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Prevalence and prediction factor of atlanto:axial subluxation in early polyarthrititis (Espoir cohort)

Aurore Le Quellec

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**PREVALENCE AND PREDICTION FACTORS OF ATLANTO-AXIAL
SUBLUXATION IN RHEUMATOID ARTHRITIS (ESPOIR COHORT)**

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INTRODUCTION :

Cette thèse comporte 2 articles :

Un premier article, intitulé *Reproducibility and diagnostic value of a new method using ratios to diagnose anterior atlanto-axial subluxation on plain radiographs*, détaille la méthodologie utilisée pour rechercher les patients présentant une luxation atlanto-axoïdienne antérieure.

Le second article, intitulé *Prevalence and prediction factor of atlanto-axial subluxation in rheumatoid arthritis (espoir cohort)*, recherche la prévalence de la luxation atlanto-axoïdienne antérieure dans la cohorte ESPOIR et les facteurs prédisposants.

REPRODUCIBILITY AND DIAGNOSTIC VALUE OF A NEW METHOD USING RATIOS TO DIAGNOSE ANTERIOR ATLANTO-AXIAL SUBLUXATION ON PLAIN RADIOGRAPHS

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AUTHORSHIP: All individuals listed as authors qualify for authorship according to the following four ICMJE criteria

KEYWORDS: Cervical spine; Radiography; Atlanto-Axial Subluxation; rheumatoid arthritis

SIGNIFICANCE & INNOVATION:

- Atlanto-axial subluxation is classically detected in rheumatoid arthritis using measurements on dynamic cervical spine radiograph.
- In everyday practice, measurements are not possible or reliable for several reason (computed radiographs or printed digital radiographs without scales, radiographs digitized in formats .jpeg, magnification effect)

- The aim of this study was to evaluate reproducibility of extrapolated anterior and posterior atlanto-dental intervals obtained from ratios measured on plain radiographs and their sensitivity and specificity versus classical measure in millimetre.
- Measures extrapolated from the ratios could be used to detect atlanto-axial subluxation.

COMPETING INTERESTS

The authors have no competing interests to declare.

FUNDING

This research received no specific funding from the public, commercial, or not-for-profit sectors.

ETHICAL APPROVAL INFORMATION

The study was conducted on a set of anonymous data from a single center.

DATA SHARING STATEMENT

Data are available via Alain Saraux, principal investigator.

PATIENT AND PUBLIC INVOLVEMENT

Patients and public were not involved in the design, conduct and reporting of the research

ABSTRACT

OBJECTIVES: Measures on conventional radiography are used to detect, especially in rheumatoid arthritis, upper cervical spine instabilities (CSIs) with the anterior and posterior atlanto-dental intervals (AADI and PADI) measurements. Our objective was to evaluate the diagnostic performance and reliability of AADIs and PADIs extrapolated based on ratios in assessing anterior atlanto-axial subluxation (aAAS) when plain radiographs do not allow the measures.

METHODS: Radiographies of 119 patients were randomly selected. Two blinded observers performed two measurements of the odontoid sagittal diameter (O), axis body base sagittal diameter (C2), AADI, PADI, Clark station and Ranawat index, and the AADI/O, AADI/C2, PADI/O and PADI/C2 ratios were calculated. The diagnostic value of AADI and PADI extrapolated from the AADI/O, AADI/C2, PADI/O and PADI/C2 ratios was evaluated using ROC curves, with AADI >2.99 mm used as the gold standard.

RESULTS: Among the 119 patients, 12 patients had aAAS (AADI >2.99 mm), 6 patients had severe aAAS (AADI >8.99 mm and/or a PADI <14 mm), and 6 patients had vertical AAS (Clarks station=2 or 3 and/or Ranawat index <13 mm). The AADI extrapolated from the AADI/O and AADI/C2 ratios has excellent intra and interobserver reproducibility. The diagnostic value of the extrapolated AADI was high for aAAS (sensitivity 92%; specificity of 100%) and severe aAAS (sensitivity 75%; specificity 100%). The diagnostic value of the extrapolated PADI was good but lower than the diagnostic value of the extrapolated AADI.

CONCLUSION: Extrapolated AADI can be used instead AADI to detect aAAS and severe aAAS.

Abbreviations and acronyms

CSI: cervical spine instability
AADI: anterior atlanto-dental interval
PADI: posterior atlanto-dental interval
aAAS: anterior atlanto-axial subluxation
vAAS: vertical atlanto-axial subluxation
AAS: atlanto-axial subluxation
O: Odontoid sagittal diameter
C2: Axis body base sagittal diameter
RA: rheumatoid arthritis
PACS: picture archiving and communication system

INTRODUCTION

Many congenital and acquired diseases, including trauma, can result in upper cervical spine instabilities. Most of these instabilities are referred to as atlanto-axial subluxation (AAS). AAS has mostly been reported in individuals with rheumatoid arthritis (RA), but it has also been observed in individuals with spondyloarthropathies, mixed connective tissue disease, systemic lupus erythaematosus, trisomy 21 and Behcet's disease (1,2). Diagnosing AAS is essential because it can be asymptomatic and may lead to spinal cord compression, vascular compression and death (3,4). It can also affect anaesthetic management, and it is important to avoid unprotected manipulations of the neck under anaesthesia (5,6).

The dynamic cervical spine radiograph is the essential screening tool for ruling out cervical spine instability (7–9). As such, the anterior (AADI) and posterior (PADI) atlanto-dental intervals have been widely used to diagnose aAAS and as markers for evaluating motion and potentially predicting neurologic cord compromise at the atlantoaxial junction (10–12). To diagnose vAAS (also known as basilar impaction or basilar invagination), numerous radiographic criteria have been described, such as the McRae line, Chamberlain line, McGregor line, Redlund-Johnell criterion, Ranawat criterion, Sakaguchi-Kauppi method and Clark station. (13)

Most of these radiographic criteria require measurements using the metric system (except for Sakaguchi-Kauppi method (14) and Clarks Station). However, in everyday practice, aAAS are more common than vAAS, and to our knowledge, there is no method to diagnose aAAS without the need of metric scale. These metric measurements are not always possible or reliable for several reasons: computed radiographs or printed digital radiographs do not always include scales, radiographs sometimes are digitized in formats that do not allow measurements to be taken (.jpeg or .bmp, for example), and radiographs may exhibit the magnification effect, which can affect the reliability of measurements and is caused by there

being a distance from the patient to the film and the space from the film to the X-ray tube (15,16). The proportions are preserved in all of these situations, and using ratios has been suggested as a solution by many authors (17–19).

This problem also arises for the evaluation of the cervical spine in the French prospective multicentric ESPOIR cohort study, which was established to monitor the clinical, laboratory and radiographic data from patients with recent-onset inflammatory arthritis consistent with RA (20). Indeed, neutral and dynamic cervical plain radiographs were obtained 12 years after patient inclusion, but these radiographs were digitized and included in the ESPOIR database in the .bmp and .jpeg formats, which did not allow the typical measurements to be taken.

The purpose of this study was to evaluate and compare the diagnostic performance and inter-/intraobserver reliability of indexes using ratios in the assessment of upper cervical spine instabilities such as anterior atlanto-axial subluxation (aAAS).

METHODS

Study population

A total of 119 patients (female:male ratio = 1.55:1; age range 15-92 years, mean 43.71 ± 18.55 years; height range 145-192 cm, mean 171 ± 8.4 cm) were randomly selected from a PACS (picture archiving and communication system) database with deidentified data in our institution. Fourteen of the 119 patients were known to have CSI.

Radiograph evaluation

Lateral cervical spine radiographs obtained in the full flexion position were retrospectively and independently analysed twice by two observers, a junior radiologist (TG) and a junior rheumatologist (ALQ). For each radiograph, the odontoid sagittal diameter (O), axis body base sagittal diameter (C2), AADI, PADI, Clark station and Ranawat criterion were measured (Figure 1):

- The odontoid sagittal diameter (O) is the distance from the anterior to the posterior border of the dens.
- The axis body base sagittal diameter (C2) is the distance from the anterior to the posterior border of the base of the vertebral body of the axis (excluding osteophytes, if present).
- The AADI is the distance from the posterior margin of the anterior C1 arch to the anterior border of the dens.

- The PADI is the distance from the posterior margin of the odontoid to the anterior border of the posterior ring of C1.
- For the Clark station, the station of the atlas is determined by dividing the odontoid process into three equal parts in the sagittal plane. If the atlanto-axial facet is level with the middle third (station II) or the caudal third (station III) of the odontoid process, basilar invagination (or vAAS) is diagnosed.
- For the Ranawat criterion, the distance between the centre of the second cervical pedicle and the transverse axis of the atlas is measured along the axis of the odontoid process. A distance of less than 13 mm is indicative of vAAS.

Definition of subluxation

The presence of subluxation was determined according to the average of the measured values using common definitions found in the literature (12,21–23):

- aAAS was defined in patients with an AADI >2.99 mm.
- vAAS was defined in patients with a Ranawat value <13 mm and/or Clark station = 2 or 3.
- Severe aAAS was defined by an AADI >8.99 mm and/or a PADI <14 mm. Severe aAAS is associated with an increased risk of neurological complications and requires surgical advice and a radiological follow-up (11,21,24).

