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ORIGINAL ARTICLE

# Validity, reliability and responsiveness of the Japanese version of the Neck Disability Index

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**Abstract**
*Background* The Neck Disability Index (NDI) is one of the most widely used questionnaires for neck pain. The purpose of this study was to validate the Japanese NDI.
*Methods* We performed two surveys with an 8-week interval in 130 patients with neck pain, radiculopathy and myelopathy. We asked patients to answer two versions of the Japanese NDI: the original NDI, which had been completed by a forward–backward translation procedure, and the modified NDI, which has the phrase "because of neck pain" to the phase "because of neck pain or numbness in the arm." The other parameters examined were the strength of pain and numbness, the Japanese Orthopaedic Association Cervical Myelopathy Evaluation Questionnaire, the Hospital Anxiety and Depression Scale, and Short Form 36. Attending surgeons judged the symptom severity. Patients were asked to report the patient global impression of change (PGIC) at the second survey. The internal consistency, criterion-related and discriminative validity, and reliability were evaluated.
*Results* The original NDI and the modified NDI were 26.9 ± 17.1 and 29.9 ± 15.5, respectively. The Cronbach $\alpha$ values of the original NDI and the modified NDI were 0.92 and 0.89, respectively. Both versions of the NDI had good to excellent correlative coefficients with the related domains. The modified NDI had a higher validity for numbness and mental health-related QOL. The symptom severity was significantly correlated with the modified NDI. The intraclass correlation coefficients of the two surveys of the modified and original NDI were comparable. The effect sizes of the modified and the original NDI were 0.64 and 0.55, respectively. Spearman's $\rho$ between the change of the NDI and the PGIC was 0.47 in the original NDI and 0.59 in the modified NDI.
*Conclusions* We demonstrated the validity, reliability and responsiveness of the Japanese NDI. The modified NDI was more strongly correlated with numbness and mental health-related QOL.

**Electronic supplementary material** The online version of this article (doi:10.1007/s00776-012-0304-y) contains supplementary material, which is available to authorized users.

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## Introduction

Neck pain is one of the most common complaints in the general population. Patient-reported outcome measures are primary tools used to assess the patients' condition, and the Neck Disability Index (NDI) [1], a symptom-specific questionnaire modified from the Oswestry Disability Index [2] for neck pain by Vernon, has been used extensively to evaluate patients with neck pain and cervical disorders [3].

There has been no report of the Japanese version of the NDI so far. The purpose of this study was to validate the Japanese version of the Neck Disability Index (NDI).

This study was supported by the Japanese Society for Spine Surgery and Related Research, and study approval was given by the institutional review board of the Clinical Research Support Center of the University of Tokyo Hospital.

## Materials and methods

### Translation of the NDI into Japanese

The NDI has ten questions with numerical responses on a six-point scale (0–5). The questions cover pain, personal care, lifting, reading, headaches, concentration, work, driving, sleeping and recreation. The raw total score of the NDI is calculated by summing the scores of the questions. The NDI is usually described as a percentage of raw scores divided by the full scores of answered questions. The final % score ranges from 0 to 100, and lower scores indicate a better state of health.

We translated the English NDI into Japanese by forward translation. The Japanese NDI was then successively translated into English as a back-translation. Finally, the original NDI was completed after we received suggestions from Dr. Vernon, the original developer of the NDI. However, during the preliminary survey at the university hospital, some patients with cervical disorders left comments on the questionnaire sheet indicating that their disability resulted not from neck pain, but from numbness in the arm. Therefore, we made the modified NDI (Supplementary material) by changing the phrase "because of neck pain" to the phase "because of neck pain or numbness in the arm" in the questions. Therefore, we included a comparative study between the two versions of the NDI in this validation study. We asked patients to answer both of the NDIs and then compared the validity between the two versions. The two Japanese versions of the original and modified NDI can be seen by downloading the files in the Supplementary material.

