

CLINICAL ASPECTS IN THE LATE STAGE OF WHIPLASH INJURY

Bertel Rune Kaale



Department of Surgical Sciences, University of Bergen.

2009

1.0	ACKNOWLEDGEMENTS	4
2.0	LIST OF PAPERS	6
3.0	INTRODUCTION	7
3.1	<i>The whiplash syndrome (WAD)</i>	7
3.2	<i>Existing models for the understanding of the chronic whiplash syndrome</i>	9
3.2.1	Organic models - biomechanical mechanisms	9
3.2.2	Psychosocial models	10
4.0	AIMS OF STUDY	12
4.1	<i>The biomechanics of the cranio-cervical junction</i>	12
4.1.1	The ligaments	13
4.1.2	The membranes	14
5.0	MATERIAL AND METHODS	15
5.1	<i>Study population</i>	15
5.1.1	Random selection of WAD patients	15
5.1.2	Random selection of control persons	16
5.2	<i>The questionnaires and the clinical tests</i>	18
5.2.1	The NDI questionnaire	18
5.2.2	The AROM test and the clinical test of passive mobility	19

5.3	<i>The MRI examinations</i>	20
5.3.1	Blinded MRI evaluations	20
6.0	RESULTS	22
6.1	<i>Article 1</i>	22
6.2	<i>Article 2</i>	22
6.3	<i>Article 3</i>	23
6.4	<i>Article 4</i>	24
7.0	DISCUSSION	26
7.1	<i>Additional information on study participants</i>	27
7.1.1	The patient group	27
7.1.2	The time of the injury	28
7.1.3	The control group	29
7.2	<i>Validity and reliability of clinical methods and patient-given information</i>	30
7.2.1	Neck Disability Index Score (NDI)	30
7.2.2	Head position and impact direction	31
7.2.3	Active range of motion (AROM)	32
7.2.4	Clinical assessment based on manual therapy techniques	34
7.2.5	Stressful life events and personality as parameters in predicting the duration and severity of symptoms after a whiplash trauma	36

7.2.6 MRI method	36
7.3 General discussion of results	39
7.3.1 Associations between MRI-findings and clinical symptoms	39
7.3.2 MRI-verified lesions, WAD vs. control	41
7.3.3 Additional evidence for ligament and membrane injury	42
7.3.4 Associations between MRI findings and accident related factors	42
8.0 SUMMARY AND CONCLUSIONS	45
9.0 PERSONAL REMARKS	45
10.0 REFERENCES	46

1.0 ACKNOWLEDGEMENTS

This research has given me a thorough introduction to project work. Furthermore, I have been inspired to continue working with scientific research related to clinical issues.

The planning of this project started already in 1991. I realize now, 18 years later, that my eagerness, curiosity, and will at that time were stronger than my scientific background. The registration of the whiplash material started before my master study, before the results from the QTF (Spitzer et al. 1995), before the MRI technology was well enough developed for this purpose, and before many medical doctors even knew what whiplash really was. Also, many medical doctors were not familiar with the anatomical structures in the upper cervical spine that this project would like to assess. All the registration work was done without any expert help or guidance throughout the process.

This pilot project was performed without any external financial founding. From 1999 and until today I have been a PhD student at the University of Bergen. I have been given all the support through excellent co-workers and unlimited use of the Haukeland University Hospital's MRI equipment. The Haukeland University Hospital (HUH) and the University of Bergen (UoB) have given the project full support during the entire study period.

Great thanks to my co-worker Jostein Kråkenes, who has followed this work from the early beginning. His enthusiasm and personal support, as well as his excellent medical knowledge, has been an important part of my work and my life during the last fourteen years.

Statistician Grethe Albrektsen has given me invaluable statistical support. Her deep insight in statistical analysis and advice regarding such analyses has been an important part of this work. As my second supervisor, she has suffered a considerable workload by her important contributions to this work.

Especially, I will give honour to my first supervisor, Professor Knut Gustav Wester, Institute of surgical sciences, UoB and Department of Neurosurgery, HUH. His great experience

and his extraordinary patience has given me personal growth, lifted my scientific thinking, and made this work come true.

I am also in debt to all the doctors that participated in the recruiting of the patients. We share a common hope that our work will bring the whiplash challenge one step forward.

Finally, my thoughts go to my dear wife, four sons and one daughter for continuous support. Now, it's my turn to reflect love and patience, give care, and to show me as the husband and father I was supposed to be.

2.0 LIST OF PAPERS

Article 1

Kaale BR, 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(4):466-75.

Article 2

Kaale BR, Krakenes J, Albrektsen G, Wester K.

Head position and impact direction in whiplash injuries: associations with MRI-verified lesions of ligaments and membranes in the upper cervical spine. J Neurotrauma. 2005;22(11):1294-302.

Erratum in: J Neurotrauma. 2006;23(6):1048.

Article 3

Kaale BR, Krakenes J, Albrektsen G, Wester K.

Active range of motion as an indicator for ligament and membrane lesions in the upper

Cervical spine after a whiplash trauma. J Neurotrauma 2007;24(4):713-21.

Article 4

Kaale BR, Krakenes J, Albrektsen G, Wester K.

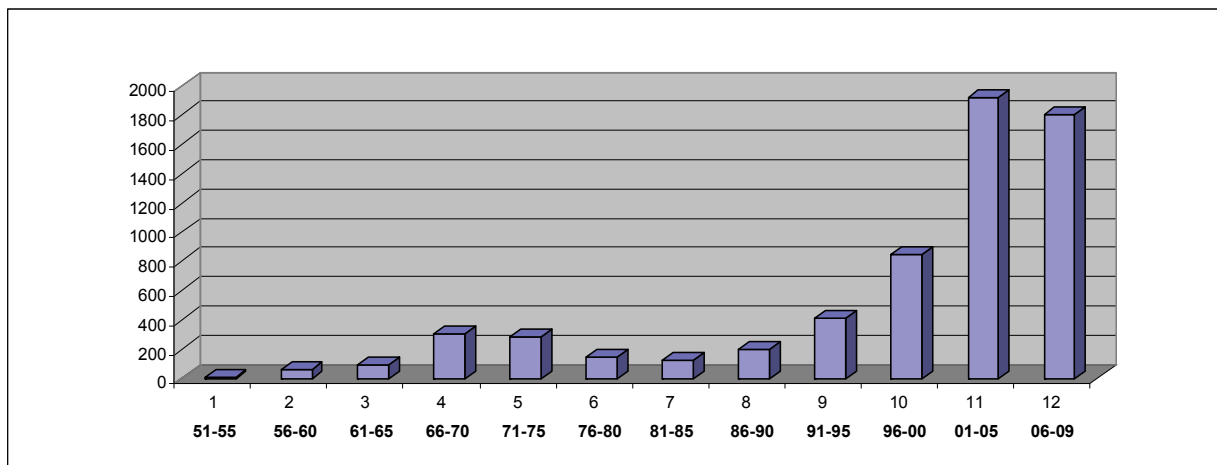
Clinical assessment techniques for detecting ligament and membrane injuries in the upper cervical spine region - a comparison with MRI results. Man Ther. 2008 Oct;13(5):397-403.

3.0 INTRODUCTION

3.1 *The whiplash syndrome (WAD)*

Harold Crowe was the first to use the term “whiplash” in 1928 to describe the manner in which the head is moving to produce a neck sprain (Crowe 1928). The term “whiplash injury” appeared for the first time in a medical journal in 1953 (Gay et al. 1953). Since 1951 and until today there are registered approximately 6200 scientific articles on the term “whiplash”. The interest in the whiplash syndrome has exploded over the last years, as judged by the number of publications revealed by a literature search (PubMed, February 2009: “Whiplash”). More than 4500 are published after 1996, above all after 2001 (Figure 1). Earlier studies, from the nineteen-seventies until the -nineties, focused mainly on in vitro studies, biomechanical laboratory testing and histological studies (Fielding et al. 1974, Dvorak et al. 1987 a, b and c, Dvorak et al. 1998, Saldinger at al. 1990, Panjabi et al. 1991 a, b), whereas an increasing number of studies focusing on psychosocial stress and cognitive and psychosocial aspects related to the late whiplash syndrome appeared from the nineteen-nineties (Van der Donk et al. 1991, Schrader et al. 1996, Karlsborg et al. 1997, Richter et al. 2004, Kivioja et al. 2004).

Figure 1: Number of publications found in a literature search (1951 – January 2009) on PubMed. Search word: whiplash.



Radanov described in 1992 two different groups of syndromes after whiplash injuries. One syndrome was called the “cervicocephalic syndrome”, characterized by headache, balance problems, disturbed accommodation, poor concentration, increased sensitivity to light, and pronounced fatigue. The other syndrome was called the “lower cervical syndrome” and was characterized by cervical and cervico-brachial pain. Radanov argued that whiplash associated disorders had not been recognized in clinical practice, as the clinicians often did not enquire about changes of the cranio-cervical complex when they referred a patient for further radiological or neurological examinations (Radanov et al. 1992).

The Québec Task Force presented their widely accepted definition of whiplash in 1995. They found from reviews of the literature a great heterogeneity of definitions and classifications of all aspects related to WAD. They concluded that this syndrome was an acceleration-deceleration mechanism of energy transfer to the neck. This mechanism could result in bony or soft tissue injuries, which in turn may lead to a wide variety of clinical manifestations. The Quebec Task Force Classification divided whiplash-associated disorders (WAD) into 5 groups (Table 1) (Spitzer et al. 1995):

Table 1. Clinical Classification of Whiplash-Associated Disorders

<u>Grade</u>	<u>Clinical presentation</u>
0	No complaint about the neck. No physical sign(s)
1	Neck complaint of pain, stiffness or tenderness only No physical sign(s)
2	Neck complaint and musculoskeletal sign(s) ^a
3	Neck complaint and neurological sign(s) ^b
4	Neck complaint and fracture or dislocation

a Musculoskeletal signs include decreased range of motion and point tenderness

b Neurological signs include decreased or absent deep tendon reflexes, weakness and sensory deficits

(Spitzer et al. 1995).

3.2 Existing models for the understanding of the chronic whiplash syndrome

The underlying causes of symptoms and complains among WAD patients are not well known or understood. Both psychosocial and organic models have been proposed and most previous studies have focused on either of these two main models. Probably, both organic and psychosocial mechanisms may be at work, as it is in most patients with chronic pain (Hulsebosch et al. 2008, Jenewein et al. 2009). It is beyond the scope of this thesis to give a full account of all launched theories and models. However, a few aspects and models will be dealt with briefly below.

3.2.1 Organic models - biomechanical mechanisms

Clinical studies, in vitro studies, biomechanical laboratory testing, radiological studies and histological studies have over time focused on soft tissue injuries in the cranio-cervical junction as a possible consequence after a whiplash trauma (Fielding et al. 1974, Dvorak et al. 1987 a, b and c, Dvorak et al. 1998, Saldinger et al. 1990, Panjabi et al. 1991 a and b, Bogduk et al. 2001, Krakenes et al. 2001, 2002, 2003 a, b, Myran et al. 2008). Adams has in fatal cases demonstrated that serious neck injury with atlanto-occipital and atlanto-axial dislocations occur

in traffic accidents (Adams 1992 a and b). These authors focused on specific soft tissue lesions as a possible explanation for the long lasting consequences in chronic whiplash syndromes. The work by the Québec Task Force group emphasized this possibility of an organic origin to the chronic whiplash syndrome (Spitzer et al. 1995). The biomechanical “limit of harmlessness” in two-car rear-end collisions is assumed to be a velocity change due to the collision of between 10-15 km/h. Morphological and anatomical signs of injury to the cervical spine have not been demonstrated below this change of speed range (Castro et al. 1997).

Studies have demonstrated that nerve root compressions after whiplash injuries can produce pain. Such nerve root compression can mediate nociceptive cellular changes, and thresholds for pain and nociceptive pathophysiology may be lower after neck injuries (Rothman et al. 2005, Hubbard et al. 2008). Injuries to the brainstem and the circulatory system after whiplash injuries have also been demonstrated by Endo et al. Vertebrobasilar artery insufficiency may lead to cervical vertigo and dizziness after whiplash injuries (Endo et al. 2006).

