Alterations of the Transverse Ligament: An MRI Study Comparing Patients With Acute Whiplash and Matched Control Subjects

Erika Jasmin Ulbrich[1,2]
Sandra Eigenheer[1]
Chris Boesch[3]
Juerg Hodler[4]
André Busato[5]
Christian Schraner[1]
Suzanne E. Anderson[1,6]
Harald Bonel[1]
Heinz Zimmermann[7]
Matthias Sturzenegger[8]

Keywords: contrast media, MRI, swelling, transverse ligament, whiplash injury

DOI:10.2214/AJR.10.6321

Received November 12, 2010; accepted after revision February 23, 2011.

Presented at the 2009 annual meeting of the Radiological Society of North America, Chicago, IL.

Supported by the National Research Program (NRP 53, "Musculoskeletal Health: Chronic Pain") of the Swiss National Science Foundation (project number 405340-104531), Von Hevesy Foundation, and Inselspital Research Foundation.

[1]Department of Diagnostic, Interventional and Pediatric Radiology, University Hospital and University of Bern, Inselspital, Switzerland.

[2]Present address: Department of Radiology, Orthopedic University Hospital Balgrist, Forchstrasse 340, 8008 Zurich, Switzerland. Address correspondence to E. J. Ulbrich (erikajulbrich@googlemail.com).

[3]Department of Clinical Research, Magnetic Resonance Spectroscopy and Methodology, University of Bern, Inselspital, Switzerland.

[4]Department of Radiology, University Hospital, Zurich, Switzerland.

[5]Institute for Evaluative Research in Orthopedic Surgery, University of Bern, Inselspital, Switzerland.

[6]Medical Imaging School of Medicine Sydney, The University of Notre Dame, Sydney, Australia.

[7]Department of Emergency Medicine, University Hospital and University of Bern, Inselspital, Switzerland.

[8]Department of Neurology, University Hospital and University of Bern, Inselspital, Switzerland.

AJR 2011; 197:961–967

0361–803X/11/1974–961

OBJECTIVE. The objective of our study was to evaluate whether there is injury to the transverse ligament of the atlas in patients with acute whiplash.

MATERIALS AND METHODS. Ninety patients with an acute (< 48 hours) symptomatic whiplash-associated injury and 90 healthy age- and sex-matched asymptomatic control subjects (mean age of patients and control subjects, 36 years) were included. The maximal sagittal thickness of the transverse ligament was measured on midsagittal T1 volumetric interpolated breath-hold examination (VIBE) images and transverse reformatted VIBE images. The signal intensity of the transverse ligament was measured on transverse STIR images and on transverse reformatted T1 VIBE images before and after IV administration of gadoterate. Contrast between the transverse ligament and CSF and alterations of contrast after gadoterate injection were calculated.

RESULTS. Patients had a minimally thicker transverse ligament (posttraumatic swelling) than control subjects, and the difference in thickness was significant in men only ($p = 0.03$). In patients, a significant signal alteration of the transverse ligament ($p = 0.03$) was seen on STIR (posttraumatic edema) and native VIBE sequences. The contrast between the transverse ligament and the CSF on VIBE images was significantly ($p = 0.005$) lower in patients than in control subjects. With the application of a contrast agent, the contrast difference between the transverse ligament and CSF in patients and control subjects was less pronounced ($p = 0.038$). There was no abnormal uptake of contrast agent by the transverse ligament or CSF.

CONCLUSION. The results of our study indicate possible involvement of the transverse ligament in whiplash injury. Although MRI may be helpful to study injury-related changes of anatomic structures in cohorts, it is not suited for individual diagnosis because the alterations are too small.

Neck pain and head pain are the most prominent symptoms in the acute and chronic phases of whiplash-associated injuries. As to which structures are damaged and to what extent are subjects of debate. Diagnosis of altered structures may allow more specific treatment strategies and potentially prevention. Important forces thought to damage neck structures are translational forces acting on zygapophyseal joints of the cervical spine [1], which are stabilized by the cervical spine muscles in a complex arrangement.

In experimental dynamic cervical spine load studies with simulated rear-end impacts, the craniocervical junction was the most vulnerable region [2]. At the C0-C1 and C1-C2 levels there are, however, no facet joints anchoring the vertebral bodies. Therefore, the effect of translational forces at the craniocervical junction may be most pronounced on ligaments and muscles. Many MRI studies have focused on the craniocervical region in patients with chronic whiplash, typically focusing on the alar ligaments [3–7]. In this study, contrary to previously published ones, patients with whiplash-associated injuries were evaluated in the acute phase. In this substudy of a larger whiplash project, we focused on only the transverse ligament; all other ligaments of the craniocervical junction are reviewed in detail in another study. Our hypothesis was that patients with acute symptomatic whiplash injuries may have swelling, edema, and an abnormal tissue-blood barrier of the transverse ligament due to traumatic injury.

Materials and Methods

This study was approved by the responsible ethics committees, and all patients and control subjects provided written informed consent before study inclusion.

