



# REVISTA BRASILEIRA DE REUMATOLOGIA

www.reumatologia.com.br



Original article

## Radiographic changes of the cervical spine in rheumatoid arthritis

Juan Marcelo Fernandez Alcala<sup>a</sup>, Diogo Douat<sup>b</sup>, Diogo Lago Pinheiro<sup>b</sup>, Douglas Jun Kamei<sup>a</sup>, Fábio Raimundo M dos Santos<sup>a</sup>, Marília B Silva<sup>a</sup>, Thelma L Skare<sup>a,\*</sup>

<sup>a</sup>Faculdade Evangélica de Medicina do Paraná, Curitiba, PR, Brazil

<sup>b</sup>Unit of Diagnostic Imaging, Hospital Universitário Evangélico de Curitiba, Curitiba, PR, Brazil

### ARTICLE INFO

#### Article history:

Received May 13 2012

Accepted March 14 2013

#### Keywords:

Rheumatoid arthritis  
Cervical spine  
Atlanto-axial luxation  
Basilar invagination  
Subaxial instability

### ABSTRACT

**Introduction:** The involvement of the cervical spine is a common feature of rheumatoid arthritis (RA).

**Objective:** To study the prevalence of radiographic changes of the cervical spine in patients with RA and their association with clinical and serological profiles of the disease.

**Methods:** We analysed lateral (neutral position, hyperextension, hyperflexion) and transoral views of cervical spine radiographs from 80 individuals with RA to investigate the presence of atlanto-axial subluxation (AAS), basilar invagination (BI), and subaxial instability (SAI). Demographic, clinical (nodules, interstitial pneumonitis, secondary Sjögren's syndrome, medications etc.), and serologic (rheumatoid factor - RF, cyclic citrullinated peptide antibody - anti-CCP, and antinuclear factor - ANF) data were obtained from the clinical records.

**Results:** Cervical spine misalignments were identified in 26/80 (32.5%) participants; AAS occurred in 12/80 (15%) participants, BI in 6/80 (7.5%), and SAI in 13/80 (32.5%). Odontoid erosions were identified in 16/80 (20.0%) participants. Cervical spine misalignment exhibited associations with age at onset and disease duration ( $P = 0.03$  and  $0.02$ , respectively). No associations were identified between the cervical spine changes and the participants' ethnicity or gender, presence of nodules, interstitial pneumonitis, secondary Sjögren's syndrome, RF, ANF, or anti-CCP. The participants with cervical spine misalignment exhibited higher frequencies of odontoid erosion ( $P = 0.03$ ).

**Conclusions:** Cervical spine misalignment was a common radiographic finding and occurred more frequently in participants with earlier onset and longer length of RA.

© 2013 Elsevier Editora Ltda. All rights reserved.

\* Corresponding author.

E-mail: tskare@onda.com.br (T.L. Skare).

## Alterações radiográficas da coluna cervical em artrite reumatoide

### R E S U M O

#### Palavras-chave:

Artrite reumatoide  
Coluna cervical  
Luxação atlanto-axial  
Invaginação basilar  
Instabilidade subaxial

**Introdução:** O envolvimento da coluna cervical é comum na artrite reumatoide (AR).

**Objetivo:** Estudar a prevalência das alterações radiológicas de coluna cervical em pacientes com AR e sua associação com perfil clínico e sorológico da doença.

**Métodos:** Analisaram-se as radiografias de coluna cervical em perfil neutro hiperextensão, hiperflexão e transoral de 80 pacientes com AR para presença de subluxação atlanto-axial (LAA), invaginação basilar (IB) e instabilidade subaxial (ISA). Dados de perfil demográfico, clínico (nódulos, pneumonite intersticial, síndrome Sjögren secundária, uso de medicamentos etc.) e sorológico (FR, anti-CCP e FAN) foram obtidos por revisão de prontuários.

**Resultados:** Havia alguma alteração de eixo de coluna cervical em 26/80 (32,5%); em 12/80 (15%) havia LAA; em 6/80 (7,5%) existia IB; em 13/80 (16,2%) existia ISA. Erosões em odontoide foram vistas 16/80 (20,0%). As alterações do eixo cervical estavam associadas com idade de início da doença e duração da mesma ( $P = 0,03$  e  $0,02$ , respectivamente). Não se encontrou associação das alterações em coluna cervical com raça, gênero, nódulos, pneumonite intersticial, Sjögren secundário, FR, FAN ou anti-CCP. Pacientes com alterações do eixo cervical apresentavam mais erosões de odontoide ( $P = 0,03$ ).