### Participants

The first survey was performed in the hospital or in the clinic at six institutions after the institutional review board had approved the study. Signed informed consent was obtained from each patient. We recruited patients who had one of the three diagnoses below: (1) neck pain without neurological symptoms (the neck pain group), (2) cervical radiculopathy or (3) cervical myelopathy. The neck pain group included patients with acute and chronic neck pain without neurological symptoms. Patients who experienced pain after traffic vehicle accidents were included. A diagnosis of cervical radiculopathy (the radiculopathy group) was made when (1) a patient suffered from pain in an upper extremity and (2) arm pain was provoked by a specific head position or with a specific exercise, or a physician found an imaging abnormality related to the arm pain. Patients with pain only around the scapula were excluded. Cervical myelopathy (the myelopathy group) was confirmed from both the neurological and magnetic resonance imaging findings. Patients with rheumatoid arthritis, cerebral palsy and other systemic diseases that might have influenced neck conditions were excluded. Patients who suffered from both radiculopathy and myelopathy (radiculomyelopathy) were also excluded.

### Data collection

The questionnaire set of the first survey included questions about patient backgrounds (age, sex, height, weight, occupation, marital status, education, smoking status) and previous treatment. It also included the original and modified versions of the Japanese NDI, the 11-grade strength of pain and numbness using a drawing of the body divided into six parts (Fig. 1), the Japanese Orthopaedic Association Cervical Myelopathy Evaluation Questionnaire (JOACMEQ) [4], the Hospital Anxiety and Depression Scale (HADS) [5, 6] and the Short Form 36 (SF-36) [7, 8].

The JOACMEQ is a disease-specific scale for cervical myelopathy proposed by the Japanese Orthopaedic Association. This patient-reported outcome measure has two components. The first component has 24 questions that comprise five domains: (1) cervical function, (2) upper extremity function, (3) lower extremity function, (4) bladder function and (5) quality of life (QOL). Each domain is calculated by a weighted sum of the involved questions, ranging from 0 to 100, with higher scores indicating a better health state. The second component has three visual analog scales for pain and numbness. We adopted only the first component in this study.

The HADS is a self-reported questionnaire for anxiety and depression. The HADS has 14 questions, and its total score ranges from 0 to 21 for each scale of anxiety and depression. A higher score indicates higher stress.

The SF-36 is a generic health-related QOL measure with 36 questions. The SF-36 consists of eight domains from the weighted sum of specific questions: physical functioning

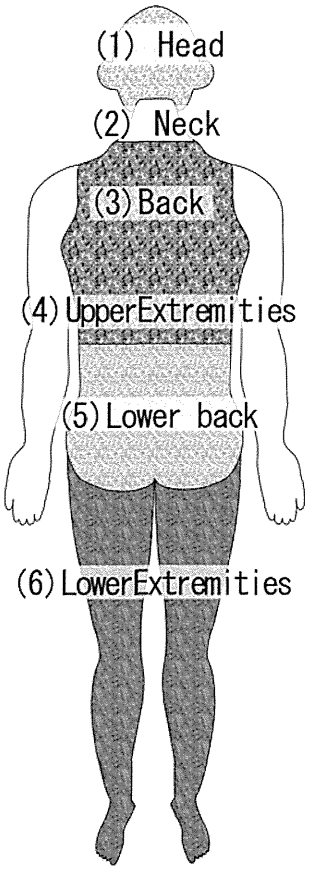


**Fig. 1** The body part figure used for the question about the intensity of the pain and numbness

(PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social role (SF), role emotional (RE) and mental health (MH). The raw score of each domain ranges from 0 to 100, with higher scores indicating better health. Two representative scores are also calculated: the Physical Component Score (PCS) and the Mental Component Score (MCS), which are expressed in norm-based scoring. Each component score has the same mean and standard deviation (50 and 10, respectively) in a normal population.

We asked the attending surgeons to report diagnoses of the cervical disorders, symptom severity, comorbidities and treatment. The symptom severity judged by surgeons had three grades: severe, moderate and slight. The surveyed comorbidities were diabetic mellitus, shoulder disorder and peripheral nerve disorders.

The second survey for repeatability/responsiveness was performed by mail 8 weeks after the first survey. A question about the patient global impression of change (PGIC) was added in the questionnaire set. The PGIC was composed of seven answers: much better, better, slightly better, unchanged, slightly worse, worse and much worse.