3.2.2 Psychosocial models

Several researchers have focused on psychosocial aspects as a possible explanation of the chronic whiplash syndrome. Psychosocial factors may influence the posttraumatic course after a whiplash injury in at least two different ways, either by a premorbid personality that makes the patient more susceptible to develop chronic pain, or a change of the personality in a negative direction caused by the chronic pain. It appears difficult to distinguish with any certainty between these two possibilities (Van der Donk et al. 1991). The work done by the Québec Task Force in 1995 focused on a possible psychosocial model together with an organic model for the understanding of the whiplash syndrome (Spitzer et al. 1995).

Results from other studies have given some support to the psychosocial explanation model for WAD2. Schrader and co-workers studied the natural course of head and neck

symptoms after rear-end car collision in Lithuania. They concluded that the chronic symptoms were usually not caused by the car accident. On the contrary, they argued that expectation of disability, a family history, and symptoms existing prior to the trauma may be more important determinants for the evolution of the late whiplash syndrome than organic changes caused by the accident (Schrader et al. 1996). Karlsborg et al. was of the opinion that the acute symptoms after whiplash traumas can be explained by the neck sprain, but that the pathogenesis of the “late whiplash syndrome” and the reasons why only some people have persistent symptoms after more than 6 months remain unknown. They concluded that long-lasting distress and poor outcome after a whiplash trauma were more related to the occurrence of stressful life events than to clinical findings after neck trauma (Karlsborg et al. 1997). Richter et al. later supported this understanding. They focused on prognostic factors for the duration and severity of acute symptoms in subjects with grade 1 or 2 whiplash injuries. They found no correlation between severity and duration of symptoms and collision parameters, and concluded that psychological factors were found to be more relevant than collision parameters in predicting the duration and severity of symptoms (Richter et al. 2004).

Kivioja et al. have compared psychiatric morbidity between two groups: patients having chronic symptoms after a whiplash injury and patients who recovered completely. Their results showed that a history of psychiatric disease or stress was more common in patients with chronic neck and head symptoms after a whiplash trauma; therefore they concluded that psychiatric morbidity might be a patient-related risk factor for the development of chronic symptoms after a whiplash injury (Kivioja et al. 2004).

4.0 AIMS OF STUDY

The aim of the present study was to explore the possibility that symptoms and signs, and also abnormal neck movements in WAD patients, could be related to organic changes in the cranio-cervical region, as judged by MRI. We also explored whether the MRI-verified changes could be related to accident-related factors among WAD patients (Krakenes et al. 2002, 2003a, b).

A total of five different neck structures assumed to be particularly vulnerable to forces acting during a whiplash episode were evaluated. A brief description of the anatomical function of these structures may be helpful and is therefore given below.

4.1 *The biomechanics of the cranio-cervical junction*

The following is an attempt to explain some of the basic principles underlying the biomechanics of the cranio-cervical junction, with special emphasis on the 5 structures studied in the present thesis: the left and right alar ligaments, the transverse ligament, the tectorial membrane and the posterior atlanto-occipital membrane.

Ligaments are in general less elastic than membranes, as the content of collagen fibres is higher in ligaments. This applies also to the structures studied here. The tectorial membrane is a broad, strong band. Also the atlanto-occipital membrane is broad, but much thinner compared with the tectorial membrane (Williams et al. 1980). The ligaments and membranes may affect the function in the cranio-vertebral junction in two possible ways. They may limit the excursions in the joints simply by acting as passive restraints, or they may affect the function through their proprioceptive innervation, and thus indirectly modify the active movements in the region.

Lesions to ligaments elsewhere in the body may contribute to local pain and disturbance of coordination and proprioception. Human ligaments may vary, also between individuals, with variations in density and pattern of distribution of nociceptors and mechanoreceptors

(Cavalcante et al. 2004, Hagert et al. 2005, Tamai et al. 1999, Petrie et al. 1998, Schutte et al. 1987). This may give individual differences in pain and biomechanical dysfunction after a soft tissue lesion. (Cavalcante et al. 2004, Hagert et al. 2005, Morisawa 1998, Schutte et al. 1987, Tamai et al. 2000, Petrie et al. 1998, Mashoof et al. 2001).

Stability of the spine and specifically the cranio-cervical junction is one of the major objectives during a neck trauma (Dvorak et al. 1988). In the cranio-cervical junction, the alar and transverse ligaments provide much of this stability. The alar ligament restrains rotation, flexion and side bending, whereas the transverse ligament restricts flexion as well as anterior displacement of the atlas (Dvorak et al. 1987, 1988).

4.1.1 The ligaments

The alar ligaments and the transverse ligaments are very strong, with an approximate in vitro strength of 200 N and 350 N respectively (Dvorak et al. 1987, 1988). The alar ligament is stretched, and thus possibly more vulnerable to overstretching, when the head/neck is rotated and in addition flexed. A neck trauma could lead to irreversible overstretching or rupture of the ligaments since they consist mainly of collagen fibres (Dvorak et al. 1987, 1988). An in-vitro study from Tominago et al. investigated the strength of neck ligaments following a whiplash trauma, with the aim to determine the dynamic mechanical properties of whiplash-exposed human cervical spine ligaments. Bone-ligament-bone specimens were tested. They investigated the anterior and posterior longitudinal ligaments, capsular ligaments, interspinosus and supraspinous ligaments and the flavum ligament. The results showed that neck ligament strength was decreased following a whiplash trauma. They concluded that this decrease in ligament strength provides support for the ligament-injury hypothesis of the whiplash syndrome (Tominago et al. 2006). Panjabi et al. came to the same conclusions. They tried to quantify the strains in the cervical spine ligaments during simulated frontal impact and investigated the injury mechanisms. They focused on the supraspinosus and interspinosus ligaments and the

flavum ligament. Their results indicated that excessive strain during frontal impacts puts strain on ligaments, and that the investigated ligaments therefore may be at risk for injury (Panjabi et al. 2004).

4.1.2 The membranes

The passive stability in the cranio-cervical junction provided by the cranio-cervical membranes is not well defined. Farley supports the idea that the tectorial membrane is a primary stabilizer of the occiput-C2 region (Farley et al. 2005), implying that injury to this specific membrane will induce instability in this region. There is also some evidence that damage to the posterior atlanto-occipital membrane may influence the posterior aspect of the cranio-cervical stability (Zumpano et al. 2006, Nash et al. 2005).

5.0 MATERIAL AND METHODS

These aspects are described under the same heading in the 4 separate publications of this thesis. More details on the process behind the inclusion of patients and controls persons, and other aspect in the Material and Methods chapters are given below.

5.1 *Study population*

This study comprises information about 92 persons with a diagnosis of whiplash-associated disorder, grade 2 (Quebec Classification of Whiplash-Associated Disorders - Spitzer et al., 1995) and 30 control persons. The study has been approved by The Regional Committees for Medical Research Ethics and The National Data Inspectorate Board.

5.1.1 Random selection of WAD patients

The WAD-2 patients included in this study was a randomly drawn sample of persons diagnosed with WAD-2 after being involved in a car accident in 7 communities in the county of Sogn and Fjordane, Norway during the period 1992 to 1998. The diagnosis was set by local physicians. A total of 342 persons had been diagnosed during this period. These 342 persons were referred to Firda medical centre shortly after the medical assessment for treatment by a physiotherapist.

The WAD-2 inclusion criteria were neck complaint and musculoskeletal signs after the consensus findings in Quebec in 1995. The diagnosis was based on symptoms and signs after a car accident. A final establishment of the diagnosis was made after 12-16 weeks, ensuring that only patients with chronic symptoms were recorded. Plain X-rays of the neck were normal and no patient had neurological deficits. During the period from 1992 to 1995, and thus before publication of the Quebec consensus (Spitzer et al 1995), the medical doctors followed the

criteria from Hirsh et al. and Norris et al. (Norris et al. 1983, Hirsch et al. 1988). The grading system of Norris et al. is very similar to the QTF classification system. The classification according to Norris et al. has only 3 groups, with neurological signs only in group 3, while the QTF grading have four groups, with neurological deficits in groups 3 and 4.

At time of diagnosis, and thus shortly after the accident, all the WAD patients completed a questionnaire on accident-related factors. The patients were asked to give information on whether they had been sitting with the head/neck turned to one side at the time of impact or not, and also on the direction of impact, that is whether the car was hit in front or from behind. Only patients who were able to give information on these aspects of the accident were included in the study. Moreover they were instructed to report date of the accident, and report on any occurrence of prior car accidents. The questionnaire was completed at the medical office or at the first visit at Firda physiotherapy centre (Attachment 1).

In 1999, the final recruitment of study participants took place. Of the initial 342 eligible patients, a total of 45 were excluded because information on accident-related factors was missing or incomplete, they had sustained a previous neck injury, or they had been sitting in the back seat. Of the remaining 297 eligible WAD-2 patients, a total of 100 individuals, 50 randomly drawn from each of the two groups defined by neck position, were invited to participate in the study. Information about the research project was attached (Attachment 2). Of the 100 invited persons, a total of 93 gave their informed consent to participate, whereas 7 rejected or did not answer.

5.1.2 Random selection of control persons

A total of 300 persons that fulfilled pre-defined inclusion criteria for serving as control, were identified. Inclusion criteria were that the persons had been treated by a manual therapist at Firda Medical Center (FMC) for conditions unrelated to neck problems during the same period as the recording and inclusion of the WAD patients (1992-98). Exclusion criteria for the control

group were any known previous neck injury or neck complaints. On an initial annual list we ranked all patients in the order they had arrived at the medical center. To secure a chronologically even distribution, we tried to include approximately 40 - 50 eligible persons every year. The number of selected controls each year was not completely equal, since the diagnostic system in our software before 1995 had more diagnoses that were less specific, such as “myalgia” and “muscle-skeleton dysfunction”. We excluded persons with such non-specific diagnoses, since they could imply that the person also had neck problems. We also category matched on gender, that is we selected the same proportion of males and female patients as in the total population of 297 eligible WAD patients. No specific routines were followed to get a similar age distribution. FMC had the only manual therapist in the county of Sogn and Fjordane at that time, and the control persons were thus recruited from the same geographic area as the WAD patients.

A total of 100 individuals, randomly drawn from the list comprising 300 names, received a preliminary request about participation in the study, together with information about the research project, and a question on whether they had experienced a neck trauma since the previous treatment sessions. Of 75 control persons that were willing to participate, 5 had been exposed for a WAD trauma. A final control group comprising 50 individuals was then randomly drawn from the 70 eligible control persons without neck trauma, and a final invitation for participation was sent out. Of these 50 persons, a total of 38 agreed to participate, whereas 12 gave a negative or no answer.

In our original study protocol, we planned to draw control persons from the general population in the county of Sogn and Fjordane. For practical reasons, however, partly related to a time delay caused by reduced capacity within Statistics Norway for selecting control persons, we were advised to select control persons from a specific patient population instead. Unfortunately, the description of the control material was not updated when the first paper

(Kaale et al. 2005a) was published. However, an erratum has been published, together with a conflict of interest statement (Kaale et al. 2006; enclosed as attachment to Article no. 1).

5.2. The questionnaires and the clinical tests

It was the intention of the study to approach the WAD complex from different points of view, with the hope of exposing important clinical aspects of the condition. Some aspects of these methods will be presented below.

The 93 WAD patients and the 38 control person who had agreed to participate in the study were assigned a date for clinical examination as well as MRI. The clinical testing of passive mobility of neck, as well as the tests for active range of motion in different directions (AROM), was performed on the same day, and 4-6 days before the MRI assessment. All these test procedures and collection of data on clinical symptoms were performed during the period September 1999 to March 2000. Eight of the control persons (7 men and 1 woman) did not show up on the MRI examination day. Moreover, due to a claustrophobic condition that made it impossible to perform an MRI examination, one of the WAD patients was later excluded. The final study population thus comprised 92 WAD-2 patients and 30 control persons. The mean time from the collision to the MRI examination was 6 years (range 2.0-9.0 years).

