Research Article

Factors associated with an excellent outcome after conservative treatment for patients with proximal cervical spondylotic amyotrophy using electrophysiological, neurological and radiological findings

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Objective: To investigate factors associated with excellent outcomes after conservative treatment in patients with proximal cervical spondylotic amyotrophy (CSA) using electrophysiological, radiological, and neurological findings.

Design: Retrospective study.

Setting: Yamaguchi University Hospital.

Participants: Seventy-seven patients.

Interventions: Erb-point-stimulated compound muscle action potentials (CMAP) were recorded in deltoid and biceps. The percentages of CMAP amplitudes on the affected side compared to the normal side in deltoid (PD) and biceps brachii (PB) were calculated. Central motor conduction time was calculated by subtracting peripheral motor conduction time from the onset latency of motor evoked potentials. Cervical lordotic angles, the diameter of C5 canal, and the intervertebral range at C4–C5 and C5–C6 levels were assessed on plain radiographs. Magnetic resonance imaging was used to assess the width of the intervertebral foramen (WIF) at C4–C5 and C5–C6 levels in the axial views. First visit and final follow-up strengths of most atrophic muscles were evaluated using manual muscle testing (MMT). Improvements in strength were classified as excellent (five grades recovered), good (more than one grade recovered), unchanged (no improvement), or poor (worsened).

Results: The outcomes were excellent in 27 patients (35.1%), good in 22 (28.6%), unchanged in 26 (33.8%), and poor in two (2.5%). Factors associated with excellent outcomes were WIF at C4–C5 and C5–C6 on the normal side, PB, and CMAP amplitudes of the deltoid on the normal side.

Conclusions: Patients with excellent outcomes originally had wide WIF at C4–C5 and C5–C6 levels and the absence of symptomatic spinal cord compression at C3–C4 and C4–C5 levels.

Keywords: Cervical spondylotic amyotrophy, Conservative treatment, Magnetic resonance imaging, Neurological findings, Compound muscle action potentials

Introduction

We previously reported the outcomes, pathology, and preoperative factors for the surgical treatment of proximal cervical spondylotic amyotrophy (CSA) using compound muscle action potentials (CMAP) of the deltoid and biceps brachii muscles and central motor conduction time (CMCT).^{1,2} We suggested that patients with CMCT-abductor digiti minimi (ADM) values $\geq$

6.8 ms have compressive cervical myelopathy, and those with CMCT-ADM values < 6.8 ms have only a ventral nerve root disorder.³ We therefore propose that cervical surgery should be performed in patients with CMCT-ADM values ≥ 6.8 ms. However, some patients with CMCT-ADM values ≥ 6.8 ms refused surgery, and some with CMCT-ADM values < 6.8 ms did not recover full function. There have been few reports on the outcomes of conservative management for proximal CSA.^{4–8} It is still unclear how these patients recover shoulder abduction and elbow flexion. We collected

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data on patient age; duration of clinical history (DCH); and electrophysiological, radiological, and neurological findings. The purpose was to evaluate the predictive factors for an excellent outcome after conservative treatment in patients with proximal CSA using electrophysiological, radiological, and neurological findings.

Materials and methods

A retrospective study was performed for 77 patients (67 men) with proximal CSA who underwent conservative treatment for proximal CSA between April 1997 and July 2016 at our hospital. These patients did not include those who underwent cervical surgery. Mean age was 60.5 ± 11.1 years (range 34–93 years). Mean DCH before electrophysiological examination was 6.2 ± 11.6 months (range, 1–72 months). Mean duration of post-electrophysiological examination follow-up was 29.0 ± 26.8 months (range, 6–120 months). All 77 patients had unilateral atrophy of the shoulder girdle muscles, but the intrinsic muscles were intact. There were no patients with gait disturbance. Patients with bilateral atrophy of the shoulder girdle muscles were excluded.

To differentiate among motor neuron diseases such as amyotrophic lateral sclerosis (ALS) and CSA, we performed electromyography (EMG) for all patients in whom motor neuron diseases were suspected. When ALS and other motor neuron diseases were suspected, we consulted neurologists. Based on consensus between the investigators and the neurologists, it was determined that the proximal CSA patients did not have these diseases. This study was approved by the institutional review board at our hospital.

Conservative treatment

Conservative treatment consisted of intermittent cervical immobilization with a soft collar, the use of vitamin B12 and/or anti-inflammatory medications, physical therapy including exercise and thermal therapy, and the active discouragement of high-risk activities and avoidance of risky environments (physical overloading, manipulation therapies, and vigorous flexion and extension of the head).

Evaluation of neurological findings

We examined muscle strength during shoulder abduction, elbow flexion, forearm supination, the biceps tendon reflex (BTR), the triceps tendon reflex (TTR), grip strength on the affected and normal side, the presence of sensory disturbance on the radial side and radicular pain in the affected upper extremity. We used

National Institute of Neurological Disorders and Stroke reflex scale.⁹

Assessment of muscle strength

First-visit and final follow-up strengths of the most atrophic muscles were evaluated using manual muscle testing (MMT). Improvements in strength were classified as excellent (five grades recovered by MMT), good (more than one grade recovered by MMT), unchanged (no improvement by MMT), or poor (worsened by MMT). A final grade of 5 indicated an excellent result.

