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MRI of the transverse and alar ligaments in rheumatoid arthritis: feasibility and relations to atlantoaxial subluxation and disease activity

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Abstract
Introduction Dysfunctional transverse and alar craniovertebral ligaments can cause instability and osseous destruction in rheumatoid arthritis (RA). This study examined (1) the feasibility of high-resolution magnetic resonance imaging (MRI) of these ligaments in RA and (2) the relation between ligament high-signal changes and atlantoaxial subluxation and RA duration/severity.
Methods Consecutive RA patients (n=46) underwent clinical examination, functional radiography, and high-resolution MRI. Two blinded radiologists rated MRI image quality, graded ligament high-signal changes 0–3 on proton-weighted sequences using an existing grading system, and assessed cervical spine rheumatic changes on short tau inversion recovery images. Agreement was analyzed using kappa and relations using multiple logistic regression.
Results MRI images had good quality in 42 (91.3%) of 46 patients and were interpretable in 44 (32 women and 12 men, median age/disease duration 60.4/9.1 years). MRI grades 2–3 changes of the transverse and alar ligaments showed moderate and good interobserver agreement (kappa 0.59 and 0.78), respectively, and prevalence 31.8% and 34.1%. Such ligament changes were more frequent with increasing anterior atlantoaxial subluxation (p=0.012 transverse, p=0.028 alar), higher erythrocyte sedimentation rate (p=0.003 transverse), positive rheumatoid factor (p=0.002 alar), and neck pain (p=0.004 alar).
Conclusion This first study of high-resolution MRI of these ligaments in RA showed high feasibility and relations with atlantoaxial subluxation, RA disease activity, and neck pain. The clinical usefulness of such MRI needs further evaluation.

Keywords Alar ligament · Transverse ligament · Rheumatoid arthritis · Magnetic resonance imaging · Radiography

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Introduction

The transverse and alar ligaments stabilize the craniovertebral junction (CVJ) [1–4] and prevent atlantoaxial instability [5–9]. Rheumatoid arthritis (RA) often affects these ligaments, and atlantoaxial subluxation is reported on functional radiography in 23–86% of adult RA patients [10]. Both

ligaments contain fibrocartilage, and fibrocartilage epitopes are targeted by the autoimmune reaction in RA [11–13]. Structural changes in these ligaments could therefore be an early sign of cervical RA. The transverse and alar ligaments should also be regarded as important to prevent osseous destruction at the CVJ in chronic RA, since mechanical instability due to ligament dysfunction can cause destruction even in the absence of active synovitis [14].

These ligaments are not accessible for biopsy or during surgery, and no non-invasive method has been established to study their structure in cervical RA. Magnetic resonance imaging (MRI) was applied in one small study from 1991 [15] to examine the transverse ligaments of four RA patients. More recently, high-resolution MRI has been used to visualize the detailed structure of the transverse and alar ligaments in patients with previous neck trauma and in non-injured volunteers [16–20] but not in RA patients, where joint dislocations and pain can make such time-demanding MRI a challenge.

The aim of this study was to examine the feasibility of high-resolution MRI of the transverse and alar ligaments in different stages of adult RA and to explore whether high-signal ligament changes are related to other imaging and clinical features. We hypothesized that such changes are related to increasing atlantoaxial subluxation and increasing severity and duration of RA.

Methods

Patients

Consecutive patients with adult RA were prospectively recruited from the Department of Rheumatology, Haukeland University Hospital, from October 2006 to May 2007. The inclusion criteria, met by 84 patients, were confirmed RA according to the American College of Rheumatology criteria [21], age 18–80 years, and no surgery during the last 4 weeks (to avoid influence of surgery on serological laboratory test results). We excluded patients with reported neck injury (n=4), severe head injury (n=1), prior cervical spine operation (n=2), current cancer (n=2), other serious somatic (n=5) or psychiatric diseases (n=3), known cervical nerve root syndrome (n=0) or myelopathy (n=0), contraindications to MRI (n=1), those declining to participate (n=14), and non-Norwegian speaking (n=2). This left 50 patients eligible for the study; all gave their written informed consent to participate, but four did not complete the MRI due to claustrophobic discomfort. The remaining 46 patients underwent MRI and constitute the study sample. The Regional Committee for Medical Research Ethics, Western-Norway approved the study.