**Table 1** Patient characteristics ($n = 130$)

| | *N* | *N* % | Mean | SD |
|---|---|---|---|---|
| Height (cm) | 129 | | 163.0 | 8.5 |
| Weight (kg) | 129 | | 64.4 | 12.7 |
| BMI | 129 | | 24.2 | 3.8 |
| Occupation | | | | |
| Full-time job | 59 | 46.9 | | |
| Part-time job | 9 | 7.0 | | |
| Housemaker | 20 | 15.6 | | |
| Retired | 20 | 15.6 | | |
| Other | 19 | 14.8 | | |
| Marital status | | | | |
| Married | 95 | 74.2 | | |
| Single | 33 | 25.8 | | |
| Education | | | | |
| Middle-school | 8 | 6.3 | | |
| High school | 53 | 41.4 | | |
| Training college | 16 | 12.5 | | |
| University | 42 | 32.8 | | |
| Graduate-school | 4 | 3.1 | | |
| Other | 5 | 3.9 | | |
| Smoking | | | | |
| Never | 50 | 38.5 | | |
| History of smoking | 51 | 39.2 | | |
| Present smoker | 29 | 22.3 | | |
| Related comorbidities | | | | |
| Worker's compensation | 1 | 0.8 | | |
| Diabetes mellitus | 7 | 5.4 | | |
| Other | 2 | 1.5 | | |

Numbers do not always add up to the total number because of missing values

*SD* standard deviation, *BMI* body mass index

## Statistical analysis

### *Internal consistency, criterion-related validity and discriminative validity*

The internal consistency was evaluated by the Cronbach $\alpha$. In general, $\alpha \geq 0.9$ is regarded as excellent, $\alpha \geq 0.8$ as good and $\alpha \geq 0.7$ as acceptable [9]. The criterion-related validity was evaluated by calculating the correlation coefficients (Spearman's $\rho$) between two NDIs and other outcomes: the 11-grade severity of pain and numbness in body parts, JOACMEQ, HADS and the SF-36. In general, $\rho = 0.1$ is regarded as a weak association, $\rho = 0.3$ as a moderate association and $\rho = 0.5$ as a strong association [10]. The discriminative validity was evaluated by performing analysis of variance (ANOVA) between two versions of the NDI and the symptom severity.

**Table 2** The outcomes of the first survey

| | *N* | Mean | SD | Min | Median | Max |
|---|---|---|---|---|---|---|
| Japanese NDI (0–100) | | | | | | |
| Original | 118 | 26.9 | 17.1 | 0 | 26 | 72 |
| Modified | 118 | 29.9 | 15.5 | 0 | 28 | 70 |
| Pain (0–10) | | | | | | |
| Head | 130 | 1.6 | 2.3 | 0 | 1 | 8 |
| Neck | 130 | 4.2 | 2.8 | 0 | 4 | 10 |
| Back | 128 | 3.0 | 2.7 | 0 | 2 | 10 |
| Upper ext | 128 | 3.5 | 2.9 | 0 | 3 | 10 |
| Lower back | 129 | 2.8 | 2.9 | 0 | 2 | 10 |
| Lower ext | 128 | 2.4 | 3.0 | 0 | 1 | 10 |
| Numbness (0–10) | | | | | | |
| Head | 129 | 1.0 | 2.0 | 0 | 0 | 9 |
| Neck | 129 | 1.8 | 2.5 | 0 | 0 | 9 |
| Back | 126 | 1.7 | 2.4 | 0 | 0 | 10 |
| Upper ext | 128 | 3.9 | 2.8 | 0 | 4 | 10 |
| Lower back | 128 | 1.7 | 2.7 | 0 | 0 | 10 |
| Lower ext | 129 | 2.7 | 3.1 | 0 | 1 | 10 |
| JOACMEQ (0–100) | | | | | | |
| Cervical | 127 | 60.0 | 27.8 | 0 | 62.5 | 100 |
| Upper ext | 129 | 84.3 | 19.1 | 0 | 85.7 | 100 |
| Lower ext | 126 | 74.6 | 22.8 | 16.7 | 75 | 100 |
| Bladder | 128 | 76.9 | 19.8 | 20 | 80 | 100 |
| QOL | 124 | 49.1 | 16.0 | 6.5 | 51.6 | 90.3 |
| HADS (0–21) | | | | | | |
| Anxiety | 128 | 6.3 | 3.9 | 0 | 6 | 18 |
| Depression | 127 | 6.1 | 4.0 | 0 | 6 | 19 |
| SF-36 | | | | | | |
| PF (0–100) | 129 | 70.7 | 22.8 | 10 | 80 | 100 |
| RP (0–100) | 129 | 61.4 | 27.8 | 0 | 62.5 | 100 |
| BP (0–100) | 129 | 45.9 | 20.4 | 0 | 41 | 100 |
| GH (0–100) | 129 | 45.7 | 17.1 | 0 | 45 | 87 |
| VT (0–100) | 129 | 48.4 | 22.3 | 0 | 50 | 100 |
| SF (0–100) | 128 | 68.5 | 26.2 | 0 | 75 | 100 |
| RE (0–100) | 129 | 68.1 | 31.3 | 0 | 75 | 100 |
| MH (0–100) | 129 | 60.9 | 23.9 | 5 | 60 | 100 |
| PCS | 127 | 34.9 | 16.5 | −10.1 | 38.2 | 63.4 |
| MCS | 127 | 45.2 | 11.6 | 14.6 | 46.3 | 75.1 |