Measurement of CMCT

Self-adhesive surface recording electrodes were placed on the target muscles using a standard belly-tendon method. Motor evoked potentials (MEPs) from the ADM muscle were recorded during voluntary contraction. Transcranial magnetic stimulation was delivered using a round 14-cm outer diameter coil (Magstim, Machida City, Tokyo, Japan). The center of the coil was held over the vertex of the skull. Magnetic stimulus intensity was set at 20% above the threshold of the MEPs during voluntary contraction. All stimuli were repeated at least four times.

CMAP and F-waves were also recorded following supramaximal electric stimulation (square wave 0.2 ms) of the ulnar nerve at the wrist. Sixteen serial responses were obtained and the shortest latency of the F-waves was measured. All muscle responses were amplified, filtered at 5–5000 Hz, and recorded using standard electromyography (Viking Select; Nicolet Biomedical Madison, WI, USA). The peripheral motor conduction time (PMCT), excluding the turn-around time at the spinal motor neuron (1 ms), was calculated from the latencies of the CMAP and F-waves as follows: (latency of CMAP + latency of F-waves – 1)/2. Conduction time from the motor cortex to the spinal motor neurons (i.e. CMCT) was calculated by subtracting the PMCT from the onset latency of MEPs.

Measurement of CMAPs

Erb-point stimulated CMAP were recorded in the deltoid and biceps in all patients. A disc electrode (diameter, 11 mm) was placed over the middle of the deltoid as an active electrode, on the acromion as a reference electrode for the deltoid, over the middle of the biceps brachii muscle, and on the lateral epicondyle of the humerus in the biceps brachii muscle. Underlying skin was treated with an abrasive solution to reduce impedance, and a ground strap was wrapped around the elbow. The bipolar stimulator probe provided a pair of bare metal contacts (diameter, 3 mm) with an adjustable

inter-electrode distance that was set to 25 mm. Stimulus intensity was gradually increased until the size of the recorded response was no longer altered. Measurement of CMAP included the negative peak amplitude from baseline to peak. The percent amplitude of CMAP was calculated in comparison with the opposite side.

Evaluation of radiological findings

The radiological findings on plain radiographs and magnetic resonance imaging (MRI) were evaluated. The cervical lordotic angles (cervical curvature: α , Cobb angle: β) (Fig. 1) and the diameter of the canal at the C5 vertebral level (C5 canal) were assessed on a lateral radiograph in the neutral position, and the intervertebral ranges at the C4–C5 (γ) and C5–C6 intervertebral level (δ) were assessed using lateral radiographs in flexion and extension positions. The alignment of the cervical spine was classified as lordotic ($>5^\circ$), straight ($-5^\circ \leq \alpha \leq 5^\circ$), sigmoid, or kyphotic ($\alpha < -5^\circ$). MRI was performed with a 1.5-T system (Magnetom Vision; Siemens Medical System, Erlangen, Germany). MRI was used to assess the number of levels of compression (NLC), the presence of a high intensity area (HIA) in the spinal cord on a T2-weighted sagittal view, and the width of the intervertebral foramen (WIF) at the C4–C5 and C5–C6

intervertebral levels on T2-weighted axial views (Fig. 2). The anteroposterior diameters of C4–C5 and C5–C6 foramen were measured at the narrowest point as the WIF.

Statistical analysis

Statistical analyses were performed using general purpose statistical software (StatFlex version 6.0; Artech Co, Ltd, Osaka, Japan; <http://www.statflex.net/>).

At the first visit, the following clinical parameters of each patient were examined as possible factors associated with the outcome of conservative management: average percentage of CMAP amplitude on the affected side compared with the normal side in the deltoid and biceps brachii muscles (AP); percentage of CMAP amplitude on the affected side compared with the normal side in the deltoid (PD); percentage of CMAP amplitude on the affected side compared with the normal side in the biceps brachii muscle (PB); age; DCH; duration of follow-up, MMT of shoulder abduction on the affected and normal sides; MMT of elbow flexion on the affected (MMT-EA) and normal (MMT-EN) sides; BTR and TTR on the affected and normal side; CMAP amplitudes of the deltoid and the biceps brachii on the affected and normal sides; CMAP onset latency of the deltoid and the biceps brachii on the affected and normal sides; α ; β ; C5 canal; γ ; δ ; NLC; the presence of HIA; and WIF at C4–5 and C5–C6 on the affected and normal sides. Univariate statistical analysis of each parameter in relation to the outcome was performed using the

Figure 1 Cervical curvature (α) and Cobb angle (β) at the C2 to the C7 on a plain radiograph in the neutral position.

Figure 2 The measurement of anteroposterior diameter of C4–C5 and C5–C6 foramen at the narrowest point (arrow).