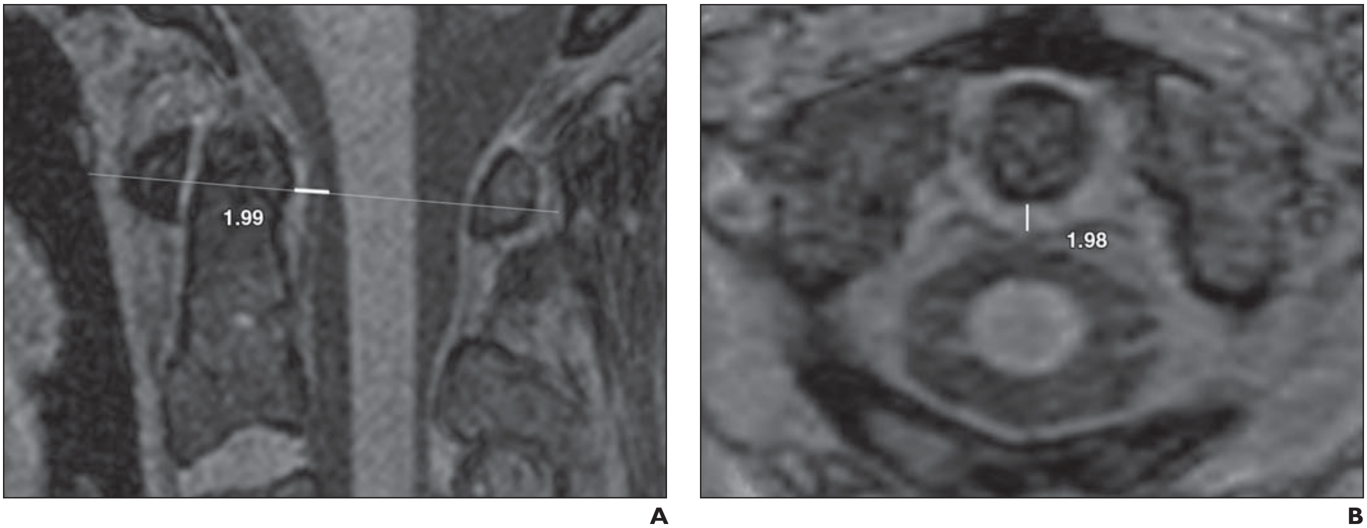


Fig. 1—Measurement of thickness of transverse ligament (retrodental soft tissue) in 31-year-old woman who presented to emergency department after being injured in motor vehicle crash.
A, Thickness of transverse ligament was measured on midsagittal T1 volumetric interpolated breath-hold examination (VIBE) image from posterior border of dental cortical bone to tectorial membrane parallel to reference line from most anterior point of anterior atlantic arch to most anterior point of posterior atlantic arch (volume increase). Long line = reference line, short line = thickness of transverse ligament.
B, Maximum thickness of transverse ligament (*line*) was measured on transverse reformatted 1-mm VIBE image on reference line from most anterior point of anterior atlantic arch to most anterior point of posterior atlantic arch (volume increase).

Patients were recruited by the emergency departments of two university hospitals. The subjects analyzed in this study are part of a larger prospective multicenter study supported by the Swiss National Science Foundation aimed at evaluation of MRI findings in patients with acute (i.e., within 48 hours of injury) whiplash and during follow-up.

Subjects

Patients presenting with acute whiplash-associated injury grade I or II, as defined by the Quebec Task Force [8], after a rear-end motor vehicle crash with a mechanism of forceful flexion and extension of the cervical spine with persistent symptoms of at least neck pain and stiffness were eligible for recruitment. We included 30 patients of three different age categories each: 20–29, 30–39, and 40–60 years. The first 90 consecutive patients of this ongoing study fitting into the three age categories with completed diagnostic evaluation and their age- and sex-matched control subjects were recruited between August 2005 and June 2008. Eligibility criteria were checked with a standardized questionnaire and included whiplash injury less than 48 hours before MRI, age of older than 18 years, sufficient knowledge of the German language to understand the various documents relating to this investigation and to give written informed consent.

Patients were excluded if any of the following aspects were found: fracture or subluxation of the cervical spine as diagnosed on standard radiographs or CT scans, direct head and brain injury, spinal tract and nerve root injury, prior head or spine surgery, prior whiplash injury with persisting pain, musculoskeletal inflammatory disorders or other severe illnesses with chronic pain or inability to work, preexisting head or neck pain, psychiatric disorders, drug or alcohol abuse, neoplastic disease of the head and neck, and contraindications to MRI (claustrophobia, pacemaker and other devices precluding MRI, or pregnancy).

The patients were examined on arrival in the emergency departments by a team of emergency physicians designated to the study for recruitment and to clinically exclude severe injury, such as multiple trauma, and significant head or serious neck injury, such as fracture-dislocation or subluxation. For the study purposes, radiographs, CT scans, or radiographs and CT scans of the cervical spine were then reviewed by the emergency radiology team in collaboration with the emergency physicians to ensure the patient was suitable for study inclusion. Eligible patients underwent a clinical examination and completed questionnaires to determine the severity of symptoms and impairment of quality of life. Subsequently, an MRI examination was performed within the first 48 hours after the motor vehicle crash.

Healthy control subjects were recruited by advertisement within the involved university institution and were matched to patients for age and sex. The same inclusion and exclusion criteria were used as in the patient group.