Clinical evaluation

An experienced rheumatologist (R.A.) performed a clinical examination including a 28-joint count [22]. The same day, the patient filled out a questionnaire including the Modified Health Assessment Questionnaire (MHAQ) [23] and visual analog scale (VAS) scores of the last 7 days' RA disease activity and neck pain. Further clinical data were obtained from their hospital medical journals. Serological laboratory tests, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) were taken within 6 days before or after the clinical examination. Immunological laboratory tests, rheumatoid factor, and anti-cyclic citrullinated peptide (CCP) were ordered if not taken within 6 months before admission. A disease activity score in 28 joints (DAS28 score) was calculated [22].

Radiography protocol

Lateral cervical spine radiographs in both flexion and extension and an anterior–posterior open-mouth view were taken with tube distance 1.50 and 1.00–1.15 m, respectively. Patients were imaged in upright position while sitting or standing. The radiographs were taken 0–33 (median 2) days after the clinical examination.

Radiographic evaluation

One radiologist (N.V.) blinded to clinical data and MRI findings interpreted all radiographs in random order. The anterior atlantodental interval (AADI) was measured on the lateral views in both flexion and extension. AADI represents the midline distance between the posterior part of the anterior tubercle of atlas and the anterior surface of the odontoid process [24–26]. AADI > 3 mm indicated anterior atlantoaxial subluxation. Vertical dislocation was evaluated on the lateral radiographs according to Kauppi [27]. Vertical subluxation was defined as present when the sclerotic ring of C2 reached the inferior line of the atlas.

MRI protocol

Within 0–32 (median 2) days after the clinical evaluation, all patients underwent MRI with the same 1.5 T scanner (Symphony Mastroclass, Siemens Medical System, Erlangen, Germany), using a standard one-channel receive-only head coil, with head and neck in a neutral position. To visualize the delicate craniovertebral ligaments with high spatial resolution while maintaining adequate imaging contrast and signal-to-noise ratio, an established MRI protocol was used [20]. It included proton-density-weighted fast spin echo (FSE) sequences in three orthogonal planes, axial, coronal, and sagittal: repetition time (TR)/echo time (TE) 2,150–2,660/

15 ms, slice thickness 1.5 mm, interslice gap 0–0.3 mm, field of view (FOV) 175×200 mm or 200×200 mm, voxel size 0.6–0.7×0.4×1.5 mm^3 and echo train length (ETL) 13.

A focused sagittal short tau inversion recovery (STIR) sequence with the same FOV, slice number, slice thickness, and interslice gap as the sagittal proton sequence was added to assess inflammatory changes at the craniovertebral junction: TR/TE 6,990/88 ms, inversion time (TI) 150 ms, flip angle 160°, voxel size 1.0×0.5×1.5 mm^3, and ETL 13. This allowed coupling of sagittal STIR and proton images to ensure adequate anatomic delineation when reading the STIR images, which showed fewer anatomic details due to a lower signal-to-noise ratio resulting from the suppression of fat signal.

To evaluate the whole cervical spine, we also included a sagittal STIR sequence with a larger FOV, covering through the apophyseal joints on both sides: TR/TE 5,680/51 ms, TI 160 ms, flip angle 160°, slice thickness 3.0 mm, interslice gap 0.3 mm, number of slices 19, FOV 180×180 mm^2, voxel size 0.8×0.6×3.0 mm^3, and ETL 13. The summarized acquisition time for the five sequences was 31 min 5 s.

MRI evaluation

Using a previously reported classification system, the alar and transverse ligaments were graded 0–3 on the proton sequences based on the ratio between any high-signal part and the total cross section area of the ligament [16, 20, 28]. No high signal was graded 0, high signal in one third or less of the total cross section was graded 1, high signal in one third to two thirds of the total cross section was graded 2, and high signal in two thirds or more of the total cross section was graded 3. The right and left sides were graded separately. The image with the largest cross-sectional area of high signal was used for grading. Any high signal had to be seen in at least two imaging planes to be graded 1–3; otherwise, it was graded 0 (no high signal). Homogenous gray ligaments were graded 2. On the focused STIR sequence, the intensity of any high signal from these ligaments was compared to the signal from adjacent craniovertebral bone marrow and cerebrospinal fluid (CSF).