The average AADI/O, AADI/C2, PADI/O and PADI/C2 ratios were calculated for each patient.

Reliability

We also evaluated intra- and interobserver reliability for all measurements (AADI, PAADI, Ranawat value <13 mm and Clark station) and ratios (AADI/O, AADI/C2, PADI/O and PADI/C2).

Extrapolation of AADI and PADI from the ratios

It is possible to evaluate the diagnostic value of the AADI/O, AADI/C2, PADI/O and PADI/C2 ratios using a ROC curve, but the cut-off values of these ratios will differ from the original AADI and PADI, and it may be confusing for clinicians who prefer to keep the AADI and PADI values. Therefore, we used a plot with the ratios on the x-axis and metrics on the y-axis, as published previously (25), to obtain the $y=ax+b$ equation needed to convert the differing cut-off values for AADI and PADI. Then, it was possible to evaluate the diagnostic

value of the extrapolated AADI and PADI obtained from the ratios using the same cut-off values.

Statistical analysis

Statistical analyses were performed using SPSS 25.0. First, we used the intraclass correlation coefficient (ICC) to determine intra- and inter-observer reliability for every measurement and ratio. An ICC > 0.8 was considered to be excellent. Then, we evaluated the correlation between ratios and AADI/PADI measurements using Spearman's rho coefficient. Finally, we calculated the AADI and PADI values extrapolated from the ratios, evaluated the correlation between the AADI/PADI extrapolated from the ratios and AADI/PADI measurements using Spearman's rho coefficient, and studied the diagnostic value of these AADI and PADI values extrapolated from the ratios using receiver operator characteristics (ROC) curves.

RESULTS

Of the 119 patients included, 14 patients had a CSI (11.8%). Twelve patients had aAAS (10.1%), 6 of them were severe (5.0%), and 6 patients had vAAS (5.0%). Four patients with vAAS also had aAAS, and 3 of them had severe aAAS. All the average measurements and ratios are reported in Table 1.

Inter- and intraobserver agreement

The ICCs for inter- and intraobserver agreement are displayed in Table 2. The inter- and intraobserver agreement were excellent (>0.8) concerning the AADI/O, AADI/C2, PADI/O and PADI/C2 ratios.

Correlation between distances and ratios

AADI/O and AADI/C2 had strong correlations with the AADI measurement (Spearman's rho correlation coefficients of 0.933 and 0.915, respectively; $P < 0.001$). PADI/O and PADI/C2 had moderate correlations ($p < 0.0001$) with the PADI measurement (Spearman's rho correlation coefficients of 0.646 and 0.600, respectively; $P < 0.001$).

Extrapolation of the AADI and PADI from ratios

Figure 2 shows the formulae obtained from the equation $y = ax + b$ and used to extrapolate the AADI and PADI from ratios in order to have the same cut off that is usually used with distances to define instability (3 and 9 for the AADI to diagnose aAAS and severe aAAS and

14 for the PADI to diagnose severe aAAS). For example, we used the equation $y = 11.63x + 0.32$ to extrapolate the AADI from the AADI/O ratio. Hence, an AADI/O ratio = 0.6 corresponds to a standardized AADI = 7.298.

Correlation between distances and the AADI/PADI extrapolated from ratios

Supplemental figure 1 shows the scatter plot between the original and extrapolated AADI and PADI. The AADI extrapolated from AADI/O and AADI/C2 had a strong correlation with the AADI measurement (Spearman's rho correlation coefficients of 0.969 and 0.969, respectively; $P < 0.001$). PADI/O and PADI/C2 had moderate correlations with the PADI measurement (Spearman's rho correlation coefficients of 0.769 and 0.793, respectively; $P < 0.001$).

Diagnostic performances of ratios

The ROC curves for the identification of aAAS and severe aAAS generated using the standardized AADI and PADI values obtained from ratios are displayed in Figure 3.

Using AADI > 2.99 as the gold standard (figure 3a), an AADI extrapolated from the AADI/O ratio had a sensitivity of 92% and a specificity of 100% to diagnose aAAS. Using the same gold standard, the extrapolated AADI obtained from the AADI/C2 ratio had a sensitivity of 92% and a specificity of 100% to diagnose aAAS. Figure 4 shows an example of a both measurement and extrapolation in a patient with aAAS on lateral flexion plain radiograph. When standard measurement found an AADI = 7.02 mm, AADI extrapolated from AADI/O ratio is 5.79.

Using AADI > 8.99 mm as the gold standard (data not shown), the AADI extrapolated from the AADI/O ratio had a sensitivity of 75% and a specificity of 100% to diagnose severe aAAS, but for a cut-off value at 8.0, both the sensitivity and specificity were 100%. Using the same gold standard, an AADI extrapolated from the AADI/C2 ratio had a sensitivity of 75% and a specificity of 100% to diagnose severe aAAS, but for a cut-off value of 8.0 mm, the sensitivity was 100% and specificity was 99%.

Using PADI < 14.00 mm as the gold standard (figure 3b), the PADI extrapolated from the PADI/O ratio had a sensitivity of 83% and a specificity of 99% to diagnose severe aAAS. Using the same gold standard, the PADI extrapolated from the PADI/C2 ratio had a sensitivity of 83% and a specificity of 100% to diagnose severe aAAS.

DISCUSSION

This study demonstrates that using the standardized AADI obtained from the AADI/O or AADI/C2 ratios to diagnose aAAS or severe aAAS could be an excellent alternative when the usual measurement methods are not possible. The ratios, as well as the extrapolated indexes, are strongly correlated with the original measurements.

So that the results were easy to interpret, we chose to use a standardization methodology already described for disease activity scores in rheumatic diseases (25). Thus, we could use the same cut-offs of “3” and “9” to diagnose aAAS and severe aAAS with the extrapolated AADI. In addition, the measurements of these ratios were reproducible by 2 observers, although they had distinct specialities (one radiologist and one rheumatologist) and had a low level of experience, demonstrating that this method is suitable for a variety of clinicians, irrespective of their medical specialty or experience level.

We did not find in the literature other methods to diagnose aAAS or severe aAAS on plain radiographs without using raw distances, while there are already such methods to diagnose vAAS (14). Many ratios are used in radiology, such as the cardio-thoracic index for the diagnosis of cardiomegaly and the Caton-Deschamps and Insall-Salvati indexes to assess the height of the patella. The advantages of these ratios are that they are easy to use and they can be applied to many people. Compared to raw distances such as the transverse cardiac diameter, these ratios remain usable, regardless of the size, sex, ethnicity or age of the patient, without the need for charts. In our case, we can assume that the calculated ratios are subject to little variability caused by differences in these parameters.

In 1987, Pavlov et al. demonstrated that the spinal canal/vertebral body ratio (also known as Pavlov’s ratio) was more than 2.5 times more sensitive and more specific than the conventional metric in screening for spinal stenosis. One of the principal reasons mentioned by the author was that the ratio method was not affected by magnification factors. Indeed, the sagittal diameter of the spinal canal and that of the vertebral body are in the same anatomic plane and are similarly affected by magnification (18).

In our study, we used the AADI, PADI, sagittal diameter of the odontoid (O) and that of the base of the axis (C2), which are also in the same anatomic plane; therefore, our ratios were not affected by magnification factors. In 2019, Lin et al. considered the utility of the C1:C2 ratio measured on open mouth odontoid radiographs to predict transverse ligament injuries in patients with atlas fractures; the authors hypothesized that using this ratio was useful in eliminating the issue of magnification and calibration and was more accurate than absolute distances. Despite the small sample size, they found that the C1:C2 ratio had the same

sensitivity and specificity as an absolute distance (the difference between the atlas lateral diameter and axis lateral diameter) (19).

This study has several limitations. First, this is a study using a population included in a deidentified database, so positive and negative predictive values cannot be calculated. The CSI group (n=14) was smaller than the control group (n=107), and the amount of available clinical data on patients was limited. The CSI group was known to have RA, while the RA status of the control group was unknown. Nonetheless, in a population targeted for the use of these ratios, a prevalence of approximately 10% seems consistent. All radiograph measurements were performed on good-quality DICOM images, whereas the aim of this study was to evaluate the feasibility of ratios in diagnosing CSI in cases where classic measurements are not feasible, such as when the images are of bad quality or in the wrong format. However, despite these limitations, we observed significant results that support a meaningful conclusion.

To conclude, the standardized AADI obtained from the AADI/O and AADI/C2 ratios can be used to diagnose aAAS and severe aAAS in daily practice and can be useful for clinical research when the available data do not allow the classic radiograph measurements to be performed.

TABLES AND FIGURES

Figure 1: Lateral flexion plain radiograph showing the method used for the following measurements:

1a. AADI, PADI, O and C2

1b. Ranawat criterion (double arrow): The distance between the centre of the second cervical pedicle and the transverse axis of the atlas.

1c. Clark station: The odontoid process is divided into 3 equal parts or stations. The position of the anterior arch of the atlas is assessed relative to these stations.