MR Acquisition

MR images were obtained using a 1.5-T magnet (Sonata, Siemens Healthcare). The parameters for the STIR transverse conventional spin-echo sequence were as follows: TR/TE, 5110/28; inversion time, 150 ms; flip angle, 180°; pixel matrix, 256 × 512; FOV, 210 × 158 mm; slice thickness, 3 mm; 20 slices; and turbo factor, 7. The parameters for the unenhanced and enhanced (after 5 minutes) sagittal 3D volumetric interpolated breath-hold examination (VIBE) sequence consisted of a TR/TE of 6.86/3.34; flip angle, 12°; pixel matrix, 256 × 256; FOV, 180 × 124 mm; nominal voxel size, 0.7 × 0.7 × 1 mm^3; slice thickness, 1 mm; and 72 slices. Gadoterate meglumine (Dotarem, Guerbet) was administered at a flow rate of 3 mL/s (dose, 0.2 mL/kg). A subtraction image of these two sequences was then obtained to increase conspicuity of any contrast alterations. A dedicated neck coil and a spine array coil were used with the patient in the supine position. Saturation pulses placed over the upper airways were used to reduce breathing and vessel-related artifacts.

The sagittal 3D VIBE slices were centered on the cord at the C4 level (72 images) with the most superior point at the midpoint of the cerebellum. The 20 transverse STIR images were obtained perpendicular to the posterior surface of the vertebral body in the middle of the respective vertebral body, with the most superior point at the midpoint of the cerebellum.

Image Analysis

The images were analyzed using the lead hospital's PACS. Blinded review of images of patients and control subjects was performed by two observers,

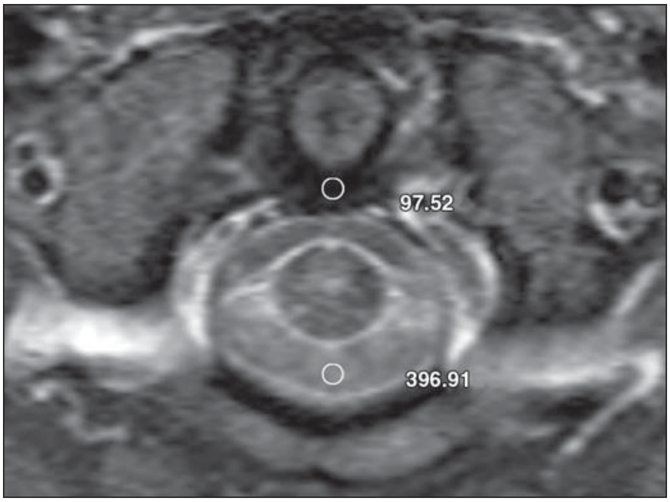


Fig. 2—Measurement of mean signal intensities (standardized region of interest) of transverse ligament (*upper circle*) and CSF (*lower circle*) in 31-year-old woman who presented to emergency department after being injured in motor vehicle crash. STIR sequence was performed at level where transverse ligament has largest diameter (edema).

one with 3 years of experience in radiology and one with 6 months of training reading MRI. Eight measurements were performed per subject.

Thickness of the transverse ligament—The thickness of the transverse ligament was measured in the midsagittal T1 VIBE sequence from the posterior border of the cortical bone of the dens to the tectorial membrane parallel to a line drawn between the most anterior part of the anterior atlantic arch to the most anterior part of the posterior atlantic arch (Fig. 1).

The thickness of the transverse ligament was also measured on the transverse reformatted 1-mm VIBE images.

Signal intensity of the transverse ligament—Measurements of the mean signal intensity of the transverse ligament and the CSF were obtained on the transverse STIR images using a small region of interest (ROI) at the level where the transverse ligament had the largest diameter (Fig. 2).

As a measurement of image contrast, the difference between the mean signal intensity of the transverse ligament and that of the CSF was divided by the sum of the same measurements.

Signal alterations of the transverse ligament after IV injection of contrast material—Measurements of the mean signal intensity of an ROI in the transverse ligament before and after contrast administration were performed using transverse reformatted 1-mm VIBE images. Measurements were also obtained in the CSF on the same transverse reconstructed VIBE images before and after contrast administration (Fig. 3).