Mann–Whitney *U* test for comparison of numerical parameters, and the chi-square test for the categorical parameters. To identify the predictive factors associated with excellent versus good/unchanged/poor outcomes, multivariate logistic regression analysis (MLRA) was performed. In this study, a dummy variable indicating the occurrence of an excellent outcome was set as an objective variable, and all the above parameters were set as the explanatory variables. Sensitivity, specificity, and area under the curve (AUC) of the receiver operating characteristic (ROC) curve were calculated to assess the utility of combining explanatory parameters in a regression model for the prediction.

Results

The outcomes were excellent in 27 patients (35.1%), good in 22 (28.6%), unchanged in 26 (33.8%), and poor in two (2.5%). Three of the patients with good outcomes and two patients with poor outcomes recovered briefly but worsened again (second attacks). The timing of when patients started to recover was 2.5 ± 1.3 months for patients with excellent outcomes and 3.5 ± 1.7 months for patients with good outcomes. The timing was significantly shorter in those with excellent outcomes compared to those with good outcomes ($P < 0.05$).

The clinical outcomes were classified into four groups (Group 1: patients with excellent outcomes, Group 2: patients with good outcomes, Group 3: patients with unchanged outcomes, and Group 4: patients with poor outcomes). The follow-up periods were 20.5 ± 22.7 months for Group 1 and 33.7 ± 28.0 months for Groups 2–4. Age and DCH were significantly different between Group 1 and Groups 2–4 ($P < 0.05$) (Table 1).

Electrophysiological findings

CMCT on the affected side

CMCT was performed for 65 patients (Group 1: 25 patients, Group 2: 20 patients, Group 3: 18 patients, and Group 4: two patients). CMCT was 5.3 ± 1.5 ms for Group 1 and 6.0 ± 1.7 ms for Groups 2–4 ($P > 0.05$) (Table 1). CMCT-ADM values ≥ 6.8 ms were observed in one patient from Group 1 and 11 from Group 2–4 (Group 2: three patients, Group 3: 7 patients, Group 4: 1 patient). CMCT-ADM values < 6.8 ms were observed in 24 patients from Group 1 and 29 from Groups 2–4 (Group 2: 17 patients, Group 3: 11 patients, Group 4: 1 patient).

CMAP

CMAP were performed for all 77 patients (Table 1). AP was significantly higher in Group 1 patients ($37.6\% \pm$

31.7%) than in Group 2–4 patients ($17.2\% \pm 21.5\%$; $P < 0.05$). PD and PB were significantly higher in Group 1 than in Group 2–4 patients ($P < 0.05$). The CMAP amplitudes of the deltoid on the affected side were 6.2 ± 3.1 mV in Group 1 patients and 1.9 ± 1.8 mV in Group 2–4 patients ($P < 0.05$). The CMAP amplitudes of the biceps brachii on the affected side were 8.4 ± 2.7 mV and 4.3 ± 2.2 mV in Group 1 and Group 2–4 patients, respectively ($P < 0.05$). The CMAP amplitudes of the deltoid on the normal side were 11.5 ± 1.7 mV and 9.1 ± 2.7 mV in Group 1 and Group 2–4 patients, respectively ($P < 0.05$). The CMAP amplitudes of the biceps brachii on the normal side were 12.8 ± 3.2 mV and 11.0 ± 2.7 mV in Group 1 and Group 2–4 patients, respectively ($P < 0.05$). The CMAP onset latency of the deltoid on the normal side was 3.3 ± 0.7 ms and 3.7 ± 0.6 ms in Group 1 and Group 2–4 patients, respectively ($P < 0.05$). The CMAP onset latency of the deltoid and biceps brachii on the affected side and biceps brachii on the normal side were not significantly different between Group 1 and Group 2–4 patients ($P > 0.05$). Among those with AP $> 60\%$ and CMCT-ADM values < 6.8 ms, 15 (60.0%), three (15.0%), zero (0.0%), and zero (0.0%) patients were in Group 1, 2, 3, and 4, respectively (Fig. 3).

Radiological findings (Table 1)

In plain radiographs, the alignment of the cervical spine (sigmoid and kyphotic), α° , β° , and γ° were not significantly different between Group 1 and Groups 2–4. The diameter of C5 canal was significantly wider in Group 1 than in Group 2–4 patients ($P < 0.05$).

For MRI, NCL and the presence of HIA on T2-weighted MRI were not significantly different between Group 1 and Groups 2–4. WIF at C4–C5 and C5–C6 intervertebral levels on the affected and normal side were significantly wider in Group 1 than in Group 2–4 patients ($P < 0.05$).

Neurological findings

MMT of shoulder abduction, elbow flexion, BTR, and TTR, grip strength on the bilateral side were evaluated for all 77 patients. MMT of bilateral forearm supination and grip strength were evaluated for 44 patients. MMT of elbow flexion and forearm supination, and grip strength on the affected side were significantly higher in Group 1 patients ($n = 19$) than in Group 2–4 patients ($n = 25$) ($P < 0.05$). BTR on the normal side was significantly higher in Group 1 patients than in Group 2–4 patients ($P < 0.05$). Radicular pain in the affected

Table 1 Neurological, electrophysiological and radiological assessments of Group 1 and Groups 2–4.

