

EXTENDED REPORT

High prevalence of asymptomatic cervical spine subluxation in patients with rheumatoid arthritis waiting for orthopaedic surgery

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Objective: To study the prevalence of cervical spine subluxation in patients with rheumatoid arthritis waiting for orthopaedic surgery, and symptoms that might be associated with the disorders.

Methods: 194 patients with rheumatoid arthritis were referred for orthopaedic surgery at Jyväskylä Central Hospital, 154 (79%) of whom volunteered for the present study including clinical examination, laboratory tests, radiographs of the cervical spine, hands, and feet, and self report questionnaires. Definition of anterior atlantoaxial subluxation (aAAS) was >3 mm and of subaxial subluxation (SAS) ≥3 mm. Atlantoaxial impaction (AAI) was analysed following to the Sakaguchi-Kauppi method.

Results: 67 patients (44%) had cervical spine subluxation or previous surgical fusion. The prevalence of aAAS, AAI, SAS, or previous fusion was 27 (18%), 24 (16%), 29 (19%), and 8 (5%), respectively; 69% of patients with cervical spine subluxations (those with fusions excluded) reported neck pain, compared with 65% of patients without subluxations ($p=0.71$). The prevalence of occipital, temporal, retro-orbital, and radicular pain in upper extremities was similar in patients with or without cervical spine subluxations (54% v 43%; 17% v 31%; 25% v 24%; 47% v 48%, respectively). However, patients with subluxations were older, had longer disease duration, more active disease, poorer function according to the Health Assessment Questionnaire, and had more often erosive disease.

Conclusions: Asymptomatic cervical spine subluxation is common in patients with rheumatoid arthritis waiting for orthopaedic surgery. Regardless of symptoms, the possibility of cervical spine subluxation in patients with severe rheumatoid arthritis should be considered in preoperative evaluation.

Cervical spine subluxations—that is, anterior atlantoaxial subluxation (aAAS), atlantoaxial impaction (AAI), and subaxial subluxation (SAS)—are common disorders in patients with rheumatoid arthritis.^{1–3} At an early stage of the disease rheumatoid inflammation of cervical spine structures may lead to subluxation.⁴ Sustained inflammation increases the prevalence of these subluxations. After a follow up period of 20 years, cervical spine subluxations were found in 42% of patients with destructive rheumatoid arthritis.⁵ Severe subluxation may cause compression of brain stem or spinal cord, leading to myelopathy and in the worst cases even to sudden death or quadriplegia.^{6–9} The risk of irreversible paralysis has been reported to be high if the posterior atlantodental interval is 14 mm or less.¹⁰

Inflammatory mechanisms in rheumatoid arthritis cause both peripheral joint destructions and cervical spine subluxation, and it is natural that disorders in these areas are associated with one another.^{11–13} Thus patients who present with cervical spine subluxation often need surgical intervention in other joints, including preventive, reconstructive, and fusion surgery.^{14, 15} To take into account the possibility of cervical spine subluxation in patients with rheumatoid arthritis, preoperative evaluation of cervical spine radiographs has been recommended before orthopaedic surgery requiring endotracheal intubation.^{16, 17}

The prevalence of cervical spine subluxations in patients with rheumatoid arthritis undergoing total knee or hip replacement has been evaluated in three retrospective studies. Collins *et al*¹⁶ reported a 61% prevalence of aAAS, AAI, or SAS, while Kauppi *et al*¹⁸ reported a 35% prevalence of AAI in patients with knee or hip replacement. In a recent study by Grauer *et al*,¹⁹ the prevalence of cervical spine instability was 41% in rheumatoid patients who had

undergone total knee or hip replacement. In a study by Collins *et al*,¹⁶ 50% of the patients with cervical spine subluxation had no signs or symptoms of it.

Our aim in the present study was to evaluate the prevalence of cervical spine subluxations in patients with rheumatoid arthritis who were referred for orthopaedic surgery and to analyse the symptoms and clinical factors that might be associated with subluxations.