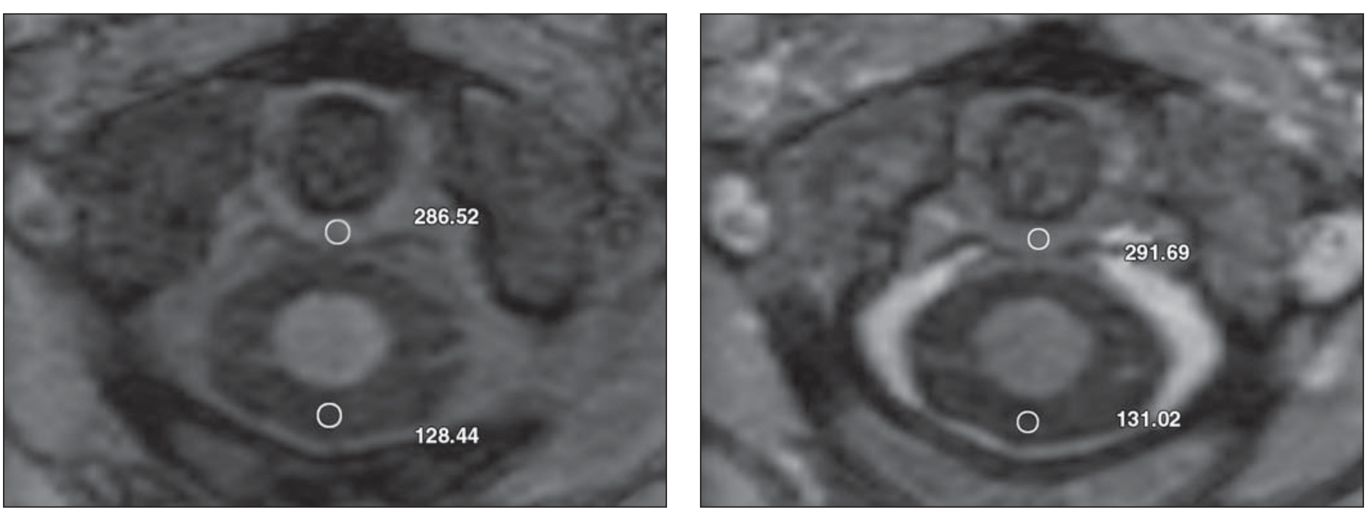
The 1-mm transverse VIBE images were reformatted on the workstations from the sagittal VIBE sequence.

Distance and ROI measurements were traced manually using a PACS (Easy Vision PACS Viewing and Reporting Workstation, Philips Healthcare) with Core software (Easy Vision IDSS, release 11, version 11.4.1, Sectra). The size of the ROI was standardized for each measurement (ROI = circle diameter, 0.6 mm; circle area, 1.13 mm^2).

To correct for arbitrary amplification of the signal intensities due to coil loading and other factors, we calculated contrasts between tissues (i.e., transverse ligament vs CSF) and relative changes of signal intensities before and after the uptake of contrast agent as described in Appendix 1.

Statistical Analysis

Differences between patients and control subjects for each of the tissue measurements were assessed using nested linear models with group (case or control); observer; and age, sex, and body mass index (BMI) of the patient nested within sex as explanatory factors. In addition, a sex-stratified analysis was performed with sex omitted from the models. Residual statistics were used to check model assumptions and no violations were detected. The agreement of measurements between the two observers was determined using interclass correlation coefficients. To estimate the reproducibility of the image analysis, one of the two observers repeated the measurements. Although only the first analysis of this observer was used for the pooled calculations, the repeated measurement was used to determine the intraobserver correlation coefficients. Logistic regression and receiver operating characteristic (ROC) curve analyses were performed to obtain operator characteristics to discriminate between patients and



A **B**

Fig. 3—Transverse reformatted 1-mm volumetric interpolated breath-hold examination image obtained on reference line from most anterior point of anterior atlantic arch to most anterior point of posterior atlantic arch in 31-year-old woman who presented to emergency department after being injured in motor vehicle crash.
A and **B,** Determination of mean signal intensity (region of interest) in transverse ligament (*upper circles*) and of dorsal CSF (*lower circles*) before (**A**) and after (**B**) contrast administration.

control subjects. SAS software (version 9.2, SAS Institute) was used, and the significance level of statistical tests was set as $p < 0.05$.

Results

A total of 90 whiplash patients were recruited (mean age, 36.3 years; age range, 20–61 years): The study group included 45 women (mean age, 36.3 years; age range, 20–59 years) and 45 men (mean age, 36.4 years; age range, 20–61 years). For the 90 healthy control subjects, the corresponding demographic data were a mean age of 36.5 years and age range of 20–61 years for the entire group (women: mean age, 36.4 years; range, 20–59 years; men: mean age, 36.5 years; age range, 20–61 years). There was no significant difference between patients and control subjects with regard to age and BMI (mean BMI, 24.5 for patients and 23.5 for control subjects). For age-related analyses, the patients and their age- and sex-matched control subjects were subdivided into three age categories (20–29, 30–39, and 40–60 years) with 30 patients and 30 control subjects in each category.

Thickness of the Transverse Ligament

The thickness of the transverse ligament measured on the midsagittal T1 VIBE images and on the transverse reformatted VIBE images was slightly greater in patients (mean, 1.99 mm [sagittal] and 1.98 mm [transverse]) than in control subjects (mean, 1.91 and 1.95 mm, respectively). This difference was significant in men only ($p = 0.03$ and $p = 0.04$) (mean: male patients, 2.12 mm [sagittal] and 2.10 mm [transverse]; male control subjects, 1.93 and 1.97 mm, respectively). The difference was not significant in female patients and female control subjects (mean: female patients, 1.86 mm [sagittal] and 1.86 mm [transverse]; female control subjects, 1.89 and 1.92 mm, respectively).

Signal Intensity of the Transverse Ligament

STIR images—The contrast between the transverse ligament and the CSF on STIR images (Tables 1 and 2) was significantly ($p = 0.007$) different in patients (–0.60) as compared with control subjects (–0.63). There was not a significant contrast difference between men and women ($p = 0.395$) or between study subjects based on BMI ($p = 0.523$) or age ($p = 0.474$).