	Group 1	Group 2	Group 3	Group 4	Groups 2–4	P Group1 vs. Groups2–4
Age (y)	56.9 ± 11.5	61.0 ± 12.2	64.7 ± 8.3	50	62.5 ± 10.5	0.0353
sex	M:22,F:5	M:20,F:2	M:23,F:3	M:2	M:45,F:5	N.S
DCH (m)	2.4 ± 2.3	5.0 ± 7.6	11.5 ± 17.5	3.5	8.3 ± 13.9	0.0308
<i>Electrophysiological findings</i>						
CMCT (ms)	5.3 ± 1.5	5.6 ± 1.0	6.2 ± 1.8	8.2	6.0 ± 1.7	N.S
CMAP						
AP (%)	60.9 ± 17.8	40.0 ± 21.3	22.7 ± 12.7	27.3	30.5 ± 18.8	0.0013
PD (%)	54.2 ± 23.3	32.2 ± 25.7	10.9 ± 11.5	15.1	20.4 ± 21.6	0.0000
PB (%)	66.8 ± 17.1	47.2 ± 21.6	34.6 ± 19.1	39.6	40.3 ± 20.7	0.0000
The CMAP amplitude of deltoid on the affected side (mV)	6.2 ± 3.1	2.9 ± 1.9	0.9 ± 0.9	2.5	1.9 ± 1.8	0.0000
The CMAP amplitude of biceps brachii on the affected side (mV)	8.4 ± 2.7	4.8 ± 2.1	3.7 ± 2.2	5.2	4.3 ± 2.2	0.0000
The CMAP amplitude of deltoid on the normal side (mV)	11.5 ± 1.7	8.5 ± 2.5	9.2 ± 2.4	13.7	9.1 ± 2.7	0.0001
The CMAP amplitude of biceps brachii on the normal side (mV)	12.8 ± 3.2	11.4 ± 2.7	10.5 ± 2.7	13.2	11.0 ± 2.7	0.0111
The CMAP onset latency of the deltoid on the affected sides (ms)	3.7 ± 1.0	4.1 ± 0.9	3.6 ± 1.6	5.1	3.9 ± 1.3	N.S
The CMAP onset latency of the biceps brachii on the affected sides (ms)	4.8 ± 0.9	5.7 ± 2.0	6.9 ± 9.3	4.5	6.2 ± 6.7	N.S
The CMAP onset latency of the deltoid on the normal sides (ms)	3.3 ± 0.7	3.7 ± 0.6	3.7 ± 0.6	3.8	3.7 ± 0.6	0.0144
The CMAP onset latency of the biceps brachii on the normal sides (ms)	4.6 ± 0.6	4.9 ± 0.5	4.8 ± 0.5	4.5	4.8 ± 0.5	N.S
<i>Neurological findings</i>						
MMT of shoulder abduction on the affected side	2.4 ± 0.9	2.5 ± 1.1	2.0 ± 0.7	2.5	2.2 ± 1.0	N.S
MMT of elbow flexion on the affected side	3.3 ± 0.5	3.0 ± 0.9	2.7 ± 0.8	2.5	2.8 ± 0.9	0.0040
MMT of forearm supination on the affected side	3.3 ± 0.7	2.6 ± 0.7	2.5 ± 1.2	2.5	2.5 ± 1.1	0.0080
BTR on the affected side	0.7 ± 0.6	0.6 ± 0.5	0.8 ± 0.7	1	0.7 ± 0.6	N.S
on the normal side	1.8 ± 0.4	1.5 ± 0.6	1.4 ± 0.7	1.5	1.4 ± 0.6	0.0091
TTR on the affected side	1.9 ± 0.6	1.5 ± 0.5	1.7 ± 0.7	2.5	1.7 ± 0.7	N.S
on the normal side	2.0 ± 0.5	1.6 ± 0.5	1.9 ± 0.5	2.5	1.8 ± 0.6	N.S
Grip strength on the affected side	32.0 ± 7.7	25.4 ± 10.4	22.6 ± 9.1	-	24.1 ± 9.8	0.0206
on the normal side (Kg)	35.8 ± 6.3	35.7 ± 9.5	30.8 ± 6.8	-	34.7 ± 6.3	N.S
<i>Radiological findings</i>						
<i>Plain radiograph</i>						
α	10.6 ± 12.8	12.1 ± 13.6	10.2 ± 12.0	10.7	11.1 ± 12.4	N.S
β	10.5 ± 12.7	11.9 ± 12.0	7.4 ± 8.5	7.9	9.4 ± 10.3	N.S
γ	10.7 ± 6.3	10.4 ± 3.6	7.9 ± 3.8	6.6	9.3 ± 3.9	N.S
δ	6.7 ± 4.5	5.7 ± 4.2	7.5 ± 3.9	7.4	6.6 ± 4.0	N.S
C5 canal (mm)	15.4 ± 1.3	15.3 ± 1.3	13.9 ± 1.7	13.5	14.5 ± 1.6	0.0180
Alignment sigmoid	1	0	4	0	4	0.4846
kyphotic	6	6	4	0	10	0.5889
<i>MRI</i>						
NCL	1.0 (0–2)	1.3 (0–3)	1.8 (0–4)	1.5 (1–2)	1.5 (0–4)	N.S
Presence of HIA	2(C4–5;1,C5–6;1)	2(C4–5)	5(C4–5)	1(C5–6)	8(C4–5;7,C5–6;1)	N.S
WIF at C4–C5 intervertebral level on the affected side	3.0 ± 0.9	2.7 ± 1.3	2.0 ± 0.6	1.9	2.3 ± 1.0	0.0130
WIF at C5–C6 intervertebral level on the affected side	3.1 ± 1.1	2.2 ± 0.6	2.4 ± 0.9	1.7	2.3 ± 0.8	0.0006
WIF at C4–C5 intervertebral level on the normal side	3.6 ± 1.0	2.7 ± 0.8	2.3 ± 0.7	1.9	2.5 ± 0.8	0.0000
WIF at C5–C6 intervertebral level on the normal side	3.0 ± 1.2	2.3 ± 0.6	2.2 ± 0.8	2.1	2.2 ± 0.7	0.0005

