ligamental structures ossification.

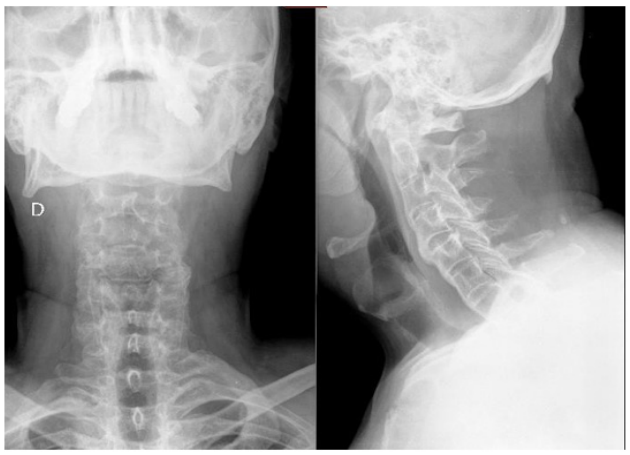
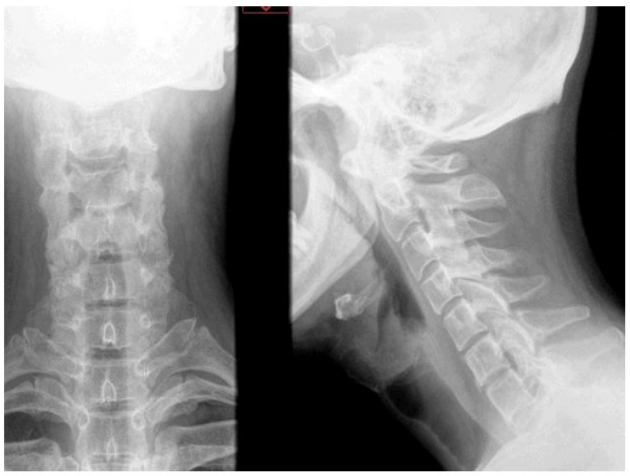


Illustration 5: Cervical bridging syndesmophytes with normal zygapophyseal joints



Ankylosis of cervical zygapophyseal joint at C2-C3, C3-C4 and C4-C5 levels.

Illustration 6: Cervical zygapophyseal joint ankylosis without syndesmophytes.

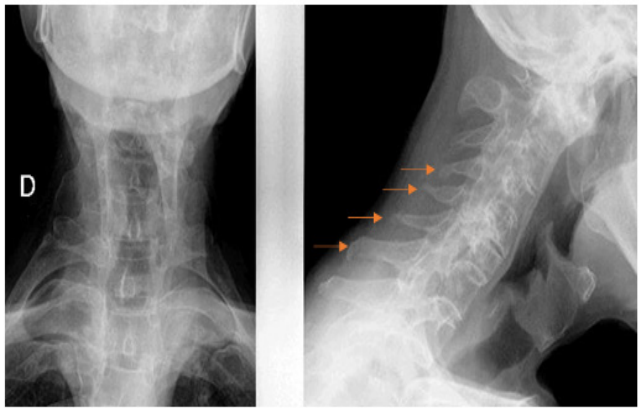


Illustration 7: Ossification of the supraspinous ligament.

Illustration 8: Extensive cervical damage.

Patient with diffuse syndesmophytes, diffuse zygapophyseal joint ankylosis and ossification of the interspinous ligament (arrow).

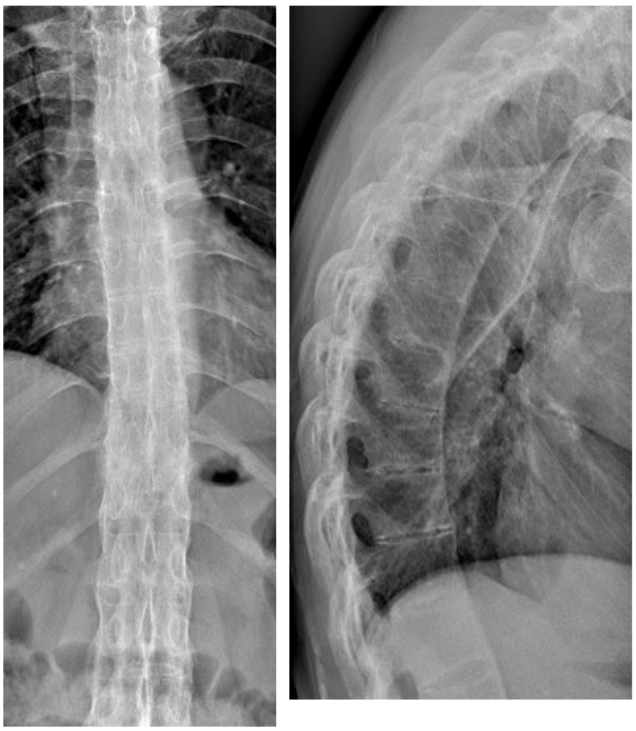


Illustration 9: Thoracic syndesmophytes.