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ORIGINAL ARTICLE

Age-related changes to the craniocervical ligaments in asymptomatic subjects: a prospective MR study

Benjamin Peters[1,2] · Paul M Parizel[1,3] · Johan W Van Goethem[1,4]

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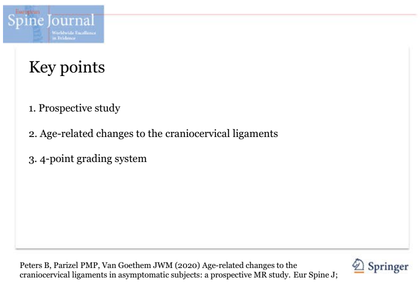
Abstract

Purpose The craniocervical junction (CCJ) is a complex of bony and ligamentous structure stabilizing CCJ. Nearly one-third of all traumatic injuries to the cervical spine involve the CCJ. Only little literature is available on this topic, and most of the studies are focused on anatomy, biomechanics or ligamentous injury in whiplash-associated disorders. We conducted a prospective study to investigate age-related changes in the craniocervical ligaments.
Methods We included asymptomatic volunteers between 16 and 99 years old who had no history of whiplash or other cervical trauma. Volunteers underwent a three-dimensional turbo spin-echo proton density-weighted sequence with variable flip-angle distribution focused on the craniocervical ligaments. The six main ligaments of the craniocervical junction were evaluated for grade of degeneration on a four-point scale by two independent readers, blinded for age and sex.
Results We included 102 volunteers. The mean age was 50.03 (16–94). Fifty-nine (58%) patients showed degeneration of at least one ligament of the CCJ. High-grade anomalous changes and multiligamentous involvement had a positive correlation with age ($p < 0.001$). The inter-rater agreement was fair to moderate, and the intra-rater agreement was moderate to substantial.
Conclusion The craniocervical ligaments show a variable degree of signal intensity and thickness in asymptomatic adults. We postulate that these changes can be due to normal aging or due to repetitive microtrauma. We propose a new grading system to evaluate changes to the craniocervical ligaments in asymptomatic volunteers.

Graphic abstract

These slides can be retrieved under Electronic Supplementary Material.



Key points

1. Prospective study
2. Age-related changes to the craniocervical ligaments
3. 4-point grading system

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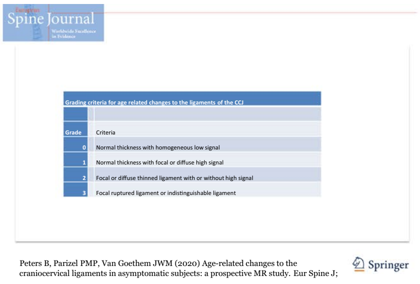

Grading criteria for age related changes to the ligaments of the CCJ

Grade	Criteria
0	Normal thickness with homogeneous low signal
1	Normal thickness with focal or diffuse high signal
2	Focal or diffuse thinned ligament with or without high signal
3	Focal ruptured ligament or indistinguishable ligament

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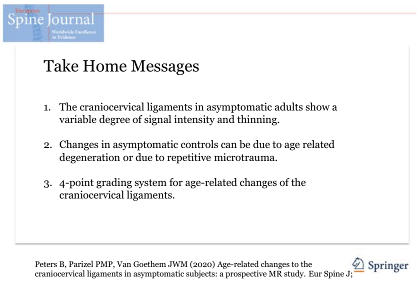

Take Home Messages

1. The craniocervical ligaments in asymptomatic adults show a variable degree of signal intensity and thinning.
2. Changes in asymptomatic controls can be due to age related degeneration or due to repetitive microtrauma.
3. 4-point grading system for age-related changes of the craniocervical ligaments.

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Keywords Craniocervical ligaments · Grading system · Degeneration · Age-related · MR · Prospective study · Whiplash-associated disorders

Introduction

The craniocervical junction (CCJ) is a complex of bony and ligamentous structures. It allows essential motion of the head in relation to the spine while safeguarding its content,

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✉ Benjamin Peters
Benjamin.Peters@jessazh.be