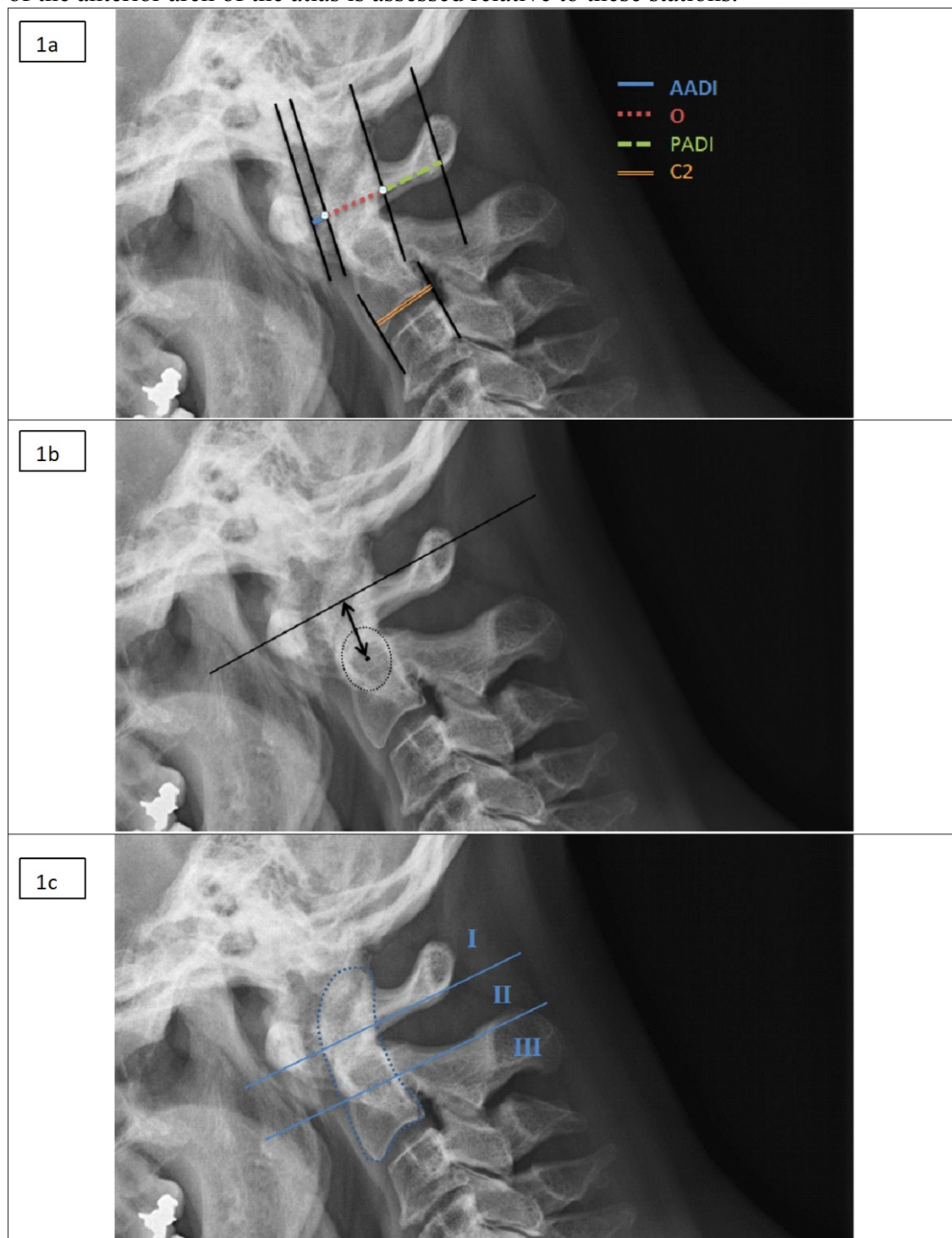


Figure 2: Formulae used to extrapolate the AADI and PADI from the ratios (Formulae to extrapolate AADI from AADI/O ratio : $y = 0.32 + 11.63 \times x$; AADI from AADI/C2 ratio : $y = 0.23 + 18.25 \times x$; PADI from PADI/O ratio : $y = 4.16 + 11.48 \times x$; and PADI from PADI/C2 ratio : $y = 5.7 + 15.74 \times x$)

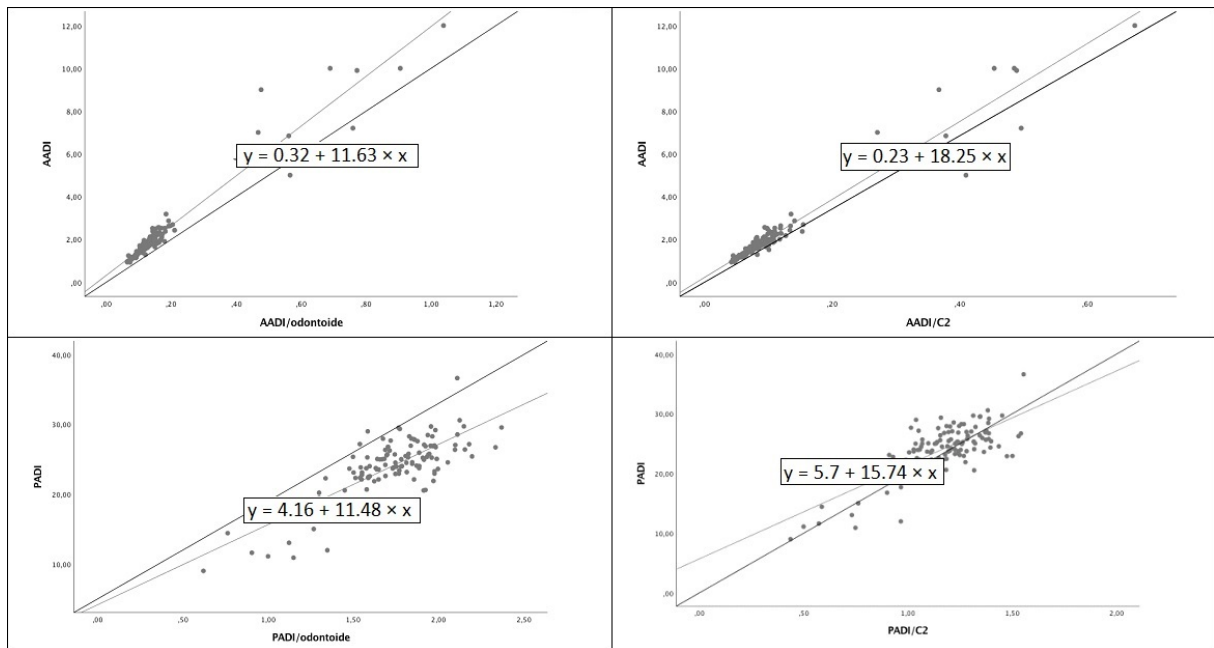


Figure 3: Scatter plot showing the strong correlation between the original and extrapolated AADI and PADI values. The AADI extrapolated from AADI/O and AADI/C2 had a Spearman's rho correlation coefficients of 0.969 and 0.969 ($P < 0.001$) with the AADI measurement, respectively. PADI/O and PADI/C2 had Spearman's rho correlation coefficients of 0.769 and 0.793 ($P < 0.001$) with PADI measurement, respectively.

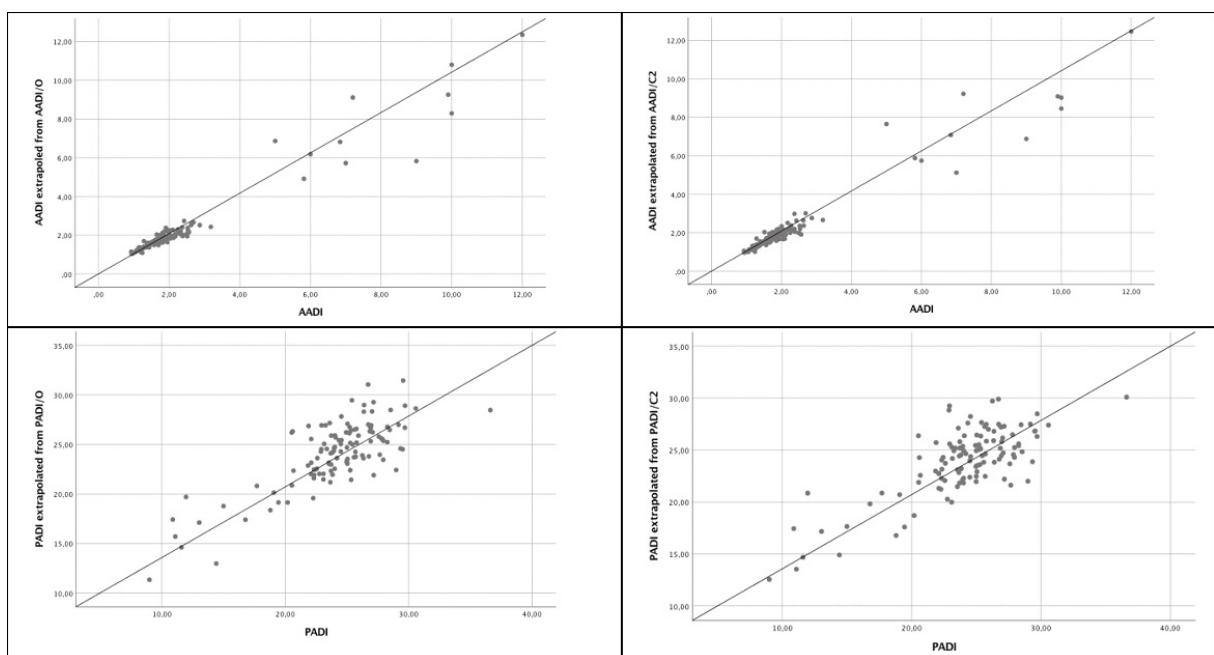


Figure 4: ROC curves showing the diagnostic value of the AADI extrapolated from the AADI/O and AADI/C2 ratios using AADI>2.99 as the gold standard (left) and the diagnostic value of the PADI extrapolated from the PADI/O and PADI/C2 ratios using PADI<14.00 mm as the gold standard (right).