The whole cervical spine was assessed for rheumatic changes on MRI. AADI was measured on the mid-sagittal proton image with the patient's neck in neutral position. Odontoid lateral mass interval (OLMI) was measured on coronal or axial sequences as the smallest distance between the medial part of the lateral mass of C1 and the lateral surface of the odontoid process [29, 30]. If OLMI on one side exceeded OLMI on the opposite side by 2 mm or more, lateral atlantoaxial subluxation (LAAS) was recorded [29]. Erosion was defined as a bone defect with sharp margins visible in at least two planes, synovitis as intermediate to high-signal intensity on STIR images of a thickness greater than the width of the joint capsule, and bone edema as a poorly defined area within the trabecular bone with high-signal intensity on STIR consistent with increased water content [31, 32]. Absent CSF signal in both anterior and posterior subarachnoidal spaces on sagittal STIR images was regarded as stenosis at the spinal cord or brain stem level. Decreased cord/brainstem diameter at the stenotic level indicated cord/brainstem compression [31]. Signal changes within the cord and brainstem were evaluated on STIR sequences.

Two independent radiologists (6 and 26 years experience) who were blinded to clinical data and radiography findings interpreted all MRI images, which were completely de-identified and presented in random order interspersed between similar images of individuals without RA. They thereafter solved all disagreements in consensus by joint reinterpretation of images. This consensus grading was used in all analyses except observer agreement analyses. To prevent RA suspicion from findings on the STIR sequences, the proton sequences were graded before the STIR sequences were made available. Both radiologists, in consensus only, evaluated the image quality as good, reduced (but images interpretable), or poor (images not interpretable) based on ligament visualization and artifacts, noise, and contrast.

Statistical analyses

Weighted kappa (linear weights) was applied to assess interobserver agreement on grading of high-signal ligament changes, using all four grades. In all further analyses, we dichotomized this grading system by combining grades 0 and 1 and grades 2 and 3, as was also done in most previous comparable studies [16, 19, 20]. Kappa was calculated for interobserver agreement on the presence or not of grades 2–3 changes. Fisher's exact test was used to compare proportions between patients with and without grades 2–3 ligament changes. To compare means, we used the Mann–Whitney U test as normality could not be assumed. Stepwise, backward, binary logistic regression was performed with grades 2–3 ligament changes as outcome variable and mutual adjustments done for continuous and categorical variables, using likelihood-ratio tests. The regression model included all variables with $p<0.2$ in the univariate analysis. SPSS 16.0 was used to analyze data. $p\leq0.05$ indicated statistical significance.

Results

MRI image quality and patient characteristics

The image quality was good in 42 (91.3%) of the 46 patients, reduced for proton sequences in one patient

(2.2%), and reduced for the focused STIR sequence in one (2.2%). Two patients (4.3%) had non-interpretable proton sequences, leaving 44 patients eligible for analysis.

Table 1 shows clinical and imaging characteristics of these 44 RA patients; 32 (72.7%) were women, median age was 60.4 years and median RA disease duration 9.1 years. Neck pain during the last week was reported by 23 (52.3%). AADI was larger on flexion radiography than on neutral position MRI: median 2.0 (range 1.0–8.5) mm versus 1.2 (range 0.0–4.3) mm ($p<0.001$, Wilcoxon signed ranks test). On MRI, three (6.8%) patients had dens erosion. No patient had compression or signal changes of the cord or brainstem.

Ligament changes on MRI

MRI showed grades 2–3 transverse ligament changes (Fig. 1) in 14 (31.8%; 95% confidence interval (CI), 17.5% to 46.1%) and grades 2–3 alar ligament changes (Fig. 2) in 15 (34.1%; 95% CI, 19.5% to 48.7%) of the 44 RA patients. Interobserver agreement on ligament changes was moderate (weighted kappa 0.57 for the transverse ligament and 0.52 for the alar ligaments) and moderate to good for grades 2–3 versus grades 0–1 changes (kappa 0.59 for the transverse and 0.78 for the alar ligaments).