METHODS

Patients

All 194 patients with rheumatoid arthritis who were on the waiting list for orthopaedic surgery at Jyväskylä Central Hospital (population 265 000) in December 2002 were informed of the study by letter. Of these, 154 (79%) volunteered to attend the study. The volunteers were seen at an outpatient clinic between March and May 2003 for clinical examination, radiographs, laboratory tests, and physical function tests. They all met the American College of Rheumatology 1987 criteria for rheumatoid arthritis.²⁰ Mean (SD) age of the 154 patients was 62 (11) years and median (IQR) duration of rheumatoid arthritis 16 (9.9 to 28) years. One hundred and seventeen of the patients (76%) were female, 109 (71%) were rheumatoid factor (RF) positive, and 129 (84%) had radiographic erosions in their hands or feet.

All but two of the 154 patients had taken disease modifying anti-rheumatic drugs (DMARDs) over the course

Abbreviations: aAAS, anterior atlantoaxial subluxation; AAI, atlantoaxial impaction; DAS, disease activity score; DMARD, disease modifying anti-rheumatic drug; HAQ, Health Assessment Questionnaire; IQR, interquartile range; SAS, subaxial subluxation; S-K, Sakaguchi-Kauppi; VAS, visual analogue scale

Table 1 Prevalence of subluxations and previous surgical fusions of the cervical spine in 154 patients on the waiting list for orthopaedic surgery

Subluxation/fusion	N (%)
Cervical spine subluxation or previous surgical fusion	67 (44)
Prevalence of disorders*	
aAAS (>3 mm)	27 (18)
AAI (S-K grade II-IV)	24 (16)
SAS (\geq 3 mm)	29 (19)
Atlantoaxial fusion	7 (5)
Subaxial fusion	1 (1)
No subluxation of fusion	87 (56)

*A patient may have more than one disorder.

AAAS, anterior atlantoaxial subluxation; AAI, atlantoaxial impaction; S-K, Sakaguchi-Kauppi method; SAS, subaxial subluxation.

of the disease. At the time of evaluation, 70 (46%) were taking methotrexate, 40 (30%) traditional DMARDs, seven (5%) leflunomide, five (3%) tumour necrosis factor inhibitors, one was taking chlorambucil, and one was taking cyclophosphamide. Sixty two per cent of these 122 patients were taking DMARDs in various combinations. Thirty patients (20%) were not taking DMARDs.

The demographic and disease related variables in the 40 patients who did not attend were comparable: mean (SD) age, 63 (15) years; median (IQR) duration of rheumatoid arthritis 12 (4.0 to 24) years; 85% were female; 71% were RF positive; 83% had erosive disease. Four patients were known to have atlantoaxial subluxation, two of whom had previously undergone surgical fusion.

The study was approved by the ethics committee of Jyväskylä Central Hospital.

Clinical data

Clinical examination was carried out in all patients by a rheumatologist (HM). The disease activity score (DAS), including 28 tender and swollen joints, patient's self report general health (on a 0–100 mm visual analogue scale (VAS)), and erythrocyte sedimentation rate (ESR) were used to evaluate clinical disease activity. Serum C reactive protein and blood haemoglobin content were measured.

Patients completed questionnaires about possible symptoms related to cervical spine disorders. The presence of pain in the neck, occipital, temporal or retro-orbital areas, and radicular pain in the upper extremities was queried, with response alternatives "yes" or "no". Pain in the neck and upper extremities and headache were also assessed by a 100 mm VAS. Neck disability was assessed by a modified neck and shoulder pain and disability index²¹ and Vernon's Neck Disability Index.²² The neck and shoulder pain and disability index is the mean of 13 100 mm VAS scores which query the intensity of pain and disability caused by neck pain. Vernon's Neck Disability Index is a sum of a 10 item questionnaire, with a maximum score of 50 (maximum of 5 on each of 10 items) assessing the disability caused by neck pain. The patients also completed the Health Assessment Questionnaire (HAQ) for overall functional disability.^{23 24}