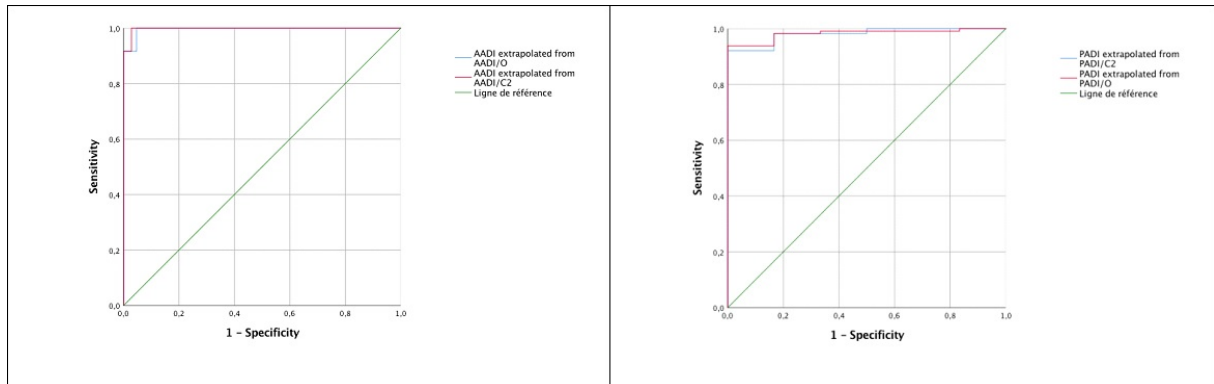


Figure 5: Lateral flexion plain radiograph showing an example of a patient with aAAS. Standard measurement found an AADI = 7.02 mm and a PADI = 18.80 mm in favour of non-severe aAAS.

With our method, we found concordant findings with extrapolated AADI>2.99 and extrapolated PADI ≥ 14.00.

- AADI extrapolated from AADI/O ratio = $0.32 + 11.63 \times 0.47 = 5.79$
- AADI extrapolated from AADI/C2 ratio = $0.23 + 18.25 \times 0.27 = 5.16$
- PADI extrapolated from PADI/O ratio = $4.16 + 11.48 \times 1.23 = 18.28$
- PADI extrapolated from PADI/C2 ratio = $5.7 + 15.74 \times 0.71 = 16.88$

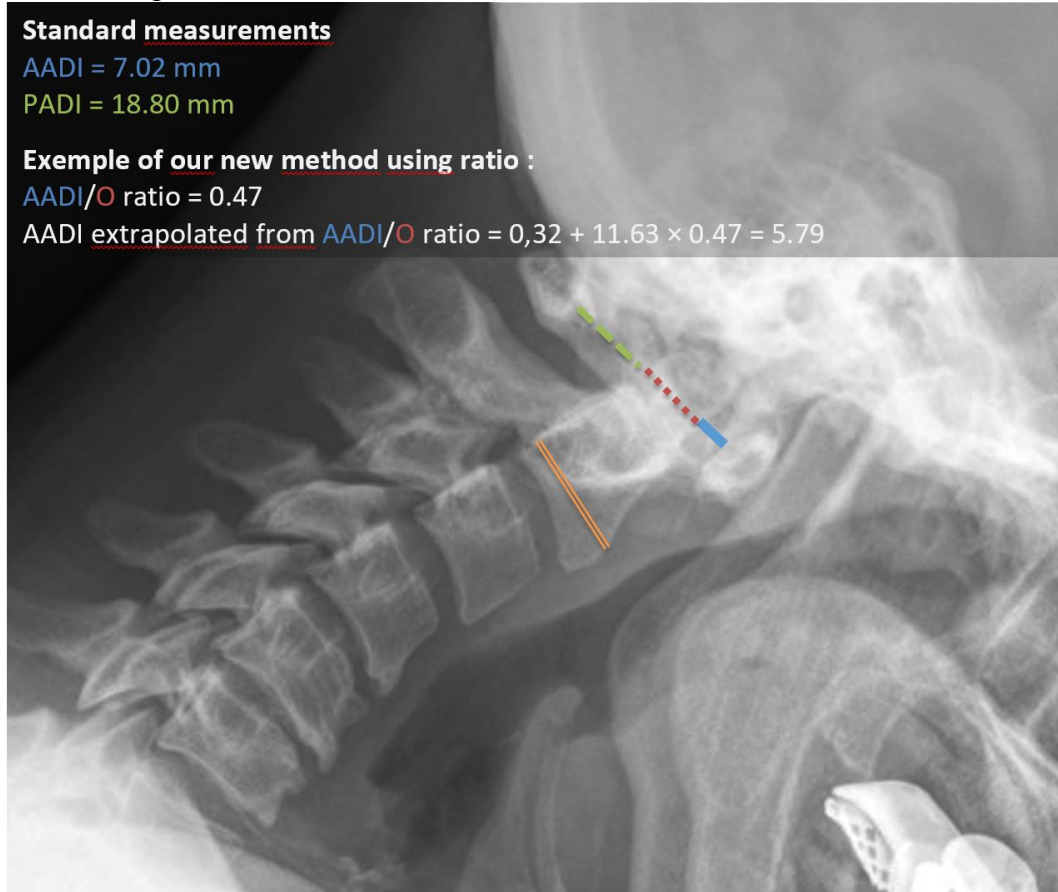


Table 1. Mean values \pm standard deviations of the distances and ratios in populations with and without AAS

Average values	All patient n = 119	No aAAS n = 107	aAAS n = 12	Severe aAAS n = 6	vAAS n = 6
AADI	2.38 \pm 2.00	1.79 \pm 0.53	7.66 \pm 2.55	9.02 \pm 2.49	
PADI	24.02 \pm 4.38	24.96 \pm 2.59	15.57 \pm 7.37	11.26 \pm 1.60	
AADI/O	0.18 \pm 0.17	0.13 \pm 0.04	0.61 \pm 0.24	0.79 \pm 0.17	
AADI/C2	0.12 \pm 0.11	0.09 \pm 0.03	0.40 \pm 0.14	0.50 \pm 0.09	
PADI/O	1.73 \pm 0.31	1.79 \pm 0.23	1.18 \pm 0.39	1.02 \pm 0.26	
PADI/C2	1.16 \pm 0.22	1.21 \pm 0.16	0.79 \pm 0.30	0.66 \pm 0.20	
Clarks station	1.03 \pm 0.16				1.5 \pm 0.55
Ranawat criterion	18.72 \pm 2.85				11.57 \pm 1.95

Table 2. Intra- and inter-observer agreement

	Reader 1 (ALQ)	Reader 2 (TG)	Reader 1 vs Reader 2 (inter-observer agreement)
	ICC (95% CI)	ICC (95% CI)	ICC (95% CI)
AADI	0.96 (0.94-0.97)	0.98 (0.97-0.99)	0.966 (0.951-0.976)
PADI	0.94 (0.92-0.96)	0.96 (0.95-0.97)	0.91 (0.88-0.94)
AADI/O	0.96 (0.95-0.97)	0.98 (0.97-0.98)	0.80 (0.73-0.86)
AADI/C2	0.96 (0.94-0.97)	0.98 (0.97-0.99)	0.96 (0.94-0.97)
PADI/O	0.87 (0.82-0.91)	0.94 (0.92-0.96)	0.92 (0.89-0.95)
PADI/C2	0.90 (0.86-0.93)	0.94 (0.92-0.96)	0.88 (0.84-0.92)
Clarks station	1	1	1
Ranawat criterion	0.85 (0.79-0.89)	0.87 (0.82-0.91)	0.83 (0.77-0.88)

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PREVALENCE AND PREDICTION FACTOR OF ATLANTO-AXIAL SUBLUXATION IN RHEUMATOID ARTHRITIS (ESPOIR COHORT)

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ABSTRACT :

BACKGROUND: Atlantoaxial subluxation (aAAS) has been reported in rheumatoid arthritis (RA). We don't know whether and when cervical x-rays could be of interest in the follow up.

OBJECTIVES: The aims of this work were first to define, in the ESPOIR cohort, the prevalence of aAAS with AADI/O ratio, at 12 years of development of polyarthritis. The secondary objectives were to look for predictive factors of aAAS.