5.2.1 The NDI questionnaire

The participants completed and returned the neck disability index (NDI) questionnaire at the time of the clinical examination (Attachment 3). This questionnaire was a modification of the Oswestry Low Back Pain Index translated into Norwegian, comprising 10 single items related to activity of daily living. The scores reflected self experienced and self reported degree of neck pain and/or difficulties with performing certain activities due to neck

pain. The participants completed and returned the neck disability questionnaire at the time of the clinical examination, i. e. 1 – 9 years after the accident.

5.2.2 The AROM test and the clinical test of passive mobility

These clinical tests were performed on the same day, a few days before the MR examination. For three persons, who became worse after testing, we had to postpone the MRI examination, which however took place within 2 weeks. The goal with the clinical tests was to find out if they could be used as indicators for soft tissue lesions in WAD patients. The clinical test attempted to assess the passive mobility in the upper cervical spine, by testing specific ligaments and membranes. The test of active range of motion (AROM) focused on active movements, to see if they were restricted or if the WAD patients had larger movement ranges than normal controls.

The test of active range of motion (AROM) focused on the ROM as a possible indicator for increased or reduced total cervical ROM as a consequence after a neck trauma. Five WAD patients and 1 control person got more severe symptoms in the head and neck after a manual pre-testing, and did therefore not undergo the subsequent AROM testing. The number of study participants in the paper presenting results from AROM (Kaale et al. 2007) thus differs slightly from the other papers.

The two tests were performed a few days before the MR examination. For three persons, who became worse after the AROM test and the clinical test for passive mobility, we had to postpone the MRI examination, which however took place within 2 weeks. Another five persons belonging to the WAD2 group and one person in the control group got more severe symptoms in the head and neck after a manual pre-testing, and did therefore not undergo the subsequent AROM testing.

5.3 The MRI examinations

The MRI examinations were performed during the period September 1999 to March 2000. All participants underwent MRI with a 1.5 T system (Magnetom Vision; Siemens Medical System, Erlangen, Germany). A standard head coil was used, and all images were obtained with the head and neck in a neutral position. More details about the MRI protocol and reliability of the MRI assessments are given elsewhere (Krakenes et al. 2001, 2002, 2003a, b) and will not be repeated here. The mean time and time range from the collision to the MRI examination varied between 6 years (range 2.0-9.0 years) and 5.7 years (range 1.9-9.0). The reason for this difference was that fewer patients were included in Article 3, see above.

The MRI examinations were in general performed within 1 week after the clinical tests. However, three persons felt bad after AROM test and clinical testing, and we had to postpone the MRI assessment, which took place within 2 weeks.

5.3.1 Blinded MRI evaluations

All MRI evaluations were performed blinded for study groups as well as for results for the clinical tests. The manual therapist (BRK) that performed the clinical testing was not blinded for study group, but was blinded for the MRI results.

Thus, the comparisons of NDI-score between WAD patients and control persons were blinded for study group, as were the analyses of possible associations between NDI-score and the severity of MRI findings among WAD patients (Kaale et al. 2005a). Moreover, the comparisons of MRI results between WAD patients and control persons, and according to accident-related factors (Kaale et al. 2005b), were also performed blinded for study group. The comparison of AROM between WAD patients and control persons (Kaale et al. 2007) however, was not blinded for study groups since the clinical testers had been the patients' therapists. When relating AROM to severity of MRI findings among WAD patients, however, the analyses were blinded for study group. When evaluation reliability of the clinical test, using MRI as gold

standard (Kaale et al. 2008), in joint analyses of results for WAD patients and controls, classifications made by the two raters were mutually blinded.

6.0 RESULTS

Detailed accounts of the results are given in the included 4 articles. Here only brief summaries will be given.

6.1 Article 1

In the first study we examined if WAD patients differed from control persons regarding symptoms and level of daily living as represented by a Neck Disability Index (NDI) score. We also examined if there were associations between self-reported symptoms, and the extent of changes in the MRI signals of the included structures, and whether WAD patients differed from control persons in these respects. Our results showed that WAD patients scored significantly higher on the 10 single items in the neck disability index (NDI) score than the control persons did. The difference was particularly pronounced for problems with neck pain, reading, headache, concentration, car driving, and overall activity level.

Among the WAD patients, the NDI score increased significantly with increasing severity of MRI abnormalities of the alar ligaments. For the other included structures: the transverse ligament, the posterior atlanto-occipital membrane, or the tectorial membrane, we did not find any significant association between the NDI scores and the observed MRI changes. However, the disability score increased with increasing number of abnormal (grade 2-3) structures among the WAD patients.

6.2 Article 2

In the second study we examined whether the MRI findings were associated with accident-related factors hypothesised to be of importance for severity of the injury.

Our results showed for all neck structures considered, that the chronic whiplash patients had significantly more MRI high-grade changes than the controls. Changes in the alar ligaments were most common; as 66% of the patients had pronounced MRI changes (grades 2 or 3) in this structure. The lowest prevalence of high-grade MRI changes was seen for the tectorial membrane. None of the control persons had the most pronounced MRI change (grade 3) in any of the 5 investigated structures, but grade 2 change was observed for the alar ligaments and the posterior occipital-membrane in three persons.

WAD patients who reported that they had the head rotated at the instant of collision had more often high-grade MRI changes of the alar ligaments than those with the head in a neutral position. Nearly two thirds (61.7%) of the patients with rotated neck position had alar ligament grade 3 changes, as opposed to only 4.4 % in the patient group that had reported a neutral neck position. The association between assumed head position and high-grade changes (grade 2-3) of the alar ligaments was more pronounced in rear-end than in front collision. High-grade changes in the transverse ligament were also more common among patients with the head turned at the instant of collision.

Pronounced MRI changes in the transverse ligament and the posterior atlanto-occipital membrane were considerably more common in front-end than in rear-end collisions. Almost one third (31.5%) of the patients with a front-end collision had grade 3 changes of the transverse ligament, compared with 2.6 % for patients with a rear-end collision. The corresponding figures for the posterior atlanto-occipital membrane were 20.4 % and 0.0 %, respectively.

6.3 Article 3

In this study we examined whether the range of active neck motion (AROM) differed between patients and controls, and whether the range of motion in any way was associated with the MRI findings. If ligaments and membranes are overstretched during an accident, one might

expect that this would lead to a hyper-mobility at the cranio-cervical junction. Such a neck hyper-mobility could not be demonstrated in the patients. On the contrary, the WAD patients had on average a shorter range of active neck motion for all movements compared with the control group.

Gender- and age-specific analyses revealed a significant difference between the patients and the controls in flexion and extension among men only, whereas the difference in rotation and side bending was most evident for women, in particular in women below 45 years.

For both the right and left alar ligaments, the maximal range of active *flexion* decreased significantly with increasing severity of the MRI changes among the WAD patients. No significant association was found between changes in the alar ligaments and maximal *extension*. The range of active *rotation*, however, decreased with increasing severity of MRI changes in the alar ligaments. Maximal range of active rotation also decreased with increasing severity of changes in the posterior atlanto-occipital membrane.

No significant association was found between AROM and MRI changes in the transverse ligament or the tectorial membrane.

The associations between flexion and rotation on one side and MRI changes in the alar ligaments on the other remained statistically significant in gender and age adjusted analyses.

6.4 Article 4

In our fourth work we examined if there was any association between the range of *passive* mobility, as estimated by manual techniques, and the MRI findings. Considering all four-response categories/grades, the kappa coefficient showed moderate agreement (range 0.45-0.60) between the clinical evaluations, as revealed by clinical tests and the MRI classifications. Most disagreements were close, however, and when adding weight also to cases without complete agreement in the calculations, the weighted kappa coefficient indicated good agreement (range 0.62-0.78). When dichotomising the classification results by combining the

two best (0-1) and two worst (2-3) categories, agreement was good for the ligaments (values close to 0.70), and very good for the two membranes (values above 0.90). The very high degree of agreement for the membranes is probably partly related to the low prevalence of abnormal findings for these structures.

In the case of disagreement, the structures were rated significantly lower by the clinical test than by the MRI classification. However, in most cases the clinical and MRI classifications differed by only one grade.

The sensitivity, specificity and positive and negative predictive values of the clinical test vs. MRI for the different ligaments and membranes were in general rather good. For the two ligaments, however, about 30-35% of the abnormal MRI results did not have a clinically detectable correlate (sensitivity of 0.69, 0.72 and 0.65 for the right and left alar ligaments, and the transverse ligament, respectively).

7.0 DISCUSSION

The overall aim of the present study was to examine whether clinical symptoms and signs in WAD patients could be related to physical injuries to specific soft tissue structures in the neck region, as judged by MRI. In the present series of studies, we found that WAD patients reported significantly more pain and functional disability than control persons; the prevalence of abnormal MRI findings was also significantly higher in WAD patients. Among WAD patients, the MRI verified changes were related to severity of symptoms, range of passive and active neck mobility, as well as accident-related factor.

So far, these results have not been reproduced by other investigators. In a sensitive and much disputed area of medicine as this, it is of the utmost importance that the association between radiological and clinical findings is reproduced. Until so happens, our results must be interpreted with caution, as always should be the case when new evidence is presented. Larger sample size is also needed to achieve more precise results. The costs associated with the use of the hospital's MRI equipment and personal resources, precluded a larger number of participants in the present study.

Our results are discussed in details in the included articles. Those discussions will not be duplicated here. Instead, certain aspects of the methodology, particular those related to validity and reliability, but also some other aspects, will be discussed. Some of these methodological aspects were too detailed to fit into the frame of the individual articles, whereas others simply did not cross my mind until I had started the process of writing this thesis together.

7.1 Additional information on study participants

To which extent one can generalize the results from this work depends very much on how representative the samples of WAD2 patients and control persons are. The use of inclusion and exclusion criteria, together with the sample sizes may directly influence the results. The inclusion and selection of patients was based on information given by the patients themselves in addition to information given by the local doctors. Thus, the quality of this information is also of importance.

Regarding the validity of the results, it is important that the clinical methods are correctly performed, and that correct methods are chosen for the analyses of the results.

7.1.1. The patient group.

The WAD-2 group seems to be a rather homogeneous group related to the inclusion-criteria from the Quebec report (Spitzer et al. 1995). At the first and second medical assessment they fulfilled the criteria by neck complaint and musculoskeletal signs. Musculoskeletal signs included decreased range of motion and point tenderness. When the project started in 1999, no new WAD classification was performed. It is thus possible that the WAD-2 group is more heterogeneous than what was the intention. In comparison with results from other studies, either with respect to severity of symptoms, or to prevalence of MRI-verified changes, it is important to bear this in mind.

Seven medical offices participated in the collection of patients, employing all together an average of 24 medical doctors. Due to heavy workload and possible lack of priority, it is possible that the quality of data given at the additional form at the medical offices was suboptimal. An indication of this is that for more than half of the patients, the additional information regarding the car accident was given on the physiotherapy form and not on the extra form distributed at the medical offices.

On the first medical assessment, the patients were asked to answer some questions regarding the car accident. One of the questions was if the patient had sustained “only one neck injury” (attachment 1). The purpose of this question was to locate persons suffering after only one injury, as it then would be easier to associate clinical findings with that specific accident. Therefore, this question was emphasized in the letters to the medical doctors, and by the first clinical assessment performed at the FMC. When starting up the project in 1999, we therefore hoped that we had eliminated those with more than one neck injury.

Today, in 2009, we have not the same certainty regarding this issue. FMC has now developed a rehabilitation program for neck injured persons, and 52 participants in the present study did come back to participate in this rehabilitation program. Rather unexpectedly, several of these patients gave new information indicating that they in fact had sustained more than one neck injury. These “new” traumas could either be another car accident, or neck injuries of other types. When asked why this had not been reported earlier, different answers were given. Some of the patients had not been aware that it was that important that they had sustained only one injury; for others, it was the registered injury that after their opinion gave them the largest symptoms. Others had not been sure of what the criteria were for “a neck injury”, and some also had an unfinished case with the insurance company, and therefore it was important for them to register only one neck case.

7.1.2 The time of the injury

In some cases we probably had the wrong date for the neck injury. Some of the patients did not see a medical doctor immediately after the injury. In some cases, the patients thought that the pain and functional disability should disappear; in others the pain and functional disability gradually increased over time. Thus, it later turned out that the date given by some of the patients as the date of the accident was the date they first realized the pain or decided to seek medical advice. The exact number is not known.