Radiographs

Radiographs of the cervical spine included lateral views taken in flexion, neutral, and extension positions of neck, and anteroposterior and odontoid projection views. A diagnosis of aAAS was made if the distance between the anterior aspect of the dens and the posterior aspect of the anterior arch of atlas was more than 3 mm during flexion. Lateral view radiographs taken in the neutral position of the neck were used to evaluate AAI. AAI was diagnosed using the Sakaguchi-Kauppi (S-K) method, which has been developed for

screening purposes in particular and evaluates the position of the atlas in relation to the axis.¹⁸ It divides the condition into four grades (grade I represents normal and grades II–IV abnormal). SAS was diagnosed if a vertebra had moved 3 mm or more in relation to the next vertebra when measured from the posterior line of the vertebral bodies. In addition, the posterior atlantodental interval was measured from lateral view radiographs.¹⁰ A distance of \leq 14 mm was determined to be critical, as it has been reported to predict paralysis in rheumatoid patients with cervical spine involvement. Cervical spine radiographs were evaluated by a spine surgeon (MHN).

Radiographs of the hands and feet were taken in posterior-anterior projection, and evaluated according to the Larsen score²⁵ by an experienced rheumatologist (TS). The presence of erosions was reported.

Statistical methods

Data analyses were undertaken using SPSS 11.0 software (SPSS Inc, Chicago, Illinois, USA). The results are expressed as mean or median, standard deviation (SD), or interquartile range (IQR). Differences between the mean values of normally distributed continuous variables were compared and tested for statistical significance with Student's *t* test. Differences between median values of non-normally distributed continuous variables were compared and tested for statistical significance using the Mann–Whitney test. Differences between categorical values were compared for statistical significance using the χ^2 test.

RESULTS

Cervical spine subluxation or previous surgical fusion was found in 67 of the 154 patients (44%) (table 1). The prevalence of aAAS, AAI, SAS, and fusion was 27 (18%), 24 (16%), 29 (19%), and 8 (5%), respectively. Surgical fusion had previously been performed at level C1–2 in seven patients and at level C4–5 in one patient. Pseudoarthrosis was found in four of the C1–2 surgical fusions and two of the patients with fusions also had SAS. The patient with C4–5 fusion also had SAS at another level, as well as AAI. All patients who were referred for shoulder surgery (five patients: two joint replacements and three ruptures of the biceps tendon or the rotator cuff or both) or for revision arthroplasty of the hip (two patients) had cervical spine subluxation or previous surgical fusion. A posterior atlantodental interval of \leq 14 was found in six patients (4%), of whom two had previously undergone C1–2 surgical fusion. However, both of these presented with pseudoarthrosis.

Patients with cervical spine subluxation (those with fusions were excluded in these analyses) were slightly older than the other patients (table 2). The median duration of rheumatoid arthritis was 24 years in patients with subluxation and 12 years in the other patients ($p < 0.001$). Disease activity measured by DAS28, ESR, and C reactive protein was significantly greater in patients with cervical spine subluxation than in the other patients. Moreover, a significantly higher proportion of patients with cervical spine subluxation had erosive rheumatoid arthritis compared with the remainder ($p = 0.001$), and functional capacity according to the HAQ was worse in the patients with cervical spine subluxations than in the others (table 2).