METHODS: Dynamic spine radiographs were retrospectively and independently analyzed by two observers. For each radiograph, the odontoid sagittal diameter (O) and the anterior atlanto-dental interval (AADI) were measured in pixels to obtain AADI/O. The cut-off AADI/O > 0.229 which correspond to an AADI>2.99 was chosen to defined aAAS. We then investigated clinical, biological, radiological factors at inclusion and 10 years to find which could predict aAAS at 12 years.

RESULTS: 323 patients were included. 15 patients had an aAAS. At the inclusion visit, only the presence of IgA RF was statistically associated with aAAS ($p = 0.025$). CRP>6mg/L (9/15 vs 58/295; $p = 0.001$) and Rheumatoid factor (13/15 vs 152/299; $p = 0.007$) at ten years are statistically associated with aAAS at 12 years.

CONCLUSION: The prevalence of aAAS is 4.6% in the ESPOIR cohort. Given the low incidence of aAAS, systematic screening would have a low yield. It seems difficult to predict which patient is at risk of aAAS in early arthritis. The presence of rheumatoid factor and CRP over 6mg/L at 10 years could be interesting factors to guide the prescription of dynamic cervical x-rays.

KEYWORDS : Rheumatoid Arthritis , Cervical spine, Radiography, Atlanto-Axial Subluxation

KEY POINTS : The aim of this study was to evaluate the prevalence of anterior atlanto-axial subluxation using ratios on plain radiograph.

Abbreviations and acronyms :

CSI : cervical spine instability

AADI : anterior atlanto-dental interval

PADI : posterior atlanto-dental interval

aAAS : anterior atlanto-axial subluxation

vAAS : vertical atlanto-axial subluxation

AAS : atlanto-axial subluxation

O : odontoid sagittal diameter

C2 : axis body base sagittal diameter

RA : rheumatoid arthritis

RF : rheumatoid factor

ACPA : anti-citrullinated protein auto-antibodies

INTRODUCTION :

Atlantoaxial subluxation has mostly been reported in individuals with rheumatoid arthritis (RA). In RA, chronic inflammatory involvement of the synovial membranes of the cervical spine leads to bone erosions and ligament laxity, responsible for spinal instability and, as it progresses, neurological damage [1,2].

In the literature, the anterior atlanto-axial subluxation is defined with an AADI > 2.99 mm. Severe aAAS was defined by AADI > 8.99 mm and/or a PADI < 14 mm. Severe aAAS is associated with an increased risk of neurological complications and requires surgical advice and radiological follow-up [3,4]. Vertical atlanto-axial subluxation (vAAS) is defined in patients with Clark station grade 2 or 3, and/or Sakaguchi-Kauppi from grade 2 to 4 [5,6].

Radiographic cervical involvement was found in approximately 47.5% of patients with RA, according to the ACR criteria [5–10], and up to 80% of patients had some degree of cervical involvement, all imaging modalities combined (radio, CT, MRI) [1,11–13]. The most frequent radiological presentation is atlantoaxial subluxation (from 7 to 42.5% depending on the study) [2,5,6,10,12,14,15]. It is agreed that cervical involvement should not be sought systematically but only in the event of suggestive symptoms [16].

Among all symptoms in connection with C1-C2 cervical involvement in RA reported in the various studies, we note: neck pain, headache, nausea [17], progressive neurological deficit [18]. However, no association between symptoms and radiological abnormalities was found, except when a neurological deficit was present. Cervical instability is very often asymptomatic [8,17,19,20]. It is even described that the intensity of pain at the C1-C2 level decreases with increasing distance of the ventral atlantoaxial subluxation ($p < 0.001$) [9]. Cervical myelopathy is rare (5%) [21] but the prognosis is severe. In symptomatic forms, patients often have sequelae despite surgery [17].

On the other hand, therapeutic advances in recent decades have allowed a significant improvement in the course of the disease with better control and, as a consequence, a decrease in complications. In clinical practice and in some studies this also seems to apply to the destruction of the cervical spine [1,12,21–23]. In the meta-analysis of Zhang and Pope in 2015 [21], the prevalence of aAAS decreased from 36% (95% confidence interval (CI), 30% to 42%) before 1980s to 24% (95% CI, 13% to 36%) in the 2000s ($p = 0.004$).

Cervical involvement has been described in studies beyond 5 years [10], 10 years [15] or 12 years [24] of evolution. Living with RA for more than 10 years seems to be the most determining parameter for predicting the risk of cervical damage [17]. In previous studies, the following factors were identified as being significantly associated with cervical involvement in RA: age of onset less than 45 years, neck pain, neurological symptoms, increased CRP, structural lesions of the hands and / or feet and changes in Sharp score, prolonged use of corticosteroids, failure of DMARDs, cervical instability at entry into the study and FR seropositivity [6,15,17,18].

Currently we do not know if it could be interesting to offer systematic screening for cervical lesions, for example after 10 years, for all patients suffering from RA or for a part of them with risk factors.

The aim of this work was first to define the prevalence of anterior atlanto-axial subluxation (aAAS) in a cohort of early polyarthritis (ESPOIR cohort) with AADI/O ratio, on lateral cervical x-rays, in flexion, at 12 years of development of polyarthritis. The secondary objective was to look for clinical and biological predictive factors of aAAS at 12 years, at inclusion and 10 years. And to see if the modified sharp score on the x-ray of hands and feet at 2, 5 and 10 years can be predictive of luxation.

METHOD

The ESPOIR cohort is a French prospective multicentric cohort of patients with early arthritis, which was established to monitor the clinical, biological and radiographic data from patients with recent-onset of inflammatory arthritis consistent with RA [25].

Esipoir cohort: ESPOIR is a longitudinal prospective cohort of adults (18-70 years) with possible early RA (clinicalTrials.gov NCT03666091). Patients were referred by rheumatologists and general practitioners to one of the 14 regional centers in France. The 813 patients were included from 2003 to 2005. The main inclusion criteria were at least 2 inflammatory joints for at least 6 weeks up to 6 months ; clinical diagnosis of RA as certain or probable ; no prescription of Disease Modifying Drugs (DMARDs) or glucocorticoids (except if prescribed for < 2 weeks with a maximum of 20mg/day prednisone or intra-articular injection < 4 weeks before inclusion). The main exclusion criteria were other inflammatory arthritis or connective tissue diseases clearly determined according to usual criteria. Patients were routinely treated and followed by their rheumatologists according to standard of care and without predefined therapeutic strategies. All patients were referred to each regional center every 6 months during the first 2 years, then every year. At baseline and at each visit, data for a set of clinical and biological variables recommended for the management of early arthritis were recorded. Patients underwent testing for baseline erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) level (normal < 5 mg/l), IgM and IgA rheumatoid factor (RF), anti-citrullinated peptide antibodies (ACPA (anti-CCP2)), and human leukocyte antigen (HLA) DRB1* alleles) in a central lab. At each visit, patients completed function, quality-of-life self-administered questionnaires (Health Assessment Questionnaire Disability Index [HAQ DI] and 36-item Short Form Health Survey [SF-36]) and globally assessed disease, pain and fatigue on a visual analog scale (VAS). Patients underwent hands and feet radiographs. Baseline, 1-year, 2-year, 5-year, 7-year and 10-year central X-ray readings using van der Heijde-modified Total Sharp Score (mTSS). The 10-years database has been locked in January 2018. The protocol of the ESPOIR cohort study was approved in July 2002 by the ethics committee of Montpellier, France (N° 020307). All patients gave their signed informed consent before inclusion. Only RA patients according to 2010ACR/EULAR criteria [26] were selected for the current study.

Cervical radiographs: Neutral and dynamic cervical plain radiographs were obtained 12 years after patient inclusion, but these radiographs were digitalized and included in the ESPOIR database in .bmp and .jpeg formats, which did not allow usual measurements to be taken. The proportions are preserved in these situations, and one of our previous study demonstrates that using the standardized AADI obtained from AADI/O or AADI/C2 ratios to diagnose aAAS or severe aAAS could be an excellent alternative when the usual measurement methods cannot be used (both sensitivity and specificity >95%).

Lateral cervical spine radiographs evaluation: Lateral cervical spine radiographs obtained in the full flexion position were retrospectively and independently analyzed by two observers, a junior radiologist (TG) and a junior rheumatologist (ALQ). For each radiograph, the odontoid sagittal diameter (O), anterior atlanto-dental interval (AADI), Clark station and Sakaguchi-Kauppi criterion were measured in pixels (Figure 1) :

- The odontoid sagittal diameter (O) is the distance from the anterior to the posterior border of the dens.
- The AADI is the distance from the posterior border of the anterior ring of C1 to the anterior margin of the odontoid.
- For the Clark station, the station of the atlas is determined by dividing the odontoid process into three equal parts in the sagittal plane. If the anterior ring of the atlas is level with the middle third (station II) or the caudal third (station III) of the odontoid process, basilar invagination (or vAAS) is diagnosed.
- For the Sakaguchi-Kauppi criterion the grade is determined with regard to the location of the superior facets of C2 compared to the line drawn along the inferior borders, the midpoints or the superior borders of the arches of C1.

