

# Radiological Cervical Spine Involvement in Patients with Rheumatoid Arthritis: A Cross Sectional Study

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**ABSTRACT. Objective.** To investigate the frequency and the severity of radiological cervical spine involvement in patients with rheumatoid arthritis (RA).

**Methods.** We investigated 165 consecutive unselected patients with RA who fulfilled the revised American College of Rheumatology criteria for RA. All patients had a complete physical and laboratory evaluation. Patients had a radiological evaluation that included hand and wrist radiographs, as well as cervical spine radiographs in anteroposterior, lateral, and lateral in full flexion views. Hand radiographs were evaluated according to the Larsen criteria, while cervical radiographs were evaluated according to Winfield classification.

**Results.** There were 143 women and 22 men, with a mean age of  $59.6 \pm 12.5$  and disease duration  $12.3 \pm 13.9$  years. Positive rheumatoid factor was found in 63.6% of patients. One hundred forty-six patients presented radiological findings related to cervical spine involvement: atlantoaxial subluxations were found in 20.6% and erosions of the odontoid process in 2.4%; none presented vertical subluxation. Subaxial subluxations were found in 43.6%, disc space narrowing at C2–C3, C3–C4, C4–C5 levels in 66.1%, and vertebral plate sclerosis and erosions in 43.6%.

**Conclusion.** Cervical spine radiological involvement is a frequent finding in our patients with RA, but the severity of the disease is rather mild, possibly related to the ethnic background. (J Rheumatol 2005;32:801–6)

*Key Indexing Terms:*  
CERVICAL SPINE  
ATLANTOAXIAL

RHEUMATOID ARTHRITIS

PREVALENCE  
SUBAXIAL SUBLUXATIONS

Rheumatoid arthritis (RA) is a chronic, systemic inflammatory disorder of unknown etiology characterized by erosive synovitis. It affects roughly 1% of the general population. Articular inflammation may be remitting, but if continued usually results in progressive joint destruction, deformity, and finally variable degrees of functional disability<sup>1</sup>. Cervical spine involvement in RA characteristically involves the atlantoaxial complex, the most mobile part of the spine, with the radiological abnormalities being classified into those of atlantoaxial subluxation (AAS), which may be horizontal or vertical in direction. However, significant subaxial disease is common and usually coexists with

the AAS<sup>2,3</sup>. Although these radiological abnormalities remain asymptomatic for years, these patients are at continued risk from a range of neurological complications and even sudden death from medullary compression<sup>2,3</sup>.

The association between various clinical factors and cervical spine involvement in RA has been reported<sup>4–8</sup>. However, there has been little investigation determining the factors that influence which patients may be affected, when they are, and the roles of disease duration, disease severity, extraarticular manifestations, and other factors.

Studies have shown that RA in Greece is milder, with less radiological joint destruction and fewer extraarticular manifestations, compared to northern European countries<sup>9,10</sup>. We investigated the frequency and the severity of cervical spine involvement in Greek patients with RA.

## MATERIALS AND METHODS

From January 2002 to September 2002, 165 consecutive unselected patients with RA being followed at the outpatient rheumatology clinic of the University Hospital of Ioannina were investigated. All patients fulfilled the revised American College of Rheumatology criteria<sup>11</sup>. Patients had a complete physical examination that included the following:

1. Symptoms and signs of peripheral joint involvement such as morning stiffness (minutes), grip strength (mm Hg), number of swollen and tender joints and Disease Activity Score for 28 joint indices (DAS28)<sup>12</sup>.
2. Symptoms and signs of cervical spine involvement, such as neck pain,

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stiffness, and neurological symptoms. Specifically, patients were asked about neck pain according to the following scale: stage 0 (no pain), stage I (intermittent pain responsive to standard analgesics), stage II (intermittent pain partially responsive to standard analgesics — need for immobilization by a cervical collar), and stage III (incapacitating continuous pain unresponsive to analgesics)<sup>13</sup>. In addition, patients were asked about neck stiffness and also muscle weakness and tingling and numbness affecting the fingers of the hands and feet. In addition, any dysfunction of the bladder (incontinence or urinary retention) was recorded in all patients. Clinical evaluation included neck assessment (range of motion: flexion extension, lateral flexion, and rotation), muscle strength of the upper and lower extremities, tendon reflexes, “marble” sensation in the trunk and limbs, and Babinski sign.

