Clinical and Finite Element Analysis of Acute Whiplash

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Abstract: Study Design: A prospective 1-year follow-up study of whiplash patients presenting with neurological signs/or symptoms (WADIII), and whiplash patients with neck pain but no neurologic findings (WADI/II).

Objective: We hypothesize that WADI/II and WADIII are distinct entities, with regards to clinical presentation, pathoanatomy, and prognosis.

Summary of Background Data: symptoms associated with whiplash injury range from mild neck pain (WADI/II), to injuries associated with neurologic sequellae (WADIII). To date, literature considers whiplash associated disorders (WAD) a single clinical and pathologic entity, with different grades of severity (WADI-IV).

Methods: Thirty one subjects were divided into a WADIII study group and a WADI/II comparison group. All subjects underwent H&P, radiographic evaluations, and clinical outcome measures (collected at 3, 6, and 12 months). Statistical analysis was performed (Student T-test, Wilcoxon Signed-Rank test) with significance set at p=0.05. A finite element analysis (FEA) technology (SCOSIA©) was used to predict stresses within the neuraxis.

Results: At day 0: Better neurologic assessments, functional performances, and higher quality-of-life measurements were noted in WADI/II compared to WADIII. VAS scores were comparable.

At 12 months: Both groups reported improvements in neurologic status and disability symptoms. However functional recovery and quality-of-life measures significantly improved in WADIII, and conversely deteriorated in WADI/II along with notable worsening of pain symptoms. Litigation claims were comparable. FEA predicted higher stress within the neuraxis of WADIII, notably in subjects with preexisting stenosis and odontoid retroflexion.

Conclusion: WADI/II and WADIII are distinct entities. Musculoskeletal injury precipitates WADI/II pain symptoms while neuronal stretching leads to WADIII neurologic injuries, which are mostly recoverable.

Keywords: Whiplash, whiplash associated disorder (WAD), neck pain, cervical cord stress injury, finite element analysis.

BACKGROUND

There are 1.5 million cases of whiplash each year in the United States. Whiplash is most commonly the result of acceleration deceleration injuries during motor vehicle accidents, but can also occur from a fall or the result of a sports injury. Neck pain resulting from whiplash injury is traditionally considered the result of muscular and/or ligamentous injuries. Imaging studies (i.e. radiographs, MRI, and CT) most often show no evidence of fracture, instability or significant soft tissue disruption [1]. Symptoms associated with whiplash injury range from mild neck pain with no physical findings to debilitating injuries with long-term neurological sequellae. Patients may complain of paresthesia, dysesthesia, weakness, and changes in vision, audition, imbalance, vertigo, altered memory, personality change, dysarthria, dysphagia, and sleep apnea.

To improve communication among practitioners and assist with prognosis, a classification system for whiplash associated disorders (WAD) was described as follows [2]: WAD I are those injuries with neck pain but no physical findings; WADII are those injuries with neck pain and physical exam findings such as tenderness to palpation of the posterior neck; WAD III includes injuries with associated neurological signs or symptoms, and WAD IV have an associated fracture or dislocation. Numerous studies have evaluated outcomes following acute whiplash injury, but are retrospective and include a wide range of injury. The past literature has suggested that the more severe injuries are associated with worse long term outcomes, and persistent, often disabling symptoms [3, 4].

In this report the authors hypothesize that whiplash patients with neurological findings (WAD III) are distinct from whiplash patients with neck pain but no neurological findings (WAD I/ II) not only in terms of clinical presentation, but in terms of pathoanatomy and prognosis. In the following prospective comparison of subjects presenting with acute whiplash injury, the authors show that deformative stress injury of the brainstem and spinal cord was evident in the WAD III subjects, but not the WAD I/II subjects. Illustrative finite element analyses of the neuraxis under conditions of deformative stress in the two groups are presented. The authors suggest that in addition to a primary trauma related injury to the neural elements, a preexisting, underlying condition or deformity may predispose some individuals to pathological deformative stress of the neural elements at the time of the injury, in contrast to others who

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manifest only muscular/ligamentous injury. Therefore, these two groups of subjects should be considered as distinct in terms of etiology, treatment, range of associated conditions and prognosis.

MATERIALS AND METHODS

Following Institutional Review Board (IRB) approval, subjects between the age 18 and 80 years involved in a MVA or fall presenting to a Level I trauma center with complaints of neck pain were reviewed for eligibility. Exclusion criteria included: fracture, dislocation, instability (WAD IV patients); patients with a potentially atraumatic etiology of neck pain, including infection, tumor, congenital or metabolic disease; patients requiring spine surgery following their presentation (i.e. for degenerative, traumatic, infectious, or neoplastic pathology); and patients presenting late following their whiplash injury.