**Conclusões:** Alterações radiológicas em eixo de coluna cervical são comuns e aparecem mais frequentemente em indivíduos com diagnóstico mais precoce de AR e maior tempo de doença.

© 2013 Elsevier Editora Ltda. Todos os direitos reservados.

## Introduction

One of the characteristics of rheumatoid arthritis (RA) is the involvement of the cervical spine.<sup>1</sup> The main alterations occur in the spine's most mobile region: its upper portion.<sup>1</sup> Typical alterations include anterior atlanto-axial subluxation, atlanto-axial impaction or basilar invagination (also known as vertical atlanto-axial subluxation), and subaxial disease.<sup>1,2</sup> All of these alterations are due to chronic local inflammation.<sup>1,2</sup>

Anterior atlanto-axial luxation occurs when the ligaments that stabilise this area are damaged. Under such circumstances, whenever the neck is moved, the head weight pulls the atlas away from the axis.<sup>2</sup> When inflammation affects the atlanto-axial joints by destroying the cartilage and bone structure, the skull presses the atlas down towards the axis, causing basilar invagination.<sup>2</sup> Subaxial disease is less frequently observed and usually occurs in association with the remainder of the deformities.<sup>1</sup> This pathology is due to inflammation of the facet joints below the second cervical vertebra.<sup>3</sup>

One meta-analysis reported that cervical spine alterations are frequent in patients with RA, occurring in 5.5 to 73% of the cases (average of 32%). These alterations are associated with neurologic signs and/or symptoms in 17% of cases.<sup>1</sup>

Atlanto-axial subluxation occurs early,<sup>1,2</sup> within the first two years of disease onset.<sup>2</sup> Diagnosis is established when a distance greater than 3 mm is measured between the anterior arch of the atlas and the odontoid process of the axis. When the diameter between the posterior arch of the atlas and the odontoid process of the axis is equal to or less than 14 mm, the risk of myelopathy is high. The first neurologic sign associated with atlanto-axial subluxation is headache in the occipital area due to compression of the greater occipital nerve (Arnold's neuralgia), which is followed by sensory and motor deficit affecting the arms and legs.<sup>4</sup> Further com-

plaints include neck stiffness, earache due to compression of the greater auricular nerve, vertigo, gait abnormalities, loss of balance, and tinnitus due to alterations of the vertebral artery flow.<sup>5</sup> When the neck is bent forwards, Lhermitte's sign could be triggered, which is an electric-like shock sensation running down the back into the limbs.<sup>5</sup> Quadriparesis, chronic hydrocephalus, cerebral infarction, and sudden death are complications of established disease.<sup>2,4</sup>

The problems associated with basilar invagination tend to appear later in the progression of disease and occur more commonly in the most severe cases of RA.<sup>2</sup> These symptoms appear in 4 to 34% of the cases, and the upward migration of the odontoid process might result in compression of the brainstem.<sup>1,6</sup> The prevalence of axial subluxation varies from 7 to 29%<sup>1,6</sup> and might occur as an isolated deformity or may affect multiple levels. The latter case results in the onset of a deformity with a "staircase" appearance.<sup>1,6</sup>

Corbett et al.<sup>7</sup> assessed 102 individuals who developed atlanto-axial luxation within the first two years of RA and determined that it occurred in association with erosive disease and resulted in poor functional prognosis. However, early administration of disease-modifying antirheumatic drugs (DMARDs) and the advent of more powerful agents for the control of inflammation allows for alteration of the natural disease progression of RA. Such modulation also affects the severity of the cervical spine involvement. It is believed that early and effective use of DMARDs might prevent or limit the pannus growth, thus reducing the space it occupies and its destructive potential.<sup>1,8</sup> As a consequence, it is expected that both the prevalence of and the risks associated with RA cervical complications will decrease.

In this study, we investigated the prevalence of radiographic changes in the cervical spine of Brazilian individuals with RA and sought to establish the clinical, serological, and demographic characteristics associated with these changes.