Definition of instability: In our previous study [27], both AADI/O and AADI/C2 had strong correlations with the AADI measurement, AADI/O having the strongest correlation (Spearman's rho correlation coefficients of 0.933 and 0.915, respectively; $p < 0.0001$). In this previous study the intraclass correlation coefficient for inter- and intraobserver agreement were excellent (> 0.8). The cut off found for diagnosing aAAS with AADI/O was $> 0,229$ (corresponding to anterior Atlantodental interval (AADI) greater than 2.99 mm), and severe aAAS was defined as AADI/O > 0.74 (corresponding to an AADI greater than 8.99 mm) on lateral cervical x-rays, in flexion (figures 1). So we chose to use the same cut off in our study. Vertical atlanto-axial subluxation (vAAS) was defined in patients with Clark station grade 2 or 3, and/or Sakaguchi-Kauppi from grade 2 to 4.

Measurements in the ESPOIR cohort: Two blinded observers read all the cervical dynamic x-ray of the ESPOIR cohort. They performed two measurements in pixel of the Odontoid sagittal diameter (O), AADI, Clark Station and Sakaguchi-Kauppi criterion and the AADI/O ratio was calculated. In case of discrepancy between the 2 readers in diagnosing luxation using AADI/O, we carried out a 2nd reading of the 2 blind proofreaders. If any discrepancy persisted, a final open reading was organized with a discussion to decide on the values to be taken into account in the study. Thereby we found the prevalence of patients with anterior atlanto-axial subluxation in the ESPOIR cohort at 12 years.

Statistical analysis: Univariate analysis was used to determine the association between aAAS and other characteristics of the population. We investigated clinical and biological factors at baseline and 10 years, as well as radiological factors (the modified Sharp score [26]) at baseline, 2 years and 5 years to find out which of these factors were associated with aAAS at 12 years. The association with the following data were analyzed: Current tobacco use, current alcohol consumption; Clinical features of arthritis (duration of morning stiffness, pain at rest and on mobility on a 0–100 mm visual analog scale), number of tender and swollen joints in 28 joints, joint topography (bilateral), rachialgia. Fatigue . Extra-articular manifestations,

Disease Activity Score in 28 joints–erythrocyte sedimentation rate (DAS28-ESR), HAQ-DI, Use of corticosteroid between inclusion and 10 years. Treatment with csDMARDs or bDMARDs at 10 years. Biological features . Hands and feet radiographs .

Since some of the patients included had missing data, the denominator varied across variables. All percentages were calculated based on the number of patients for whom the variables were available.

Data are presented either as frequencies (%) or as the mean (Standard Deviations) where appropriate. The χ^2 test (or Fisher's exact test) was used for binary variable and Mann-Whitney U test was used to compare continuous variables. The p values < 0.05 were considered significant and all statistical tests were two-sided.

RESULTS:

Descriptive statistics: Of the 813 patient enrolled in the ESPOIR cohort, 521 (64.1%) were followed up for 10 years. Among them, 323 patients had dynamic cervical spine x-rays and were able to be included (Flow-chart, Figure 2). They were all diagnosed with rheumatoid arthritis (average age 47.9 +/- 11.2). At the end of this first reading, an aAAS was found in 8 patients, with converging conclusion from the 2 examiners. At the end of the 1st reading, different findings were noted in 18 patients. A second blind reading by the 2 examiners was then carried out for the 18 patients in which discordant conclusions had been drawn, making it possible to draw converging conclusions in 16 of them with 5 aAAS. For the 2 remaining x-rays with discordant conclusions, a 3rd reading was carried out openly with deliberation between the 2 readers to choose which value should be integrated. Both x-rays were considered to show pathological ratios. In total 15 patients had an aAAS (4.6%), and no patients had severe aAAS. 5 patients had vAAS for both readers, all grade 2 using the Sakaguchi-Kauppi criterion (1.5%) and none had vAAS using the Clark station. Among the patient with aAAS, 187 (58%) had csDMARDs and 53 (16.4%) had bDMARDs at 10 years.

Statistical analysis: At the inclusion visit, no clinical or radiological characteristics were associated with aAAS, only the presence of RF IgA with a rate over 30 IU/ml is statistically correlated (p = 0.025). The diagnostic value of RF IgA and IgM at the inclusion was evaluated (IgA : Se 60%, Sp 70% ; IgM : Se 40%, Sp 80%) showing modest relevance (figure 3). The modified sharp at 2 years and 5 years were not associated with aAAS at 12 years according to the Man-Whitney test. Symmetric arthritis at 10 years (9/15 vs 107/301; p = 0.044) is statistically correlated with aAAS at 12 years and rheumatoid arthritis of hands is almost statistically significant (10/14 vs 134/301 ; p = 0.057). The use of oral corticosteroids between inclusion and 10 years (8/15 VS 83/303; p = 0.04), the presence of biological inflammatory syndrome (CRP>6mg/L) (9/15 VS 58/295; p = 0.001) and the presence of Rheumatoid factor (13/15 VS 152/299 ; p = 0.007) are also statistically associated with aAAS at 12 years. The diagnostic value of CRP associated with FR at 10 years was evaluated using ROC curve (Se 60%, Sp 90%) (figure 3). Among the 15 patients with aAAS, 9 had both RF and increased CRP, 4 had only RF without increased CRP, none had increased CRP without RF, 2 had neither increased CRP nor RF.

DISCUSSION

We found 4.6% of aAAS in the ESPOIR cohort. It is less luxation than was found in previous papers (36% before 1980s and 24% in the 2000s [21]), and no severe aAAS. The ESPOIR cohort began in 2003, so the cervical x-rays were taken in the 2010s. This data goes in the direction of improving the course of the disease. Probably with better control thanks to therapeutic advances in the recent decades and, as a consequence, a decrease in complications.

Diagnosing AAS is important because it can be asymptomatic and may lead to spinal cord compression, vascular compression and death [30,31]. It can also affect anesthesia management, and it is important to avoid unprotected manipulations of the neck under anesthesia [32,33]. But given the low incidence of aAAS, systematic screening would have a low yield and since cervical instability is very often asymptomatic, other predictive factors could be helpful to guide the screening.

At the beginning of the follow-up, it seems very difficult to predict which patients will have aAAS. IgA RF is statistically correlated but with modest relevance. However it has already been mentioned in the literature, that the IgA RF could be predictive in more severe forms. In particular, it has been reported that high pretreatment levels of IgA RF are associated with a poor clinical response to TNF- α inhibitors [34].

Regarding the 10 years follow up, symmetric arthritis is a classic sign of rheumatoid arthritis and the use of corticosteroids is relatively common. All the more as the frequency and the dosage of corticosteroid administration were not specified for each patient in the data base. Nevertheless prolonged use of corticosteroids [18] have already been mentioned to be associated with cervical involvement in RA. If the CRP is still high at 10 years it can be worth looking for luxation, but this criterion alone is not sufficient. If patients are only tested for CRP, as is done in current follow-up practices, 27% (4/15) of aAAS could be missed. In previous studies, RF seropositivity was associated with cervical involvement in RA [15,17]. In our study, although IgM RFs at baseline is not predictive of aAAS, the presence of RF at 10 years is associated with aAAS. Among patients with RF, 8% were dislocated (13/165). Patients without RF at 10 years have a low risk of luxation at 12 years (2/149, 1,3%). It has been shown that a progressive decrease in RF levels parallels the decrease of clinical activity in patients treated with traditional DMARDs [35] or biologic agents [36–39]. Until now, no relevance had been found for RFs in the follow-up (monitoring disease activity [40] and treatment response [41]) but it appears it could be interesting to look for RF at 10 years to help decide which patients require cervical dynamics x-rays.

Although structural lesions of the hands and / or feet and changes in Sharp score [6,15,17,18] had already appeared to be associated with cervical involvement in RA, the Sharp modified was not correlated with aAAS in our population. Nevertheless it was not the modification but the mean Sharp score which was investigated. Failure of DMARDs was identified in previous study as being associated significantly with cervical involvements in RA [18]. In our population no association was found between treatment with csDMARDs or bDMARDs but it is difficult to conclude with only 15 aAAS.

Concerning the reading of cervical radiographs in clinical practice, it is interesting to note that these ratios will differ from the original AADI and PADI, and it may be confusing for clinicians who prefer to keep the AADI and PADI values. It is possible to use standardization methodology so that the results are easy to interpret in clinical practice. In the previous study we used a plot with the ratios on the x-axis and metrics on the y-axis [42], to obtain the $y=ax+b$ equation needed to convert the differing cut-off values for AADI and PADI. Thus, we

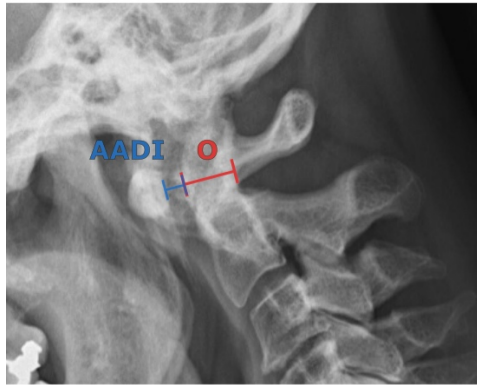
could use the same cut-off « 3 » and « 9 » to diagnose aAAS and severe aAAS with the extrapolated AADI. The ratios, as well as the extrapolated indexes, were strongly correlated with the original measurements.

