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Original article

Reproducibility and diagnostic value of a new method using ratios to diagnose anterior atlanto-axial subluxation on plain radiographs

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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 > 2.9 mm used as the gold standard.
Results: Among the 119 patients, 12 patients had aAAS (AADI > 2.9 mm), 6 of them had severe aAAS (AADI > 8.9 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 inter-observer reproducibility. The diagnostic value of the extrapolated AADI was high for aAAS (sensitivity 92%; specificity of 100%) and severe aAAS (sensitivity75%; 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.

1. 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 Behçet'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 atlanto-axial 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

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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).

2. Methods

2.1. Study population

A total of 119 patients (female:male ratio = 1.5:1; age range: 15–92 years, mean: 43.7 ± 18.5 years; height range: 145–192 cm, mean: 171 ± 8.4 cm) were randomly selected from a picture archiving and communication system (PACS) database with deidentified data in our institution. Fourteen of the 119 patients were known to have CSI.

2.2. 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 (Fig. 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 odontoid process is divided into 3 equal parts ("stations") from cranial to caudal in the sagittal plane. The results are positive if the anterior arch of the atlas is in the second or third station. 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.

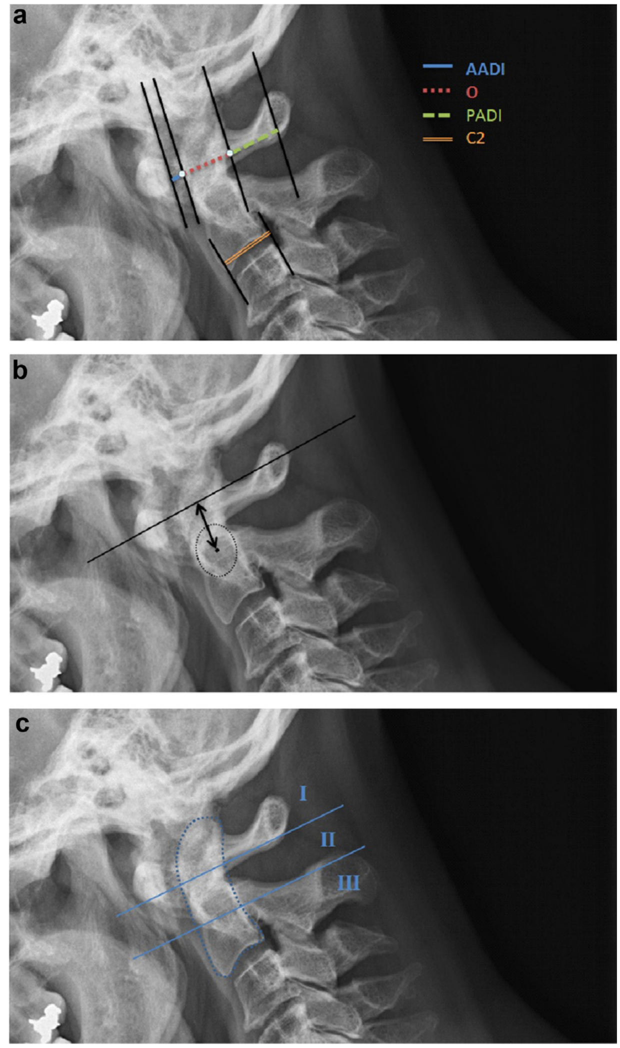

Fig. 1. Lateral flexion plain radiograph showing the method used for the following measurements: a: anterior atlanto-dental intervals (AADI), posterior atlanto-dental intervals (PADI), odontoid sagittal diameter (O) and axis body base sagittal diameter (C2); b: Ranawat criterion (double arrow): the distance between the centre of the second cervical pedicle and the transverse axis of the atlas; c: 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.

2.3. 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 > 2.9 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 > 8.9 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.