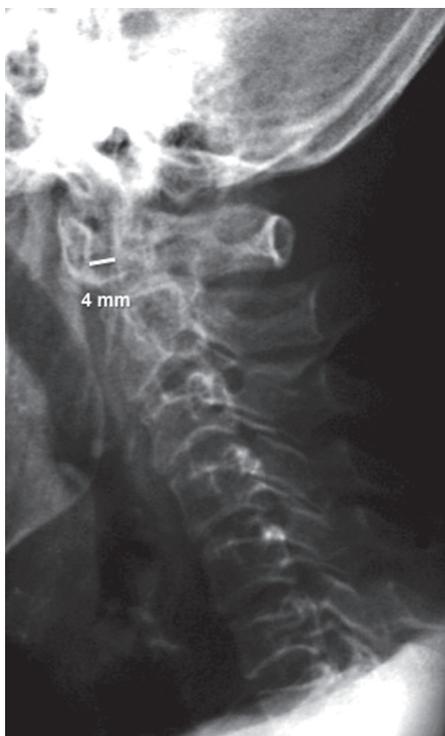
## Methods

This study was approved by the institutional research ethics committee, and all participants signed an informed consent form. Individuals from both genders who met at least four of the classification criteria formulated in 1987 by the American College of Rheumatology<sup>9</sup> were invited to participate in the study. The participants were selected based on their order of consultations and their availability to participate in the study, which was conducted from July to December 2011. In addition, their RA diagnosis should have been established before age 16. Pregnant women and individuals with histories of cervical spine trauma or with intellectual incapacities hindering them from understanding the terms of the informed consent form were excluded.

Lateral-view radiographs of the cervical column were performed for all of the participants in the neutral position and in hyperextension and hyperflexion. Two radiologists blinded to the participants' clinical data independently analysed all of the images.

The parameters assessed were: atlanto-axial subluxation, basilar invagination, erosion of the odontoid process of the axis, and subaxial instability. Atlanto-axial subluxation was considered to be present when the distance between the anterior arch of the atlas and the odontoid process of the axis was larger than 3 mm (Fig. 1).<sup>10,11</sup>

Basilar invagination was assessed using the Redlund-Johnell and Pettersson method<sup>12</sup>, which involves drawing a line from the posterior margin of the hard palate to the inferior cortical surface of the occipital bone on a lateral radiograph

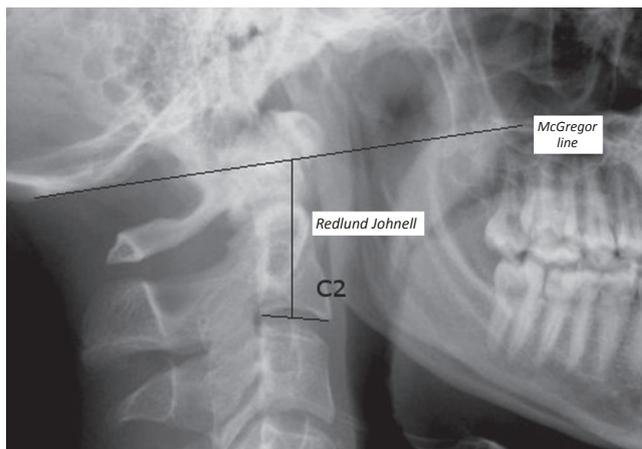


**Fig. 1** – Lateral radiograph (hyperflexion) showing increased space between the posterior margin of the anterior arch of the atlas and the anterior surface of the odontoid process of the axis, indicative of atlanto-axial subluxation.

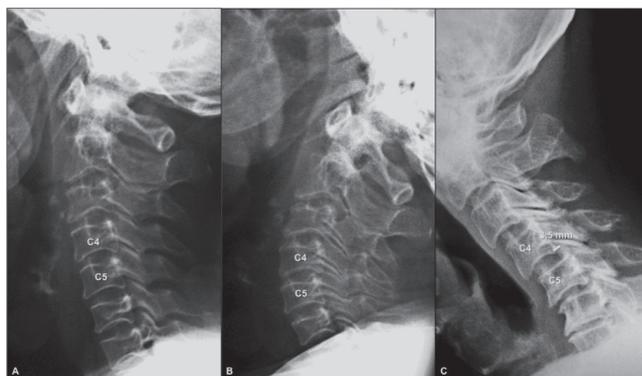
and measuring the distance between that line and the centre of the lower end plate of C2 vertebral body. The normal values of that line are 34 mm or more in males and 29 mm or more in females. This method is appropriate for the assessment of basilar invagination because it avoids the use of measurements involving the tip of the odontoid process as reference, as it is frequently eroded in individuals with RA (Fig. 2).<sup>12</sup>