Extended author information available on the last page of the article

the spinal cord. The CCJ includes three bony elements, the occiput, the atlas (first cervical vertebra) and the axis (second cervical vertebra). These form the atlanto-occipital joints (C0–C1) and the atlanto-axial joints (C1–C2). Two symmetric atlanto-occipital joints arise between the atlas and the occipital condyles on both sides. The biomechanics of the atlanto-occipital joint is mainly determined by its bony structures [1, 2]. The atlanto-axial joint is composed of three elements: the midline atlanto-axial joint, between the atlas and the odontoid process and the lateral atlanto-axial joints, between the lateral mass of the atlas and the axis on both sides. The biomechanics of the atlanto-axial joint are primarily determined and limited by ligamentous structures [3]. The craniocervical ligaments are a complex of ligaments stabilizing the craniocervical joints while allowing significant mobility of the CCJ [3, 4]. The ligaments of the CCJ can be classified into intrinsic and extrinsic ligaments. The transverse and alar ligaments are the most important and strongest intrinsic ligaments [2, 5, 6]. The transverse ligament is located posterior of the odontoid process and attaches on the lateral tubercles of the atlas on both sides. The normal transverse ligament is 6–7 mm thick. The two alar ligaments run from the occipital condyles to the lateral aspect of the odontoid process. The thickness of a normal alar ligament is around 7 mm. The tectorial membrane is an intrinsic ligament forming an upward continuation of the posterior longitudinal ligament onto the clivus. The posterior atlanto-occipital ligament is an extrinsic ligament extending from the posterior arch of the atlas to the posterior rim of the foramen magnum [2, 3].

Whiplash injuries usually result from motor vehicle accidents (MVA), typically rear-end collisions. Whiplash-associated disorder (WAD) is the term for the ensuing clinical manifestation(s). WAD may result in chronic clinical symptoms and pain and carries a high medical care cost [2, 7]. The role of ligamentous lesions of the CCJ caused by whiplash injuries and the role of these lesions in WAD are strongly debated in the literature, with at least as many studies supporting this theory [8–13] as there are studies rejecting it [13–15]. However, little literature is available on the normal MR appearance of the ligaments of the CCJ, mostly part of a study as a control population compared to patients with WAD [8–15]. Moreover, most studies in a normal population are focused on the alar ligaments, neglecting the other ligaments of the CCJ [16–19]. Also the normal appearance of these ligaments in different age groups has not been studied. We performed a prospective study to evaluate the normal appearance of the CCJ ligaments in asymptomatic subjects [8] and we evaluated age-related changes to these ligaments, introducing a new and simple grading system (Table 1). This will allow further research, with more confidence, into possible lesions of these ligaments caused by whiplash injuries.

Table 1 Grading system to evaluate the craniocervical ligaments of the CCJ

Grade	Criteria
Grading criteria for age-related changes to the ligaments of the CCJ	
0	Normal thickness with homogeneous low signal
1	Normal thickness with focal or diffuse high signal
2	Focal or diffuse thinned ligament with or without high signal
3	Focal ruptured ligament or indistinguishable ligament

Materials and methods

Subjects

Our prospective study was approved by the ethics committee of our institution. The inclusion criteria of our study are composed of volunteers between 16 and 99 years old. The subjects of the study were recruited from patients that were scheduled for brain MRI not related to cervical problems. Subjects with acute or chronic cervical pain or with a history of whiplash or any other cervical trauma that needed medical attention were excluded. All subjects were included between February 2018 and October 2018. Informed consent was obtained from all individual participants included in the study.

Data acquisition

All MR examinations were performed with a dedicated neck coil on the same 3T MRI scanner (Siemens, Magnetom Prisma, Erlangen, Germany). The MRI protocol consisted of a three-dimensional turbo spin-echo intermediate proton density to T2-weighted sequence with variable flip-angle distribution (3D SPACE) focused on the craniocervical ligaments, with imaging acquisition parameters TR: 1000 ms, TE 34 ms and a voxel size of $0.64 \times 0.55 \times 0.73$ mm.

Analysis of MR images

Analysis was performed on a GE PACS running AW server with multiplanar reconstructions. The six main ligaments of the craniocervical junction were evaluated: right alar ligament, left alar ligament, right transverse ligament, left transverse ligament, tectorial membrane and posterior atlanto-occipital ligament. We split the transverse ligament in left and right, as the ligament can be affected differently on each side. All these ligaments were evaluated on a four-point scale 0–3: 0 (homogeneous low signal intensity with normal thickness), 1 (high signal intensity with normal thickness), 2 (reduced thickness) and 3 (full thickness rupture or indistinguishable from surrounding