3. Symptoms and signs of extraarticular manifestations such as Raynaud’s phenomenon, rheumatoid nodules, pleurisy, sicca syndrome, scleritis, episcleritis, etc. In addition, the following laboratory indicators were investigated in all patients: C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and IgM rheumatoid factor (IgM RF).

Patients with neck trauma, neck infections, or congenital abnormalities were excluded from the study.

**Radiological assessment.** The radiological evaluation consisted of radiographs of cervical spine (anteroposterior, lateral in neutral and flexion position), and wrist and hand in posteroanterior position. Cervical spine radiographs were evaluated according to the modified Winfield classification<sup>14,15</sup>.

AAS was measured by recording the shortest distance between the posterior surface of the anterior arch of the atlas to the anterior surface of the odontoid peg. A distance  $\geq 2.5$  mm was taken as significant. Vertical subluxation was recorded as present if the tip of the odontoid peg lay  $> 4.5$  mm above the line described by McGregor (a line drawn between the hard palate and the most caudal point of the occipital curve). Radiological evaluation of the cervical spine did not include open-mouth anterior-posterior view of C1–C2, thus we did not assess C1–C2 lateral joint destruction and lateral AAS.

Multiple subaxial subluxation (SAS) was recorded as present if displacement between adjacent vertebral bodies was  $> 1$  mm. A shift  $> 1$  mm is considered abnormal according to the Smith criteria<sup>4</sup>.

Disk space narrowing at C2–C3, C3–C4, and C4–C5 was recorded only if there was a relative lack of osteophytosis. Disk space narrowing at lower levels in the cervical spine was not documented, since degenerative changes are frequently superimposed. Vertebral plate erosions, often accompanied by localized areas of reactive sclerosis, were noted.

Apophyseal joint erosions and sclerosis were also investigated. The obliquity of the apophyseal joints, however, frequently obscured the definition of these joints on a plain lateral radiograph, making erosions difficult to visualize. Osteoporosis was assessed subjectively as present or absent.

In addition, pairs of hand and wrist radiographs were evaluated using Larsen’s criteria<sup>16</sup>. The following joints were assessed: 4 proximal interphalangeal, 5 metacarpophalangeals, and the wrist bilaterally. Scoring of each joint was by 6 stages from 0 (normal) to 5. The wrist was considered as a unit and the score was multiplied by 5. Thus, the score ranges from 0 to 140<sup>16</sup>. Erosive changes were considered mild or moderate when the score ranged between 0 and 80, and severe when the radiological score was  $> 80$ . The radiographs were interpreted by one radiologist (AKZ) who was blinded to the patients’ clinical status.

**Statistical analysis.** Association of each radiological finding from cervical spine with clinical, laboratory, and radiological measures was analyzed by chi-square test. These measures were considered categorical according to the following classifications: age ( $\leq 45$ ,  $> 45$  yrs), sex (female/male), disease duration ( $\leq 5$ ,  $> 5$  yrs), extraarticular manifestations (yes/no), ESR ( $\leq 30$ ,  $> 30$  mm Hg), IgM RF (yes/no), Larsen score ( $\leq 80$ ,  $> 80$ ), DAS28 ( $\leq 3.2$ ,  $> 3.2$ ), CRP (yes/no), cervical spine radiograph (yes/no), clinical signs (yes/no). Multivariate analysis was based on a logistic regression model, using as dependent variable the presence of any radiological finding.

## RESULTS

The demographic and clinical characteristics of our patients are shown in Table 1. There were 143 women (86.7%) and 22 men (13.3%), with a mean age of  $59.6 \pm 12.5$  years, mean disease duration of  $12.3 \pm 13.9$  years, and followup of  $8.9 \pm 5.1$  years. One hundred five patients presented with IgM RF. Sixty-six RA patients presented clinical findings related to cervical spine involvement. The most common clinical symptom was neck pain and stiffness, and the majority of those patients had decreased range of motion of the cervical spine. Only one patient presented symptoms and signs of neurological impairment<sup>17</sup> (Table 2). Forty patients used major analgesics, while 4 were carrying soft cervical casts. On the other hand, 146 patients presented radiological findings suggesting cervical spine involvement. All patients were refractory to many disease modifying antirheumatic drugs (DMARD). The current treatment was as follows: 88 patients were taking methotrexate (MTX; 12.5–20 mg/week) plus prednisone ( $< 7.5$  mg/day), 23 were taking

Table 1. Demographic, clinical, and radiological data of patients with RA.