2.4. Reliability

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

Table 1
Mean values ± 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	2.4 ± 2.0	1.8 ± 0.5	7.7 ± 2.5	9.0 ± 2.49	
PADI	24.0 ± 4.4	25.0 ± 2.6	15.6 ± 7.4	11.3 ± 1.6	
AADI/O	0.2 ± 0.2	0.1 ± 0.04	0.61 ± 0.2	0.79 ± 0.2	
AADI/C2	0.12 ± 0.1	0.1 ± 0.03	0.4 ± 0.1	0.5 ± 0.1	
PADI/O	1.7 ± 0.3	1.8 ± 0.23	1.2 ± 0.4	1.0 ± 0.3	
PADI/C2	1.2 ± 0.2	1.2 ± 0.16	0.8 ± 0.30	0.7 ± 0.2	
Clarks station	1.03 ± 0.2				1.5 ± 0.5
Ranawat criterion	18.7 ± 2.8				11.6 ± 1.9

AADI: anterior atlanto-dental intervals; PADI: posterior atlanto-dental intervals; aAAS: anterior atlanto-axial subluxation; O: odontoid sagittal diameter; C2: axis body base sagittal diameter; vAAS: basilar invagination.

2.5. *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 cutoff 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 cutoff 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 cutoff values.

2.6. *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 > 0.80 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.

3. 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.

3.1. *Inter- and intra-observer agreement*

The ICCs for inter- and intra-observer agreement are displayed in Table 2. The inter- and intra-observer agreement were excellent (> 0.80) concerning the AADI/O, AADI/C2, PADI/O and PADI/C2 ratios.

3.2. *Correlation between distances and ratios*

AADI/O and AADI/C2 had strong correlations with the AADI measurement (Spearman's rho correlation coefficients of 0.93 and 0.91, respectively; $P < 0.001$). PADI/O and PADI/C2 had moderate correlations ($P < 0.001$) with the PADI measurement (Spearman's rho correlation coefficients of 0.65 and 0.60, respectively; $P < 0.001$).

3.3. *Extrapolation of the AADI and PADI from ratios*

Fig. 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 cutoff 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 $y = 11.6x + 0.3$ to extrapolate the AADI from the AADI/O ratio. Hence, an AADI/O ratio = 0.6 corresponds to a standardized AADI = 7.3.

3.4. *Correlation between distances and the AADI/PADI extrapolated from ratios*

Supplemental Fig. S1 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 0.97 and 0.97, respectively; $P < 0.001$). PADI/O and PADI/C2 had moderate correlations with the PADI measurement (Spearman's rho correlation coefficients of 0.77 and 0.79, respectively; $P < 0.001$)

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)	0.96 (0.95–0.98)
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)

ALQ: Aurore Le Quellec; TG: Thibaut Guyard; ICC: intraclass correlation coefficient; AADI: anterior atlanto-dental intervals; PADI: posterior atlanto-dental intervals; aAAS: anterior atlanto-axial subluxation; O: odontoid sagittal diameter; C2: axis body base sagittal diameter; vAAS: basilar invagination.