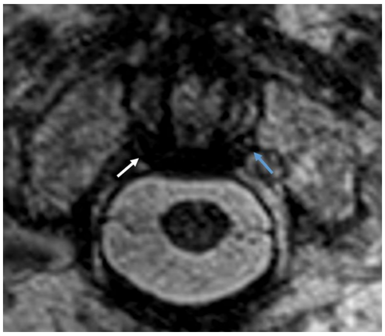

Fig. 1 Axial reconstruction of the transverse ligament shows a homogeneous hypointense signal, grade 0, in the right transverse ligament (white arrow) and a hyperintense lesion with normal ligamentous thickness, grade 1, in the left transverse ligament (blue arrow)

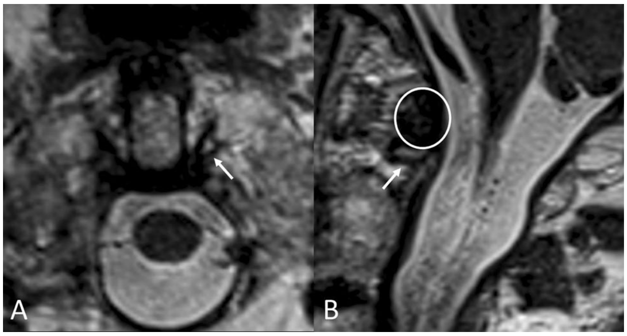

Fig. 2 Axial (**a**) and sagittal (**b**) reconstruction. **a** Hyperintense signal in and thinning, grade 2, of the left transverse ligament (white arrow). **b** The thinning of the transverse ligament (white arrow) compared to the normal thickness of the alar ligament (white circle). Note the small hyperintense lesion (grade 1) in the right transverse ligament in **a**

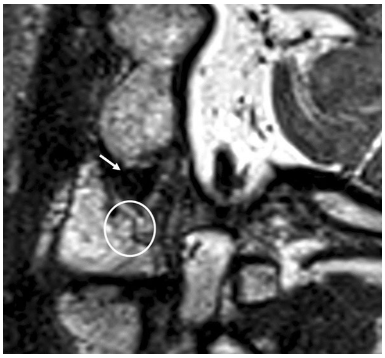

Fig. 3 Oblique reconstruction shows an absent transverse ligament, grade 3, on the lateral tubercle (white circle). Note the normal aspect of the alar ligament (white arrow)

structures) (Table 1, Figs. 1, 2, 3). Ligaments with a score of 0 were described as normal. Ligaments with a score of 1, 2 or 3 were described as anomalous. This can be due to degenerative changes, microtrauma or another etiology, whether that is normal or abnormal for age. All data were anonymized. Acquired images should be diagnostic for the evaluation of the craniocervical ligaments. All images were evaluated for diagnostic quality in consensus. Two independent readers (with 30-year and 4-year experience) evaluated each ligament, blinded for age and sex. Eight weeks prior to the first readout, the readers did a training session together of 20 random cases. After 6 weeks, reader 2 performed a second readout of all data to evaluate for intra-reader variability.

Statistical analysis

To perform statistical analysis, we used IBM SPSS Statistics 25. We performed a Spearman test to correlate age and changes to the ligaments of the CCJ. We used Cohen's kappa test to evaluate for inter- and intra-rater agreement. K values were interpreted as follows: $k < 0$ reflects poor agreement,' $k = 0–0.20$ 'slight agreement,' $k = 0.21–0.4$ 'fair agreement,' $k = 0.41–0.60$ 'moderate agreement,' $k = 0.61–0.8$ 'substantial agreement' and $k > 0.81$ 'almost perfect agreement.'

Results

One hundred and six subjects were scanned during the study period. Four studies were excluded due to severe motion artifacts and insufficient diagnostic quality. Fifty-one male and 51 female subjects were included. The mean age was 50.3 (16.04–94.29; standard deviation 19.25). Reader 1 evaluated 59 (58%) subjects with changes to at least one ligament, and reader 2 evaluated 68 (67%) with changes to at least one ligament. All readouts are found in Table 2. Reader 1 found 7 (7%) anomalous changes in the tectorial membrane, 1 (1%) anomalous change in the posterior atlanto-occipital ligament, 33 (32%) anomalous changes in the right alar ligament, 39 (38%) anomalous changes in the left alar ligament, 25 (25%) anomalous changes in the right transverse ligament and 24 (24%) anomalous changes in the left transverse ligament. In the first assessment, reader 2 found 13 (13%) anomalous changes in the tectorial membrane, 2 (2%) anomalous changes in the posterior atlanto-occipital ligament, 34 (33%) anomalous changes in the right alar ligament, 42 (41%) anomalous changes in the left alar ligament, 24 (24%) anomalous changes in the right transverse ligament and 29 (28%) anomalous changes in the left transverse ligament. Multiple anomalous changes and high-grade anomalous changes have a positive correlation with age ($p < 0.001$) for both readers. The inter-rater reliability