No. of patients	165
Women/men	143/22
Mean age ( $\pm$ SD) (range), yrs	59.6 (12.5) (17–85)
Mean disease duration ( $\pm$ SD) (range), yrs	12.3 (13.9) (1–20)
Mean followup ( $\pm$ SD) (range), yrs	8.9 (5.1) (0–20)
Extraarticular manifestations, n (%)	76 (46.1)
Clinical findings of cervical spine involvement, n (%)	66 (40)
Radiological findings of cervical spine involvement, n (%)	146 (88.5)
DMARD therapy, n (%)	
MTX + prednisone	88 (53.3)
MTX + cyclosporin A + prednisone	23 (13.9)
MTX + infliximab	21 (12.7)
Cyclosporin A + prednisone	20 (12.1)
Other DMARD	13 (7.9)

DMARD: disease modifying antirheumatic drug.

Table 2. Clinical features of cervical spine involvement in RA patients.

Symptoms and Signs	No. of Patients	%
Neck pain	66	40
Neck stiffness	42	25.5
Decreased range of motion		
Flexion	66	40
Extension	48	29.1
Lateral flexion	52	31.5
Rotation	49	29.7
Tingling or numbness	1	0.6
Brisk tendon reflexes	5	3.0
Babinski sign	1	0.6
“Marble” sensation	0	0
Neurological stage*		
Class I	65	39.4
Class II	1	0.6
Class IIIa	0	0
Class IIIb	0	0

\* Ranawat classification<sup>17</sup>.

MTX (12.5–17.5 mg/week) plus cyclosporin A (CSA; 2.5–3 mg/kg/day) plus prednisone (< 7.5 mg/day), 21 were taking MTX (12.5–17.5 mg/week) plus infliximab (3 mg/kg at Week 0, 2, and 6 and every 8 weeks thereafter), 20 were taking CSA (2.5–3 mg/kg/day) plus prednisone (< 7.5 mg/day), and finally, 13 patients were undergoing other DMARD therapy.

Anterior AAS was found in 34 patients (20.6%; Figure 1), while none had vertical subluxation and only 4 patients presented erosive lesions of the odontoid process. Seventy-two patients presented SAS (Figure 2), while a significant number of patients presented upper disc space narrowing and sclerosis, and vertebral plate erosions and sclerosis (Table 3). The majority of our patients with anterior AAS had atlantodental interval between 2.5 and 5.0 mm. More specifically, 19 patients had anterior AAS only in flexion position, whereas anterior AAS was observed in 15 patients during both neutral and flexion position (Table 4). Radiological findings of cervical spine involvement were not related to sex, disease duration, extraarticular manifestations, clinical symptoms and signs of cervical spine involvement, ESR, RF, and DAS28. In contrast, radiological findings of cervical spine involvement were more frequent in patients older than 45 years and in those with Larsen score > 80 (Table 5).



Table 3. Radiological findings of 165 patients with RA.

Radiological Findings	No. of Patients	%
Atlantoaxial subluxation	34	20.6
Verticle subluxation	0	0
Odontoid erosions	4	2.4
Subaxial subluxation > 1 mm	72	43.6
Upper disc space narrowing	109	66.1
Vertebral plate erosion and sclerosis	72	43.6
Apophyseal joint erosion and sclerosis	31	18.8

Logistic regression analysis adjusted for age showed that radiological findings of cervical spine involvement (AAS and SAS) were not associated with any variable studied (Table 6). No differences were found between patients with radiological cervical spine involvement and the therapeutic intervention. Finally, only one patient with radiologic findings of the cervical spine required surgical intervention. This patient had class II neurological findings according to the Ranawat classification<sup>17</sup> (Table 2).

## DISCUSSION

In our study anterior AAS was found in 20.6% of patients and 2.4% presented lesions of the odontoid process.