To conclude the prevalence of anterior atlanto-axial subluxation (aAAS) is 4.6% in the ESPOIR cohort. Given the low incidence of aAAS, systematic screening would have a low yield. It seems difficult to predict which patient is at risk of aAAS in early arthritis. However the use of corticosteroids between inclusion and 10 years, symmetric arthritis, the presence of rheumatoid factor at 10 years, and CRP over 6mg/L at 10 years are statistically correlated with aAAS. Patients suffering from RA are not tested for RF in the current follow-up, but it could be an interesting factor to monitor the risk of aAAS after 10 years and guide the prescription of dynamic cervical x-rays.

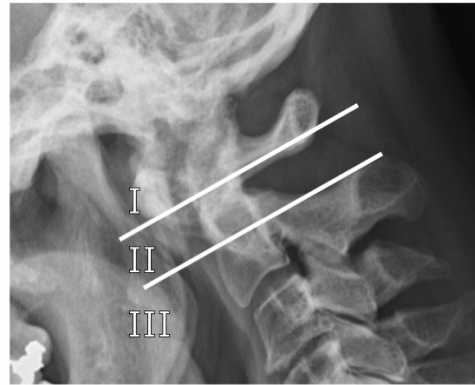
TABLES AND FIGURES

Figure 1 : Schematic representation of the AADI and O measure. Clark station and Sakaguchi method for grading of vertical dislocation.

a) Lateral flexion plain radiograph showing the method used for AADI and O measurements

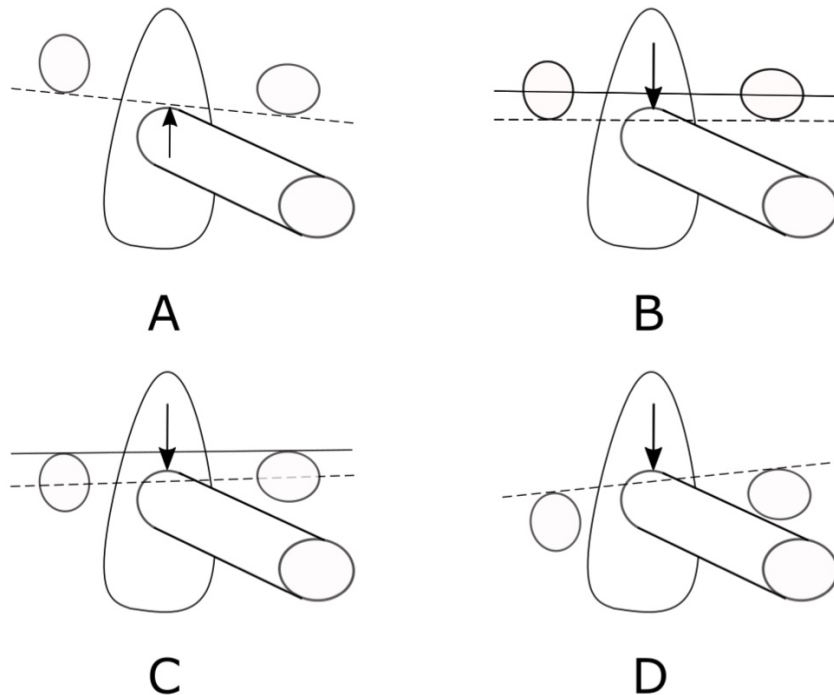


b) Clark station



The station of the first cervical vertebra is determined by dividing the odontoid process into three equal parts in the sagittal plane. If the anterior ring of the atlas is level with the middle third (station II) or caudal third (station III) of the odontoid process, basilar invagination is diagnosed

c) Schematic representation of the Sakaguchi method for grading of vertical dislocation (VD)



- A. Grade1 (normal) : the most cranial parts of the superior facet of C2 (arrow) are located below the dashed line drawn along the inferior borders of the anterior and posterior arches of C1.
- B. Grade 2 : the superior facets of C2 (arrow) are located above the dashed line drawn along the inferior borders of arches of C1 but below the line drawn through the midpoints of the arches.
- C. Grade 3 : the superior facets of C2 (arrow) are located above the dashed line drawn through the midpoints of the arches but below the line drawn along the superior borders of the arches.
- D. Grade 4 : the superior facets of C2 (arrow) are located above the dashed line drawn along the superior borders of anterior and posterior arches of C1.

Figure 2 : Flow-chart of patients included in the study.

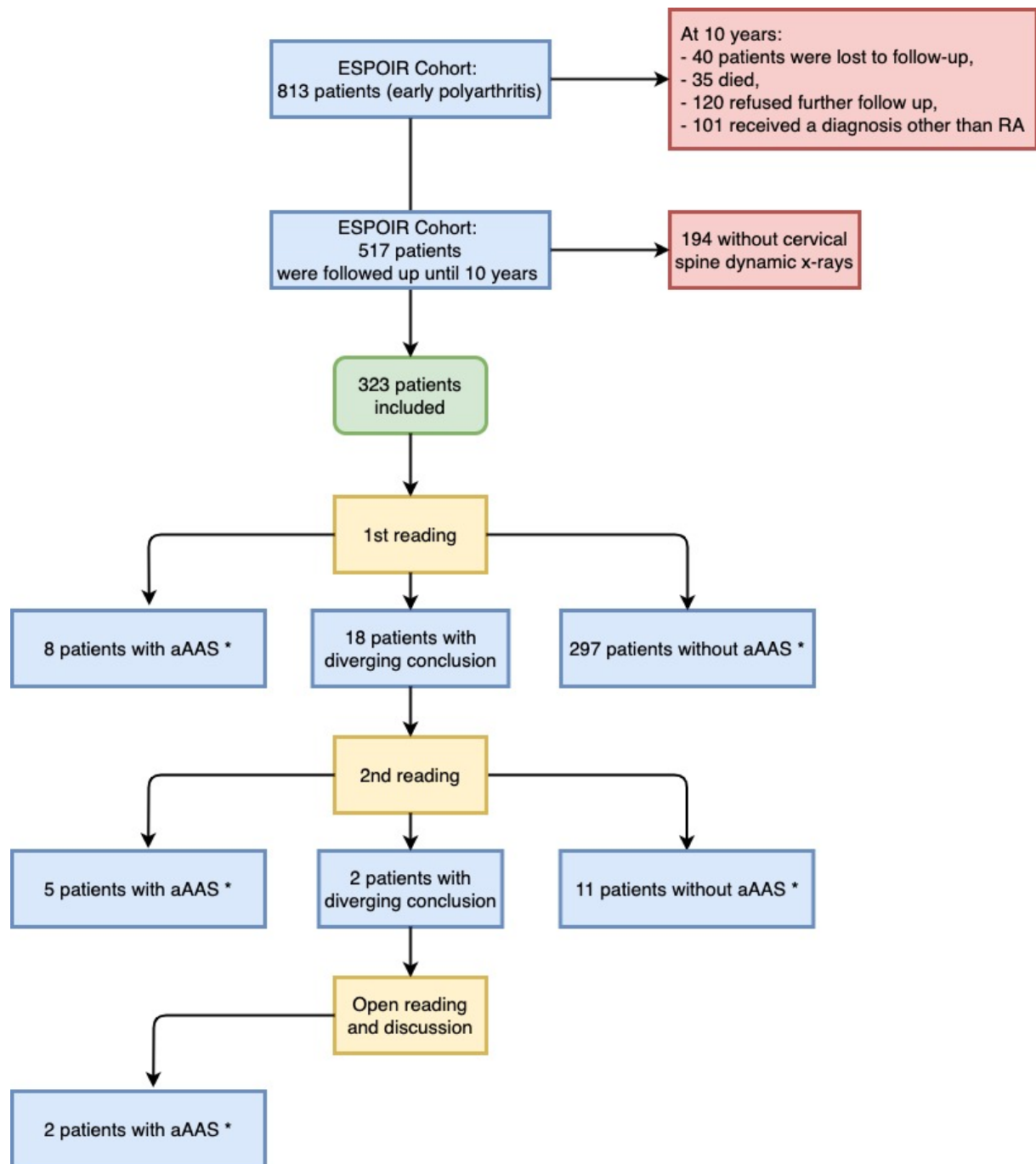


Figure 3 : ROC curves showing the pronostic value of RF IgA and RF IgM at inclusion and CRP associated with RF at 10 years to predict aAAS at 12 years.