Volumetric interpolated breath-hold examination images before and after IV injection of contrast agent—The contrast between the transverse ligament and the CSF on VIBE images (Tables 1 and 2) was also significantly ($p = 0.005$) different in patients (0.38) as compared with control subjects (0.40). With the application of contrast agent, the significance for a different contrast between the transverse ligament and the CSF in patients versus control subjects was less pronounced ($p = 0.038$).

Signal Alterations of the Transverse Ligament and CSF After IV Injection of Contrast Material on Volumetric Interpolated Breath-Hold Examination Images

Signal changes after application of contrast agent did not reach significance for the transverse ligament or for CSF (Tables 1 and 2).

Separation of Patients From Control Subjects Based on Contrast Between Transverse Ligament and CSF

Although the contrasts reached significance between patients and control subjects in the cohorts, the ROC curves were very close to the diagonal. That is, there is no possibility to find a value for the contrast that separates control subjects from patients purely on the basis of this measurement.

Interobserver Reliability and Reproducibility

The interobserver agreement of the thickness measurements was moderate (sagittal, 0.59; transverse, 0.46). Interobserver agreement was classified as poor (≤ 0), slight (0.01–0.20), fair (0.21–0.40), moderate (0.41–0.60), substantial (0.61–0.80), or almost perfect (0.81–1.00) [9]. The repeatability in two analyses of observer A (intraobserver agreement) was almost perfect for sagittal (0.820) and transversal (0.817) thickness measurements.

The interobserver agreement for all performed measurements was significantly lower (between fair and substantial) than the intraobserver agreement (between substantial and almost perfect) as shown in Table 3.

Discussion

Although some studies have found a consistent association between chronic symptoms and MRI abnormalities [6, 7], the role of imaging in detecting posttraumatic alterations in patients with acute whiplash-associated injury has been a subject of debate [3–5, 10, 11]. In whiplash-associated trauma, damage to the alar ligaments [3], the transverse ligament [5], and the tectorial and posterior atlantooccipital membranes [6] has been postulated. The MRI findings may be subtle and have not been verified by large study groups obtained from different institutions. However, the results of experimental studies of animals [12] and cadavers [13–17] suggest that these structures may, indeed, be at risk with mechanisms probably working in whiplash injuries.

TABLE 1: Calculated on the STIR Sequence and on the Volumetric Interpolated Breath-Hold Examination (VIBE) Sequence Before and After Application of Contrast Agent

	Contrast Between Transverse Ligament and CSF			Uptake of Contrast Agent (% Change in Signal Intensity)	
Group	STIR	Unenhanced VIBE	Contrast-Enhanced VIBE	By Ligament	By CSF
All patients	–0.60 (–0.628 to –0.579)	0.38 (0.362–0.395)	0.38 (0.362–0.395)	3 (0.1–5.6)	3 (–0.2 to 6.9)
All control subjects	–0.63 (–0.659 to –0.611)	0.40 (0.381–0.415)	0.40 (0.379–0.416)	5 (2–7.1)	5 (1.4–9.1)
Patients					
Female	–0.60 (–0.632 to –0.559)	0.37 (0.351–0.393)	0.39 (0.364–0.408)	4 (0.6–7.8)	2 (–3.7 to 6.8)
Male	–0.61 (–0.645 to –0.577)	0.39 (0.359–0.411)	0.37 (0.344–0.397)	2 (–2.9 to 5.9)	5 (0.3–10.1)
Control subjects					
Female	–0.63 (–0.663 to –0.590)	0.41 (0.384–0.435)	0.41 (0.388–0.439)	2 (–0.8 to 5.4)	2 (–2.9 to 6.9)
Male	–0.64 (–0.675 to –0.610)	0.39 (0.362–0.41)	0.38 (0.355–0.409)	7 (2.8–10.9)	8 (2.5–14.4)

Note—The values in parentheses are the 95% CIs.

TABLE 2: Significance Levels for Contrasts and Uptake of Contrast Agent by Transverse Ligament and CSF for the Different Variables

Calculated Value	*p*				
	Rater	Age	Patients Versus Control Subjects	Females Versus Males	Body Mass Index
Contrast between transverse ligament and CSF					
STIR	**0.001**	0.474	**0.007**	0.395	0.523
Unenhanced VIBE	**0.022**	**0.035**	**0.005**	0.641	0.411
Contrast-enhanced VIBE	**0.033**	**0.244**	**0.038**	0.874	0.978
Uptake of contrast agent					
By ligament	0.888	0.627	0.363	0.956	0.945
By CSF	0.701	0.259	0.212	0.484	0.731