Table 2 depicts clinical and imaging characteristics of RA patients with and without grades 2–3 high-signal ligament changes. Patients with transverse ligament changes had higher ESR, larger AADI on radiography, and more often dens erosion on MRI. Patients with alar changes had higher ESR and CRP, more often dens erosion and were more likely men. Other clinical and imaging characteristics given in Table 1 did not differ significantly between patients with and without grades 2–3 ligament changes; Table 2 shows all characteristics with $p<0.2$.

The mutually adjusted multiple logistic regression analysis (Table 3) confirmed that grades 2–3 transverse ligament changes were related to ESR ($p=0.003$) and AADI on radiography ($p=0.012$). Grades 2–3 alar ligament changes were related to gender ($p=0.001$), neck pain

Table 1 Clinical and imaging characteristics of the 44 analyzed RA patients.

	N (%)	Median (range)
Clinical characteristics		
Women	32 (72.7)	
Age (years)		60.4 (19.8–79.6)
RA duration (years)		9.1 (0.0–34.6)
DAS28 score		5.3 (2.9–7.9)
MHAQ score (possible scores 1.0 to 4.0)		1.5 (1.0–3.4)
Last week neck pain intensity, VAS score (0 to 10)		3.0 (0.0–10.0)
ESR (mm/h)		29.0 (7.0–107.0)
CRP (mg/l)		9.5 (1.0–67.0)
Positive rheumatoid factor	25 (56.8)	
Positive anti-CCP	35 (79.5)	
Methotrexate treatment	24 (54.4)	
TNF inhibitor treatment	9 (20.5)	
Radiographic findings		
Anterior atlantoaxial subluxation (flexion)	11 (25.0)	
Anterior atlantodental interval (flexion), mm		2.0 (1.0–8.5)
Vertical subluxation	5 (11.4)	
MRI findings C0–C2		
Lateral atlantoaxial subluxation (LAAS)	8 (18.2)	
Dens erosion	3 (6.8)	
Peridental synovitis	8 (18.2)	
Bone edema	7 (15.9)	
Atlantooccipital joint erosion/synovitis	2 (4.5)	
Lateral atlantoaxial joint erosion/synovitis	7 (15.9)	
Spinal or brainstem stenosis	0	
MRI findings C3–C7		
Bone edema	7 (15.9)	
Erosion/synovitis at endplate and/or apophyseal joint	6 (13.6)	
Spinal stenosis	2 (4.5)	

DAS 28 disease activity score in 28 joints, *MHAQ* Modified Health Assessment Questionnaire, *VAS* visual analog scale, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein, *anti-CCP* anti-cyclic citrullinated peptide, *TNF* tumor necrosis factor, *MRI* magnetic resonance imaging