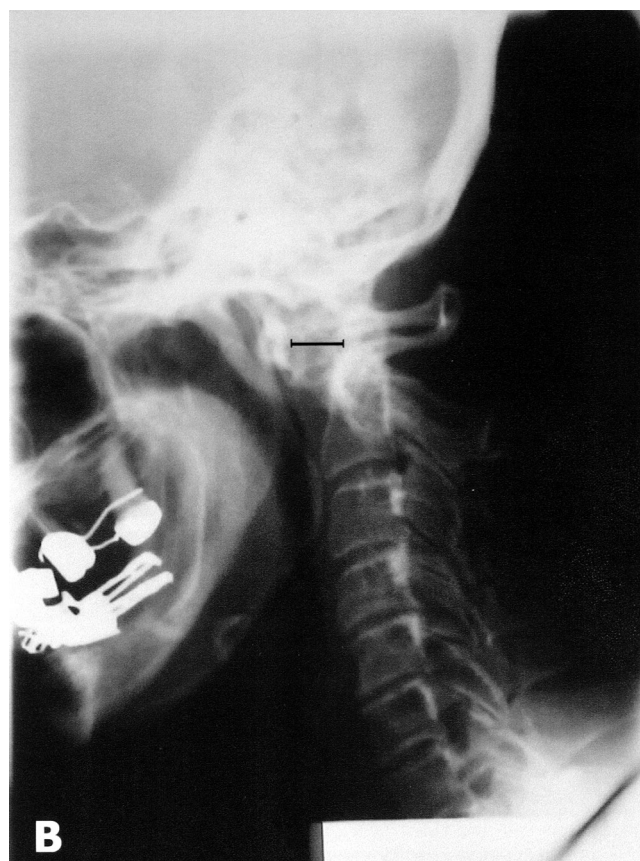


Figure 1. A 62-year-old patient with a 12 year history of RA with neck pain, without neurological signs. Lateral radiographs show (A) in neutral position, normal atlas-dental interval; (B) in flexion position, a 12 mm AAS (black line).



Figure 2. A 53-year-old patient with a 6 year history of RA: lateral radiograph of the cervical spine shows SAS at C4–C5 level (arrow).

Table 4. Severity of anterior atlantoaxial subluxation in 165 patients with RA.

Atlantodental Interval, mm	No. of Patients	%
< 2.5	131	79.4
2.5–5	27	16.3
6–8	4	2.4
9–12	3	1.8

However, a significant number of our patients presented radiological features of SAS, as well as subaxial disc space narrowing and sclerosis and apophyseal joint abnormalities. Vertical subluxation was not observed, probably because we used the McGregor method for its evaluation. Although this method is sufficient, in some cases the tip of the odontoid process is not visible in all radiographs. We tried to overcome this inconvenience by repeating the unacceptable radiographs. C1–C2 lateral joint destruction, lateral subluxation, and rotatory dislocation, previously described in some patients with RA, require an open-mouth anteroposterior view. This was not undertaken in this study and therefore our patients were not evaluated for these lesions and derangements of these joints.

There are a number of RA disease related and patient related factors that might contribute to the development of cervical spine involvement: (1) Severe polyarthritis is common in patients with cervical spine involvement, most of whom have rheumatoid nodules. Severe progressive radiological destruction is often present in the hands and feet, as

well as at the hip and knees<sup>5,18,19</sup>. (2) Patients with IgM RF are at higher risk for cervical spine involvement. There is general agreement that seronegative disease is less severe<sup>20</sup>. CRP concentration at onset of RA may predict the subsequent development of cervical spine involvement<sup>18,21</sup>. (3) Older patients are more likely to have lesions in the lower spine. Degenerative disk disease may contribute to the development of dislocation of the cervical vertebrae<sup>4</sup>. (4) The effect of disease duration is controversial. Cervical spine involvement has been reported within 2 years of RA onset<sup>15</sup>. In a 5 year study by Pellicci, *et al*<sup>22</sup> in 106 RA patients, radiological evidence of cervical spine involvement was present in 43% of patients at baseline and 76% at last followup, indicating that routine monitoring of the cervical spine is in order. Similarly, Fujiwara, *et al*<sup>18</sup> reported cervical spine involvement in 31% of patients at baseline and 43% after mean followup of 5.9 years. Among patients with cervical spine involvement at baseline, half showed radiological progression during followup<sup>18</sup>. In another study, disease duration greater than 10 years was associated with a higher risk of cervical spine involvement<sup>4</sup>. (5) The role of longterm corticosteroid therapy is also controversial. According to one hypothesis, corticosteroid therapy may promote the occurrence of cervical spine damage by alleviating pain, which otherwise prompts the patient to limit movement of the neck. In addition, corticosteroid therapy induces osteoporosis, which may decrease the mechanical strength of the cervical spine<sup>18,19,23</sup>, although this hypothesis has been challenged<sup>5</sup>. In a study by Rudge, *et al* in non-

Table 5. Relationship of radiological findings of cervical spine involvement to patients' characteristics.