Whiplash patients with no neurological signs or symptoms (WAD I/II) were enrolled into the comparison or control group. Whiplash patients with associated neurological signs and/or symptoms (WAD III) were enrolled into the study group. Upon presentation, patients underwent routine cervical spine x-rays, including anteroposterior (AP), lateral, and odontoid views. Where the x-ray series was inadequate (C7-T1 not visualized), a cervical CT scan with coronal and sagittal reconstructions was performed. All patients (i.e. study and comparison groups) underwent a cervical MRI.

A history and physical examination was performed on each subject, including history of the traumatic event (i.e. mechanism, speed of vehicle, direction of impact, loss of consciousness, presence of seatbelt, associated injuries) as well as the nature, severity, and location of the pain and any associated neurological symptoms. Pain was assessed objectively using the Visual Analog Scale (VAS) ranging 0 (no pain) to 10 (extremely severe pain). The patient's neurological status was assessed with the American Spinal Injury Association (ASIA) Impairment Scale. Brainstem disability was assessed using the Brainstem Disability Index [5], a collation of 20 symptoms of brainstem dysfunction, see Table **1**. Function was assessed with the Karnofsky Performance Scale and Neck Disability Index. Quality of life was assessed with the SF-36 physical component and mental component questionnaires. Clinical outcome measures were repeated at 3, 6, and 12 months following the injury for the study group and at 12 months for the comparison group. At 12 months all subjects were questioned on litigation status. All data collected was entered into a computerized database.

The data were collected by a research assistant, and therefore not subject to the influence of the investigator in the patient interview. The SF-36 is a widely approved instrument for measurement of physical functioning, bodily pain, general health, vitality, social functioning, and mental health, and is valid when tested against outcome instruments [6-8]. While the ASIA scale does not measure spasticity, coordination or gait- it is useful as a metric to register subtle changes in sensory and motor function. The Karnofsky Index was designed as a functional index for cancer patients, but has also been used in other areas as a reliable means of assessing function [9]. The Brainstem Disability Index [5] used in this report is not validated, but is used by the authors to measure improvement in the panoply of symptoms generally attributed to neurological dysfunction of the brainstem based upon the encyclopedic descriptions of others [10-21]. A score of 100 represents the presence of all 20 symptoms and significant disability (Table **1**).

Table 1. Brainstem Disability Index

The following 20 symptoms may be referable to pathology at the level of the brainstem. Please indicate yes or no whether you have any of the following symptoms on a recurring or chronic basis.

Double vision
Memory loss
Dizziness
Vertigo
Ringing in the ears
Speech difficulties
Difficulty swallowing
Sleep apnea
Snoring or frequent awakening
Choking on food
Hands turn blue in cold weather
Numbness in your arms and shoulders
Numbness in your back and legs
Get tired very easily
Unsteady walking
More clumsy than you used to be
Urinate more often (every 1-2 hours)
Irritable bowel disease or gastro esophageal reflux disease
Weaker than you would expect in your arms or hand
Weaker in your legs
5% each positive response, 0-100%

All data were entered into a computerized database managed by a third-party (Elder Research Inc., Charlottesville, VA). Data were de-identified, time-stamped, and redundantly backed up. Cryptographic signatures derived from content of the data and times of entry were used to ensure against accidental loss or modification of data.

Groups were compared both with Student T-tests and with non-parametric Wilcoxon Signed-Rank tests, in order to lessen reliance upon the normality assumption. Our null hypothesis was that there was no significant difference in prognosis between the two groups. Statistical significance was set at $p = 0.05$.

A finite element analysis (FEA) program (PRIMEGen) was adapted for the purpose of modeling the brainstem and cervical and upper thoracic spinal cord under dynamic loading and strain. The resulting Spinal Cord Stress Injury Analysis (SCOSIA ©) technology computes predicted relative magnitude and location of stress within the brainstem and upper spinal cord [5].

The SCOSIA system utilizes a simplified model of the brainstem and spinal cord. The model is constructed from

Table 2. Gender, Age, and Mechanisms of Injury Distribution

	Gender	Age (mean)	MVC	Fall	Sports	Miscellaneous (Hyper-extension)
Cases *n=21*	62%M *vs*. 38%F	45y + 7months	57.14%	28.57%	14.29%	0%
Controls *n=10*	60%M *vs*. 40%F	47y + 4months	40%	50%	0%	10%
P-value	*>0.05*	*>0.05*	*>0.05*	*>0.05*	*>0.05*	*>0.05*

quadrilateral elements extruded along parametrically generated cubic lines that are fit to the specific geometric properties, including curvature, of each subject in the neutral position. Assumptions include isotropy for all grey and all white matter, constant material properties regardless of stress, and boundary interfaces at the pons and mid thorax. The model uses the Young's modulus of elasticity for bovine grey and white matter provided by Ichihara *et al.* [22], and Poisson's ratio of 0.4. Ichihara demonstrated that the grey matter is more rigid (Young's modulus of $6.56x10^5$ Pa) and more fragile than the white matter (Young's modulus of $2.77x10^5$ Pa). Other reports by Ichihara *et al.* also note little difference in the elastic properties of live *vs*. dead spinal cord tissue [23], and compression of the bovine cervical spinal cord produced the same histo-pathologic changes as compression of the human cervical spinal cord [24]. Thus, it was reasonable to use the material properties derived by Ichihara *et al.* for bovine spinal cords in a human spinal cord model.