Table 2 A summary of all the readouts of the two different readers. Reader 2 evaluated all the ligaments a second time (2B) with an interval of 6 weeks. The inter- and intra-rater agreement was calculated

	Reader 1	Reader 2A	Reader 2B	*K* value Inter	*k* value Intra
Tectorial membrane				0.509353	0.605501
0	95	89	89		
1	6	13	12		
2	1	0	1		
3	0	0	0		
AOP				0.328947	0.488294
0	101	100	98		
1	0	2	3		
2	1	0	1		
3	0	0	0		
Alar right				0.493377	0.683476
0	69	68	62		
1	31	28	36		
2	2	6	4		
3	0	0	0		
Alar left				0.516862	0.628415
0	63	60	58		
1	35	38	37		
2	4	4	7		
3	0	0	0		
Transverse right				0.504132	0.517910448
0	77	78	77		
1	13	17	21		
2	9	7	3		
3	3	0	1		
Transverse left				0.39782	0.54393
0	78	73	76		
1	12	19	17		
2	9	8	7		
3	3	2	2		

was moderate ($k=0.51$) for the tectorial membrane, fair ($k=0.33$) for the atlanto-occipital ligament, moderate ($k=0.49$) for the right alar ligament, moderate ($k=0.49$) for the left alar ligament, moderate ($k=0.50$) for the right transverse ligament and fair ($k=0.4$) for the left transverse ligament. The intra-rater reliability was substantial ($k=0.61$) for the tectorial membrane, moderate ($k=0.49$) for the atlanto-occipital ligament, substantial ($k=0.68$) for the right alar ligament, substantial ($k=0.63$) for the left alar ligament, moderate ($k=0.52$) for the right transverse ligament and moderate ($k=0.54$) for the left transverse ligament.