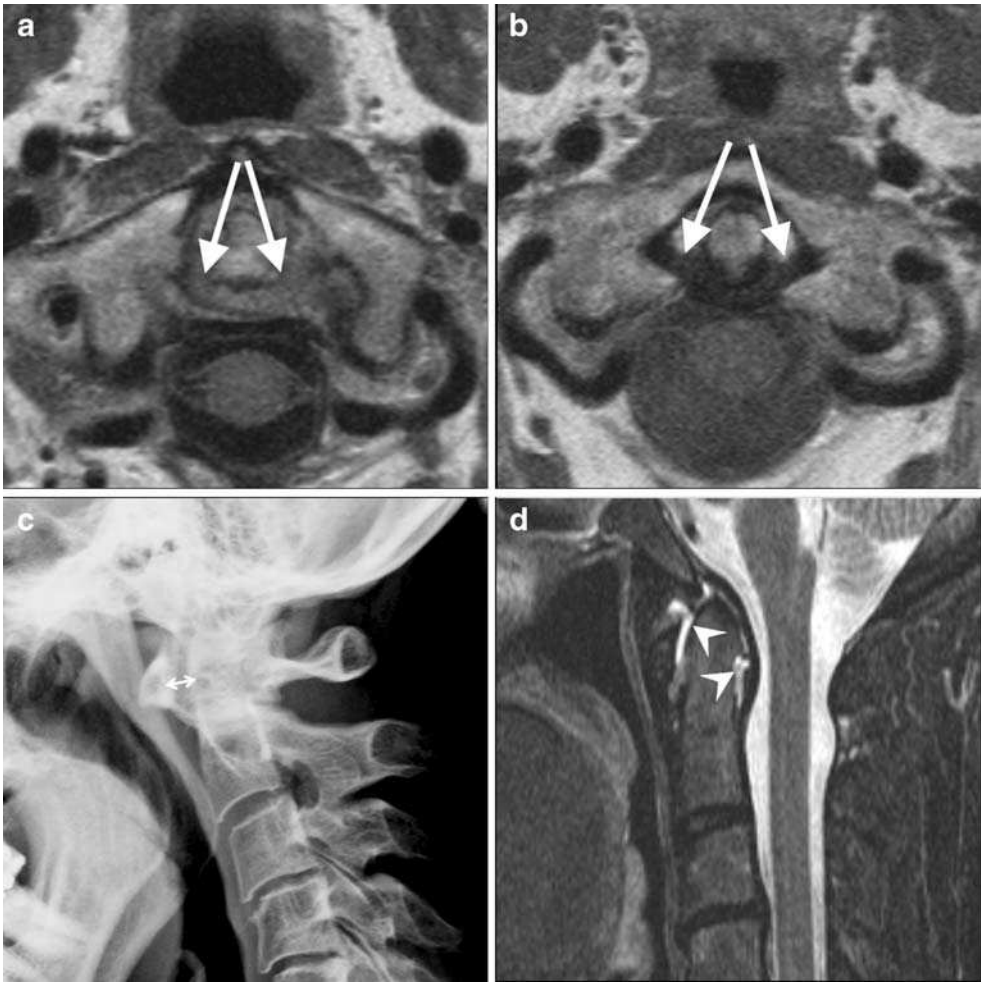

Fig. 1 **a**–**d**. Grade 3 high-signal changes bilaterally (**a**) and normal (**b**) transverse ligament at axial proton-weighted MRI sections of transverse ligaments in two different RA patients (*arrows*), flexion lateral radiography (**c**) with increased anterior atlantoaxial interval, AADI, (*double arrow*) and mid-sagittal STIR MRI section (**d**) indicating anterior and posterior peridental synovitis (*arrowheads*) in same RA patient as in **a** and **c**

intensity (p=0.004), rheumatoid factor (p=0.002), and AADI on radiography (p=0.028). Dens erosion could not be included in the regression models (all patients with erosion had grades 2–3 changes) but was nearly significant in further unadjusted analyses using Cytel Studio8, StatXact (p=0.055 for transverse and p=0.069 for alar changes).

On the focused STIR sequence, only one transverse ligament and no alar ligament had signal intensity higher than bone marrow. No ligament had STIR signal as intense as CSF.

Discussion

In this study, for the first time a high-resolution MRI technique for assessing high-signal changes of craniovertebral ligaments has been applied on RA patients. High-resolution MRI provided high-quality images and reliable evaluation of the transverse and alar ligaments in different stages of adult RA disease. MRI ligament changes were related to atlantoaxial subluxation, neck pain, and markers of disease activity: elevated ESR and rheumatoid factor.

The MRI sequences used in the current study are possible to perform and interpret in most adult RA patients. The patients in our study accepted the long acquisition times despite the fact that they had more severe RA (higher DAS28 scores) than patients in a general RA population [33]. Their ligaments were graded with similar interobserver reliability as reported for non-RA subjects [16, 19, 20] and for many radiological examinations in daily use [34–36].

The present high-resolution FSE sequences with 1.5 mm slice thickness allow a more detailed evaluation of the ligament structure than the 3-mm gradient-echo slices that were applied on four RA patients in the study by Dickman et al. [15]. They reported alterations of the transverse ligament but did not describe the signal characteristics.