	No. of Patients*	%	p
Women	125/143	87.4	NS
Men	21/22	95.5	
Age, yrs			0.05
≤ 45	16/21	76.2	
> 45	130/144	90.3	
Disease duration, yrs			NS
≤ 5	26/33	78.8	
> 5	120/132	90.9	
Extraarticular manifestations			NS
No	75/89	84.3	
Yes	71/76	93.4	
Symptoms and signs of cervical spine			NS
No	91/99	91.9	
Yes	55/66	83.3	
ESR, mm/h			NS
< 30	78/87	89.7	
> 30	66/76	86.8	
IgM rheumatoid factor			NS
Negative	51/60	85.0	
Positive	95/105	90.5	
Larsen score			< 0.05
≤ 80	102/120	85.0	
> 80	43/45	97.7	
Disease Activity Score for 28 joint indices			NS
≤ 3.2	55/62	88.7	
> 3.2	91/103	88.3	

\* Total number of patients in each category.

Table 6. Logistic regression analysis. Dependent variable: radiological findings of atlantoaxial subluxation and subaxial subluxation (adjusted for age).

Independent Variable	Odds Ratio	95% CI	p
Sex (men/women)	2.62	0.54–7.93	NS
Disease duration (> 5, < 5 yrs)	1.14	0.71–2.09	NS
Extraarticular manifestations (yes/no)	1.21	0.66–2.57	NS
Symptoms and signs of cervical spine	1.18	0.82–1.60	NS
ESR (> 30, < 30 mm/h)	0.68	0.34–1.59	NS
IgM rheumatoid factor (+/–)	1.35	0.49–3.66	NS
Larsen score (> 80, < 80)	1.38	0.55–3.77	NS
Disease Activity Score for 28 joint indices (≤ 3.2, > 3.2)	1.54	0.63–3.39	NS

rheumatoid patients, corticosteroid treatment was associated with increased SAS and was related to the duration of steroid therapy<sup>24</sup>. Recent studies also suggest that early and aggressive treatment with DMARD may prevent or retard the development of cervical spine disorder<sup>25</sup>.

There is general agreement that the symptoms and signs vary widely across patients and show no correlation with the severity of radiological damage. At least 15% of patients with radiological lesions are asymptomatic<sup>26,27</sup>. This makes it difficult to determine the optimal timing and methods of radiological monitoring, particularly as subluxation can develop rapidly. Pain in the cervical spine and/or suboccipital region is the most common manifestation. Cervico-

brachial or occipital neuralgia can occur. Decreased range of motion is common. Neurological manifestations usually occur in patients with known cervical lesions. They consist of nerve root compression and/or spinal cord compression.

We found using multivariate regression analysis that cervical spine radiological involvement was not associated with any clinical, laboratory, or radiological indicator, in contrast to a recent study showing that early and extensive erosion in peripheral joints predicts AAS<sup>8</sup>. Although we found a high frequency of radiological cervical spine involvement, the severity of the disease was rather mild. This may be due to a mild disease process of RA in Mediterranean countries and to aggressive therapy<sup>9,10,28</sup>.

Our results suggest that cervical spine radiological involvement is a frequent finding in patients with RA. However, only a small number of them had severe disease and there was no correlation with clinical symptoms and signs. Therefore, plain radiographs of the cervical spine should be obtained regularly to seek cervical spine manifestations, even in patients without cervical symptoms. What is lacking from the literature is a prospective, community based study investigating the incidence of cervical spine involvement at predefined time intervals, that is, at 2, 5, or 10 years.