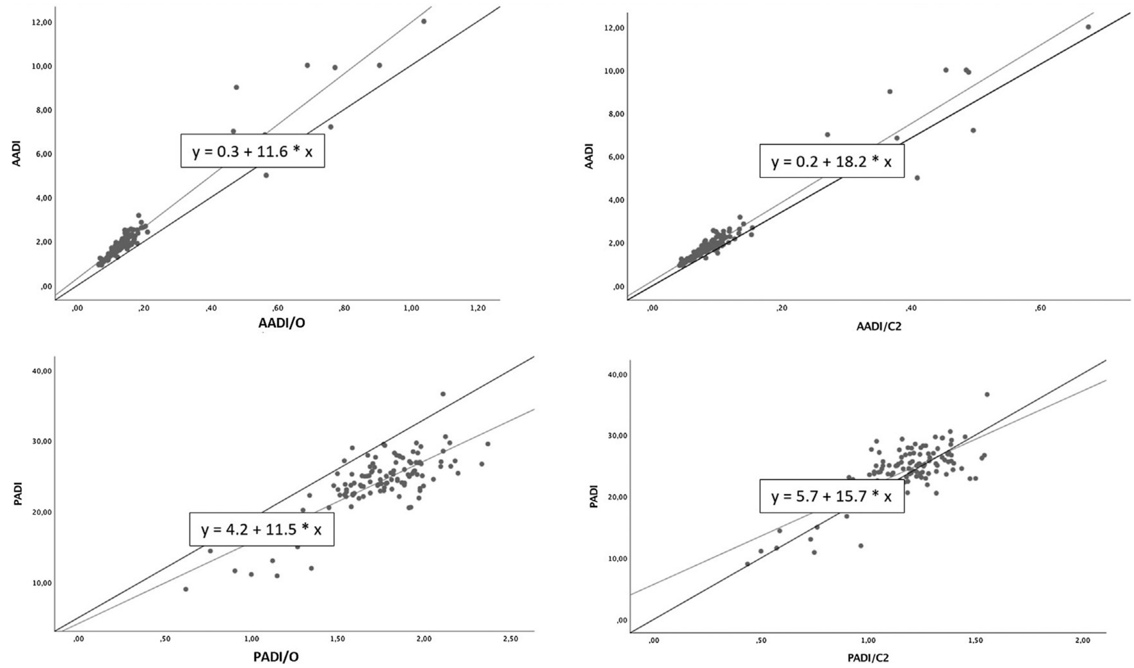

Fig. 2. Formulae used to extrapolate the anterior atlanto-dental intervals (AADI) and posterior atlanto-dental intervals (PADI) from the ratios (formulae to extrapolate AADI from AADI/odontoid sagittal diameter (O) ratio: y = 0.3 + 11.6 × x; AADI from AADI/axis body base sagittal diameter (C2) ratio: y = 0.2 + 18.2 × x; PADI from PADI/O ratio: y = 4.2 + 11.5 × x; and PADI from PADI/C2 ratio: y = 5.7 + 15.7 × x).

[Fig. S1; see the supplementary material associated with this article online].

3.5. 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 Fig. 3.

Using AADI > 2.9 as the gold standard (Fig. 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. Fig. 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 = 7.0 mm, AADI extrapolated from AADI/O ratio is 5.8.

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 cutoff value at 8.0, both the sensitivity and specificity were 100%. Using the same gold standard, an AADI extrapolated from the AADI/C2