Subaxial instability was diagnosed when vertebral slippage was greater than 3 mm (Fig. 3).<sup>13,14</sup>

The participants' demographic data, along with duration, age at onset of disease, clinical profile (i.e., presence of nodules, associated interstitial lung disease, secondary Sjögren's syndrome, peripheral neuropathy, and eye involvement), and medication use, were collected from the clinical records. To establish the presence of secondary Sjögren's syndrome, the



**Fig. 2** – Redlund-Johnell's method for identifying basilar invagination. On a lateral radiograph, a line is drawn from the posterior margin of the hard palate (A) to the inferior cortical surface of the occipital bone (B). The distance from the centre of the lower end plate of C2 vertebral body (C) and line A-B is measured on a line parallel to the longitudinal axis of the odontoid process. The normal values of that distance are 34 mm or more in males and 29 mm or more in females.



**Fig. 3** – Lateral cervical spine radiographs in the neutral position (A), hyperextension (B), and hyperflexion (C). The C4 vertebral body exhibits anterior slippage of 3.5 mm relative to the C5 vertebral body only on the radiograph performed in hyperflexion (C), indicating subaxial instability.

classification criteria formulated by the American-European consensus group<sup>15</sup> were used. The participants were asked about any clinical complaints they had regarding the cervical region (i.e., pain, stiffness, paresthesia, and weakness of the upper limbs).

The data were grouped into frequency and contingency tables; the measures of central tendency used were medians and interquartile ranges in cases of non-parametric data and means and standard deviations in cases of parametric data. Associations between nominal data were assessed using Fisher's exact test, and the Mann-Whitney test and unpaired Student's t-test were used in cases of numerical data. The level of significance was established as 5%, and analyses were performed using the Graph Pad Prism version 5.0 software.

## Results

### Descriptive analysis of the investigated population

Among the 80 individuals included in the study, 10 (12.5%) were male, and 70 (87.5%) were female; 18 (22.5%) were Afro-descendants, and 62 (77.5%) were Caucasian. The average age of the sample was  $55.4 \pm 11.9$  years (26-82 years), the average duration of disease was nine years (1-29 years), and the age at disease onset ranged from 17 to 75 years (average of  $45.0 \pm 12.6$  years).

Eleven (13.7%) participants exhibited interstitial lung disease on chest radiograph or tomography, nine (11.2%) exhibited subcutaneous nodules, two (2.5%) had scleritis, one (1.25%) had vasculitis, and one (1.25%) had peripheral neuropathy. Nineteen (23.7%) participants exhibited secondary Sjögren's syndrome. Fifty-four participants tested positive for rheumatic factor (RF), 19 (25.0%) for antinuclear factor (ANF), and 22 (70.9%) for the cyclic citrullinated peptide antibody (anti-CCP). Regarding treatment, 66 (82.5%) participants used methotrexate, 39 (48.7%) used antimalarial agents, 37 (46.2%) used glucocorticoids, 27 (33.7%) used leflunomide, nine (11.2%) used anti-tumour necrosis factor (TNF)- $\alpha$  agents, and four (5%) used azathioprine. Ten (12.5%) participants used four DMARDs, 24 (30.0%) used three, 31 (38.7%) used two, and 15 (18.7%) used only one.

The prevalence rates of the various types of radiographic changes observed in the cervical spine are depicted in Figure 4.

The distance between the anterior arch of the atlas and the anterior surface of the odontoid process in the individuals with atlanto-axial luxation varied from 3.5 to 5.5 mm (average of  $4.3 \pm 0.7$  mm), and the distance between the odontoid process and the posterior arch of the atlas varied from 14.0 to 23.0 mm (average of  $20.4 \pm 2.1$  mm). This alteration was noted on the lateral radiograph in the neutral position in only one of the 12 participants with atlanto-axial luxation. The distance from the anterior arch of the atlas to the odontoid process exhibited a median difference of 2.7 mm between the radiographs acquired in the neutral position and neck hyperflexion.