RESULTS

Thirty-one subjects meeting study criteria presented between March 2006 and December 2007. There were 19 males and 12 females.

The study group (WAD III), consisted of 21 subjects, 13 male and 8 female. The comparison group (WAD I/II) included ten subjects (6 male and 4 female). The average age of all subjects was 46 years (range 21 years to 71 years). There was no significant difference in the age (Mean age in study group = 46 years, mean age in comparison group = 47 year) or sex distributions among the whiplash and comparison groups (Table **2**).

Mechanisms of Injury

Within the study group (WAD III), twelve subjects suffered MVA (57%), 6 subjects a fall (29%), and 3 subjects a sports related injury (14 %). In the comparison group, four suffered MVA (40%), 5 subjects a fall (50%), and 1 subject a hyperextension sports related injury (10%).

Neurological Assessment

At day 0 the WAD III group scored significantly lower (i.e. more pathological) than the comparison group on the ASIA scale (284 *vs*. 324 points) (*p<0.01*). At 12 months, the WAD III group improved their neurological scoring by 34 points (total 318 points), and this improvement was statistically significant (*p = 0.05*). The comparison group maintained their original ASIA score (324 points) (Table **3**). The difference in prognosis between the two groups was statistically significant with p = 0.013.

Table 3. Objective Neurologic Assessment - ASIA Score

ASIA	0 months	12 months	*P-values*
Cases	284	318	*0.0002*
Controls	324	324	*0.5*
P-values	*0.01*	*0.0139*	

At day 0 the WAD III group showed numerous bulbar symptoms with an average score of 84.55% (16.9 bulbar symptoms out of the 20 listed) on the brainstem disability scale. The control group presented with an average score of 15% (3 out of 20 symptoms). The difference between these groups was significant at p<0.001. At 12 months the WAD III group noted improvement of symptoms reflected by a significant improvement in brain-stem score to an average of 35.60% (7.14 out of 20 possible bulbar symptoms), (*p=0.05*) (Table **4**).

Table 4. Brainstem Disability Index Scores

HMBSS (0-20 points)	0 months	12 months	*P-values*
Cases	84.55% (16.9/20)	35.60% (7.14/20)	*0.05*
Controls	15% (3/20)	8.45% (1.66/20)	
P-values	*<0.001*		

The most common presenting bulbar symptoms were dizziness, vertigo and numbness or weakness in the arms and hands. Resolution was most commonly seen in vertigo, clumsiness, gait changes, and weakness in the arms and hands. At 12 months, persistent bulbar symptoms included sleep disturbances (including apnea and frequent awakening), sexual difficulties and fatigue.

Pain Assessment

At day 0 the WAD III group had a mean pain score of 5.6/10 which was similar to the mean score of the comparison group, 6/10. At 12 months, the WAD III group had improved to an average VAS score of 1.6/10, which was lower than the mean score for the comparison (WAD I/II) group of 3.8/10. The difference in these results at 12 months

was significant ($p<0.05$). Improvement within each group was statistically significant (Table **5**).

Table 5. Pain Assessment – Visual Analogue Scale (VAS)

VAS (0-10 points)	0 months	12 months	*P-values*
Cases	5.55	1.65	*<0.001*
Controls	6.00	3.87	
P-values	*0.15*	*<0.001*	

At day 0 mean NDI score in the WAD III group was 42.24 and mean score in the comparison group was 52.75 ($p=0.02$). At 12 months, NDI score improved to 19.6 in the WAD III group and 27.0 in the comparison group ($p=0.01$). Improvement within each group was statistically significant ($p<0.05$) (Table **6**).

Table 6. Neck Disability Index Score

NDI	0 months	12 months	*P-values*
Case	42.24	19.60	*< 0.001*
Control	52.75	27.00	
P-values	*0.02*	*0.01*	

Function Assessment

At day 0 mean KPS score was 70.16% in the WAD III group and 86% in the comparison group. This difference was statistically significant with $p < 0.001$. At 12 month follow up, subjects in the WAD III group scored significantly higher with mean of 88.13% ($p<0.001$). The comparison group had a non-significant decrease in mean score to 84.24%. (Table **7**) The difference between the two groups at 12 months was significant at $p=0.01$.

Table 7. Disability Assessment – Karnofsky Performance Scale (KPS)

KPS	0 months	12 months	*P-values*
Case	70.16%	88.13%	*<0.001*
Control	86%	84.24%	
P-values	*< 0.001*	*0.01*	

Quality of Life Surveys

At day 0 the WAD III group had mean SF-36 physical score of 32.61 while the comparison group had mean score of 54.59. These scores were significantly different, $p<0.001$. At 12 month follow up, the WAD III group showed significant improvement in SF-36 score (mean of 49.17), while the comparison group showed a significant decline in SF-36 score (mean of 44.74) ($p<0.05$). Absolute comparisons between WAD III and comparison group at 12 month follow up were not statistically significant, but comparisons between mean improvement (or decline) in each group were ($p<0.001$) (Table **8**).