Having examined feasibility and reliability, a next step in evaluating a new imaging method is to explore relations between imaging findings and clinical variables. To ensure valid results for such relations, our prospective study included nonselected RA patients, the same experienced rheumatologist examined all patients, and the radiologists graded the ligaments blinded to presence/severity of RA

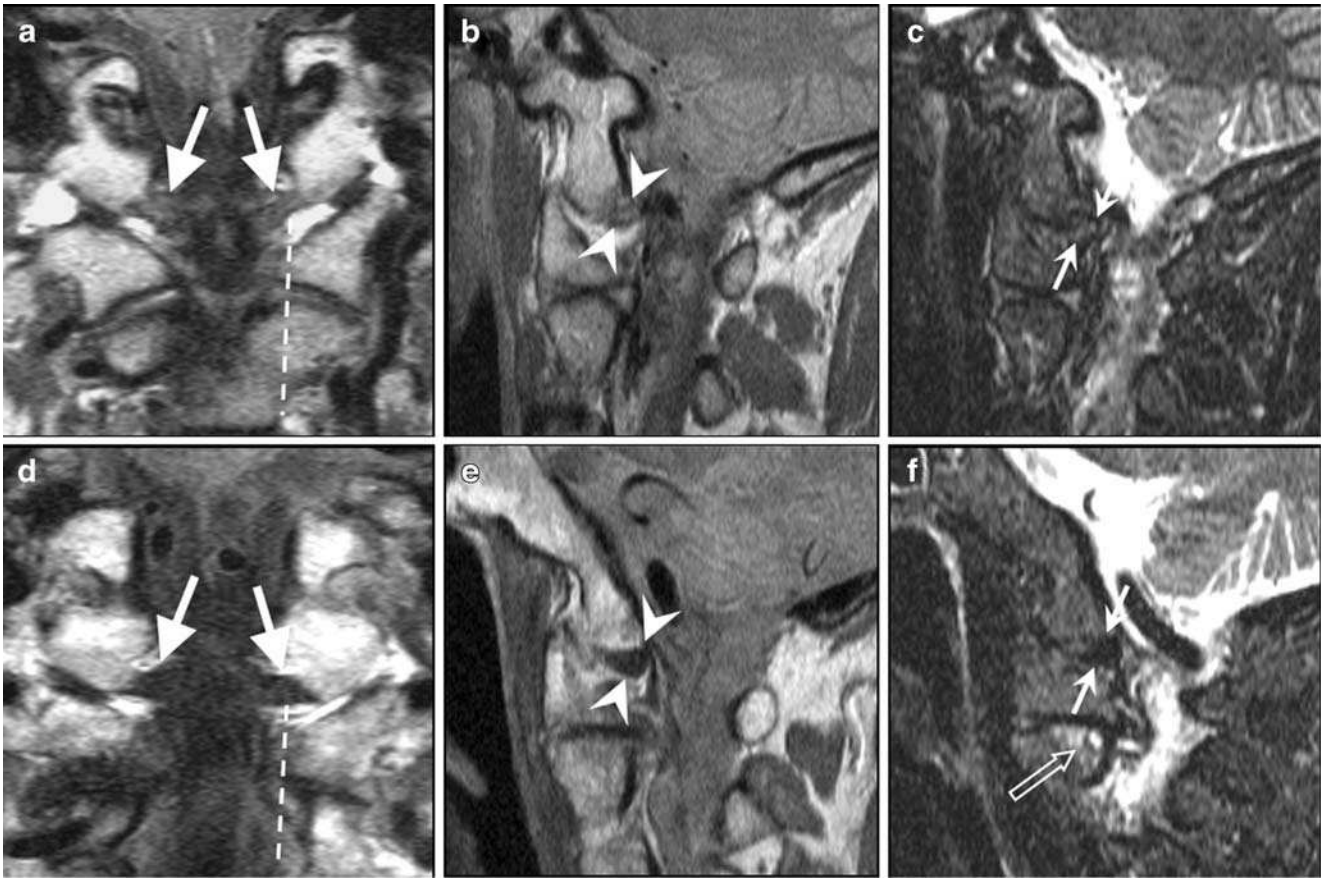

Fig. 2 **a**–**f** Grade 3 high-signal changes (**a**, **b**) and normal (**d**, **e**) alar ligaments (*arrows*/*arrowheads*) at coronal (**a**, **d**) and sagittal (**b**, **e**) proton-weighted MRI sections of alar ligaments in two different RA patients. Respective sagittal STIR MRI sections (**c**, **f**) show signal intensity similar (**c**) and lower (**f**) compared to adjacent bone marrow (*small arrows*). *Broken lines* mark the sagittal plane. Note bone edema (*open arrow*) at the left lateral atlantoaxial joint (**f**)

and subluxation. Short time from clinical assessment to MRI further enhanced the validity of the relations found between clinical variables and ligament changes on MRI. We tested a priori hypotheses and found statistically significant relations despite the small sample.