The measure of vertebral slippage in the six participants with basilar invagination varied from 20.0 to 28.0 mm (average of  $25.6 \pm 2.8$  mm). Vertebral slippage in the 13 participants with subaxial instability varied from 3.5 to 5.0 mm (median of 4.0 mm).

No participant exhibiting radiographic alterations reported clinical complaints that could be attributed to them.

### The association between radiographic changes in the cervical spine and the clinical and laboratory profiles

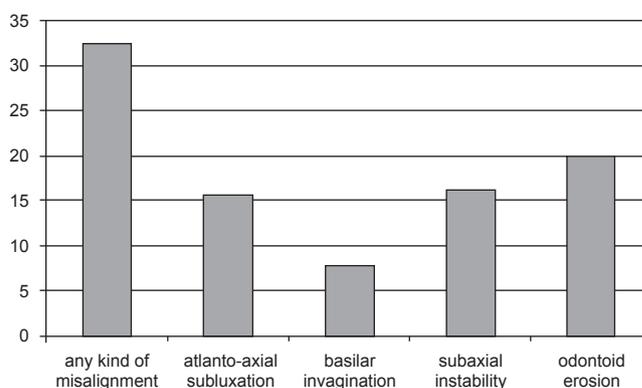
The results of the comparison of the group of participants with some type of cervical spine misalignment with the remainder of the participants are described in Table 1. The prevalence of radiographic changes in the cervical spine was higher in the participants with longer disease duration and with earlier disease onset.

## Discussion

The sample assessed in this study exhibited a high prevalence of cervical spine abnormalities (31%). In agreement with the literature,<sup>1</sup> basilar invagination was the least frequent alteration. Interestingly, all of the participants in this case series were clinically asymptomatic, and the literature indeed stresses that silent development is characteristic of basilar invagination.<sup>2</sup> Therefore, clinicians must actively evaluate patients for this pathology.<sup>1,2</sup>

Therefore, routine follow-up of patients with RA must include radiographs of the cervical spine, which should be performed in other positions in addition to the neutral position; otherwise, many alterations might not be identified. According to Kauppi et al.,<sup>10</sup> 50% of subluxations are undiagnosed when radiographs are taken in the neutral position only. In this case series, atlanto-axial luxation would have been diagnosed in only one participant if radiographs had been performed in only the neutral position. There are no definite guidelines in the literature for the interval between radiographic assessments. Although the results of this study do not allow for any conclusions to be drawn in that regard, they indicate that individuals with longer disease duration or earlier disease onset should be monitored more carefully.

Cervical myelopathy usually appears many years after the onset of atlanto-axial subluxation.<sup>14</sup> This delay is believed to be due to the accumulated effects of repeated microtrauma on an unstable cervical spine over the course of many years,



**Fig. 4 – Prevalence rates (%) of radiographic changes in the cervical spine of 80 individuals with RA (atlanto-axial subluxation in 12/80, basilar invagination in 6/80, subaxial instability in 13/80, and odontoid erosion in 16/80).**

**Table 1 – Comparison of the demographic, clinical, and serological profiles of patients with and without cervical spine misalignment.**

	With some luxation n = 26/80 = 32.5%	Without luxation n = 54/80 = 67.5%	P
Age (years)	26-75 mean 53.9 ± 13.9	34-82 mean 56.0 ± 10.9	0.46
Disease duration (years)	2-29 mean 11.0 IQR 7.5-16.5	1-27 mean 7,0 IQR 4.0-12.0	0.02
Age at disease onset (years)	17- 63 mean 40.5 ± 13.4	23-75 mean 47.0 ±11.8	0.03
Gender	4 males 22 females	6 males 48 females	0.72
Ethnicity	21 Caucasian 5 Afro-descendants	41 Caucasian 13 Afro-descendants	0.77
Nodules	2/26 (7.6%)	7/54 (12.9%)	0.71
Lung fibrosis	4/26 (15.3%)	7/54 (12.9%)	0.74
Secondary Sjögren's	5/26 (19.2%)	14/54 (25.9%)	0.28
Rheumatoid factor	15/26 (57.6%)	39/53 (73.5%)	0.19
Antinuclear factor	4/26 (15.3%)	15/50 (30.0%)	0.10
Cyclic citrullinated peptide antibody	8/13 (61.5%)	14/18 (88.8%)	0.43
Odontoid erosion	9/26 (34.6%)	7/54 (12.9%)	0.03

which results in both neuronal and glial cell death and spinal cord atrophy.<sup>1,4,16</sup> Microtrauma seems more relevant for the genesis of myelopathy than ischaemic injury.<sup>5</sup> Once myelopathy manifests itself, the clinical state of deteriorates rapidly, and the prognosis becomes poorer.<sup>1</sup>