Table 8. Physical Health Survey – (SF36 Physical)

SF36-Physical (0-90 points)	0 months	12 months	*P-values*
Case	32.61 points	49.17 points	*< 0.001*
Control	54.59 points	44.74 points	
P-values	*< 0.001*	*0.05*	

At day 0 the WAD III group had mean SF-36 mental score of 40.16, while comparison group had mean of 54.75. This difference was statistically significant, $p < 0.001$. At 12 month follow up, the WAD III group's mean score had improved to 49.05, a statistically significant improvement ($p<0.05$). Mean score in the comparison group declined to 54.22 at final follow-up. This decline was not statistically significant. The difference in SF-36 mental score remained significant at 12 months ($p<0.05$) (Table **9**).

Table 9. Mental Health Survey – (SF36 Mental)

SF36-Mental (0-90 points)	0 months	12 months	*P-values*
Case	40.16 points	49.05 points	*< 0.001*
Control	54.75 points	54.22 points	
P-values	*< 0.001*	*< 0.001*	

Litigation

At 12 month follow-up, the two groups were similar in regards to pending litigation claims. 19% of subjects within the WAD III group (4 patients) and 20% of the control group (2 patients) were involved in litigation.

Finite Element Analysis (FEA)

FEA was performed on two representative patients. FEA of the neuraxis (brainstem and spinal cord) of a WAD III subject with pre-existing spinal stenosis and retroflexion of the odontoid process upon flexion of the neck is compared to a subject from the WAD I/II group. A comparison of these axial representations of predicted stress that is developed during flexion provides insight into the pathophysiology underlying the neurological findings of subjects with whiplash injuries.

Whiplash Subject with Spinal Stenosis and Retroflexion of Odontoid

WAD III subject 10 was neurologically intact prior to the incident. Following the motor vehicle accident (rear-end collision) the subject reported moderate pain (3/10), headache, sleeping disturbances, numbness in the arms, shoulders, hands, and legs; weakness in the arms and hands. His gait was unsteady. His KPS score of 70 reflected moderately severe disability. The flexion X-Ray revealed retroflexion of the odontoid which violated Wackenheim's line, thereby constituting mild basilar invagination on full flexion (Fig. **1**). The radiograph demonstrated stenosis, presumably preexisting, at C3-4, C4-5, C5-6, C6-7.

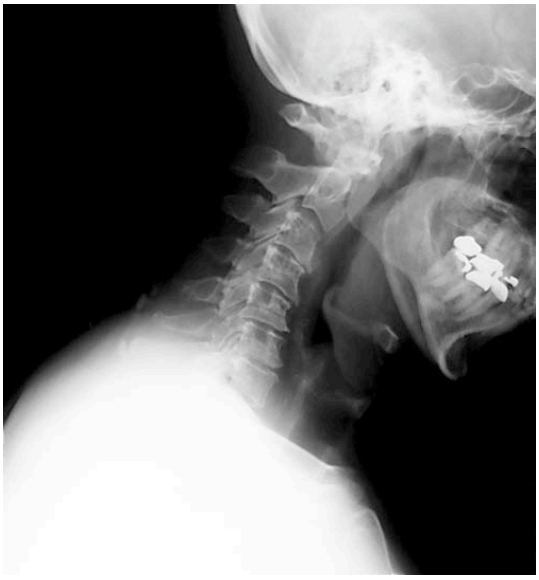

Fig. (1). Flexion X-Ray of WAD III subject J10.

The axial views of the upper spinal cord (Figs. **2A-C**) show very high predicted von Mises stresses (the aggregate of strain and compression). Predicted stresses in the lower medulla were evident, most prominently in the dorsal areas. The FEA predicted high stresses of 58N/cm^2 in the mid-region of the cord, in the region of the corticospinal tracts. Lower in the spine, the stresses were predominately dorsal, reflecting injury to the dorsal columns. At 12 months the patient reported no pain, weakness, or sensory loss; no headache, no sleep disturbances. He reported the ability to carry on normal activities with minimal discomfort, and a quality of life that was approaching his pre-injury quality of life.