These uncertainties may have influenced the results and conclusions of article two, where the aim was to find out if the MRI findings could be associated with accident related factors. With the possibility of more than one trauma, this correlation becomes doubtful. This new knowledge impairs our conclusions, and we therefore have to use the results with caution. For the three other articles, it is highly unlikely that this bias could interfere with the results and conclusions.

7.1.3 The control group

The control material was randomly drawn among persons that were referred for physiotherapy for diagnoses outside the head and neck area. That means that the control persons probably were more affected by muscle and skeleton problems than completely healthy control persons would have been and consequently, that they scored higher on the disability index (Kaale et al. 2005a) than more healthy controls would have done. It is a possibility that our control group had a higher level of muscle and skeleton problems to the lower back and extremities compared to a general population group. Thus, the difference between WAD persons and control persons may have been even larger if we had drawn control persons from the general population. On the other hand, WAD person may have exaggerated their symptoms.

In summary, we believe that the results from this study are based on a fairly representative sample of WAD-2 patients and control persons without a diagnosis of WAD.

7.2 Validity and reliability of clinical methods and patient-given information

7.2.1 Neck Disability Index Score (NDI)

The NDI questionnaire is a condition specific instrument, thought to be sensitive to changes in symptoms, and easy to use in clinical practice (Ackelman et al. 2002). In Sweden, a Swedish version of the NDI has been used, demonstrating good validity, sensitivity and test-retest reliability, but not optimal specificity (Ackelman et al. 2002). It is important to map all aspects of WAD. Consequently, some authors have suggested incorporating questions regarding social and emotional matters (Ackelman et al. 2002, Hoving et al. 2003, Cleland et al. 2006, Vos et al. 2006). On the other hand, others have claimed that there has been a trend to over-psychologise the WAD patients, and thereby overlook the somatic origin for their symptoms and functional disabilities (Cote 2001, Bergholm 2003, Johansson 2006, Maak 2006). We wanted to emphasise on the possible *somatic* aspects, and therefore did not include such questions in our questionnaire.

Co-morbidity may be a problem when a patient tries to estimate the degree of a particular disability. For instance, headache is quite common in the general population and is not necessarily a part of the neck syndrome. Ackelman et al. showed in their study that for the concurrent validity, a high degree of pain for the chronic neck pain patients in most cases did not correspond with high levels of NDI. Misunderstanding of this issue could result in an overestimation of the scores of this particular item, and also influence the answers for the other questions. A possible modification of the NDI instrument could be that the patient was asked to emphasise only disability due to neck pain. In the present study, however, this would make comparison with responses in the control group difficult.

The NDI questionnaire does not reflect the full spectrum of disabilities judged to be important by the WAD patient. Issues concerning emotional and social functioning are not

addressed properly in this questionnaire (Hoving et al. 2003). For the WAD patient group it is important to assess issues concerning emotional and social function to daily life. The results from Hoving et al. indicate that the social consequences of the pain and functional disability are important aspects of the subject's situation that is not covered by the NDI.

Correction for missing values has been a challenge using the NDI. For instance, the item concerning driving may be an unanswered question (Vos et al. 2006). In our study, no correction for missing values was necessary for any item.

A study by Cleland reported poor construct validity using the NDI questionnaire. This questionnaire was less responsive to changes in each item compared to other questionnaires. They propose using the Patient Specific Functional Scale (PSFS). The PSFS exhibited significantly greater changes in score, while changes in the NDI did not differ between improved and stable patients (Cleland et al. 2006).

7.2.2 Head position and impact direction

Through the Firda rehabilitation program, we followed-up the question regarding neck position at the time of accident (Kaale et al. 2005b). That work gave us some new information. Our goal in the present study was to register either front or rear end collision, and connect the individual cases with either neutral or rotated neck position during the time of accident.

With increasing knowledge over the years regarding the biomechanical conditions around a car accident, we now realize that the information given to the patients at the first registration was insufficient. Sometimes it can be difficult to register the first strike in a car collision. A car collision may also often contain more than one hit, from different directions and with different hit points. Thus, there might have been problems with the patients' registering and estimating the force on the neck and head in a fast upcoming series of blows during the accident. Impulses from high noises and scaring sights may also have influenced the total impression of the car accident, and thereby influenced the patients' perception of the direction of the impact.

With regards to neck position, we only asked whether the neck was rotated at the moment of the accident or not. However, there may be a difference between going *into* a rotated neck position and going *out* of it, as these are two completely different movements. Going into rotation stretches some types of soft tissues, whereas going from a rotated position back to a more neutral position may relax the same tissue tension. This important distinction was not clear to the patients or to us at the time of registration. Thus, there may be some uncertainties regarding the information given by the patients about hit-directions and neck position.

7.2.3 Active range of motion (AROM)

The cervical range of motion (CROM) device employed in this study is easy to use, and it seems to be a potentially useful tool for the clinician. Studies have shown acceptable intra tester and inter tester reliability (Capuano-Pucci et al. 1991, Youdas et al. 1991, Youdas et al. 1992). Capuano-Pucci investigated a healthy group, and Youdas et al. did their works on both a healthy and a patient group. In my previous MSc graduation project (Kaale 1996), reliability of AROM was assessed on a control group (n=61) and four whiplash groups (n= 20 x 4), using the same device as in the present research project. The test/re-test results did not fall within the predefined acceptable limits of deviation in each direction, set to $\pm 4^\circ$. Intra tester reliability was shown to be more reliable than inter tester reliability. Comparison of the results between control and patient groups showed a higher degree of conformity for the patient groups. There were no demonstrable differences between large and small movements.

In clinical work, it is essential that clinicians are able to obtain the same measurement when a subject is retested. Likewise, testers must be confident that the inter tester reliability is acceptable. Tousignant et al. have evaluated the validity of the CROM device (Tousignant et al. 2000, 2002, 2006). The CROM device was found to be valid for measurements of active neck motion. Based on these studies, the CROM may be a useful tool for assessing AROM in the neck for both a normal population and for different patient groups.

Experience from the present study (Kaale et al. 2007) shows that patients with neck problems, compared to persons with normal neck function, is often more difficult to assess, since neck symptoms can influence the test results. The individual level of neck function and level of symptoms may also vary from day to day. My experience with the CROM device used on a whiplash group includes several challenges, as indicated below.

The subjects were given verbal instruction concerning the purpose of the testing. We tried to give the same information each time. We tried to control our voice, giving the information with the same speed and the same sensitivity and level of influence for each person. We experienced that it was difficult to control or adjust the person's own experience of our message. How far to go into a direction of motion, their own ability to control their own movement, when to stop, different level of acceptance of pain, how to cope with their own anxiety of possible pain, or consequences after neck motion were all challenges we had to cope with. We experienced that these challenges were not stable, and that they thus may have influenced the reliability and validity of our tests.

We performed the test with a warm-up period consisting of three repetitions of each of 6 movements; extension, flexion, side bending (left and right) and rotation (left and right). Two measurements were taken for each of the six cervical motions. The second measurement was recorded and used in the analyses. Our patients had individual symptoms and functional deficits, as revealed in one or several of the testing directions. We experienced that the order of test direction could influence the result. If the main problem was extension, and that was the first testing direction, pain and functional provocation by that test movement could influence the results of other test directions.

Sometimes a patient's level of pain and functional disability differed throughout the day. The changes could be a result of different activities of daily life, or a consequence of fluctuation of a soft tissue healing process. Such changes may also have influenced the reliability and validity of the AROM tests.

Changes in AROM at one time, or over time, do not necessarily reflect real changes in AROM. Changes to the better or worse may be a result of different impacts. To secure a proper use of the CROM device, it is vital to try to control for these artefacts.

We summarise this work by emphasising the uncertainty that the CROM device not necessarily reflect real changes in the AROM due to a neck injury. Changes in AROM may also be the result of patient related or method related fluctuations.

7.2.4 Clinical assessment based on manual therapy techniques

When testing passive intervertebral motion by the use of clinical techniques, it is a challenge to prove the level of intra and inter tester reliability.

Van Trijffel et al. have conducted a systematic review to determine inter examiner reliability of passive assessment of segmental intervertebral motion in the cervical spine (Van Trijffel et al. 2005). Nineteen studies were included in this review. Two studies satisfied criteria for external and internal validity, of which one found fair to moderate reliability. Assessment of motion segments C1-2 and C2-3 almost consistently reached at least fair reliability. Overall, inter examiner reliability was poor to fair. However, most studies were found to be of poor methodological quality.

Fernández-de-las-Peñas C et al. conducted a study to determine if the lateral gliding test for the cervical spine was a valid clinical test compared with radiological assessment as a tool for the diagnosis of intervertebral joint dysfunction in the lower cervical spine in patients with mechanical neck pain. They concluded that the lateral gliding test for the cervical spine was as good as a radiological assessment for the diagnosis of intervertebral dysfunction in the lower spine (Fernández-de-las-Peñas C et al. 2005).

Piva et al. conducted a study on inter tester reliability of passive intervertebral movement (PIM). Measurements of PIM tests resulted in moderate reliability of assessing atlanto-occipital

mobility. They concluded that results of PIM tests were affected by neck pain reproduced by the tests. (Piva et al. 2006).

These studies indicate that PIM tests of the cervical spine have poor to moderate inter tester reliability. Poor reliability and high levels of measurement errors reduce the usefulness of a test, and limits the extent to which tests results can be generalized. The tests in our study have not been through reliability tests, so we have no values indicating the level of reliability. The goal of our study was to see if changes in PIM could be verified by another diagnostic tool, the MRI. Changes in PIM may be a direct consequence after a soft tissue lesion. These possible soft tissue lesions may then be visualized by MRI. The level of agreement between clinical tests and radiological assessment may however tell us something about both the validity of the clinical tests, and what clinical consequences a positive MRI results may give in clinical testing for a specific tested motion.

In summary, results from research performed by other authors on the reliability of PIM tests, indicate that these test so far do not meet the standards and levels of secure information. The level of intra and inter tester reliability is too low. We are not sure if the results reflect real clinical changes or if they are consequences of a methodological weakness. Our results indicate a connection between the MRI findings and the manual PIM tests. To secure a more reliable use of these clinical tests, a proper protocol has to be made on a scientific basic. With a proper protocol, this clinical approach may strengthen the assessment, and further choose those who need a radiological assessment. The recommendation from Jansen et al. was that only those who were classified as WAD 3 and 4 with neurological findings were justified for an MRI assessment (Jansen et al. 2008). The use of MRI verifying soft tissue lesion in ligaments, membranes and capsules in the upper cervical spine is still doubtful because of weakness with different types of MRI equipment and protocols, inadequate knowledge about clinical findings after a neck trauma, and normal variation of soft tissue structures.

7.2.5 Stressful life events and personality as parameters in predicting the duration and severity of symptoms after a whiplash trauma

The present study did not have as an aim to investigate these aspects of the whiplash syndrome. Nevertheless, they may be of importance and will therefore be dealt with briefly below.

Laxity in the ligaments in the upper cervical spine after a neck injury, with possible change in biomechanical function, may be an origin of pain. Even so, we cannot exclude psychosomatic causes of pain and functional deficit. Psychosocial factors may influence the posttraumatic course after a whiplash trauma, either by a premorbid personality that makes the patient more vulnerable to develop chronic pain, or because the chronic pain over time induces a change of personality in a direction that negatively influences the rehabilitation. Low expectation of personal success, low self image in family- and work relations combined with long-lasting distress, may predispose for a poor outcome after a whiplash trauma. A family history showing problems to deal with personal challenges and expectations of disability and possible neck symptoms existing prior to the trauma may be risk factors for development of chronic symptoms after a whiplash trauma, in some cases possibly more important than the organic changes caused by the accident itself (Van der Donk et al. 1991, Schrader et al. 1996, Karlsborg et al. 1997, Richter et al. 2004).