Grades 2–3 ligament changes were related to larger AADI on flexion radiography, but which came first is not clear from this cross-sectional study. Longitudinal studies are needed to test the hypothesis that MRI ligament changes increase the risk of larger AADI and later subluxation. If so, MRI ligament changes can justify early RA treatment to prevent subluxation. Transverse ligament changes could be particularly relevant as this ligament is the most important structure preventing anterior dislocation of atlas on axis; a functionally intact transverse ligament usually prevents AADI from exceeding 3 mm [2, 5, 7, 9].

LAAS was not related to grades 2–3 alar ligament changes, despite the fact that it has been postulated that dysfunctional alar ligaments can cause LAAS in RA patients [30]. However, the role of the alar ligaments in the development of LAAS is not clear since the odontoid process can deviate laterally on MRI also in asymptomatic non-RA individuals [37].

Our findings suggest that MRI ligament changes are related both to general and local RA disease activity. Patients with transverse changes had higher ESR, patients with alar changes were more often rheumatoid factor positive, and both groups tended to have more dens erosions. However, MRI ligament changes were not significantly related to DAS 28, anti-CCP, or disease duration. In DAS 28, the subcategories patients' peripheral joint status and assessment of global health to a lesser degree reflect cervical RA activity, and most (79.5%) of the RA patients were anti-CCP positive, making a relation with ligament changes hard to prove statistically. Rheumatic cervical spine changes usually appear within 2 years of RA disease onset [38]. Most of our patients had longer disease duration (median 9.1 years), making a relationship with ligament changes less likely.

High-signal alar ligament changes were associated to neck pain but were also found in RA patients without neck pain. Thus, such changes are not always symptomatic, as

Table 2 Characteristics of RA patients with and without MRI ligament changes grades 2–3.

	With	Without	p^b
Transverse ligament (14 patients with grades 2–3 MRI changes[a] and 30 without)			
Neck pain intensity, median VAS score	4.5	1.0	0.054
ESR, median (mm/h)	47.0	28.5	0.003
CRP, median (mg/l)	18.5	7.0	0.123
AADI on radiography (flexion), median (mm)	3.6	2.1	0.003
Dens erosion on MRI, *n* (%)	3 (21.4)	0 (0.0)	0.027
Peridental synovitis on MRI, *n* (%)	5 (31.8)	3 (10.0)	0.087
Lateral atlantoaxial joint erosion/synovitis on MRI, *n* (%)	4 (28.6)	3 (10.0)	0.184
Alar ligaments (15 patients with grades 2–3 MRI changes[a] and 29 without)			
Men, *n* (%)	8 (53.3)	4 (13.8)	0.011
Neck pain intensity, median VAS score	4.0	2.0	0.113
ESR, median (mm/h)	38.0	24.0	0.001
CRP, median (mg/l)	19.0	7.0	0.020
Positive rheumatoid factor, *n* (%)	11 (73.3)	14 (48.3)	0.199
AADI on radiography (flexion), median (mm)	3.1	2.3	0.060
LAAS on MRI, *n* (%)	5 (33.3)	3 (10.3)	0.099
Dens erosion on MRI, *n* (%)	3 (20.0)	0 (0.0)	0.034

Only characteristics with $p<0.2$ are given

MRI magnetic resonance imaging, *VAS* visual analog scale, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein, *AADI* anterior atlantodental interval, *LAAS* lateral atlantoaxial subluxation

[a] Highest assigned grade if different between right and left side

[b] *p* values are based on Fisher's exact test or Mann–Whitney *U* test

Table 3 Logistic regression of MRI grades 2–3 transverse and alar ligament changes on potential explanatory variables.