Comparison Subject

On presentation, the comparison (WAD I/II) subject, 18 reported substantial musculo-ligamentous pain, but no neurological symptoms. On exam there were no neurological findings and no radiological abnormalities. Axial views

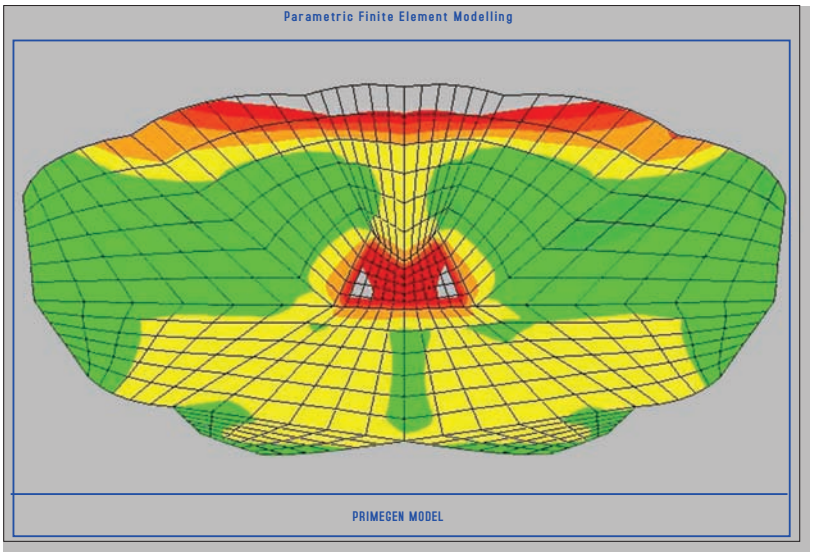

Fig. (2A). Predicted stresses in the lower brainstem on normal neck flexion in WAD III subject J10. Mild basilar invagination sets up deformative stress in the brainstem on full craniocervical flexion.

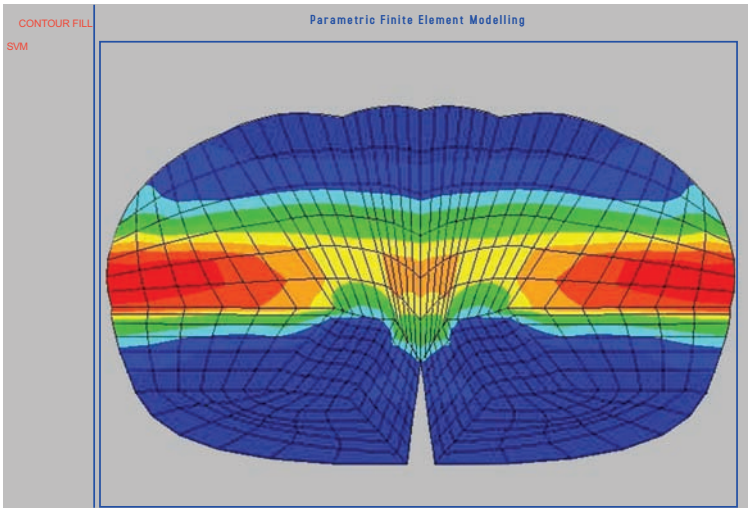

Fig. (2B). Predicted stresses at the C3 level on normal flexion in WAD III subject J10. Spinal stenosis leads to deformative stress in the cervical spinal cord on flexion.

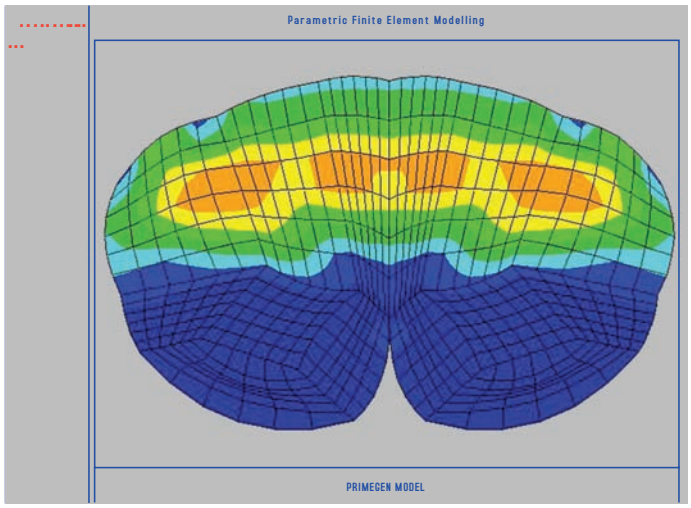

Fig. (2C). Predicted stresses at the C4 level on normal flexion in WAD III subject J10. Spinal stenosis leads to deformative stress in the cervical spinal cord on flexion.

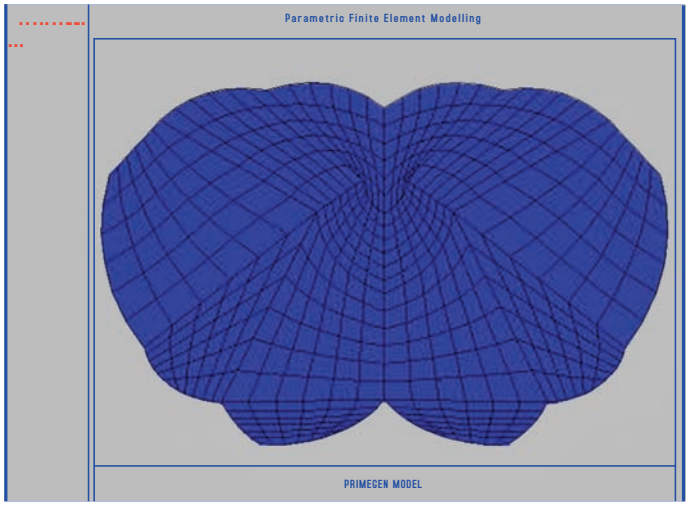

Fig. (3A). Predicted stresses in the lower brainstem on normal neck flexion in the comparison subject. Stresses are low throughout.