Group 1: excellent; Group 2: good; Group 3: unchanged; Group 4: poor; Groups 2–4: good, unchanged, and poor; y, year; DCH, duration of clinical history; m, month; CMCT, central motor conduction time; CMAP, compound muscle action potentials; AP, average percentage of CMAP amplitude on the affected side compared with the normal side in the deltoid and biceps brachii muscles; PD, percentage of CMAP amplitude on the affected side compared with the normal side in the deltoid; PB, percentage of CMAP amplitude on the affected side compared with the normal side in the biceps brachii muscle; MMT, manual muscle testing; BTR, biceps tendon reflex; TTR, triceps tendon reflex; NCL, the number of levels of compression; MCL, the most compressed level of the spinal cord; HIA, the presence of a high intensity area; WIF, the width of the intervertebral foramen.

With regard to BTR and TTR, absence is 0, hype-reflex is 1, normal is 2, and hyper-reflex is 3.

Figure 3 The relationship between surgical outcome and electrophysiological findings. The thick line showed CMCT was 6.8 ms and AP was 60%. CMCT, central motor conduction time; CMAP, compound muscle action potentials; AP, average percentage of CMAP amplitude on the affected side compared to the normal side in deltoid and biceps brachii muscles; ○: Excellent; △: Good; ×: Unchanged; □: Poor. Patients who blacked out had recovered briefly but worsened again (second attacks).

upper extremity was not significantly different between Group 1 and Groups 2–4.

Association between conservative outcomes and the level of compression of the spinal cord on MRI for patients with CMCT-ADM values < 6.8 ms (Table 2)

Compression of the spinal cord occurred in 16 (66.7%) Group 1 patients and 24 (82.8%) Group 2–4 patients (Group 2: 14 patients, Group 3: nine patients, and Group 4: one patient). The level most commonly affected by compression was C4–C5, followed by C5–C6.

Analysis of factors associated with Group 1 status

In the MLRA, the dummy variable representing Group 1 was set as the objective variable. All of the above parameters (age, DCH, AP, PD, PB, CMAP amplitude of

Table 3. Results of multiple regression analysis.

Exp Var	β	SE (β)	P	Odds ratio	95% confidence interval
Age	0.02	0.05	0.668	1.023	0.922–1.135
WIF at C4–C5 intervertebral level on the normal side	1.75	0.74	0.018	5.772	1.358–24.540
WIF at C5–C6 intervertebral level on the normal side	1.77	0.72	0.013	5.897	1.451–23.971
PB	0.08	0.03	0.004	1.526	1.146–2.031
The CMAP amplitude of deltoid on the normal side (mV)	0.76	0.27	0.004	2.139	1.268–3.609

Exp Var, explanatory variable; β , partial regression coefficient; SE, standard error; WIF, the width of the intervertebral foramen; HIA, high intensity area; PB, percentage of CMAP amplitude on the affected side compared with the normal side in the biceps brachii muscle; CMAP, compound muscle action potentials. Odds ratio for PB was computed for Δ PB.

the deltoid and biceps brachii on the affected and normal sides, CMAP onset latency of the deltoid on the normal side, MMT-EA, BTR on the normal side, C5 canal, and WIF at the C4–C5 and C5–C6 intervertebral levels on the affected and normal) were set as explanatory variables. Using the stepwise method, four parameters (WIF at C4–C5 and C5–C6 intervertebral levels on the normal side, PB, and the CMAP amplitude of the deltoid on the normal side) were considered significant factors that were all positively associated with Group 1 status (Table 3).

The diagnostic power of the predicted probability calculated by the regression model composed of the four parameters was evaluated by ROC analysis. The AUC of the predicted probability was 0.958, while the AUCs of individual parameters were 0.803, 0.688, 0.808, and 0.810 for WIF at the C4–C5 and C5–C6

Table 2. Association between outcomes and the level of compression of the spinal cord on MRI for patients with CMCT/ADM values < 6.8 ms.