*SD* standard deviation, *NDI* Neck Disability Index, *ext* extremity, *JOACMEQ* Japanese Orthopaedic Association Cervical Myelopathy Evaluation Questionnaire, *QOL* quality of life, *HADS* Hospital Anxiety and Depression Scale, *SF36* short form 36, *PF* physical functioning, *RP* role physical, *BP* bodily pain, *GH* general health, *VT* vitality, *SF* social role, *RE* role emotional, *MH* mental health, *PCS* Physical Component Score, *MCS* Mental Component Score

*Reliability and responsiveness*

The two versions of the NDI were evaluated by calculating the intraclass correlation coefficient (ICC) of first and second NDI in patients who reported being "unchanged" in the PGIC of the second survey. The ICC ranged from 0 to 1, and a higher value indicated higher repeatability. An ICC above 0.70 is accepted as good [11].

Responsiveness is the ability of an instrument to detect clinically relevant change over time. The responsiveness was evaluated from the data of patients who reported that they were "much better," "better" or "slightly better" in the PGIC of the second survey. We calculated the effect size and the standard response mean (SRM) from these data. The effect size was judged to be small if it was less than 0.2, moderate if it was around 0.5 and large if it was greater than 0.8 [10]. A higher SRM indicates higher responsiveness. We also calculated the correlation between change of the NDI and PGIC. Statistical analysis was performed by IBM SPSS 17.0 (IBM, Chicago, IL, USA).

**Table 3** The Cronbach's α values of the original and modified NDIs

| | Original NDI | | Modified NDI | |
|---|---|---|---|---|
| | *N* | Cronbach α | *N* | Cronbach α |
| Neck pain | 26 | 0.90 | 25 | 0.84 |
| Radiculopathy | 40 | 0.91 | 41 | 0.90 |
| Myelopathy | 52 | 0.94 | 52 | 0.92 |
| Total | 118 | 0.92 | 118 | 0.89 |

## Results

The first survey was performed from March 2010 to October 2010, and 130 patients completed the first study. The mean patient age was 59.4 ± 13.8 years (range 22–88 years), and there were 88 male and 42 females. The patient characteristics are shown in Table 1. The pain duration averaged 50.3 ± 66.3 months. The interval between the two surveys averaged 56.9 ± 5.6 days. Thirty-four (26.2 %) patients had received no treatment before the first survey, and of the others who had previous or ongoing treatment, 89 (68.5 %) received therapeutic drugs, 59 (45.4 %) had surgery, and 11 (8.5 %) received physical therapy (% greater than 100 because of multiple choices). The symptom severity judged by surgeons was mild in 44 (33.9 %), moderate in 70 (53.9 %) and severe in 16 (12.3 %) patients.