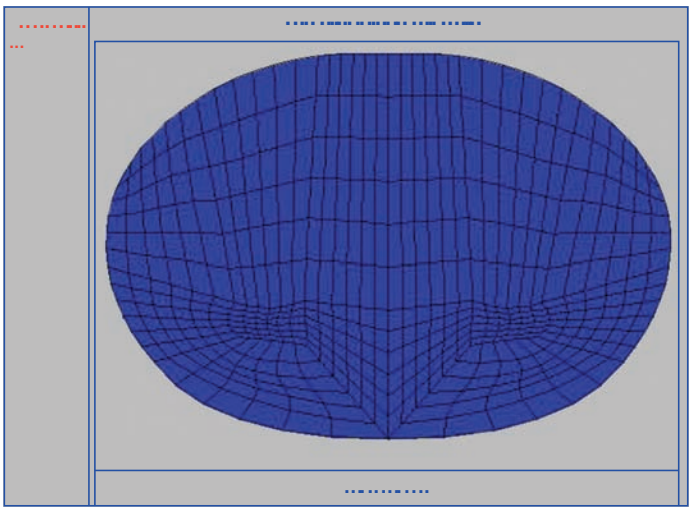

Fig. (3B). Predicted stresses at the C1 level on normal neck flexion in the comparison subject. Stresses are low throughout.

through the medulla and the spinal cord show predicted von Mises stress is very low (less than 5 N/cm^2) during flexion (Figs. **3A** and **3B**).

DISCUSSION

At one year follow up, the present study demonstrates significant improvement in neck pain and neurological

findings in both the WAD III group and the comparison (WADI/II) groups. Somewhat surprisingly, however, the magnitude of improvement was statistically greater in the WADIII group. Indeed, at one year, neck pain symptoms in the WADIII group were significantly less than the comparisons (WADI/II).

In the WAD III group, sensori-motor deficits showed significant improvement as measured by the ASIA score at one year following initial injury (Table **3**). Furthermore, the Brainstem Disability Index demonstrated a significant improvement in the WADIII group; that is, the brainstem ("bulbar") symptoms had to a large extent resolved at 12 months.

Neurological status was mirrored in function and quality of life. In the WAD III group, function measured by Karnofsky scale was significantly impaired following the acute whiplash injury (average 70 in the Karnofsky scale), but improved to near normal (average Karnofsky scale of 90) at 12 months. On the other hand, the comparison (WAD I/II) group demonstrated no improvement: the Karnofsky scale decreased slightly from 88 to 84 over the 12 month period.

Subjects' physical and mental health status assessed by the SF-36 health survey demonstrated quality of life approximately paralleled function in both groups. In the WAD III group, quality of life, though significantly impaired after the traumatic event, improved to normal at 12 months. On the other hand, in the WAD I/II group, the SF-36 scores showed a significant deterioration over the same 12 month period. This observation was evident in both the physical component and the mental component of the SF-36. The difference between the WAD III and comparison groups was highly significant.

These results are consistent with the findings of Kamper *et al.* who reported in their meta-analysis review that most of the pain recovery following whiplash occurs during the first 3 months post injury [25]. However, our results are at variance with others, who report that severe whiplash associated with neurological sequellae (WAD III) is persistent and debilitating. There has been no consistent characterization of clinical outcome for whiplash patients. Most recently, Carroll *et al.* performed a meta-analysis of the literature pertaining to whiplash injury. When considering all whiplash patients, 44% to 66% of patients had symptoms at one year, but only 12% reported daily neck pain and only 9% reported significant health impairment as a result of the whiplash injury [26-28]. Others have shown that 90% of patients presenting with neck pain and neurological signs (WAD III) have continued symptoms at one-year following the injury [29]. The severity of symptoms at initial presentation is thought to be prognostic of a poor outcome at 12 months follow-up [26].

Neurological Outcomes after Whiplash Injury

The clinical outcomes in this series are consistent with observation in experimental models that axons subjected to strain recover rapidly, both anatomically and functionally [30-32], and with neurosurgical series where anatomical alignment has been restored, and which show that even profound clinical deficits are recoverable [5, 12, 14, 17, 33-40]. Improvement in pain, bulbar symptoms, ASIA index, Karnofsky index and quality of life assessment support the concept that restoration of the neutral position of the cervical spine and craniospinal junction with a neck brace decreases the deleterious effects of flexion in the setting of erstwhile abnormal movement and anatomical abnormality.