Discussion

Changes in the ligaments of the CCJ are of great interest in patients with cervical trauma and especially in patients with chronic WAD [7]. The MR appearance of the morphology and signal intensity of the ligaments of the CCJ has been investigated in previous studies. Most studies evaluated the alar ligaments alone for orientation, morphology and signal intensity. Healthy volunteers were usually recruited as part of a control group for patients with WAD, where the mean age was relatively low [16, 17, 19]. In our study, the mean age was 50.3 with a wide range (16.04–94.29), which is relatively high compared with previous studies. A recent study by Wenz et al. investigated the signal changes in the alar ligaments in a healthy population, suggesting that dispositional factors are important in fat-related hyperintensities [17]. In our study, we studied the MR appearance of the six main ligaments of the CCJ often involved in WAD in an asymptomatic population without recollected prior cervical trauma and without acute or chronic cervical pain. In previous studies, the alar ligaments were evaluated for signal intensity based on maximal cross-sectional involvement in sagittal images going from grade 0, low signal throughout the entire cross section, to grade 3, high signal in 2/3 or more of the cross section [17, 20, 21]. We assessed the ligaments for signal intensity and thickness on a new four-point scale (Table 1), comparable with grading systems of other ligamentous structures [22]. Both readers observed the most changes in the alar ligaments (32–41%) and the transverse ligaments (24–28%), whereas the tectorial membrane (7–13%) is less frequently affected and the posterior atlanto-occipital ligament (1–4%) is rarely affected. Of all affected ligaments, grade 2 (7–9%) were most frequently seen in the transverse ligament. Grade 3 anomalous changes were only observed in the transverse ligament (1–3%) (Table 2). High-grade anomalous changes and multiligamentous anomalous changes had a positive correlation ($p < 0.001$) with age for both readers. The alar and transverse ligaments are known to be the strongest and most important stabilizing ligaments of the CCJ [3]. We postulate that the observed changes to the ligaments are due to age-related degeneration or repeated microtrauma. This is supported by the correlation between grading and age. The inter-rater agreement is moderate for the tectorial membrane, the alar ligaments and the right transverse ligament. The left transverse ligament showed only a fair ($k = 0.40$) agreement which is close to moderate agreement, and this difference with the other ligaments can be due to our relative small sample size. The inter-rater agreement of the posterior atlanto-occipital ligament is statistically low, due to the small amount of anomalous changes encountered. The intra-rater agreement is in general higher than the inter-rater agreement for all ligaments and is highest (substantial agreement) for the tectorial membrane and both alar ligaments. The inter- and intra-rater agreement of the alar ligaments is higher than that of the transverse ligaments. A possible explanation is the better visualization of the alar ligaments which are usually surrounded by more fat than that of the transverse ligaments and thus better distinguished from surrounding structures. The inter- and intra-rater agreement in our study is higher compared to that in other recent studies evaluating the signal intensity of the ligaments of the CCJ [17, 19, 23]. This can be due to several possible reasons. First, both readers did a training session together 8 weeks prior to the readouts. Second, recent studies evaluated the ligaments of the CCJ on 2D sequences. As it is known, the ligaments of the CCJ have different orientations, especially the alar ligaments, and grading on 2D sequences can be influenced by partial volume effect [24]. We evaluated each ligament on a 3D sequence with multiplanar and oblique reconstructions at hand to avoid partial volume effect. Third, several studies evaluated the ligaments of the CCJ on relatively low field strengths. It is known that the signal-to-noise ratio and the spatial resolution increase with the field strength and thus the delineation of the ligaments improves with higher field strength [18]. We performed all investigations on the same 3T MR scan (Siemens, Magnetom Prisma, Erlangen, Germany). Last, we used a different grading system. In most studies, the ligaments were evaluated as proposed by Krakenes et al. subdividing the ligaments in thirds and changes in intensity were evaluated throughout those parts [11]. The inter-rater agreement in studies using this grading system is usually low [17–19, 23]. One can imagine it is rather difficult to subdivide a small ligament in thirds and differentiate the appearance of signal intensity throughout those parts. Although this grading system can be useful to evaluate ligaments for posttraumatic changes, we tried to simplify the grading system to evaluate the ligaments of the CCJ similar to ligamentous changes in other parts of the body (Table 1) [22].

The limitations of our study are the relative small sample size, and our findings should be verified by larger cohorts. We used an intermediate proton density to T2-weighted 3D SPACE technique which does not differentiate between high intensity due to edema or due to fat infiltration and thus thinned ligament [24]. With an additional fat suppression, centrally located high-signal anomalous changes due to fatty infiltration could resolve in a grade 2 anomalous changes; thus, more high-grade anomalous changes could potentially be detected [17, 25]. We did not do a longitudinal follow-up of our volunteers. A longitudinal follow-up with large intervals could better demonstrate ligamentous changes due to aging. In conclusion, we established the normal appearance of the CCJ ligaments and their changes with age in an asymptomatic population. We established a correlation between age and changes to the ligaments probably reflecting normal degeneration and/or expected sequelae of microtrauma.

Conclusion

The craniocervical ligaments in asymptomatic adults show a variable degree of signal intensity and thinning. These changes are more common in elderly adults compared to young adults, showing a significant statistical relationship between age and ligamentous changes in the craniocervical ligaments. High-grade ligamentous anomalous changes, with partial rupture or complete rupture of the CCJ ligaments, were rare in asymptomatic volunteers. We postulate that these changes in asymptomatic controls can be due to age-related degeneration or due to repetitive microtrauma that were not recollected by the asymptomatic volunteers on questioning. We propose a new four-point grading system, comparable to ligamentous grading systems in other parts of the body, for age-related changes in the craniocervical ligaments. Knowledge of degenerative changes to the craniocervical ligaments is important in order to be able to differentiate age-related ligamentous changes and posttraumatic changes in patients with WAD or other trauma to the CCJ.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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Affiliations

Benjamin Peters[1,2] · **Paul M Parizel**[1,3] · **Johan W Van Goethem**[1,4]

[1] Department of Radiology, Antwerp University Hospital, University of Antwerp, Antwerp, Belgium

[2] Department of Radiology, Virga Jessa Hospital, Hasselt, Belgium

[3] David Hartley Chair of Radiology, Royal Perth Hospital (RPH), University of Western Australia (UWA), Perth, WA, Australia

[4] Department of Radiology, AZ Nikolaas, Sint-Niklaas, Belgium