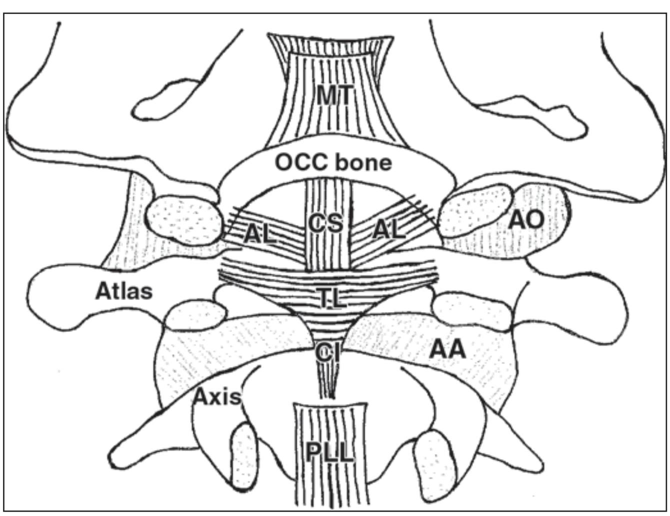
Note—**Boldface** values are less than 0.05, significance level. Tests for generalized linear models indicate no violation of basic assumptions of the models for the contrast; however, they indicate a violation for the uptake of contrast agent. The differences for the uptake of contrast are far above a significance level of 0.05.

The major stabilizers of the atlantoaxial region are the alar ligaments, the cruciate ligament of the atlas, and the anterior and posterior longitudinal ligaments. The cruciate ligament of the atlas consists of the transverse ligament and vertical fibers (a small fasciculus that continues upward [crus superius] and another downward [crus inferius]) [18] (Fig. 4A). The transverse ligament is a thick, strong band that arches across the ring of the atlas and retains the odontoid process in contact with the anterior arch [18] (Fig. 4B).

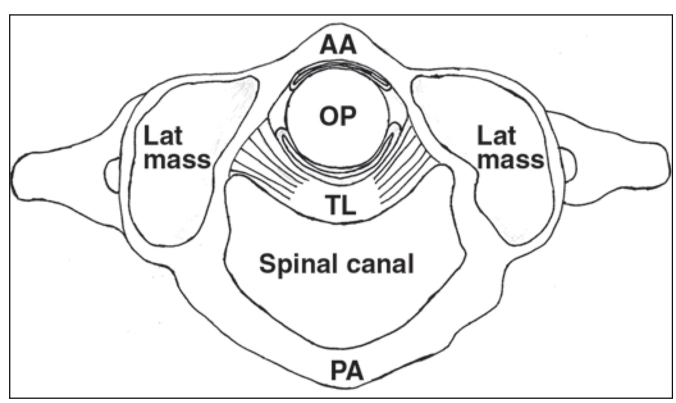
In this study, contrary to previously published studies, symptomatic patients with whiplash-associated injuries were evaluated in the very acute phase—that is, within 48 hours of injury—and were compared with matched control subjects. In addition to signal intensity, we also evaluated ligament thickness, contrast, and contrast enhancement. Krakenes et al. [3–6] looked at the ligaments in patients with chronic whiplash-associated injuries 2–9 years after injury in a motor vehicle crash on proton density–weighted images (2-mm slice thickness), whereas we selected patients within the first 48 hours after a motor vehicle crash and used STIR (3-mm slice thickness) and T1-weighted VIBE (1-mm slice thickness with isotropic voxels) images. The STIR sequence is known as the most sensitive sequence for depicting posttraumatic injury. Krakenes et al. [3–6] considered increased signal on the proton density–weighted sequence as a sign of injury. However, high signal changes of upper neck ligaments are found in asymptomatic and symptomatic noninjured control subjects and thus may also be caused by degeneration and normal aging or may represent normal variants [19]. Furthermore, in a recent study [20] high signal changes of the alar and transverse ligaments seen on imaging within 7 days after car crash in patients with acute whiplash-associated disorder (WAD) grade I or II were not related to clinical outcome at 12-month follow-up.

A study of dynamic cine MRI showed that whiplash patients with long-standing symptoms had both more abnormal signal from the alar ligaments and more abnormal movements at the C0-C2 level than control subjects [21].

In this study, patients with acute whiplash injury had a minimally thicker transverse ligament. This finding was significant for men only. Posttraumatic swelling may be the explanation.



A



B

Fig. 4—Drawings show major stabilizers of craniocervical junction.
A, Cruciate ligament, alar ligaments, membrana tectoria, posterior longitudinal ligament (PLL) are shown in coronal plane. MT = membrana tectoria, OCC = occipital, AL = alar ligament, CS = crus superius of vertical fibers, AO = atlantooccipital membrane, TL = transverse ligament, CI = crus inferius of vertical fibers, AA = atlantoaxial membrane.
B, Transverse ligament (TL) is shown in transverse plane. Lat = lateral, OP = odontoid process, AA = anterior arch of atlas, PA = posterior arch of atlas.

TABLE 3: Inter- and Intraobserver Agreement of All Calculated Contrasts and Uptake of Contrast Agent

Calculated Value	Reliability	
	Interobserver	Intraobserver
Contrast between transverse ligament and CSF		
STIR	0.323	0.734
Unenhanced VIBE	0.654	0.850
Contrast-enhanced VIBE	0.510	0.909
Uptake of contrast agent		
By ligament	0.372	0.721
By CSF	0.508	0.863
Thickness measurements		
Sagittal	0.590	0.820
Transverse	0.460	0.817

In patients, a significant signal alteration of the transverse ligament was seen on STIR and unenhanced VIBE images and, to a lesser degree, also on the VIBE series after the application of a contrast agent. This effect possibly relates to stretching and microtrauma to collagen fibers of the transverse ligament with edema. Differences between patients and control subjects are statistically sound. However, the difference is too small for diagnosis in an individual patient. Nevertheless, such imaging findings may help to increase our understanding about injury mechanisms.