On the other hand, acute whiplash injury without neurological deficit (WAD I/II) appears to be the result of osteo-musculo-ligamentous trauma. It is unclear whether symptoms from the latter may persist in the absence of clinical intervention, and the extent to which psycho-social features influence outcome. Schmitt *et al.*, found that depression and anxiety impose a negative impact on patient's recovery [41]. Carstensen reported that pre-collision psychological distress and pre-injury neck pain are predictive of poor outcome in patients with WAD [42]. Positive expectations, along with other psychosocial factors at the time of the initial injury are prognostic of good outcome [26, 43]. Carroll *et al.* showed that the recovery from WAD symptoms is comparable to the natural history of neck pain in the general population and workers [26]. Secondary gain is another concern that can also affect the reported recovery of the patient with neck pain post motor vehicle crash and/or a work related injury. The literature regarding the prognostic value of compensation and litigation is scarce [44, 45]. In our study 20% of subjects within each group were involved in a litigation claim. The low number of subjects precludes a meaningful statistical comparison.

Pathophysiology of Whiplash Injury Associated with Neurological Deficit

Flexion and extension of the cervical spine in whiplash injury result in abnormal strains that may exceed the physiological limit and result in neurological dysfunction. Experimentally, large strains have been shown to arise even from normal flexion of the spinal cord and brainstem [46-50]. The effect of strain on axons is faithfully recapitulated in experimental models of stretch- induced axonopathy where electron micrographs show clumping, loss of microtubules and neurofilaments, loss of axon transport and accumulations of axoplasmic material identified as "retraction balls" [47, 51-63], and in human histopathological studies that suggest that axon retraction bulbs are the histological substrate of stretch injury in the cortico-spinal tracts of the brainstem in infants with "Shaken Baby Syndrome" [64] and in cases of chronic brainstem deformity such as basilar invagination [52, 59, 60, 65]. Axonal injury relates directly to magnitude and rate of strain increase [66]. Rapid occurrence of these strains can exceed the material properties of the tissue, leading to tissue disruption; however, even mild stretch can induce progressive neurofilament alteration and delayed axotomy [67]. The degree of injury appears to be related to the peak strain of the tissue and the loading rate. The cord, though initially compliant to stretch, becomes progressively stiffer as the fibers bear tensile load [53, 68]. Stretching of the axolemma may result in several levels of injury: a conduction block due to myelin damage, or membrane injury with irreversible changes, decreased amplitude and increased latency [66]. Deformative stress acting upon the Na^+ channel mechanoreceptors increases Na^+ influx, causing reversal of the cation exchange pumps and

depolarization of voltage-gated Ca^{++} channels, with subsequent pathological influx of Ca^{++} [67, 69].

The deformative stress imposed upon the neuraxis by flexion of the neck and craniocervical junction, such as occurs in whiplash injury, is manifest radiologically by the measurement of increased length of the medulla and spinal cord [5, 12, 14, 17, 18, 22, 46, 49, 51, 52, 61, 64, 68, 70-79] (Figs. **4A-C**).

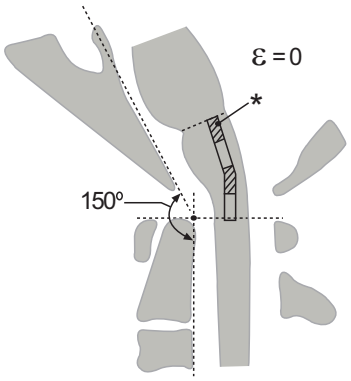

Fig. (4A). Normal craniocervical junction in the neutral position. The clivo-axial angle varies from 150-165 degrees. There is minimal or zero deformative strain in the neutral state.

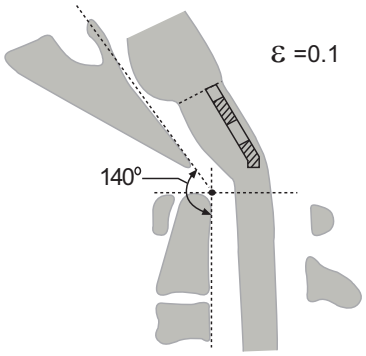

Fig. (4B). Normal craniocervical junction in flexion. The neuraxis stretches by approximately 10% of its total length with flexion of the craniocervical junction creating a strain ε = 0.1.

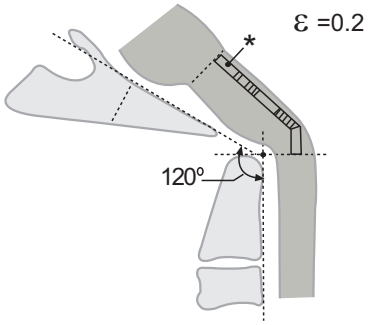

Fig. (4C). Pathological craniocervical junction with an abnormal clivo-axial angle in flexion. Upon full flexion at the craniocervical junction, the increase in the tangent arc creates a deformative strain approaching ε = 0.2. *In vivo* and *in vitro* models demonstrate decreased or loss of neurological function with strains of 0.2.