	None	C3–4	C4–5	C5–6	C3–4 C4–5	C4–5 C5–6	C4–5 C6–7	C2–3 C3–4 C4–5	C3–4 C4–5 C5–6	C4–5 C5–6 C6–7	C3–4 C4–5 C5–6 C6–7
Group 1	8	0	8 ^{#1}	0	2	6 ^{#2}	0	0	0	0	0
2	2	2	2	3	1	4 ^{#3}	1	1	1	0	0
3	3	0	3	2	0	1	0	0	0	1	1
4	0	0	0	0	0	1	0	0	0	0	0
Groups 2–4	5	2	5	5	1	6	1	1	1	1	1

Group 1: excellent; Group 2: good; Group 3: unchanged; Group 4: poor, Groups 2–4: good, unchanged, and poor; #1: One patient had the high intensity area of spinal cord at C4–5 intervertebral level. #2: One patient had the high intensity area of spinal cord at C5–6 intervertebral level. #3: One patient had the high intensity area of spinal cord at C4–5 intervertebral level, respectively.

Figure 4 ROC curves for WIF at C4–C5 and C5–C6 intervertebral level on the normal side, PB, and the CMAP amplitude of deltoid on the normal side associated with Group 1 status. The AUC of the predicted probability was 0.958, whereas those of individual parameters were 0.803 for WIF at C4–C5 intervertebral level on the normal side, 0.688 for WIF at C5–C6 intervertebral level on the normal side, 0.808 for PB, and 0.810 for the CMAP amplitude of deltoid on the normal side. ROC, receiver operating characteristic; PP, predicted probability; WIF at C4–C5-N, the width of the intervertebral foramen at C4–C5 intervertebral level on the normal side; WIF at C5–C6-N, the width of the intervertebral foramen at C5–C6 intervertebral level on the normal side; CMAP amp-DN, compound muscle action potentials amplitude of deltoid on the normal side; PB, percentage of CMAP amplitude on the affected side compared with the normal side in the biceps brachii muscle; AUC, area under curve.

intervertebral levels on the normal side, PB, and the CMAP amplitude of the deltoid on the normal side, respectively (Fig. 4).

Patients with poor outcomes

The periods of follow-up of the two patients with poor outcomes were 13 months and 31 months, respectively. However, they did not improve and had second attacks.

Discussion

The clinical outcomes of cervical traction, immobilization of the neck using a collar, physical therapy, administration of vitamin B12, injection of prostaglandin E1 (IPE), and hyperbaric oxygen (HBO) as conservative treatments have been reported.^{4–8} Tofuku *et al.* reported that HBO may facilitate the recovery of reversibly

injured anterior cells by improving the hypoxic condition of neural tissue at risk, although it had no effect on the recovery of irreversibly injured anterior cells.⁵ Shibuya *et al.* suggested that patients with anterior spinal artery syndrome may have been included among those diagnosed with CSA and reported good outcomes after IPE.⁶ Nagata *et al.* reported the outcomes of conservative management for proximal CSA in which cervical traction, immobilization of the neck using a collar, physical therapy, and administration of vitamin B12 or E were applied to their patients; 38.3% achieved full recovery.⁷ Inui *et al.* reported that 31.8% (27 patients) of the 85 patients who underwent continuous cervical traction for 2–3 weeks as an initial conservative treatment achieved full recovery with conservative management.⁸ In the present study, special conservative treatments such as cervical traction, IPE, and HBO were not performed; however, 35.1% of the patients achieved excellent outcomes. As the timing of when patients started to recover was 2.5 ± 1.3 months for patients with excellent outcomes, conservative treatment should be continued for at least 3.8 months before surgery.

CMCT is used to electrophysiologically evaluate corticospinal tract function and diagnose disorders of the corticospinal tract.^{3,10–13} Chan *et al.* reported that CMCT is helpful in localizing the clinically relevant levels of spinal cord compression in cervical spondylotic myelopathy and correlates well with motor abnormalities on clinical examination.¹⁴ Takahashi *et al.* reported that CMCT was significantly correlated with the results of clinical assessment in patients with cervical myelopathy.¹⁵ As CMCT is prolonged in certain conditions, it is of diagnostic value in several neurological disorders such as myelopathy, amyotrophic lateral sclerosis, and multiple sclerosis (MS). It could also be used as a prognostic marker in certain neurological conditions, such as myelopathy and MS.¹⁶ We suggested that patients with CMCT-ADM values ≥ 6.8 ms have compressive cervical myelopathy, and those with CMCT-ADM values < 6.8 ms have only a ventral nerve root (VNR) disorder.³ Therefore, in our view, patients with CMCT-ADM values ≥ 6.8 ms should undergo cervical surgery. However, 12 patients in the present study refused cervical surgery, and 91.7% (11/12) did not achieve full recovery. In patients with CMCT-ADM values ≥ 6.8 ms, conservative treatment may not be indicated. Of the 53 patients with CMCT-ADM values < 6.8 ms, 75.4% (40/53) had spinal cord compression on MRI, but did not show involvement of the corticospinal tract. Boden *et al.* considered that abnormal MRI findings in asymptomatic subjects are false-positive results,

since it is difficult to distinguish between ageing discs and pathologically degenerate discs which cause symptoms.¹⁷ These patients may have asymptomatic spinal cord compressions; 24.6% (13/53) may only have the involvement of the C5 ventral root and/or C6 ventral root, and 38.5% (5/13) of these patients did not recover full function. Therefore, it was difficult to achieve full recovery despite the involvement of the ventral nerve root.