7.2.6 MRI method

Advanced MRI technology has since the late nineteen-nineties made it possible to detect ligament and capsular injuries in the cranio-cervical junction. A new MRI protocol for classifications of MRI signal intensity in cranio-cervical ligaments and membranes was developed by one of the collaborators in the present study (JK). To ensure that the criteria were

mutually understood, a pilot study including ten cases was performed, and results based on the interpretations of different radiologists were compared and discussed, before this study was started (Krakenes et al. 2002). A detailed description of the classification system, as well as results from inters and intra observer variation studies are presented elsewhere (Krakenes et al. 2001, 2002, 2003 a, b) and in the thesis they were a part of (Krakenes J. “MRI analysis of craniovertebral ligaments and membranes in the late stage of whiplash injury”, Doctorial thesis, University of Bergen 2004).

In the studies from Krakenes et al., the consistency in the grading of signals changes in craniovertebral ligaments and membranes varied considerably, both between observers and for the different structures evaluated. Inter observer agreement for the right alar ligament was moderate (0.41), and for the left alar ligament fair (0,31). The respective values with weighted kappa were 0.51 and 0.50, respectively. Main reasons for disagreement were intermediate signal in parts of or in the entire ligament width, reduced image quality, or erroneous use of criteria (Krakenes et al. 2001). In another recent Norwegian study that applied a classification similar to that in the present study, inter and intra observer agreements were rather similar to those observed by Krakenes et al. (Myran et al.2008). Inter-observer agreement improved considerably in both of these studies, however, when dichotomising into normal (grade 0-1) and abnormal (grade 2-3) categories.

It is important to identify findings susceptible to different interpretations and to disclose sources of disagreement. Inconsistency in radiological diagnosis will mislead clinicians and reduce the usefulness of radiological examinations. A better understanding of the normal anatomy and injury patterns, combined with more experience in using the criteria, will probably reduce such inconsistencies.

The consensus in Euro Spine 2008 ask for more reliable MRI studies of the ligaments in the upper part of the cervical spine in whiplash-injured patients in the acute phase (Jansen et al. 2008).

MRI as an assessment tool for ligament injuries is not a new science. An example is the use of MRI detecting lesions to the cruciate ligaments. Fritz has focused on the MR imaging of meniscal and cruciate ligament injuries. The cruciate ligaments are about 38 mm long, and a width of 11 mm (Gray's Anatomy). He concluded in 2003 that MRI imaging provides clinically useful information in detecting and characterizing sports-related pathology of the menisci and cruciate ligaments in a non-invasive fashion. Acute and chronic tears of the anterior and posterior cruciate ligaments can be accurately identified and evaluated with MRI imaging (Fritz, RC 2003). The size of the cruciate ligaments is almost three times that of the alar ligaments. However, there are also studies that show how MRI can be used in really small structures. Carrino et al. has focused on magnetic resonance imaging-guided percutaneous biopsies of musculoskeletal lesions for which other imaging modalities might be inadequate. One of the main reasons for doing this work was the need for site-specific targeting within a lesion. The results showed that the performance of percutaneous biopsies can be very good for bone lesions, moderate for extra-articular soft-tissue lesions, and fair for intra-articular soft-tissue lesions. (Carrino et al. 2007).

So far, the use of MRI in the study of specific ligaments and membranes in the upper cervical spine has not yet been established as an assessment procedure after neck traumas. The Euro Spine indicates a lack of knowledge regarding MRI changes in the upper cervical spin ligaments and membranes in the normal population. They also request a better consensus using the MRI equipment and MRI procedures (Jansen et al. 2008).

In the present study we considered results from the MRI evaluation as being a correct classification of potential physical injury. The use of MRI as a gold standard is a challenge, since there so far are not established standards of MRI sequences or interprets routines (Jansen et al. 2008). As part of the reliability studies (Krakenes et al. 2000, 2001, 2003 a and b), the MRI evaluation was performed twice. When relating the MRI findings to clinical symptoms (Kaale et al. 2005a, 2007, 2008) and accident-related factors (Kaale et al. 2005b), we only

considered results from the initial MRI examination, to ensure that the evaluations were blinded for study group. The prevalence reported by Krakenes et al. are based on the second evaluation, and differ thus slightly from those presented in the present study.

7.3 General discussion of results

7.3.1 Association between MR-findings and clinical symptoms

We found that WAD patients reported significantly more pain and functional disability than the control persons, both for total score and for each of the ten single items (Kaale et al. 2005a). The disability score increased with increasing number of abnormal (grade 2-3) structures among the WAD patients. We also observed that WAD patients had on average a shorter range of active motion for all movements compared with the control group (Kaale et al. 2007). The difference was statistically significant for all measures considered, except side bending to the left. Among the WAD patients, increasing severity of lesions to the alar ligaments was associated with a decrease in maximal flexion and rotation. An abnormal posterior atlanto-occipital membrane was associated with shorter range of rotation, with a significant trend test both in analyses with and without adjustment for lesions to other structures. Regarding passive test of joint motion, we found that the MRI-verified abnormalities correlated with a clinical detectable passive hyper-mobility (Kaale et al. 2008).

The observed difference in severity of symptoms between WAD patients and control persons, together with the dose-response relationship in the analyses of associations of severity of symptoms and severity of MRI findings, indicate that subjective symptoms and complaints among WAD patients can be linked with physical injury signs to specific soft tissue structures in the upper cervical spine, in particular the alar ligaments. We cannot, however, draw conclusion

with respect to whether the MRI verified lesions is caused by the whiplash episode or to any other unfavourable event.

Results from studies like ours appear to have stimulated a debate regarding a possible organic origin of whiplash as demonstrated by MRI. Kwan et al. found the level of evidence weak: the patients were studied many years after their trauma; too little information was given about the type of trauma, any cervical manipulation that they had undergone, nor any history of other injuries. They also demand information about the prevalence of these appearances in non-traumatic neck pain (Kwan et al. 2004). So far, however, few studies have focused on the clinical aspects regarding the MRI findings on the cranio-cervical ligaments. Isolated MRI changes without clinical correlations are of little use. Clinical test of passive mobility of soft tissue structures in the upper cervical spine corresponded with signs of physical injuries, as judged by magnetic resonance imaging (Kaale et al. 2008). Considering all four-response categories, the kappa coefficient indicated moderate agreement (range 0.45-0.60) between the clinical and the MRI classification. When there was disagreement, the classifications obtained by the clinical test were significantly lower than the MRI grading, but mainly within one grade difference. When combining grade 0-1 (normal) and 2-3 (abnormal), the agreement improved considerably (range 0.70-0.90).

The use of MRI for verifying lesions in the cranio-cervical ligaments is still in an early phase regarding approach to clinical findings and symptoms. A closer approach between radiological methods and clinical findings seems urgent for a more thorough understanding of this long lasting whiplash syndrome. There is still a considerable uncertainty regarding these MRI results and the clinical consequences of these MRI changes. Findings from Krakenes et al., showing reparative changes, with lack of fibre structure with connective tissue or fat replacement in the cranio vertebral ligaments indicate soft tissue lesion after a neck trauma.

7.3.2 MRI-verified lesions, WAD vs. control

For all neck structures in the present study, that is the alar and the transverse ligaments, and the posterior atlanto-occipital and tectorial membranes, the whiplash patients had more high-grade changes (grades 2 or 3) than the control persons (Kaale et al. 2005b). The prevalence of high-grade changes was highest for the alar ligaments (66.3% graded 2 or 3). Signal changes in other structures often appeared in conjunction with lesions to the alar ligament.

Soft tissue structures in the upper cervical spine visualized by MRI have earlier been described by several authors (Pfirrmann et al. 2000, Wilmink et al., 2001, Roy et al. 2004). These studies were performed on either healthy persons (Pfirrmann et al. 2000, Roy 2004), or on very small patient groups (Pfirrmann et al. 2000, Wilmink et al 2000, Roy et al. 2004). These works were not able to find any correlation between alar injuries and WAD traumas.

In a recent Norwegian study, Myran and co-workers (Myran et al. 2008) described high-signal intensity changes in the alar ligaments among whiplash patients, patients with chronic neck pain, and in controls; no overall significant difference between the three groups was found. The authors concluded that the diagnostic value and the clinical relevance of magnetic resonance detectable areas of high intensity in the alar ligaments are questionable. However, no direct comparison of WAD patients and control persons was performed in this study. The proportion of abnormal (grade 2-3) alar ligaments in the chronic pain group was rather similar to those in the control group, whereas WAD patients more often had abnormal alar ligaments (Albrektsen et al., 2009, Myran et al, 2009; in press). Thus, results from the study by Myran et al. give some support to our findings, although the difference between WAD patients and control person was less pronounced than in our study. We considered the results from the MRI evaluation as being a correct classification of a potential physical injury. So far, however, there have not been established standards of MRI sequences or interpretation routines (Jansen et al. 2008). The consensus in Euro Spine ask for more reliable MRI studies of the ligaments in the

upper part of the cervical spine in whiplash-injured patients in the acute phase (Jansen et al. 2008).

7.3.3 Additional evidence for ligament and membrane injury

Additional studies have focused on potential injuries in specific neck structures. Johansson described pronounced anatomical changes in three patients that underwent surgical fixation of the cranio-cervical junction after a neck injury, as well as widespread injuries with scar tissue in the C0/1 and C1/2 joint capsules, open joint cavities at the C1/2 level due to these capsule injuries, injuries to the dens related capsules, and granulation changes in the alar ligaments (Johansson 2006). Other authors have also supported this ligament injury hypothesis. Panjabi et al. advocated that cervical ligaments might be at risk for injury in a whiplash trauma due to excessive strain during the impact (Panjabi et al. 2004). Tominaga et al. support these findings with their results indicating a decrease in neck ligament strength due to whiplash trauma (Tominaga et al. 2006); other authors have suggested that soft tissue injuries in facet joints and capsular ligaments may be a consequence after a whiplash trauma (Siegmund et al. 2001, Pearson et al. 2004).

Ivancic et al. have suggested that capsular ligament injuries, in the form of increased laxity, may be one component perpetuating chronic pain and clinical instability in whiplash patients. They demonstrated that the average length of the whiplash-exposed capsular ligaments was significantly greater than that of the control ligaments (Ivancic et al. 2007).

7.3.4 Associations between MRI findings and accident related factors

We found that whiplash patients who had been sitting with their head/neck turned to one side at the moment of collision more often had high-grade signal changes of the alar and transverse ligaments than those who had not turned their heads (Kaale et al. 2005b). Severe MRI

signal changes in the transverse ligament and the posterior atlanto-occipital membrane were more common in front than in rear end collisions. These findings support our theory that head position and impact direction at time of accident may influence location and degree of lesion of soft tissue structures in the neck. The association with the accident-related factors supports the hypothesis that the MRI verified signal changes in ligaments and membranes in the upper cervical spine are caused by the whiplash trauma.

Several clinical and in vitro studies have indicated that direction and strength of external forces acting at time of accident is of importance for severity of injury. In 1983 Norris et al. postulated that injury of the neck might be the result when a motor vehicle runs into another from behind. They developed a classification system based on presenting symptoms and physical signs after a neck trauma. This work was a forerunner for the later WAD classification system (Spitzer et al. 1995). At that time only impacts from behind were included. Norris et al. did not consider head and neck position during impact. Later, frontal impacts and side impacts have also been included (Kullgren et al. 2000, Panjabi et al. 2004), and head position during impact has also been considered a risk factor after a whiplash trauma (Kumar et al. 2005, Maak et al. 2006, Panjabi et al. 2006).

Panjabi et al. has performed several in vitro studies looking for soft tissue lesions after neck trauma. Investigating human cervical spine specimens, they have found that head-turned rear end impact caused significantly greater injury at C0-1 and C5-6, as compared to head-forward rear – and frontal impacts (Panjabi et al. 2006). Panjabi performed in 2004 a project, where they put up a whole cervical spine with muscle force replication model and a bench-top sledge to simulate frontal impacts. Their results concluded that the supraspinatus, interspinous ligaments and the flavum ligament were at risk for injury due to excessive strains during frontal impacts (Panjabi et al. 2004). In an in vitro study, Maak et al. focused on lesions to the alar, transverse and apical ligaments after a whiplash trauma. They concluded that these ligaments were not at risk due to head-turned rear-end impacts under 8 G (Maak et al. 2006). A new

research from 2008 by Siegmund et al. conclude in an in vitro study that head-turned posture increases the strain on facet joint capsular ligaments compared to a neutral head posture (Siegmund et al. 2008). These findings support the hypothesis that organic lesions may be a consequence after a whiplash trauma.