Twenty-eight (21.5 %) patients were classified into the neck pain group, 45 (34.6 %) into the radiculopathy group and 57 (43.9 %) into the myelopathy group. The number of patients who underwent surgical treatment after the first survey was 1 (3.6 %) in the neck pain group, 7 (15.6 %) in the radiculopathy group and 6 (10.5 %) in the myelopathy group.

The original NDI and the modified NDI of the first survey were 26.9 ± 17.1 and 29.9 ± 15.5, respectively (Table 2). No response was frequently found (6.9 and 8.5 %, respectively) for the question about driving. The ceiling effect of individual questions was small (0 to 4.8 %), but the floor effect was found more frequently in the original NDI than in the modified NDI (5.1 vs. 0.9 %). In both NDIs, the floor effect was significant for question 5 (about headaches) and 9 (about sleep) (45.3–50.8 %). The results of the NRSs, JOACMEQ, HADS and SF-36 are shown in Table 2.

In the second survey, 118 patients responded. The response to the PGIC was "much better" in 7 (5.9 %) patients, "better" in 24 (20.3 %), "slightly better" in 21 (17.8 %), "unchanged" in 55 (46.6 %), "slightly worse" in 5 (4.2 %), "worse" in 5 (4.2 %) and "much worse" in 1 (0.9 %) patient.

### Internal consistency, criterion-related validity and distinctive validity

The Cronbach α of the original NDI and the modified NDI were 0.92 and 0.89, respectively (Table 3). The subgroup analysis of the three groups showed good to excellent values for Cronbach's α.

The majority of parameters had a statistically significant correlation with the NDIs (Table 4). The original NDI had higher CCs for pain severity in the neck and back. The modified NDI had a higher correlation than the original NDI in some domains: numbness in the upper extremities, lower back and lower extremities; the upper/lower extremity function in the JOCMEQ; all mental health domains and the MCS in the SF36.

There was a statistically significant difference in the symptom severity for the modified NDI (ANOVA, $p = 0.020$), but not for the original NDI ($p = 0.142$).

### Reliability and responsiveness

A total of 118 patients responded to the PGIC questionnaire, and 55 patients (46.6 %) answered "unchanged" in the PGC in the second survey. Their responses were analyzed for the test–retest repeatability. The ICC of the original and modified NDI was accepted as good (0.77 and 0.78, respectively).

Spearman's $\rho$ between the two versions of the NDI and the PGIC was 0.47 ($p < 0.0001$) in the original NDI and 0.59 ($p < 0.0001$) in the modified NDI (Fig. 2).

Fifty-two patients (44.1 %) reported a positive change at the second survey ("much better," "better" and "slightly better"). The effect size of the original and modified NDI was judged to be moderate (0.55 and 0.64, respectively). The SRMs of the original and modified NDI were −0.52 and −0.66, respectively.

## Discussions

Our study demonstrated that both of the Japanese NDIs had good to excellent validity, repeatability and responsiveness.

We compared the internal consistency and repeatability of the Japanese NDI with the NDIs in other languages (Table 5) and found that the internal consistency of the Japanese NDI was comparable to the NDI in other languages. The reliability was marginally acceptable, possibly