The mechanically induced stretching of the axon is an important epigenetic factor in gene expression. Deformative stress results in up-regulation in neurons of N-Methyl D-Aspartate receptors, and heightened vulnerability to subsequent challenges of reactive oxygen species and peroxynitrites, concomitant mitochondrial dysfunction and DNA fragmentation [80]. Calpain activation may contribute to progressive intra-axonal structural damage after stretch injury [62], or apoptosis of neurons and oligodendrocytes [52, 80-83].

Cranio-Cervical Anatomical Abnormalities that may give Rise to Increased Neurological Deficit with Acute Whiplash Injury

The authors believe that whiplash injury may be exacerbated by underlying craniocervical or cervical deformity, stenosis or compression. Deformative stress due to chronic flexion extension injuries were noted in patients with angulation of the brainstem [76, 78, 79, 84] and attributed to the fulcrum effect of the medullo-spinal junction draped over the odontoid [17]. Deformative stress is evident in achondroplasia [85-89], platybasia [84, 90, 91], acquired bone-softening conditions such as rickets, hyperparathyroidism, spondyloepiphyseal dysplasia, acroosteolysis, Hurler's Syndrome, osteomalacia, achondromalacia, renal osteodystrophy, Paget's disease, and degenerative conditions such as rheumatoid arthritis [35, 51, 72, 92-99] and osteogenesis imperfecta [100, 101]. The horizontally tipped odontoid may deform the brainstem, especially in flexion [18, 102]. Our illustrative case J10 was emblematic of the ventral brainstem compression that results from a retroflexed odontoid in pathological flexion, as occurs in a whiplash injury. Platybasia results in anterior concavity of the brainstem with consequent medullary kink [10, 34]. The significance of the Clivo-vertebral angle in causing neurological deficit has been noted by many [5, 10, 20, 34, 71, 76, 79, 103].

Stress Modeling with Finite Element Analysis

Notwithstanding its potential utility, FEA modeling in the neuraxis is nascent and simplistic. The analysis used in this report assigns different moduli of elasticity to white and gray matter, but assumes stereotypic response and uniform properties under various degrees of strain and compression; presently FEA does not take into account strain rate, or alteration of compliance due to age, previous injury, metabolic and circulatory factors, such as ischemia. Use of FEA should be considered non-validated, and only an approximation of relative stress. The stresses are virtual computations, and do not integrate measurements of stress over time and over the full length of the tract. Clearly, the shortcomings of FEA need to be addressed. Nevertheless, the authors concur with others that FEA generated stress calculations may help in understanding the underlying pathophysiology of acute and chronic deformative stress injuries of the spinal cord and brainstem [46, 48, 75, 104].

KEY POINTS

- Whiplash- associated disorders (WAD) encompasses a wide variety of clinical presentations, including neck pain with and without neurologic findings (WADI/II and WADIII respectively).
- A series of clinical evaluation, quality-of-life measures, radiographic assessment, and a finite element analysis (Spinal Cord Stress Injury Analysis –

SCOSIA© software) were used to compare patients with WADIII (cases) to those with WADI/II (controls).

- Our study findings, conversely to the classic literature, suggest that WADIII and WADI/II are of distinct etiologies, pathoanatomy, and expected outcomes.
- Injuries to the musculo-ligamentous envelope of the cervical spine are thought to result in WADI/II; these injuries are expected to have a worst functional and pain outcome than WADIII.
- Stretch injuries to the cervical cord and medulla, especially in patients with pre-existing canal stenosis and/or odontoid retroflexion, are thought to result in WADIII; these injuries are expected to improve significantly with regards to neurologic function, pain scores, and quality of life measures.

CONCLUSION

Whiplash associated disorders result from a continuum of a stress injury to the cervical spine. However, depending on the affected elements we consider two distinct etiologies of WAD: deformative neuraxial stress injury resulting in the neurological findings in subjects with WAD III, and osteo-ligamentous injury resulting in chronic pain and tenderness in subjects with WAD I/II. Both etiologies result in significant pain, loss of function and poor quality of life. The improvement in pain, function, and quality of life in WAD III subjects in this study suggests that neuronal injury due to deformative stress in WAD III injuries are in many instances recoverable. This notion is supported by evidence in neuro-biological and clinical studies which demonstrate recovery of function after removal of neuraxial deformative stress.

DISCLOSURE

Authors William A. Wilson, IV., Fraser C. Henderson, Sr., and Alexander R. Vaccaro hold an equity ownership interest in Computational Biodynamics, LLC., and are entitled to royalty payments from the Spinal Cord Stress Injury Analysis (SCOSIA©) upon commercialization. Research related to potential Computational Biodynamics, LLC. products, including early-stage research essential to the development of these products, has been conducted by individuals who hold a financial stake in the successful outcome of that research.

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