In general, the CMAP amplitude reflects the number of axons that are alive. Patients with CMAP exceeding 50% of the normal side showed the most complete return of function, despite severe weakness.¹⁸ One patient with CMAP exceeding 50% of the normal side showed unchanged outcomes in this study. We propose that conservative treatments should be performed for patients with AP > 60% and CMCT-ADM values < 6.8 ms (Fig. 3).

The pathophysiology of proximal CSA involves a combination of lesions in the VNR and/or the anterior horns (AH).^{1,4,19,20} When patients only have the involvement of the VNR, AP, PD, and PB reflect the degree of VNR involvement (Fig. 5). Patients with severe and mild involvement of the VNR tend to have low value and high AP, PD, and PB values, respectively. When patients have involvement of the AH, patients tend to have the high AP, PD, and PB values because the amplitude of CMAP on the normal side is low (Fig. 6).

Factors associated with group 1 status

Nagata *et al.* reported factors associated with excellent and good outcomes for patients with proximal CSA.⁷

Figure 5 When a patient had the severe involvement of the VNR, CMAP amplitude of the deltoid were 1.0 mV on the affected side and 9.0 mV on the normal side. PD was 11.1%. When a patient had the mild involvement of the VNR, CMAP amplitude of the deltoid were 6.1 mV on the affected side and 10.9 mV on the normal side. PD was 56.0%. VNR, ventral nerve roots; CMAP, compound muscle action potentials; PD, percentage of CMAP amplitude on the affected side compared with the normal side in the deltoid.

These included absence of severe muscle atrophy of the shoulder, degenerative spondylosis at the cervical spine, a wide diameter of the C5 canal on plain radiography, and a wide WIF on computed tomography. In the present study, factors associated with Group 1 were WIF at the C4–C5 and C5–C6 intervertebral levels on the normal side, PB, and the CMAP amplitude of the deltoid on the normal side. Ahmed *et al.* reported the morphology of the human intervertebral foramina of the cervical spine.²¹ There were no significant differences between the right and the left sides from C3–C4 to C6–C7 intervertebral levels.²¹ Therefore, patients with wide WIF at the C4–C5 and C5–C6 intervertebral levels on the normal side originally tend to have wide WIF at the C4–C5 and C5–C6 intervertebral levels on the affected side. We considered that WIF at the C4–C5 and C5–C6 intervertebral levels on the affected side may have become narrower due to degenerative changes. Czervionke *et al.* reported that the cervical intervertebral foramina are oval in shape; the width of the foramen is approximately one half its heights.²² Lu *et al.* reported that compared with normal foraminal area values, reduction of 20–30% of the foraminal area was observed after 1 mm narrowing of the intervertebral disc spaces.²³ Compression of the nerve root within the intervertebral foramina after the collapse of the intervertebral disc space cannot be ignored.²³ WIF at the C4–C5 and C5–C6 intervertebral levels on the affected side were not correlated to clinical outcomes. We did not evaluate the height of intervertebral foramina at the C4–C5 and C5–C6 intervertebral levels. However, we evaluated the number of axons that were alive from VNR and AH using the amplitude of CMAP. We considered that the CMAP amplitude of the deltoid on the normal side mainly reflected the absence of symptomatic spinal cord compression at the C3–C4 and C4–C5 intervertebral levels and the absence of a narrow WIF at the C4–C5

Figure 6 When a patient had the involvement of the AH, CMAP amplitude of the biceps brachii muscle were 5.5 mV on the affected side and 7.2 mV on the normal side. PB was 76.4%. AH, anterior horns; CMAP, compound muscle action potentials; PB, percentage of CMAP amplitude on the affected side compared with the normal side in the biceps brachii muscle.

and C5–C6 intervertebral levels on the normal side. Patients with high PB did not have severe compression of the spinal cord on the affected side at the C3–C4 and C4–C5 intervertebral levels nor narrow WIF on the affected side and at the C4–C5 and C5–C6 intervertebral levels. Therefore, patients in Group 1 originally had wide WIF at the C4–C5 and C5–C6 intervertebral levels and the absence of symptomatic spinal cord compression at the C3–C4 and C4–C5 intervertebral levels.

Conclusion

Special conservative treatments such as cervical traction, IPE, and HBO were not performed, but 35.1% achieved excellent outcomes. Conservative treatments should be performed in patients with CMCT-ADM values < 6.8 ms and AP > 60%. Patients in Group 1 originally had wide WIF at the C4–C5 and C5–C6 intervertebral levels and the absence of symptomatic spinal cord compression at the C3–C4 and C4–C5 intervertebral levels.

Disclaimer statements

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Conflict of interest None.