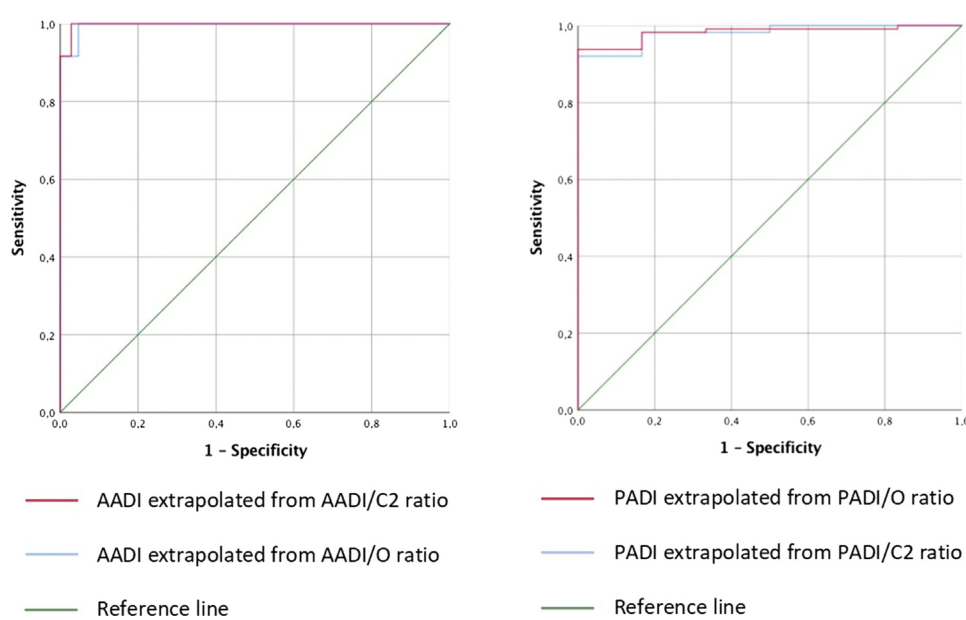

Fig. 3. Receiver operator characteristics (ROC) curves showing the diagnostic value of the anterior atlanto-dental intervals (AADI) extrapolated from the AADI/odontoid sagittal diameter (O) and AADI/axis body base sagittal diameter (C2) ratios using AADI > 2.9 as the gold standard (left) and the diagnostic value of the posterior atlanto-dental intervals (PADI) extrapolated from the PADI/O and PADI/C2 ratios using PADI < 14.0 mm as the gold standard (right).

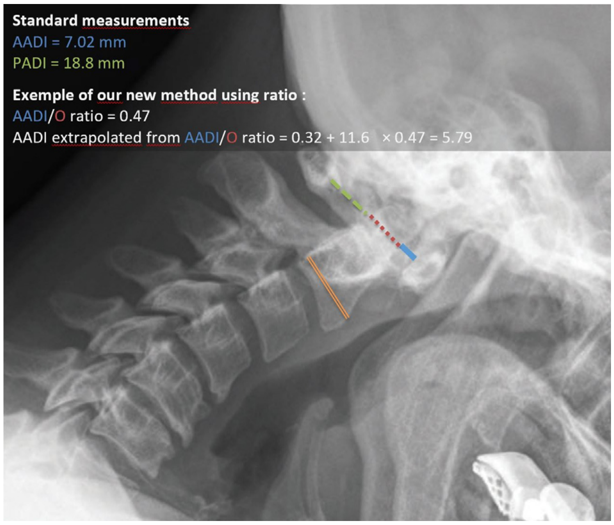

Fig. 4. Lateral flexion plain radiograph showing an example of a patient with anterior atlanto-axial subluxation (aAAS). Standard measurement found an anterior atlanto-dental intervals (AADI) = 7.0 mm and a posterior atlanto-dental intervals (PADI) = 18.8 mm in favour of non-severe aAAS. With our method, we found concordant findings with extrapolated AADI > 2.9 and extrapolated PADI ≥ 14.0. AADI extrapolated from AADI/odontoid sagittal diameter (O) ratio = 0.3 + 11.6 × 0.5 = 5.8; AADI extrapolated from AADI/axis body base sagittal diameter (C2) ratio = 0.2 + 18.2 × 0.3 = 5.2; PADI extrapolated from PADI/O ratio = 4.2 + 11.5 × 1.2 = 18.3; PADI extrapolated from PADI/C2 ratio = 5.7 + 15.7 × 0.7 = 16.9.

ratio had a sensitivity of 75% and a specificity of 100% to diagnose severe aAAS, but for a cutoff value of 8.0 mm, the sensitivity was 100% and specificity was 99%.

Using PADI < 14.0 mm as the gold standard (Fig. 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.

The presence of a vAAS had no impact on the diagnostic performance of the extrapolated AADI and PADI from ratios.

4. 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 cutoffs 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.

Authorship

All individuals listed as authors quality for authorship according to the following four ICMJE criteria.

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 measures in millimetres.

Measures extrapolated from the ratios could be used to detect atlanto-axial subluxation.

Disclosure of interest

The authors declare that they have no competing interest.

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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.

Appendix A. Supplementary data

Supplementary data (Fig. S1) associated with this article can be found, in the online version, at https://doi.org/10.1016/j.jbspin.2021.105229.

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