## REFERENCES

- Wolfe F, Hawley DJ. The longterm outcomes of rheumatoid arthritis: Work disability: a prospective 18 year study of 823 patients. *J Rheumatol* 1998;25:2108-17.
- Neva MH, Kaarela K, Kauppi M. Prevalence of radiological changes in the cervical spine — A cross sectional study after 20 years from presentation of rheumatoid arthritis. *J Rheumatol* 2000;27:90-3.
- Nakano KK, Schoene WC, Baker RA, Dawson DM. The cervical myelopathy associated with rheumatoid arthritis: analysis of patients, with 2 postmortem cases. *Ann Neurol* 1978;3:144-51.
- Smith PH, Benn RT, Sharp J. Natural history of rheumatoid cervical luxations. *Ann Rheum Dis* 1972;31:431-9.
- Winfield J, Young A, Williams P, Corbett M. Prospective study of the radiological changes in hands, feet, and cervical spine in adult rheumatoid disease. *Ann Rheum Dis* 1983;42:613-8.
- Halla JT, Harding JG Jr. The spectrum of atlantoaxial facet joint involvement in rheumatoid arthritis. *Arthritis Rheum* 1990;33:325-9.
- Oda T, Fujiwara K, Yonenobu K, Azuma B, Ochi T. Natural course of cervical spine lesions in rheumatoid arthritis. *Spine* 1995;20:1128-35.
- Neva MH, Isomaki P, Hannonen P, Kauppi M, Krishnan E, Sokka T. Early and extensive erosiveness in peripheral joints predicts atlantoaxial subluxations in patients with rheumatoid arthritis. *Arthritis Rheum* 2003;48:1808-13.
- Drosos AA, Lanchbury JS, Panayi GS, Moutsopoulos HM. Rheumatoid arthritis in Greek and British patients. A comparative clinical, radiologic, and serologic study. *Arthritis Rheum* 1992;35:745-8.
- Drosos AA, Moutsopoulos HM. Rheumatoid arthritis in Greece: clinical, serological and genetic considerations. *Clin Exp Rheumatol* 1995;13 Suppl 12:S7-12.
- Arnett FC, Edworthy SM, Bloch DA, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum* 1988;31:315-24.
- Prevoo ML, van't Hof MA, Kuper HH, van Leeuwen MA, van de Putte LB, van Riel PL. Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. *Arthritis Rheum* 1995;38:44-8.
- Pellicci P, Ranawat C, Tsairis P, Bryan W. A prospective study of the progression of rheumatoid arthritis of the cervical spine. *J Bone Joint Surg Am* 1981;63:342-50.
- Bland JH, Davis PH, London MG, Vanbuskirk FW, Duarte CG. Rheumatoid arthritis of the cervical spine. *Arch Intern Med* 1963;112:892-8.
- Winfield J, Cooke D, Brook AS, Corbett M. A prospective study of the radiological changes in the cervical spine in early rheumatoid disease. *Ann Rheum Dis* 1981;40:109-14.
- Larsen A, Dale K, Eek M. Radiographic evaluation of rheumatoid arthritis and related conditions by standard reference films. *Acta Radiol Diagn Stockh* 1977;18:481-91.
- Ranawat CS, O'Leary P, Pellicci P, Tsairis P, Marchisello P, Dorr L. Cervical spine fusion in RA. *J Bone Joint Surg Am* 1979;61:1003-10.
- Fujiwara K, Fujimoto M, Owaki H, et al. Cervical lesions related to the systemic progression in rheumatoid arthritis. *Spine* 1998;23:2052-6.
- Rasker JJ, Cosh JA. Radiological study of cervical spine and hand in patients with rheumatoid arthritis of 15 years' duration: an assessment of the effect of corticosteroid treatment. *Ann Rheum Dis* 1978;37:529-35.
- Papadopoulos IA, Katsimbri P, Katsarakis A, Temekonidis T, Georgiadis A, Drosos AA. Clinical course and outcome of early rheumatoid arthritis. *Rheumatol Int* 2001;20:205-10.
- Paimela L, Laasonen L, Kankaanpää E, Leirisalo-Repo M. Progression of cervical spine changes in patients with early rheumatoid arthritis. *J Rheumatol* 1977;24:1280-4.
- Pellicci P, Ranawat CS, Tsairis P, Bryau WJ. A prospective study of the progression of rheumatoid arthritis of the cervical spine. *J Bone Joint Surg Am* 1981;63:342-50.
- Dvorak J, Grob D, Baumgartner H, Gschwend N, Grauer W, Larsson S. Functional evaluation of the spinal cord by magnetic resonance imaging in patients with rheumatoid arthritis and instability of upper cervical spine. *Spine* 1989;14:1057-64.
- Rudge SR, Drury PL, Lloyd-Jones JK. Long-term corticosteroids and cervical subluxation in non-rheumatoid patients. *Rheumatol Rehabil* 1981;20:102-5.
- Neva MH, Kauppi MJ, Kautiainen H, et al, for the FIN-RACo Trial Group. Combination drug therapy retards the development of rheumatoid atlantoaxial subluxations. *Arthritis Rheum* 2000;43:2397-401.
- Bouchaud-Chabot A, Liote F. Cervical spine involvement in rheumatoid arthritis. A review. *Joint Bone Spine* 2002;69:141-54.
- Roche CJ, Eyes BE, Whitehouse GH. The rheumatoid cervical spine: signs of instability on plain cervical radiographs. *Clin Radiol* 2002;57:241-9.
- Papadopoulos NG, Alamanos Y, Papadopoulos IA, Tsifetaki N, Voulgari PV, Drosos AA. Disease modifying antirheumatic drugs in early rheumatoid arthritis: a longterm observational study. *J Rheumatol* 2002;29:261-6.