8.0 SUMMARY AND CONCLUSION

The results of this study give reasonable support to the existence of an organic model that in part can explain the problems of the long lasting whiplash syndrome. Results from studies published during the recent years have given additional support to such a model, but contrasting results have also been reported.

Nevertheless, psychosocial factors may still be of importance for the development of the long-lasting whiplash syndrome in combination with organic causes, and thus of relevance in predicting the outcome with duration and severity of the complaints.

Additional studies is still needed to gain better understanding of underlying biological mechanisms, possibly leading to improvements in diagnostic and therapeutic procedures.

9.0 PERSONAL REMARKS

The work with this project over a period of 18 years has been an extraordinary process of learning and challenges. Personally, it has been a long period with increasing knowledge and scientific understanding; perhaps more valuable than the end results itself. Hopefully, the present work will raise important questions regarding clinical and physical manifestations after a whiplash trauma. I hope and believe that this work has shed some new and stronger light on the existence of an organic origin of this neck problem.

10.0 REFERENCES

Ackelman BH, Lindgren U. Validity and reliability of a modified version of the neck disability index. *J Rehabil Med.* 2002;34(6):284-7.

Adams V. Neck Injuries: 1. Occipitoatlantal Dislocation – A Pathologic Study of 14 Traffic Fatalities. *J Forensic Sci.* 1992;37(2):556-64.

Adams V. Neck Injuries: 2. Atlantoaxial Dislocation – A Pathologic Study of 14 Traffic Fatalities. *J Forensic Sci.* 1992;37(2):565-73.

Albrektsen G, Kaale BR, Krakenes J, Wester K. *Spine* 2009, July 1, in press.

Bogduk N, Yoganandan N. Biomechanics of the cervical spine. Part 3: minor injuries. *Clinical Biomechanics.* 2001;16:267-275.

Bergholm U, Johansson BH. New diagnostic approach can improve treatment of whiplash injuries. Functional magnetic resonance tomography makes visualization of the injuries possible. *Lakartidningen.* 2003;100(47):3842-7.

Capuano-Pucci D, Rheault W, Aukai J, Bracke M, Day R, Pastrick M. Intratester and intertester reliability of the cervical range of motion device. *Arch Phys Med Rehabil.* 1991;72(5):338-40.

Castro WHM, Schilgen M, Meyer S, Weber M, Peuker C, Wörtler K. Do “whiplash injuries” occur in low-speed rear impacts? *Eur Spine J* 1997;6:366-375.

Carrino JA, Khurana B, Ready JE, Silverman SG, Winalski CS. Magnetic Resonance Imaging – Guided Percutaneous Biopsy of Musculoskeletal Lesions. *J Bone Joint Surg Am.* 2007;89:2179-2187.

Cavalcante ML, Rodrigues CJ, Mattar R Jr. Mechanoreceptors and nerve endings of the triangular fibrocartilage in the human wrist. *J Hand Surg Am.* 2004;29(3):432-5.

Cleland JA, Fritz JM, Whitman JM, Palmer JA. The reliability and construct validity of the Neck Disability Index and patient specific functional scale in patients with cervical radiculopathy. *Spine.* 2006;31(5):598-602.

Cote P, Hogg-Johnson S, Cassidy JD, Carroll L, Frank JW. The association between neck pain intensity, physical functioning, depressive symptomatology and time-to claim-closure after whiplash. *J Clin Epidemiol.* 2001;54:275-286.

Crowe HE. Injuries to the cervical spine. Presented at the meeting of the Western Orthopaedic Association, San Francisco, California. 1928: Ref Type: Hearing.

Dvorak J, Panjabi M, Gerber M, Wichmann W. CT-Functional Diagnostics of the Rotatory Instability of Upper Cervical Spine. 1. An Experimental Study on Cadavers. *Spine.* 1987;12(3):197-205(a).

Dvorak J, Hayek J, Zehnder R. CT- functional Diagnostics of the Rotatory Instability of the Upper Cervical Spine. Part 2. An Evaluation on Healthy Adults and Patients with Suspected Instability. *Spine.* 1987;12(8):726-731(b).

Dvorak J, Panjabi MM. Functional anatomy of the alar ligaments. *Spine.* 1987;12(2):183-9(c).

Dvorak J, Schneider E, Saldinger P, Rahn B. Biomechanics of the Craniocervical Region: The Alar and Transverse Ligaments. *J Orthopaedic Res.* 1988;6:452-61.

Endo K, Ichimaru K, Komagata M, Yamamoto K. Cervical vertigo and dizziness after whiplash injury. *Eur Spine J.* 2006 Jun;15(6):886-90.

Farley FA, Gebarški SS, Garton HL. Tectorial membrane injuries in children. *J Spinal Disord Tech.* 2005;18(2):136-8.

Fernández-de-las-Peñas C, Downey C, Miangolarra-Page JC. Validity of the lateral gliding test as tool for the diagnosis of intervertebral joint dysfunction in the lower cervical spine. *J Manipulative Physiol Ther.* 2005;28(8):610-6.

Fielding W, Cochran G, Lawsing J, Hohl M. Tears of the Transverse Ligament of the Atlas. *J Bone and Joint Surg.* 1974;56(8):1683-91.

Fritz RC. MR imaging of meniscal and cruciate ligament injuries. *Magn Reson Imaging Clin N Am.* 2003;11(2):283-93.

Gay JR, Abbot KH. Common whiplash injuries of the neck. *JAMA.* 1953;152:1698-1704.

Hagert E, Forsgren S, Ljung BO. Differences in the presence of mechanoreceptors and nerve structures between wrist ligaments may imply differential roles in wrist stabilization. *J Orthop Res.* 2005;23(4):757-63.

Hirsch SA, Hirsch PJ, Hiramoto H, Weiss A. Whiplash Syndrome – Fact or Fiction. *Orth Clin N Am.* 1988;19(4):791-95.

Hoving JL, O'Leary EF, Niere KR, Green S, Buchbinder R. Validity of the neck disability index, Northwick Park neck pain questionnaire, and problem elicitation technique for measuring disability associated with whiplash-associated disorders. *Pain.* 2003;102(3):273-81.

Hubbard RD, Quinn KP, Martínez JJ, Winkelstein BA. The role of graded nerve root compression on axonal damage, neuropeptide changes, and pain-related behaviors. *Stapp Car Crash J.* 2008 Nov;52:33-58.

Hulsebosch CE, Hains BC, Crown ED, Carlton SM. Mechanisms of chronic central neuropathic pain after spinal cord injury. *Brain Res Rev.* 2008 Dec 25. [Epub ahead of print]

Ivancic PC, Ito S, Tominaga Y, Rubin W, Coe MP, Ndu AB, Carlson EJ, Panjabi MM.

Whiplash causes increased laxity of cervical capsular ligament. *Clin Biomec* 2008;23:159-165.

Jansen GB, Edlund C, Grane P, Hildingsson C, Karlberg M, Link H, Måwe U, Portala K, Rydevik B, Sterner Y; Whiplash injuries: diagnosis and early management. The Swedish Society of Medicine and the Whiplash Commission Medical Task Force. Swedish Society of Medicine; Whiplash Commission Medical Task Force. *Eur Spine J.* 2008 Oct;17 Suppl 3:S355-417.

Jenewein J, Moergeli H, Wittmann L, Büchi S, Kraemer B, Schnyder U. Development of chronic pain following severe accidental injury. Results of a 3-year follow-up study.

J Psychosom Res. 2009 Feb;66(2):119-26. Epub 2008 Dec 16.

Johansson BH. Whiplash injuries can be visible by functional magnetic resonance imaging. *Pain Res Manag.* 2006;11(3):197-9.

Kaale BR. Nakkeskade: Reproduserbarheit av rørslemåling og konsekvensar av nakkestilling ved påkøyringskader, og nakkeskader på anna grunnlag. University of Bergen 2006.

Kaale BR, 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(4):466-75.

Kaale BR, Krakenes J, Albrektsen G, Wester K. Erratum. *J Neurotrauma.* 2006;23(6):1048

Kaale BR, Krakenes J, Albrektsen G, Wester K. Head Position and Impact Direction in Whiplash Injuries: Association with MR-Verified Lesions of Ligaments and Membranes in the Upper Cervical Spine. *J Neurotrauma.* 2005;22(11):1294-1302.

Kaale BR, Krakenes J, Albrektsen G, Wester K. Active Range of Motion as an Indicator for Ligament and Membrane Lesion in the Upper Cervical Spine after a Whiplash Trauma. *J Neurotrauma*. 2007;24(4):713-721.

Kaale BR, Krakenes J, Albrektsen G, Wester K. Clinical assessment techniques for detecting ligament and membrane injuries in the upper cervical spine region – A comparison with MR results. *Man Ther*. 2008;oct(13):397-403.

Karlsborg M, Smed A, Jespersen H, Stephensen S, Cortsen M, Jennum P, Herning M, Korfitsen E, Werdelin L. A prospective study of 39 patients with whiplash injury. *Acta Neurol Scand*. 1997;95:65-72.

Kivioja J, Själin M, Lindgren U. Psychiatric morbidity in patients with chronic whiplash-associated disorder. *Spine*. 2004;29(11):1235-9.

Krakenes J, Kaale BR, Rorvik J, Gilhus NE. MRI assessment of normal ligamentous structures in the craniovertebral junction. *Neuroradiology*. 2001;43(12):1089-97.

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(7):617-24.

Krakenes J, Kaale BR, Moen G, Nordli H, Gilhus NE, Rorvik J. MRI of the tectorial and posterior atlanto-occipital membranes in the late stage of whiplash injury. *Neuroradiology*. 2003;45(9):585-91.

Krakenes J, Kaale BR, Nordli H, Moen G, Rorvik J, Gilhus NE. MR analysis of the transverse ligament in the late stage of whiplash injury. *Acta Radiol*. 2003;44(6):637-44.

Krakenes J. MRI analysis of craniovertebral ligaments and membranes in the late stage of whiplash injury, University of Bergen 2004

Kullgren A, Krafft M, Nygren A, Tingvall C. Neck injuries in frontal impacts: influence of crash pulse characteristics on injury risk. *Accid Anal Prev.* 2000;32(2):197-205.

Kumar S, Ferrari R, Narayan Y. Looking away from whiplash: effect of head rotation in rear impacts. *Spine.* 2005;30(7):760-8.

Kwan O, Friel J. MRI of the posterior tectorial and atlanto-occipital membranes in the late stage of whiplash injury. *Neuroradiology.* 2004;46:165-166.

Maak TG, Tominaga Y, Panjabi MM, Ivancic PC. Alar, transverse, and apical ligament strain due to head-turned rear impact. *Spine.* 2006;31(6):632-8.

Mashoof AA, Levy HJ, Soifer TB, Miller-Soifer F, Bryk E, Vigorita V. Neural anatomy of the transverse carpal ligament. *Clin Orthop Relat Res.* 2001;5(386):218-21.

Morisawa Y. Morphological study of mechanoreceptors on the coracoacromial ligament. *J Orthop Sci.* 1998;3(2):102-10.

Myran R, Kvistad KA, Nygaard OP, Andresen H, Zwart JA. Magnetic Resonance Imaging Assessment of the Alar Ligaments in Whiplash Injuries. *Spine.* 2008;33(18):2012-2016.

Myran R, Kvistad KA, Nygaard OP, Andersen H, Folvik M, Zwart JA. Reply to Editorial submission on Myran R, et al by Albrektsen G, et al. *Spine* 2009, July 1, in press.

Nash L, Nicholson H, Lee AS, Johnson GM, Zhang M. Configuration of the connective tissue in the posterior atlanto-occipital interspace: a sheet plastination and confocal microscopy study. *Spine.* 2005;30(12):1359-66.

Norris SH, Watt I. The prognosis of neck injuries resulting from rear-end vehicle collisions. *J Bone Joint Surg Br.* 1983;65(5):608-11.