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References

- Imajo Y, Kato Y, Kanchiku T, Suzuki H, Taguchi T. Pathology and prognosis of proximal-type cervical spondylotic amyotrophy. New assessment using compound muscle action potentials of deltoid and biceps brachii muscles. *Spine*. 2011;36(7):E476–81.
- Imajo Y, Kato Y, Kanchiku T, Suzuki H, Yoshida Y, Funaba M, et al. Prediction of surgical outcome for proximal-type cervical spondylotic amyotrophy novel mode of assessment using compound action potentials of deltoid and biceps brachii and central motor conduction time. *Spine*. 2012; 37(23):E1444–9.
- Imajo Y, Kanchiku T, Suzuki H, Yoshida Y, Funaba M, Nishida N, et al. Effects of differences in age and body height on normal values of central motor conduction time determined by F-waves. *J Spinal Cord Med*. 2017;40(2):181–7.
- Kameyama T, Ando T, Yanagi T, Yasui K, Sobue G. Cervical spondylotic amyotrophy. Magnetic resonance imaging demonstration of intrinsic cord pathology. *Spine*. 1998;23(4):448–52.
- Tofuku K, Koga H, Yone K, Komiya S. Conservative treatment with hyperbaric oxygen therapy for cervical spondylotic amyotrophy. *Spinal Cord*. 2011;49:749–53.
- Shibuya R, Yonenobu K, Yamamoto K, Kuratsu S, Kanazawa M, Onoue K, et al. Acute arm paresthesia with cervical spondylosis: three case reports. *Surg Neurol*. 2005;63:220–8.
- Nagata K, Sato K, Tsurumi M, Matsushima T. Clinical results of cervical spondylotic amyotrophy. *Spine Spinal Cord*. 2009;22: 1117–23.(in Japanese)
- Inui Y, Miyamoto H, Sumi M, Uno K. Clinical outcomes and predictive factors relating to prognosis of conservative and surgical treatments for cervical spondylotic amyotrophy. *Spine*. 2011;36 (10):794–9.
- Hallett M. Ninds myotatic reflex scale. *Neurology*. 1993;43:2723.
- Kaneko K, Taguchi T, Morita H, Yonemura H, Fujimoto H, Kawai S. Mechanism of prolonged central motor conduction time in compressive cervical myelopathy. *Clin Neurophysiol*. 2001;112:1035–40.
- Nakanishi K, Tanaka N, Sasaki H, Kamei N, Hamasaki T, Yamada K, et al. Assessment of central motor conduction time in the diagnosis of compressive thoracic myelopathy. *Spine*. 2010; 35(26):E1593–8.
- Funaba M, Kanchiku T, Imajo Y, Suzuki H, Yoshida Y, Nishida N, et al. Transcranial magnetic stimulation in the diagnosis of cervical compressive myelopathy. *Spine*. 2015;40(3):E161–7.
- Fujimoto K, Kanchiku T, Imajo Y, Suzuki H, Funaba M, Nishida N, et al. Use of central motor conduction time and spinal cord evoked potentials in the electrophysiological assessment of compressive cervical myelopathy. *Spine*. 2017;42 (12):895–902.
- Chan KM, Nasathural S, Chavin JM, Brown WF. The usefulness of central motor conduction studies in the localization of cord involvement in cervical spondylitic myelopathy. *Muscle Nerve*. 1988;21:1220–3.
- Takahashi J, Hirabayashi H, Hashidate H, Ogihara N, Yamazaki I, Kamimura M, et al. Assessment of cervical myelopathy using transcranial magnetic stimulation and prediction of prognosis after laminoplasty. *Spine*. 2008;33(1):E15–20.
- Udapa K, Chen R. Central motor conduction time. *Handb Clin Neurol*. 2013;116:375–86.
- Tani T, Kishimoto H, Tsuboya H, Kimura J. Electrophysiologic assessment of shoulder girdle weakness in patients with cervical spondylosis: prognostic value of supraclavicular stimulation. *J Clin Neuromuscul Dis*. 2002;4:11–8.
- Boden SD, McCowin PR, Davis DO, Dina TS, Mark AS, Wiesel S. Abnormal magnetic resonance scans of the cervical spine in asymptomatic subjects. *J Bone Joint Surg Am*. 1990;72-A(8): 1178–84.
- Keegan JJ. The cause of dissociated motor loss in the upper extremity with cervical spondylosis. *J Neurosurg*. 1974;23:528–36.
- Ito T, Tsuji H, Tamaki T, Miyasaka H, Toyoda A. The clinical consideration of the dissociated motor loss syndrome (Keegan) in diseases of the cervical spine. *J Jpn Orthop Assoc*. 1980;54: 135–51.
- Ahmed SH, El-Shaarawy EAA, Ishaq MF, Moniem MHA. Morphological and radiometrical study of the human intervertebral foramina of the cervical spine. *Folia Morphol*. 2014;73:7–18.
- Czervionke LF, Daniels DL, Ho PS. Cervical neural foramina: correlative anatomic and MR imaging study. *Radiology*. 1988;169: 753–9.
- Lu J, Ebraheim NA, Huntoon M, Haman SP. Cervical intervertebral disc space narrowing and size of intervertebral foramina. *Clin Orthop Relat Res*. 2000;370:259–64.