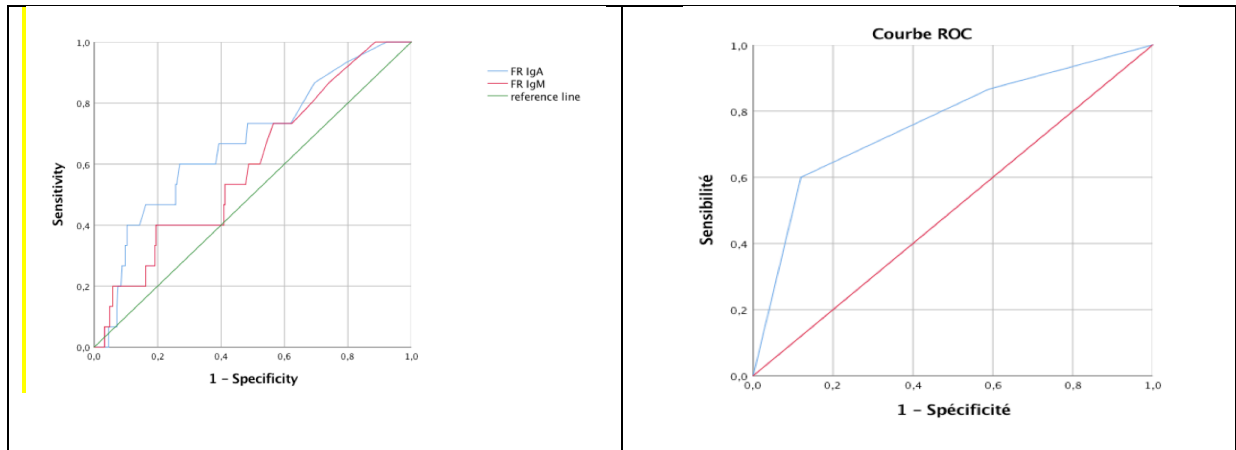


Table 1: Comparison at inclusion between the populations with and without development of a cervical luxation at 12 years.

	AADI \geq 3		AADI<3		p
Binari variables :					
Smoking	9/15	60%	144/308	47%	0.429
Alcohol	2/15	13%	51/308	17%	1
Joint swelling	1/15	7%	5/308	2%	0.25
Xerostomia	4/15	27%	71/308	23%	0,756
Xerophtalmia	3/15	20%	43/308	14%	0.79
salivary gland swelling	1/15	7%	5/308	2%	0.250
Raynaud phenomenom	2/15	13%	52/308	17%	0.731
HLA-DRB1	10/13	77%	171/296	58%	0.251
Anti-CCP antibodies	11/15	73%	146/308	47%	0.029
Continuous variables :					
	mean	SD	mean	SD	p
Age	43.620	11.172	48.10	11.22	0.120
Weight	63.6	11.73	67.5	13.1	
Size	166	618	164.86	8.253	0.432
Morning stiffness duration	54.00	37.091	106.79	222.527	0.647
Morning stiffness intensity	41.67	23.55	50.49	26.82	0.125
Asthenia	51.93	31.79	46.36	27.282	0.498
Joint pain at rest	35.07	25.82	36.97	27.72	0.926
Joint pain during mobilisation	55.07	23.31	54.63	25.778	0.877
EVA patient	55.53	23.724	59.85	25.91	0.384
EVA doctor	46.27	11.58	51.98	22.31	0.203
Number of painful joint	9.53	7.21	8.7	6.972	0.588
Number of swelling joint	7.13	6.28	7.74	5.21	0.366
DAS 28	5.23	1.23	5.13	1.34	0.684
HAQ	0.99	0.65	0.96	0.69	0.738
IgM RF	153.2	241	137.32	509.7	0.212
IgA RF	41.8	33.73	33.87	73.86	0.025
Anti-CCP	530.93	1078.629	745.81	1998.9	0.532

Table 2: Modified sharp at inclusion (M0), 2 years (M24) and at 5 years (M60)

	AADI \geq 3		AADI<3		p
	mean	SD	mean	SD	
Mean Sharp M0	3.74	4.19	2.7	5.15	0.280
Mean Sharp M24	12.13	17.48	5.6	8.64	0.378
Mean Sharp M60	20.09	20.72	7.96	12.09	0.088

Table 3: Comparison at 10 years between the populations with and without development of a cervical luxation at 12 years.

	AADI \geq 3		AADI<3		p
Binari variables :					
Oral corticosteroide	8/15	53%	83/303	27%	0,04
Morning stiffness	6/15	40%	152/302	50%	0.598
Arthritis	8/14	57%	111/301	37%	0.16
Hands arthritis	10/14	71%	134/301	45%	0.057
Symetrical arthritis	9/14	64%	107/301	36%	0.044
Nodules	2/14	14%	14/286	5%	0.155
Anti-CCP antibodies	9/15	60%	141/308	46%	0.413
RF	13/15	87%	152/299	51%	0.007
Radiological modification	9/15	60%	116/300	39%	0.111
CRP \geq 6mg/L	9/15	60%	58/295	20%	0.001
Continuous variables :					
	mean	SD	mean	SD	p
Number of painfull joint	2.93	7.35	2.07	4.32%	0.902
Number of swelling joint	1.20	1.93	0.94	2.17%	0.397
DAS28	2.82	1.51	2.49	1.27%	0.227
HAQ	0.74	0.61	0.507	0.59%	0.067
CRP (mg/L)	14.40	16.71	6.34	19.13	0.001
ESR, (mm/h)	27	30.36	13.33	13.14	0.152

CONFLICT OF INTERESTS :

The authors have no competing to declare concerning this work.

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SERMENT D'HIPPOCRATE

Au moment d'être admis(e) à exercer la médecine, je promets et je jure d'être fidèle aux lois de l'honneur et de la probité.

Mon premier souci sera de rétablir, de préserver ou de promouvoir la santé dans tous ses éléments, physiques et mentaux, individuels et sociaux.

Je respecterai toutes les personnes, leur autonomie et leur volonté, sans aucune discrimination selon leur état ou leurs convictions. J'interviendrai pour les protéger si elles sont affaiblies, vulnérables ou menacées dans leur intégrité ou leur dignité. Même sous la contrainte, je ne ferai pas usage de mes connaissances contre les lois de l'humanité.

J'informerai les patients des décisions envisagées, de leurs raisons et de leurs conséquences. Je ne tromperai jamais leur confiance et n'exploiterai pas le pouvoir hérité des circonstances pour forcer les consciences.

Je donnerai mes soins à l'indigent et à quiconque me le demandera. Je ne me laisserai pas influencer par la soif du gain ou la recherche de la gloire.

Admis(e) dans l'intimité des personnes, je tairai les secrets qui me seront confiés. Reçu(e) à l'intérieur des maisons, je respecterai les secrets des foyers et ma conduite ne servira pas à corrompre les mœurs.

Je ferai tout pour soulager les souffrances. Je ne prolongerai pas abusivement les agonies. Je ne provoquerai jamais la mort délibérément.

Je préserverai l'indépendance nécessaire à l'accomplissement de ma mission. Je n'entreprendrai rien qui dépasse mes compétences. Je les entretiendrai et les perfectionnerai pour assurer au mieux les services qui me seront demandés.

J'apporterai mon aide à mes confrères ainsi qu'à leurs familles dans l'adversité.

Que les hommes et mes confrères m'accordent leur estime si je suis fidèle à mes promesses ; que je sois déshonoré(e) et méprisé(e) si j'y manque. »

LE QUELLEC (Aurore) – Prevalence and prediction factor of atlanto-axial subluxation in early polyarthritis (Espoir cohort)

Th. : Méd. : Brest 2019.

RESUME :

INTRODUCTION : La luxation atlanto-axiale a été décrite dans la polyarthrite rhumatoïde (PR). Nous ne savons pas si et quand les radiographies dynamiques du rachis cervical auraient un intérêt dans le suivi de ces patients.

OBJECTIFS : Le but de ce travail était tout d'abord de définir, dans la cohorte ESPOIR, la prévalence de la subluxation atlanto-axiale antérieure (aAAS) à l'aide du ratio AADI/O, à 12 ans d'évolution de la PR. Le deuxième objectif était de rechercher des facteurs prédictifs de aAAS.

METHODE : Les radiographies dynamiques du rachis cervical ont été lues rétrospectivement et indépendamment par 2 observateurs. Pour chaque radiographie, le diamètre sagittal de l'odontoïde (O) et l'intervalle atlanto-dental antérieur (AADI) ont été mesurés en pixels pour obtenir AADI/O. En adéquation avec notre précédente étude, le "cut-off" AADI/O > 0,229 a été choisi pour définir les aAAS. Nous avons ensuite étudié les facteurs cliniques, biologiques et radiologiques et recherché la présence d'associations statistiquement significatives aux aAAS à 12 ans d'évolution.

RESULTATS: 323 patients ont été inclus. 15 patients avait une aAAS. A la visite d'inclusion, seule la présence de Facteur Rhumatoïde (FR) en IgA était statistiquement associée à l'aAAS ($p = 0.025$). La CRP > 6mg/L (9/15 vs 58/295; $p = 0.001$) et le FR (13/15 vs 152/299; $p = 0.007$) à dix ans étaient statistiquement associés à l'aAAS à 12 ans.

CONCLUSION: La prévalence de l'aAAS est de 4.6% dans la cohorte ESPOIR. Etant donné la faible prévalence d'aAAS, une recherche systématique aurait un faible rendement. Il semble difficile de prédire quel patient est à risque d'aAAS dans la PR débutante. La présence de FR et une CRP > 6mg/L à 10 ans pourraient être des éléments intéressants pour guider la prescription de radiographies cervicales dynamiques.

MOTS CLES : Polyarthrite rhumatoïde, rachis cervical, radiographie, subluxation atlanto-axiale

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