Panjabi M., Dvorak J., Crisco J., Oda T., Wang P., Grob D. Effects of Alar Ligament Transection on Upper Cervical Spine Rotation. *J Orthopaedic Res.* 1991;9:584-93.

Panjabi M., Dvorak J., Crisco J., Oda T., Hilibrand A., Grob D. Flexion, Extension, and Lateral Bending of the Upper Cervical Spine in Response to alar Ligament Transections. *J Spinal Disord.* 1991;4:157-67.

Panjabi MM, Pearson AM, Ito S, Ivancic PC, Gimenez SE, Tominaga Y. Cervical spine ligament injury during simulated frontal impact. *Spine.* 2004;29(21):2395-403.

Panjabi MM, Ivancic PC, Maak TG, Tominaga Y, Rubin W. Multiplanar cervical spine injury due to head-turned rear impact. *Spine.* 2006;31(4):420-9.

Pearson AM, Ivancic PC, Ito S, Panjabi MM. Facet joint kinematics and injury mechanisms during simulated whiplash. *Spine.* 2004;29(4):390-7.

Petrie S, Collins JG, Solomonow M, Wink C, Chuinard R, D'Ambrosia R. Mechanoreceptors in the human elbow ligaments. *J Hand Surg Am.* 1998;23(3):512-8.

Pfirrmann WA, Binkert CA, Zanetti M, Boos N, Hodler J. Functional MR imaging of the craniocervical junction. Correlation with alar ligaments and occipito-atlantoaxial joint morphology: a study in 50 asymptomatic subjects. *Schweiz Med Wochenschr* 2000;130:645-51.

Piva SR, Erhard RE, Childs JD, Browder DA. Inter-tester reliability of passive intervertebral and active movements of the cervical spine. *Man Ther.* 2006;11(4):321-30.

Radanov BP, Dvorak J, Valach L. Cognitive deficits in patients after soft tissue injury of the cervical spine. *Spine.* 1992;17(2):127-31.

Richter M, Ferrari R, Otte D, Kuensebeck HW, Blauth M, Krettek C. Correlation of clinical findings, collision parameters, and psychological factors in the outcome of whiplash associated disorders. *J Neurol Neurosurg Psychiatry*. 2004;75(5):758-64.

Rothman SM, Kreider RA, Winkelstein BA. Spinal neuropeptide responses in persistent and transient pain following cervical nerve root injury. *Spine*. 2005 Nov 15;30(22):2491-6.

Roy S, Hol PK, Laerum LT, Tillung T. Pitfalls of magnetic resonance imaging of alar ligament. *Neuroradiology* 2004;46:392-298.

Saldinger P., Dvorak J., Rahn B., Perren S. Histology of the Alar and Transverse Ligaments. *Spine*. 1990;15(4):257-61.

Schrader H, Obelieniene D, Bovim G, Surkiene D, Mickeviciene D, Miseviciene I, Sand T. Natural evolution of late whiplash syndrome outside the medicolegal context. *Lancet*. 1996; 347(9010):1207-11.

Schutte MJ, Dabezies EJ, Zimny ML, Happel LT. Neural anatomy of the human anterior cruciate ligament. *J Bone Joint Surg Am*. 1987;69(2):243-7.

Siegmund GP, Myers BS, Davis MB, Bohnet HF, Winkelstein BA. Mechanical evidence of cervical facet capsule injury during whiplash: a cadaveric study using combined shear, compression, and extension loading. *Spine*. 2001;26(19):2095-101.

Spitzer, WO., Skovron, M.L., Salmi, L.R., Cassidy, J.D., Duranceau, J., Suissa, S. & Zeiss, E. (1995). Scientific monograph of the Quebec Task Force on Whiplash-Associated Disorders: redefining "whiplash" and its management. *Spine*.1995;20:1S-73S.

Tamai M, Okajima S, Fushiki S, Hirasawa Y. Quantitative analysis of neural distribution in human coracoacromial ligaments. *Clin Orthop Relat Res*. 2000;4(373):125-34.

Tominaga Y, Ndu AB, Coe MP, Valenson AJ, Ivancic PC, Ito S, Rubin W, Panjabi MM. Neck ligament strength is decreased following whiplash trauma. *BMC Musculoskelet Disord*. 2006;7:103-16.

Tousignant M, de Bellefeuille L, O'Donoghue S, Grahovac S. Criterion validity of the cervical range of motion (CROM) goniometer for cervical flexion and extension. *Spine*. 2000;25(3):324-30.

Tousignant M, Duclos E, Laflèche S, Mayer A, Tousignant-Laflamme Y, Brosseau L, O'Sullivan JP. Validity study for the cervical range of motion device used for lateral flexion in patients with neck pain. *Spine*. 2002;27(8):812-7.

Tousignant M, Smeesters C, Breton AM, Breton E, Corriveau H. Criterion validity study of the cervical range of motion (CROM) device for rotational range of motion on healthy adults. *J Orthop Sports Phys Ther*. 2006;36(4):242-8.

Trijffel van E, Anderegg Q, Bossuyt PM, Lucas C. Inter-examiner reliability of passive assessment of intervertebral motion in the cervical and lumbar spine: a systematic review. *Man Ther*. 2005;10(4):256-69.

Van der Donk J., Schouten JS., Van Romunde LK., Valkenburg HA. The association of neck pain with radiological abnormalities of the cervical spine and personality traits in the general population. *J Rheumatol*. 1991;18:1884-9.

Vos CJ, Verhagen AP, Koes BW. Reliability and responsiveness of the Dutch version of the Neck Disability Index in patients with acute neck pain in general practice. *Eur Spine J*. 2006;15(11):1729-36.

Williams PL, Warwick R. *Gray's Anatomy*, 36th Edition. Churchill Livingstone 1980.

Wilmink JT, Patijn J. MRi maging of Alar ligament in whiplash-associated disorders: an observer study. *Neuroradiology* 2001;43:859-863.

Youdas JW, Carey JR, Garrett TR. Reliability of measurements of cervical spine range of motion--comparison of three methods. *Phys Ther.* 1991;71(2):98-104.

Youdas JW, Garrett TR, Suman VJ, Bogard CL, Hallman HO, Carey JR. Normal range of motion of the cervical spine: an initial goniometric study. *Phys Ther.* 1992;72(11):770-80.

Zumpano MP, Hartwell S, Jagos CS. Soft tissue connection between rectus capitus posterior minor and the posterior atlanto-occipital membrane: a cadaveric study. *Clin Anat.* 2006;19(6):522-7.

NAMN: _____ F NR: _____

ADR: _____ TLF: _____

UTSATT FOR NAKKESLENGSKADE – MND/ÅR: _____

PÅKØYRD FORFRA JA _____ NEI _____ HUGSAR IKKJE _____

EG SAT MED NAKKEN ROTERT (ANSIKTET SNUDD TIL EI SIDE) I KOLLISJONSAUGNEBLINKEN

JA _____ NEI _____ HUGSAR IKKJE _____

EG SAT MED NAKKEN NØYTRAL (ANSIKTET RETT FRAM) I KOLLISJONSAUGNEBLINKEN

JA _____ NEI _____ HUGSAR IKKJE _____

BRUKTE DU SIKKERHETSSELE

JA _____ NEI _____ HUGSAR IKKJE _____

HADDE BILEN RIKTIG INNSTILT HOVUDSTØTTE

JA _____ NEI _____ HUGSAR IKKJE _____

HAR DU TIDLEGARE VORE UTSATTT FOR BILKOLLISJON ELLER ANDRE NAKKESKADER

JA _____ NEI _____ HUGSAR IKKJE _____

BRUKTE DU NAKKEKRAGE ETTER BILULYKKA JA _____ NEI _____
DERSOM JA:

BYRJA DU Å BRUKE KRAGEN I LØPET AV 3 DGR JA _____ NEI _____

I LAUPET AV 3 TIL 7 DAGAR JA _____ NEI _____

(Legen skriv WAD kategori)

WAD KATEGORI: _____

I perioden 1993-1997 vart De registrert ved ditt lokale legekantor i høve med ditt nakkeslengtilfelle. Som De sikkert hugsar, vart det i tillegg utført ei tilleggsregistrering på eit eige ark angående nakkestilling i kollisjonsaugneblinken, påkøyringsretning etc.

Underteikna skal no gjennomføre eit prosjekt der vi ynskjer å undersøke om nakkestilling i kollisjonsaugneblinken har noko å seie for dei plager som kan oppstå etter eit slikt biluhell. Dette vil bli gjort ved hjelp av eit spørreskjema, testteknikker innan manuell terapi og MRI (røntgenundersøking).

Resultatet frå studiet vil kunne gje nytting informasjon om sittestilling i kollisjonsaugneblinken har betydning for eventuelle skader. Dette vil igjen kunne ha betydning for korleis bilfabrikantar utformer bilseter og hovudstøtte. I tillegg vil meir nøyaktig funn til skadde enkeltstrukturar kunne bidra til å gje meir målretta behandling for dei som har pådrege seg slike skader etter eit nakkeslengtraume.

Målingar for delprosjekt 1 og 2 (sjå vedlagt informasjonsskriv) vil bli gjennomført på Sandane. Alle registrerte pasientar vil få tilbod om å delta på desse to delprosjekta. Kun eit mindre utval av pasientar (ca 40 personar) vil få tilbod om å delta på delprosjekt 3,4,5, som også ofattar ein MRI undersøking. Alle målingar for desse delprosjekta vil bli gjennomført på Haukeland sykehus i Bergen. Reisekostnadar for den enkelte bil bli dekkja. Undersøkinga vil bli lagt til ein laurdag. Eit tilfeldig utval av ei pasientar som seier seg villeg til å delta på delprosjekt 3-5 vil få tilsendt innkalling om tid og sta for undersøking. Undersøkningsperioden for alle delprosjekta vil vere **april til juni 1999 (husk evt å enre)**.

Vi håpar at flest mulige er villeg til å delta, ettersom det er svært viktig for generaliserbarheten av resultatane. Ver vennleg å sende svararket tilbake i vedlagte svarkonvolutt innan dato....., også om du ikkje ynskjer å delta.

Sandane den 1. oktober 1998

Bertel Rune Kaale

Vedlegg 2b

INVITASJON TIL DELTAKING I FORSKNINGSPROSJEKT SOM KONTROLLPERSON

Underteikna skal gjennomføre eit forskningsprosjekt vedrørande nakkeslengskader (whiplash) hos trafikkskadde. Vi ynskjer å undersøke om nakkestilling i kollisjonsaugneblinken har noko å seie for dei plager som kan oppstå etter ulukka. Dette vil bli gjort ved hjelp av eit spørreskjema, testteknikker innan manuell terapi og MRI (røntgenundersøking). Resultatane frå studiet vil kunne gje nyttig informasjon om sittestilling i kollisjonsaugneblinken har betydning for eventuelle skader. Dette vil igjen kunne ha betydning for korleis bilfabrikanten utformer bilsete og hovudstøtte. I tillegg vil meir nøyaktig funn til skadde enkeltstrukturar kunne bidra til å gje ei meir målretta behandling for dei som har pådrege seg slike skader etter eit nakkeslengtraume.

For å kunne seie noko om omfanget av eventuelle skader, treng eg ei kontrollgruppe som samanlikningsgrunnlag. Ei kontrollgruppe i dette prosjektet består av personar som tidlegare ikkje har vore utsatt for nakkeslengskader ved bilkollisjon eller har hatt andre skader til nakke/rygg. Denne kontrollgruppa skal gje oss informasjon om korleis ein normal nakke fungerer. Kontrollmaterialet er blitt tilfeldig uttrekt av Statistisk Sentralbyrå basert på kjønn, alder og bustad blant pasientane. Kontrollpersonane skal gjennomgå dei same testane som whiplash-pasientane.

Målingar for delprosjektet 1 og 2 (sjå vedlagt informasjonsskriv) vil bli gjennomført på Sandane. Kun eit mindre utval pasientar (ca 20 personar i kvar gruppe) vil få tilbud om å delta på delprosjekt 3,4,5 som også omfattar ein MRI undersøking. Alle målingar for disse delprosjekta vil bli gjennomført på Haukeland sykehus i Bergen. Reisekostnadar for den enkelte vil bli dekkja. Undersøkinga vil bli lagt til ein laurdag. Eit tilfeldig utval av dei pasientar som seier seg villeg til å delta på delprosjekt 3-5 vil få tilsendt innkalling om tid og stad for undersøking. Undersøkingstida for alle delprosjekt vil vere april til juni 1999.