In one study including 37 individuals with RA and cervical myelopathy,<sup>17</sup> 19 participants died; 15 deaths occurred six months after the onset of symptoms. In that same case series, all of the individuals who had not received cervical collar treatment and half the individuals who had received treatment died within 12 months. In another study<sup>18</sup> including nine individuals with myelopathy and subjected to conservative treatment, all of the participants died within 12 months; the cause of death was attributed to spinal cord compression in four cases.

In the study conducted by Neva et al.<sup>6</sup> of Finnish patients with RA who died, review of the clinical records revealed that cervical spine abnormalities had been diagnosed in only 38 out of 853 individuals and that cervical spine deformities were severe enough to be a potential cause of death in 17 cases. Despite these findings, according to the official death certificates, cervical spine disorder was not the cause of death of any of those individuals. The data indicate that cervical myelopathy is often not given proper consideration.

There is no consensus on the treatment of cervical spine instability in patients with RA, while the available opinions and recommendations on early and prophylactic surgical stabilisation are exclusively based on retrospective studies.<sup>4,19</sup> As a rule, conservative treatment is performed in asymptomatic individuals, while indications for surgical intervention include intractable pain, neurologic disorders, involvement of the vertebral artery, and high signal intensity in the spinal cord on T1-weighted magnetic resonance imaging.<sup>20,21</sup> Although conservative treatment is only used in the milder cases, close monitoring to detect the onset of cervical spine instability is mandatory, especially in the individuals subjected to manipulation of the cervical spine, such as patients requiring orthopaedic surgery.<sup>22</sup>

Some authors<sup>19,23</sup> have reported associations between cervical spine subluxation and some features of RA, such as positive RF and the presence of subcutaneous nodules. In the present study, neither these nor other clinical features exhibited such associations, except for earlier age at onset and longer disease duration. Association with a longer-duration ECD disease has already been reported in the literature,<sup>17</sup> although contradictory findings have been described.<sup>24</sup> The disagreement relative to associations with positive RF, the presence of subcutaneous nodules, and disease duration might possibly be accounted for in more aggressive RA treatments resulting from novel data on its physiopathology. As has already been mentioned, that type of treatment tends to modify the natural history of RA, including its effects on the cervical spine.<sup>8,25</sup>

To conclude, in this study, a sample of individuals with RA exhibited high prevalence rates of asymptomatic disorders of cervical spine alignment. These disorders were more frequent in individuals with longer disease durations.

## Conflicts of interest

The authors declare that there is no conflicts of interest.

## REFERENCES

- Casey ATH, Crockard HA. The cervical spine. In: Firestein GS, Panayi GS, Wollheim FA (eds). *Rheumatoid Arthritis*. 2.ed. London: Oxford University Press, 2006; p.475-84.
- Kaupasi MJ, Barcelos A, da Silva JAP. Cervical complications of rheumatoid arthritis. *Ann Rheum Dis*. 2005;64:355-8.
- Neva MH, Kotaniemi A, Lehtinen JT, Belt EA, Kauppi M. Atlanto-axial disorders in rheumatoid arthritis associate with the destruction of peripheral and shoulder joints, and decreased bone mineral density. *Clin Exp Rheumatol*. 2003;21:179-84.
- Wolfs JFC, Kloppenburg M, Fehlings MG, von Tulder MW, Boers M, Peul WC. Neurologic outcome of surgical and