In all, 69% of the patients with cervical spine subluxations (those with fusions excluded) reported neck pain, compared with 65% of patients without subluxations ($p = 0.71$) (table 3). The prevalence of occipital, temporal, retro-orbital, and radicular pain in the upper extremities was similar in patients with or without cervical spine subluxations (54% *v* 43%, 17% *v* 31%, 25% *v* 24%, and 47% *v* 48%, respectively). The severity of experienced neck pain, headache, and pain in

Table 2 Demographic and clinical characteristics at the time of the evaluation in 146 patients with and without cervical spine subluxations

Characteristic	Patients without cervical spine subluxation (n = 87)*	Patients with cervical spine subluxation (n = 59)*	p Value
<i>Demographic variables</i>			
Age (years)	60 (11)	65 (10)	0.005
No of women	67 (77%)	44 (75%)	0.735
<i>Clinical variables</i>			
Duration of RA (years)†	12 (7 to 21)	24 (14 to 32)	<0.001
RF positive	58 (67%)	45 (76%)	0.250
No with erosive disease	65 (75%)	53 (95%)	0.001
<i>Disease activity measures</i>			
Haemoglobin (g/l)	132 (12)	130 (15)	0.326
ESR (mm/h)†	15 (8 to 29)	20 (12 to 40)	0.048
CRP (mg/l)†	4 (1 to 8)	8 (5 to 21)	<0.001
DAS28	2.9 (1.0)	3.5 (1.1)	0.002
<i>Patient questionnaires</i>			
HAQ (0–3 scale)†	0.75 (0.25 to 1.25)	1.25 (0.88 to 1.75)	0.001
Pain VAS	46 (25)	55 (26)	0.055
Global health VAS	43 (22)	46 (20)	0.417

Values are mean (SD), n (%), or †median (interquartile range).

*53–59 patients in the subluxation group and 83–87 in the non-subluxation group completed each question, had all laboratory tests, and hands and feet radiographs taken; these figures have been used to calculate the percentages.

CRP, C reactive protein; DAS28, 28 joint disease activity score; ESR, erythrocyte sedimentation rate; HAQ, Health Assessment Questionnaire; RA, rheumatoid arthritis; RF, rheumatoid factor; VAS, visual analogue scale.

upper extremities did not differ significantly between the patients with cervical spine subluxations and the others. Scores of the neck disability indices were comparable between the groups.

DISCUSSION

Our main observation was that 44% of patients with rheumatoid arthritis on a waiting list for orthopaedic surgery had subluxation or previous surgical fusion of the cervical spine. Previously, Collins *et al*¹⁶ reported a 61% prevalence of cervical spine subluxation, Kauppi *et al*¹⁸ reported a 35% prevalence of AAI, and Grauer *et al*¹⁹ reported a 41% prevalence of cervical spine instability in rheumatoid patients

who had undergone total hip or knee replacement. The high prevalence of cervical spine subluxations in the present study shows that these disorders are common in patients with rheumatoid arthritis awaiting orthopaedic surgery.

It has been reported that up to 27% of patients with rheumatoid arthritis require a large joint replacement in the long term.²⁶ They also undergo various synovectomies, fusions, and small joint replacements. Although several orthopaedic procedures can be carried out under regional anaesthesia, general anaesthesia is also widely used in these procedures. Forced movements of the neck during intubation for general anaesthesia may cause compression of the brain stem and even quadriplegia in patients with cervical spine

Table 3 Symptoms and functional neck pain indices in 146 patients with and without cervical spine subluxation

Variable	Patients without cervical spine subluxation (n = 87)	Patients with cervical spine subluxation (n = 59)	p Value
<i>Patients with symptoms in different areas</i>			
Neck pain	53 (65%)	37 (69%)	0.709
Occipital pain	34 (43%)	29 (54%)	0.202
Temporal pain	25 (31%)	9 (17%)	0.073
Retro-orbital pain	19 (24%)	13 (25%)	0.918
Radicular pain in upper extremity	39 (48%)	26 (47%)	0.974
<i>Pain, 0–100 mm VAS</i>			
Neck	15 (1 to 47)	25 (1 to 49)	0.371
Headache	7 (1 to 26)	2 (0 to 14)	0.74
Upper extremities	18 (3 to 46)	24 (4 to 53)	0.301
<i>Neck disability indices</i>			
Vernon's neck disability index (range 0 to 50)	20 (18 to 20)	20 (18 to 20)	0.871
Neck and shoulder pain and disability index (range 0 to 100)	11 (1 to 36)	20 (1 to 42)	0.336

Values are n (%) or median (interquartile range).