Vi håpar at flest mulig er villeg til å delta, ettersom det er svært viktig for generasiserbarheten av resultatane. Ver vennleg å sende tilbake svarslippen nederst på arket i vedlagte svarkonvolutt innan dato....., også om du ikkje ønskjer å delta.

Sandane 1. oktober 1998

Bertel Rune Kaale

SVARSLIPP:

Kryss av i ein av rubrikkane nedanfor både for punkt 1a og 1b:

- 1a Prosjekt uten MRI undersøking (del 1-2)
 JA, eg ynskjer å delta i prosjektet.
 Nei, eg ynskjer ikkje å delta i prosjektet.
- 1b Eg er villeg til å delta på delprosjekt 3-5, i tillegg til del 1 og 2
 JA, eg ynskjer å delta i prosjektet.
 NEI, eg ynskjer ikkje å delta i prosjektet.

Dato _____

Underskrift _____

INFORMASJONSSKRIV

Informasjon om prosjekt vedrørende samanheng mellom nakkestilling i kollisjonsaugneblinken og eventuelle nakkeskader etter traumet.

Målet med prosjektet

Forsøket er retta mot personar som har vore utsatt for ein bilkollisjon. Bakgrunnen for undersøkinga er å vurdere om nakkestilling i kollisjonsaugneblinken har noko å seie for kva skader og funksjonsforstyrningar som kan oppstå etter traumet. Når nakken og hovudet blir utsatt for ein kraftig sleng i kollisjonsaugneblinken, blir både blautdels- og leddstukturar utsett for ei stor påkjenning. Kva slags strukturar som kan bli skada, kan vere avhengig av kva stilling nakken og hovudet hadde i kollisjonsaugneblinken. For å kunne utføre ei meir nøyaktig undersøking, er det viktig å sjå om våre metodar fangar opp ei slik blautdels- og leddforandring.

Beskriving av forsøket.

Prosjektet består av fem delar.

Del 1: Du skal her svare på 10 spørsmål på eit spørjeskjema. Desse spørsmåla omhandlar daglege normale gjeremål og funksjonar i forhold til evt. nakkesmerter. Ved starten av prosjektet vil du bli informert om kva du skal gjere.

Del 2: Vi skal her utføre måling av dine aktive nakkebevegelsar. Nakkebevegelsane skal ikkje forårsake smerte. Du kan sjølv avbryte nakkerørsla dersom du føler ubehag. Som måleinstrument fester vi ein liten og lett bøylehjelm på hovudet ditt. På denne hjelmen er det festa 3 kompassliknande skiver. Desse måler utslaget i rørsla. Testen tar 4 min.

Del 3: I denne delen av prosjektet skal du ligge på ein vanleg behandlingsbenk. Eg skal teste kvaliteten på eit viktig leddband i nakken din. Testen er smertefri, og den varer berre i 30 sek. Dersom du blir uvel, avslutter vi testen.

Del 4 og 5: Vi skal her gjennomføre ein test ved hjelp av MRI. MRI er eit godt røntgenapparat som tek bilder av det samme leddbandet som eg tidlegare har testa. Du blir plassert komfortabelt på eit liggebord ved MRI maskina. Nakken blir plassert i 2 forskjellige rotasjonsstillingar. Dersom du klarer å ligge slik i 10 min. til kvar side, gir det os nok tid til å ta bilda. Det einaste du merkar til når bilda blir tatt er at det "brumer" litt i MRI maskina. Dersom

du får problem med dette, blir billedopptaket avslutta. Der il hele tida vere personar tilstades som du kan henvende deg til med eventuelle spørsmål.

Alle aktuelle tester(delprosjekt 1-2, evt. 3-5) vil bli utførde fortløpande samme dag. Vi vil kome tilbake med meir nøyaktig informasjon om tid og stad for gjennomføringa.

Du står fritt om du ynskjer å delta i forsøket. Du kan når som helst trekke deg frå forsøket uten å angje grunn, og utan at det på nokon måte vil påverke ditt tilhøve tili eventuell vidare undersøking og behandling for din nakkeskade.

Sandane okt. 1998

Bertel Rune Kaale

Spesialist i manuell terapi

INNKALLING

Vedlegg 4a

Vi takkar for din velvillighet itl å stille som deltakar i delprosjekt 1 og 2. Vi har satt deg opp på følgende timebestilling for undersøkelse av nakke gjennom spørreskjema, registrering av nakkerørsle og test av leddbandsstrukturar (dersom dette ikkje passer tar du kontakt på telefon.....)

Stad: _____

Dag: _____

Tid: _____

Ditt referansenummer: _____

Når du kjem til avtalt tid og stad, skal du ikkje opge ditt navn eller omtale din nakkeskade. Du skal kun oppgi ditt referansenummer (HUSK å ta med lappen med ditt referansenummer !)

VEL MØTT

Med helsing

Bertel Rune Kaale

INNKALLING

Vedlegg 4b

Vi takkar for din velvillighet til i stille som deltakaker i delprosjekter 3-5. Du er ein av dei som er blitt trekt ut til å delta i desse delprosjekta. Vi har satt deg opp på følgende timebestilling for undersøkelse av nakke gjennom mRI undersøkelse (dersom dette ikke passer tar du kontakt på telefon.....)

Stad: _____

Dag: _____

Tid: _____

Ditt referansenummer: _____

Når du kjem til avtalt tid og stad, skal du ikkje oppgi ditt navn eller omtale din nakkeskade. Du skal kun oppgi ditt **referansenummer** (HUSK å ta med lappen med ditt referansenummer!)

VEL MØTT

Med helsing

Bertel Rune Kaale

NAKKEFUNKSJONSINDEKS

Dette skjemaet er utformet for å gi oss informasjon om hvordan dine eventuelle nakkesmerter har påvirket din evne til å klare deg i hverdagen. Vennligst besvar hver del, og kryss av i bare EN rubrikk for hvert spørsmål. Vi er oppmerksomme på at du kan mene at to av utsagnene i enkelte deler kan gjelde deg, men vennligst kryss bare av i den rubrikken som best beskriver dine problem.

Del 1: Har du for tiden smerter i nakken ?

- 0 Jeg har ingen smerter i nakken nå.
 1 Nakkesmertene er milde nå.
 2 Nakkesmertene er moderate nå.
 3 Nakkesmertene er ganske sterke nå.
 4 Nakkesmertene er meget sterke nå.
 5 Nakkesmertene er de verst tenkelige nå.

Del 2: Påvirker dine eventuelle nakkesmerter ditt personlige stell (vask, påkledning etc) ?

- 0 Jeg kan stelle meg selv som vanlig, uten at det medfører nakkesmerter.
 1 Jeg kan stelle meg selv som vanlig, men det medfører moderate nakkesmerter.
 2 Det er smertefullt i nakken når jeg steller meg selv, det tar lang tid og jeg må være forsiktig.
 3 På grunn av mine nakkesmerter trenger jeg noe hjelp, men klarer det meste av mitt personlige stell.
 4 På grunn av mine nakkesmerter trenger jeg daglig hjelp til det meste av mitt personlige stell.
 5 På grunn av mine nakkesmerter klarer jeg ikke å vaske og kle meg selv.

Del 3: Evne til å løfte/ bære en pose med 4 liter melk i 15 minutter ?

- 0 Jeg kan løfte og bære en pose med 4 liter melk i 15 minutter uten noe besvær.
 1 Jeg kan løfte og bære en pose med 4 liter melk i 15 minutter, men det medfører moderat nakkesmerte.
 2 Jeg kan løfte en pose med 4 liter melk fra gulvet, men jeg klarer ikke å bære posen i 15 minutter.
 3 Jeg klarer ikke å løfte en pose med 4 liter melk fra gulvet.
 4 Jeg kan klare å løfte lettere ting fra gulvet.
 5 Jeg klarer ikke å løfte noe fra gulvet.

Del 4: Har du problemer med lesing på grunn av dine nakkesmerter ?

- 0 Jeg kan lese så mye jeg vil uten å få nakkesmerter.
 1 Jeg kan lese så mye jeg vil, men jeg får lette smerter i nakken.
 2 Jeg kan lese så mye jeg vil, men jeg får moderate smerter i nakken.
 3 Jeg kan ikke lese så mye jeg vil fordi jeg får moderate smerter i nakken.
 4 Jeg kan nesten ikke lese på grunn av sterke smerter i nakken.
 5 Jeg kan ikke lese i det hele tatt på grunn av sterke smerter i nakken.

Del 5: Får du hodepine på grunn av dine nakkesmerter ?

- 0 Jeg har aldri hodepine på grunn av nakkesmerter
- 1 Jeg får av og til lett hodepine på grunn av mine nakkesmerter.
- 2 Jeg får av og til moderat hodepine på grunn av mine nakkesmerter.
- 3 Jeg får ofte moderat hodepine på grunn av mine nakkesmerter.
- 4 Jeg får ofte sterk hodepine på grunn av mine nakkesmerter.
- 5 Jeg har hodepine nesten hele tiden på grunn av mine nakkesmerter.

Del 6: Har du nedsatt konsentrasjon på grunn av dine nakkesmerter ?

- 0 Jeg kan konsentrere meg fullt ut når jeg vil uten noe form for nakkesmerter.
- 1 Jeg kan konsentrere meg fullt ut når jeg vil, men jeg har moderate nakkesmerter.
- 2 Jeg har moderate vanskeligheter med å konsentrere meg når jeg vil på grunn av mine nakkesmerter.
- 3 Jeg har store vanskeligheter med å konsentrere meg når jeg vil på grunn av mine nakkesmerter.
- 4 Jeg har veldig store vanskeligheter med å konsentrere meg når jeg vil på grunn av mine nakkesmerter.
- 5 Jeg klarer ikke å konsentrere meg i det hele tatt på grunn av mine nakkesmerter.

Del 7: Kan du gjennomføre normalt husarbeid/ hagearbeid ?

- 0 Jeg kan arbeide så mye jeg vil.
- 1 Jeg klarer å utføre lett husarbeid/ hagearbeid uten stort behov for pauser.
- 2 Jeg klarer å utføre lett husarbeid/ hagearbeid men med behov for pauser på grunn av mine nakkesmerter.
- 3 Jeg klarer ikke utføre normalt husarbeid/ hagearbeid på grunn av mine nakkesmerter.
- 4 Jeg klarer nesten ikke utføre noe husarbeid/ hagearbeid på grunn av mine nakkesmerter.
- 5 Jeg klarer ikke å utføre noe husarbeid/ hagearbeid på grunn av mine nakkesmerter.

Del 8: Kan du kjøre bil så mye du ønsker ?

- 0 Jeg kan kjøre bil så mye jeg vil uten å få nakkesmerter.
- 1 Jeg kan kjøre bil så mye jeg vil, men jeg får lette nakkesmerter.
- 2 Jeg kan kjøre bil så mye jeg vil, men jeg får moderate nakkesmerter.
- 3 Jeg kan ikke kjøre bil så mye jeg vil, fordi jeg får moderate nakkesmerter.
- 4 Jeg klarer nesten ikke kjøre bil på grunn av sterke nakkesmerter.
- 5 Jeg klarer ikke kjøre bil i det hele tatt på grunn av sterke nakkesmerter.

Del 9: Har du søvnforstyrrelser på grunn av dine nakkesmerter ?

- 0 Jeg har ingen problem med å sove.
- 1 Min søvn er minimalt forstyrret av mine nakkesmerter (mindre enn 1 times søvnløshet).
- 2 Min søvn er noe forstyrret på grunn av mine nakkesmerter (1-2 timers søvnløshet).
- 3 Min søvn er moderat forstyrret på grunn av mine nakkesmerter (2-3 timers søvnløshet).
- 4 Min søvn er veldig forstyrret på grunn av mine nakkesmerter (3-5 timers søvnløshet).
- 5 Min søvn er fullstendig forstyrret av mine nakkesmerter (5-7 timers søvnløshet).