	Unadjusted		Final model[a]		
	OR	p[b]	OR	95% CI	p[b]
Transverse ligament					
Neck pain intensity, VAS score (0 to 10)	1.29	0.032			0.708[c]
ESR (per 10 mm/h)	1.63	0.001	1.69	(1.10,2.59)	0.003
CRP (per 10 mg/l)	1.28	0.198			0.457[c]
AADI on radiography (flexion) (mm)	1.93	0.005	1.81	(1.08,3.04)	0.012
Peridental synovitis on MRI (yes vs. no)	5.00	0.046			0.217[c]
Lateral atlantoaxial joint erosion/synovitis on MRI (yes vs. no)	3.60	0.129			0.825[c]
Alar ligaments					
Gender (men vs. women)	7.14	0.006	24.84	(2.69,229.91)	0.001
Neck pain intensity, VAS score (0 to 10)	1.23	0.072	1.68	(1.09,2.61)	0.004
ESR (per 10 mm/h)	1.61	0.002			0.112[c]
CRP (per 10 mg/l)	1.33	0.130			0.610[c]
Positive rheumatoid factor (yes vs. no)	2.95	0.106	29.87	(2.00,445.64)	0.002
AADI on radiography (flexion) (mm)	1.32	0.162	1.87	(1.03,3.41)	0.028
LAAS on MRI (yes vs. no)	4.33	0.074			0.327[c]

Only variables with $p<0.2$ from the univariate analysis were included in the model

MRI magnetic resonance imaging, *OR* odds ratio, *CI* confidence interval, *VAS* visual analog scale, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein, *AADI* anterior atlantodental interval, *LAAS* lateral atlantoaxial subluxation

[a] Stepwise backward by using likelihood-ratio tests

[b] *p* values are based on likelihood-ratio tests

[c] Not in the final model, *p* value for adding term to final model

confirmed for other upper cervical spine findings in RA as well [39, 40]. Alar high-signal changes also exist in asymptomatic non-RA subjects [19, 37]. Data on high-signal transverse ligament changes in asymptomatic subjects are sparse [41]. High-signal alar ligament changes may thus not necessarily represent pathologic tissue, and the histological correlate of MRI changes in the transverse and alar ligaments is not known.

The STIR images shed new light on the morphology underlying high-signal changes in the transverse and alar ligaments. Both ligaments consist almost exclusively of collagen fibers [2, 3], and are expected to show low signal on proton-weighted MRI sequences [42]. Inflammation or edema can cause high signal from ligaments on proton sequences and especially on STIR sequences, which suppress the high signal from fat [43]. Only one single ligament in our study had higher signal intensity than bone marrow on STIR. Thus, such changes more likely represent fat or fibrosis than inflammation. Postmortem and postoperative histopathological studies of bone and soft tissue specimen from the upper cervical spine in chronic RA have revealed predominantly fibrous tissue with little or no evidence of active inflammation [14, 44]. Similarly, MRI of the peridental area in chronic RA suggests fibrous tissue consistency rather than ongoing inflammation [45].

Our MRI protocol was primarily intended for optimal visualization of the ligaments, and to limit the examination time it did not include T1 sequences without/with gadolinium contrast enhancement, which are needed for ideal assessment of rheumatic MRI features [32]. Although synovitis and bone edema can be evaluated at STIR sequences alone [31, 46], the lack of gadolinium-enhanced T1 sequences probably diminished the sensitivity to such features, especially synovitis. MRI during cervical flexion, which tightens the transverse ligament [2], could have added further information on the nature of the high-signal changes since loose ligaments might show a higher MRI signal and tightening might reduce the signal [47].

To conclude, the successful and detailed visualization of the transverse and alar ligaments on high-resolution MRI provides new opportunities for research on these important structures in patients with RA. In this initial study, MRI ligament changes were related to atlantoaxial subluxation, markers of RA disease activity, and neck pain. Further studies with larger samples, longitudinal design, and control groups are needed to clarify if high-resolution MRI of transverse and alar ligaments can predict, diagnose, and help to treat cervical RA disease.

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Conflict of interest statement We declare that we have no conflict of interest.

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