*52–55 patients in the subluxation group and 77–83 in the non-subluxation group completed each question; these figures have been used to calculate the percentages.

VAS, visual analogue score.

subluxation.¹⁷ To avoid serious consequences, it has been advised to intubate these patients with the neck in the neutral position and possibly using fiberoptic instruments.^{16,17} Thus cervical spine radiographs are recommended in patients with rheumatoid arthritis before hip or knee replacements.¹⁶ Alternatively, regional anaesthesia should be considered. However, the position of neck needs a special attention during regional anaesthesia as well.

Based on a study of Boden *et al*¹⁰ in which posterior atlantodental interval ≤ 14 was reported to be a predictor of irreversible paralysis in rheumatoid patients with cervical spine involvement, Grauer *et al*¹⁹ evaluated posterior atlantodental interval values in patients who had undergone total joint replacement. Only one of their 49 patients had a posterior atlantodental interval < 14 mm, compared with 15 patients with aAAS > 3 mm. The 4% prevalence of critical posterior atlantodental interval (≤ 14) in our study is consistent with Grauer's study. However, as it may not be possible to study the degree of aAAS or the posterior atlantodental interval that could lead to complications during surgery, we believe that all subluxations have to be taken seriously.

A major issue is how to predict preoperatively which rheumatoid patients have cervical spine subluxation. In clinical experience, patients with cervical spine subluxation are often asymptomatic.²⁷ According to our results, one third of the patients with cervical spine subluxation did not report neck pain, and the median neck pain VAS in patients with subluxations was only 25/100 mm. Moreover, neck pain, or pain in the occipital, temporal, or retro-orbital areas, or radicular pain in the upper extremities, did not identify patients with subluxations. Furthermore, patients with cervical spine subluxations could not be identified by using neck pain or disability indices other than the HAQ.

Measures reflecting clinical disease activity, including the DAS, ESR, and C reactive protein, were significantly worse in patients with cervical spine subluxations than in the other patients. As expected, the duration of the disease was longer in patients with subluxations, and were more likely to suffer from erosive peripheral disease than patients without subluxations, as we have shown previously.¹²

The present cohort involved patients with rheumatoid arthritis of long duration. Furthermore, all patients were on the waiting list for orthopaedic surgery, which might be considered as representing failure of conservative treatment. Although all but two patients had been treated with DMARDs, the therapy may have not been aggressive enough to prevent severe long term complications of rheumatoid arthritis such as cervical spine subluxation. The more aggressive treatment strategies for rheumatoid arthritis that are in current use are associated with improved long term outcomes,²⁸⁻³¹ but their role in preventing cervical spine subluxation in the long term remains to be shown.

Limitations of our study include a skewed patient population—in other words, we only included patients who were waiting for orthopaedic surgery. This study therefore does not aim to provide prevalence figures for cervical spine involvement in rheumatoid arthritis in general. However, our specific aim was to study the most severe cases—that is, patients who needed orthopaedic surgery, who can be considered to be failures of conservative management. Cervical spine disorders are common in this group of patients,^{16,18,19} and health professionals should be alerted to this. Second, magnetic resonance imaging (MRI) was not included in the present study, which might be considered a limitation. However, functional radiographs measure the magnitude of aAAS more reliably than MRI,³² although MRI imaging is needed to determine canal stenosis and cord compression.

Our results show that patients with rheumatoid arthritis who have cervical spine subluxations cannot be distinguished preoperatively on the basis of symptoms. Thus in patients with longstanding and severe disease, and especially those with early erosive disease,¹² there should be a high level of suspicion concerning cervical spine pathology in those about to undergo anaesthesia.

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