- conservative treatment of rheumatoid cervical spine subluxation: a systematic review. *Arthritis Rheum.* 2009;61:1743-52.
5. Wasserman BR, Moskovicich R, Razi AE. Rheumatoid arthritis of cervical spine. *Bull NYU Hosp Joint Dis.* 2011;69:136-48.
  6. Neva H, Myllykangas-Luosujärvi R, Kautiainen H, Kauppi M. Mortality associated with cervical spine disorders: a population-based study of 1666 patients with rheumatoid arthritis who died in Finland in 1989. *Rheumatology.* 2001;40:123-7.
  7. Corbett M, Dalton S, Young A, Silman A, Shipkley M. Factors predicting death, survival and functional outcome in a prospective study of early rheumatoid disease over fifteen years. *J Rheumatol.* 1993;32:717-23.
  8. Neva MH, Kauppi MJ, Kautiainen H, Luukkainen R, Hannonen P, Leirisalo-Rapo M, et al. Combination drug therapy retards the development of rheumatoid atlanto-axial subluxation. *Arthritis Rheum.* 2000;43:2397-401.
  9. Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum.* 1988;31:315-24.
  10. Kauppi M, Neva MH. Sensitivity of lateral view cervical spine radiographs taken in the neutral position in atlanto-axial subluxation in rheumatoid diseases. *Clin Rheumatol.* 1998;17:511-4.
  11. Komusi T, Munro T, Harth M. Radiological review: the rheumatoid cervical spine. *Semin Arthritis Rheum.* 1985;14:187-95.
  12. Redlund-Johnell I, Pettersson H. Radiographic measurements of the craniovertebral region. Designed for evaluation of abnormalities in rheumatoid arthritis. *Acta Radiol Diagn (Stockh).* 1984;25:23-8.
  13. Eijk IC, Nielsen MM, van Soesbergen RM, Haumburger HL, Kertens PJS, Dijkmans BAC, et al. Cervical spine involvement is rare in early rheumatoid arthritis. *Ann Rheum Dis.* 2006;65:973-4.
  14. Souza CP, Delfino HLA. Radiographic study of cervical spine alterations and its clinical correlation in patients with rheumatoid arthritis. *Acta Ortop Bras.* 2005;13:38-41.
  15. Vitali C, Bomardieri S, Jonsson R, Moutsopoulos HM, Alexander EL, Carson SE, et al. Classification criteria for Sjögren's syndrome: a revised version of the European criteria proposed by the American European consensus group. *Ann Rheum Dis.* 2002;61:554-8.
  16. Henderson FC, Geddes JF, Crockard HA. Neuropathology of brain stem and spinal cord in end stage rheumatoid arthritis: implications for treatment. *Ann Rheum Dis.* 1993;52:629-37.
  17. Marks JS, Sharp J. Rheumatoid cervical myelopathy. *Q J Med.* 1981;50:307-19.
  18. Meijers KA, van Beusekom GT, Luyendijk W, Duijfjes F. Dislocation of the cervical spine with cord compression in rheumatoid arthritis. *J Bone Joint Sur (Br).* 1974;56B:668-80.
  19. Halla JT, Hardin JG. The spectrum of atlanto-axial facet joint involvement of rheumatoid arthritis. *Arthritis Rheum.* 1990;33:325-9.
  20. Schmitt-Sody M, Kirchoff C, Buhmann S, Metz P, Birkenmaier C, Troullier H, et al. Timing of cervical spine stabilization and outcome in patients with rheumatoid arthritis. *Int Orthop.* 2008; 32: 511-516.
  21. Christensson D, Saveland H, Rydholm U. Cervical spine surgery in rheumatoid arthritis: A Swedish nation-wide registration of 83 patients. *Scand J Rheumatol.* 2000;29:314-9.
  22. Neva MH, Häkkinen A, Mäkinen H, Hannonen P, Kauppi M, Sokka T. High prevalence of asymptomatic cervical spine subluxation in patients with rheumatoid arthritis waiting for orthopaedic surgery. *Ann Rheum Dis.* 2006;65:884-8.
  23. Rasker JJ, Gosh JA. Radiological study of cervical spine and hand in patients with rheumatoid arthritis of 15 years duration: an assessment of the effects of corticosteroids treatment. *Ann Rheum Dis.* 1978;37:529-35.
  24. de Souza MC, de Ávila Fernandes E, Jones A, Lombardi I Jr, Natour J. Assessment of cervical pain and function in patients with rheumatoid arthritis. *Clin Rheumatol.* 2011;30:831-6.
  25. Kaito T, Hosono N, Ohsima S, Ohwaki H, Takenaka S, Fujiwara S, et al. Effect of Biological Agents on Cervical Spine Lesions in Rheumatoid Arthritis. *Spine*, 2012 Apr 2. [Epub ahead of print]