**Table 4** Correlations between the two versions of the NDI and other outcomes

| | *N* | Original NDI | | Modified NDI | |
|---|---|---|---|---|---|
| | | Spearman | *p* value | Spearman | *p* value |
| Pain (0–10) | | | | | |
| Head | 118 | 0.374 | <0.0001 | 0.370 | <0.0001 |
| Neck | 118 | 0.635 | <0.0001 | 0.486 | <0.0001 |
| Back | 117 | 0.601 | <0.0001 | 0.555 | <0.0001 |
| Upper ext | 117 | 0.455 | <0.0001 | 0.499 | <0.0001 |
| Lower back | 117 | 0.221 | 0.017 | 0.219 | 0.018 |
| Lower ext | 117 | 0.271 | 0.003 | 0.319 | 0.001 |
| Numbness (0–10) | | | | | |
| Head | 118 | 0.306 | 0.001 | 0.347 | <0.0001 |
| Neck | 118 | 0.435 | <0.0001 | 0.443 | <0.0001 |
| Back | 115 | 0.407 | <0.0001 | 0.416 | <0.0001 |
| Upper ext | 116 | 0.402 | <0.0001 | 0.481 | <0.0001 |
| Lower back | 117 | 0.256 | 0.001 | 0.327 | <0.0001 |
| Lower ext | 117 | 0.286 | <0.0001 | 0.371 | <0.0001 |
| JOACMEQ (0–100) | | | | | |
| Cervical | 116 | −0.397 | <0.0001 | −0.369 | <0.0001 |
| Upper ext | 117 | −0.385 | <0.0001 | −0.454 | <0.0001 |
| Lower ext | 115 | −0.363 | <0.0001 | −0.427 | <0.0001 |
| Bladder | 118 | −0.191 | 0.039 | −0.206 | 0.026 |
| QOL | 115 | −0.677 | <0.0001 | −0.686 | <0.0001 |
| HADS (0–21) | | | | | |
| Anxiety | 116 | 0.415 | <0.0001 | 0.414 | <0.0001 |
| Depression | 117 | 0.426 | <0.0001 | 0.455 | <0.0001 |
| SF36 | | | | | |
| PF (0–100) | 117 | −0.526 | <0.0001 | −0.551 | <0.0001 |
| RP (0–100) | 117 | −0.599 | <0.0001 | −0.607 | <0.0001 |
| BP (0–100) | 117 | −0.64 | <0.0001 | −0.669 | <0.0001 |
| GH (0–100) | 117 | −0.501 | <0.0001 | −0.510 | <0.0001 |
| VT (0–100) | 117 | −0.518 | <0.0001 | −0.597 | <0.0001 |
| SF (0–100) | 116 | −0.422 | <0.0001 | −0.483 | <0.0001 |
| RE (0–100) | 117 | −0.523 | <0.0001 | −0.580 | <0.0001 |
| MH (0–100) | 117 | −0.413 | <0.0001 | −0.482 | <0.0001 |
| PCS | 115 | −0.602 | <0.0001 | −0.617 | <0.0001 |
| MCS | 115 | −0.336 | <0.0001 | −0.410 | <0.0001 |

*NDI* Neck Disability Index, *Ext* extremity, *JOACMEQ* Japanese Orthopaedic Association Cervical Myelopathy Evaluation Questionnaire, *QOL* quality of life, *HADS* Hospital Anxiety and Depression Scale, *SF36* short form 36, *PF* physical functioning, *RP* role physical, *BP* bodily pain, *GH* general health, *VT* vitality, *SF* social role, *RE* role emotional, *MH* mental health, *PCS* Physical Component Score, *MCS* Mental Component Score

because of the long interval between the two surveys; the interval between the two surveys ranged from 1 day to 2 weeks in other studies except for one subgroup. We selected an 8-week interval between the two surveys because we had planned to evaluate both the repeatability and responsiveness by separating patients into two groups based on the PGIC of the second survey.

The majority of past reports demonstrated the validity of the NDI in the neck pain population. Few validation studies of the NDI were performed in patients with cervical radiculopathy/myelopathy, who do not always have neck pain, though many studies have adopted the NDI as an assessment following conservative or surgical treatment. With regard to the patients with radiculopathy, only Cleland et al. [13] reported a good test–retest reliability (ICC = 0.68) in 38 radiculopathy patients. The Korean NDI developed by Song et al. [21] demonstrated the validity and reliability in a mixed population that included radiculopathy and myelopathy patients.