In a recent study, Dullerud et al. [22] did not find any significant differences between whiplash patients and control subjects in assessment of the alar and transverse ligaments; however, increased signal on proton density–weighted images was commonly observed in the transverse ligaments of the healthy subjects. The patients in that study [22] were examined 1–7 years after whiplash injury. In our study, we examined patients within the first 48 hours after whiplash-associated injury. Moreover, we performed a quantitative analysis, whereas Dullerud et al. made a qualitative observation. Nonetheless, in our study we found only slight differences between patients and control subjects regarding the transverse ligament.

There was no increased uptake of contrast agent of the transverse ligament (blood-tissue border) in patients compared with control subjects. This finding is understandable because ligaments do not have a high blood-rich vascular supply. The uptake of contrast agent was not different for patients or control subjects.

Further reviews of measurements of the transverse ligament in whiplash patients, like those performed in this study, might be helpful for recognizing (subtle) objective structural posttraumatic effects of whiplash.

However, our results suggest that upper neck MRI is of limited value in the initial examination of patients with WAD grade I or II and cannot be recommended for routine use in this setting.

One must realize that our analyses were performed with the patient in a static prone condition, not really reflecting real life with the cervical spine in an upright position and bearing the weight of the head. Dynamic cine MRI in a small series of chronic whiplash patients with long-standing symptoms (mean, 7.8 years) showed abnormal movements in addition to abnormal signal intensities at the C0-C2 level when compared with control subjects [21]. Whether such a dynamic examination procedure is applicable in the acute stage of whiplash injury is, however, questionable.

Limitations of the current study include motion artifacts influencing signal intensity measurements on the STIR images. The transverse ligament is a small structure, and partial volume effects may have played a role. To correct for variations of the signal intensity caused by systematic differences of the coil loading (e.g., by a relieving posture of the patients) and by the MR systems at the two participating sites, we calculated ratios of signal intensities (Appendix 1). This eliminates potential influences; however, it introduces the ambiguity that the reference—in this case, CSF—could be influenced by microhemorrhage. The CSF relaxation times and, thus, the signal intensity may be influenced by the addition of small amounts of blood. The presence of increased protein content and the formation of deoxyhemoglobin are postulated to have potential complex interactions and influence on the relaxation times [23–25]. In this study, however, the influence of blood in the CSF on the observed results is unlikely because the absolute signal intensities of CSF in patients did not differ significantly from control subjects (healthy volunteers). Therefore, we conclude that the signal intensity of CSF is a valid reference for the signal amplification by the MR systems and that, thus, changes in the ligament-CSF ratio represent changes of the ligament. Positive aspects include study numbers, excellent age and sex matching of patients and healthy control subjects, and prompt MRI after injury.

In conclusion, the results indicate a possible involvement of the transverse ligament in whiplash-associated injury. Although MRI may be helpful to study injury-related changes to anatomic structures in cohorts, it may not be suited for individual diagnosis because alterations are small.

Acknowledgments

Many thanks to our study coordinators (Nathalie Sollberger, Sandra Stiegler); MRI technicians (Jeanette Pfeiffer, Karolina Dobrowolska, Verena Beutler, and Karin Zwygart); the computer technicians of the Department of Radiology, University Hospital, Inselspital, Bern; and Vincent Im Hof, Peter Vock, and Juergen Triller.

References

1. Bogduk N, Yoganandan N. Biomechanics of the cervical spine. Part 3. Minor injuries. *Clin Biomech (Bristol, Avon)* 2001; 16:267–275
2. Ivancic PC, Panjabi MM. Cervical spine loads and intervertebral motions during whiplash. *Traffic Inj Prev* 2006; 7:389–399
3. Krakenes J, Kaale BR, Moen G, Nordli H, Gilhus NE, Rorvik J. MRI assessment of the alar ligaments in the late stage of whiplash injury: a study of structural abnormalities and observer agreement. *Neuroradiology* 2002; 44:617–624
4. Krakenes J, Kaale B, Moen G, et al. MRI of the tectorial and posterior atlanto-occipital membranes in the late stage of whiplash injury. *Neuroradiology* 2003; 45:585–591
5. Krakenes J, Kaale B, Nordli H, et al. MR analysis of the transverse ligament in the late stage of whiplash injury. *Acta Radiol* 2003; 44:637–644
6. Krakenes J, Kaale B. Magnetic resonance imaging assessment of craniovertebral ligaments and membranes after whiplash trauma. *Spine* 2006; 31:2820–2826
7. Kaale B, Krakenes J, Albrektsen G, Wester K. Whiplash-associated disorders impairment rating:

neck disability index score according to severity of MRI findings of ligaments and membranes in the upper cervical spine. *J Neurotrauma* 2005; 22:466–475 [Erratum in *J Neurotrauma* 2006; 23:1048]
8. Spitzer WO, Skovron ML, Salmi LR, et al. Scientific monograph of the Quebec Task Force on Whiplash-Associated Disorders: redefining "whiplash" and its management. *Spine* 1995; 20(suppl 8):1–73 [Erratum in *Spine* 1995; 20:2372]
9. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977; 33:159–174
10. Krakenes J, Kaale B, Rorvik J, Gilhus NE. MRI assessment of normal ligamentous structures in the craniovertebral junction. *Neuroradiology* 2001; 43:1089–1097
11. Baumert B, Wörtler K, Steffinger D, et al. Assessment of the internal craniocervical ligaments with a new magnetic resonance imaging sequence: three-dimensional turbo spin echo with variable flip-angle distribution (SPACE). *Magn Reson Imaging* 2009; 27:954–960
12. MacNab I. Acceleration injuries of the cervical spine. *J Bone Joint Surg Am 1964*; 46:1797–1799
13. Panjabi MM, Cholewicki J, Nibu K, Babat LB, Dvorak J. Simulation of whiplash trauma using whole cervical spine specimens. *Spine* 1998; 23: 17–24
14. Geigl BC, Steffan H, Dippel Ch, Muser MH, Walz F, Svensson MY. Comparison of head-neck kinematics during rear end impact between standard hybrid III, RID neck, volunteers and PMTOs. In: *Proceedings of the International Conference on Biomechanics of Impacts.* Brunnen, Switzerland: 1995:261–270
15. Geigl BC, Steffan H, Leinzinger P, Roll, Mühlbauer M, Bauer G. The movement of head and cervical spine during rearend impact. In: names of editors, eds. *Proceedings of the International Conference on Biomechanics of Impacts.* Lyon, France: 1994:127–137
16. Hodgson VR, Thomas LM. Mechanisms of cervical spine injury during impact to the protected head. *Proceedings of the 24th Stapp Car Crash Conference.* Warrendale, PA: Society of Automotive Engineers, 1980
17. Mertz HJ, Patrick LM. Strength and response of the human neck. *Proceedings of the 15th Stapp Car Crash Conference.* Warrendale, PA: Society of Automotive Engineers, 1971: SAE paper no. 710855, 207–255
18. Newell RLM. Chapter 42: Joints, craniovertebral joints, atlantoaxial joints. In: Standring S, ed. *Gray's anatomy: the anatomical basis of clinical practise*, 40th ed. London, UK: Churchill Livingston, 2008:733–735
19. Myran R, Kvistad KA, Nygaard OP, Andresen H, Folvik M, Zwart JA. Magnetic resonance imaging assessment of the alar ligaments in whiplash injuries: a case-control study. *Spine* 2008; 33: 2012–2016
20. Vetti N, Krakenes J, Eide GE, Rorvik J, Gilhus NE, Espeland A. Are MRI high-signal changes of alar and transverse ligaments in acute whiplash injury related to outcome? *BMC Musculoskelet Disord (England)* 2010; 11:260
21. Lindgren KA, Kettunen JA, Paatelma M, Mikkonen RM. Dynamic kine magnetic resonance imaging in whiplash patients and in age- and sex-matched controls. *Pain Res Manag (Canada)* 2009; 14:427–432
22. Dullerud R, Gjertsen Q, Server A. Magnetic resonance imaging of ligaments and membranes in the craniocervical junction in whiplash-associated injury and in healthy control subjects. *Acta Radiol* 2010; 51:2007–2012
23. Mohamed M, Heasely DC, Yagmurlu B, Yousem DM. Fluid-attenuated inversion recovery MR imaging and subarachnoid hemorrhage: not a panacea. *AJNR* 2004; 25:545–550
24. Grossman RI, Gomori JM, Goldberg HI, et al. MR imaging of hemorrhagic conditions of the head and neck. *RadioGraphics* 1988; 8:441–454
25. Noguchi K, Seto H, Kamisaki Y, Tomizawa G, Toyoshima S, Watanabe N. Comparison of fluid-attenuated inversion-recovery MR imaging with CT in a simulated model of acute subarachnoid hemorrhage. *AJNR* 2000; 21:923–927

APPENDIX 1: Definition of the Calculated Contrasts and Uptake of Contrast Agent

$$\text{Contrast between ligament and CSF (STIR)} = \frac{\text{STIR intensity (ligament)} - \text{STIR intensity (CSF)}}{\text{STIR intensity (ligament)} + \text{STIR intensity (CSF)}}$$

$$\text{Contrast between ligament and CSF (VIBE native)} = \frac{\text{VIBE intensity (ligament)} - \text{VIBE intensity (CSF)}}{\text{VIBE intensity (ligament)} + \text{VIBE intensity (CSF)}}$$

$$\text{Contrast between ligament and CSF (VIBE after contrast agent)} = \frac{\text{VIBE intensity (ligament)} - \text{VIBE intensity (CSF)}}{\text{VIBE intensity (ligament)} + \text{VIBE intensity (CSF)}}$$

$$\text{Uptake of contrast agent by ligament} = \frac{\text{VIBE intensity (ligament after contrast agent)} - \text{VIBE intensity (ligament native)}}{\text{VIBE intensity (ligament native)}}$$

$$\text{Uptake of contrast agent by CSF} = \frac{\text{VIBE intensity (CSF after contrast agent)} - \text{VIBE intensity (CSF native)}}{\text{VIBE intensity (ligament native)}}$$