Patients who have neurological symptoms often complain not only of pain but also variable symptoms: tingling, burning, numbness, etc. Patients with spinal disorders often complain of numbness and insist that it is different from pain, although numbness is usually regarded as one of the symptoms of neuropathic pain [23]. In a study of 892 patients with cervical ossification of the posterior

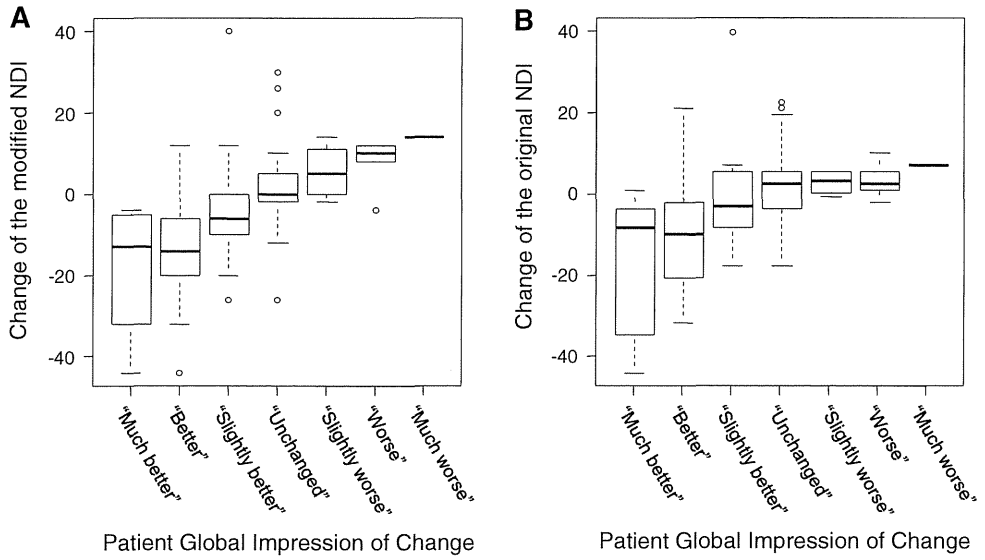


**Fig. 2** The relationship between the change in the NDI and the patient global impression of change (PGIC). **a** The modified NDI: Spearman's $\rho = 0.588$ ($p < 0.0001$, $n = 106$). **b** The original NDI: Spearman's $\rho = 0.467$ ($p < 0.0001$, $n = 106$)

**Table 5** The internal consistency and reliability of the NDI in various languages

| | *N* | Condition | Cronbach α | ICC/interval |
|---|---|---|---|---|
| English [1] | 52 | Neck pain | 0.8 | 0.89/2 days |
| French [12] | 101 | Neck pain | na | 0.93/1 day |
| Swedish [13] | 59 | Neck pain | na | 0.97/2 days (chronic) |
| | | | | 0.94/3 months (chronic) |
| | | | | 0.89/2 days (acute) |
| Dutch [14] | 187 | Acute neck pain | na | 0.90/1 week |
| Brazilian Portuguese [15] | 203 | Trauma, OA | 0.74 | 0.92/1 day |
| | | | | 0.48/1 week |
| Greek [16] | 65 | Neck pain | 0.85 | 0.93/1–2 weeks |
| Iranian [17] | 185 | Neck pain | 0.88 | 0.90/2 days |
| Catalan [18] | 150 | Whiplash | 0.87 | na |
| Spanish [19] | 221 | Neck pain | 0.89 | 0.88/2 weeks |
| Turkish [20] | 88 | Chronic neck pain | na | 0.979 |
| Korean [21] | 78 | Radiculopathy (50) | 0.82 | 0.93/2 days |
| | | Myelopathy (28) | | |
| Chinese [22] | 125 | Neck pain | 0.89 | 0.95/1 day |
| Japanese (present study) | 130 | Neck pain (28) | 0.92 (original) | 0.77/8 weeks (original) |
| | | Radiculopathy (45) | 0.89 (modified) | 0.78/8 weeks (modified) |
| | | Myelopathy (57) | | |

*NDI* Neck Disability Index, *na* not available, *OA* osteoarthritis

longitudinal ligament [24], the researchers had asked, "Which is more troublesome, pain or numbness?" Of these patients, 45.0 % responded "both pain and numbness," 25.0 % responded "numbness" and 22.2 % responded "pain." Their result indicates the clinical importance of numbness, which is often regarded by patients as another entity different from pain. In the present study, the modified NDI had a higher criterion-related validity in numbness and mental health-related QOL, while the original NDI had a higher criterion-related validity in neck pain. In other words, the inclusion of numbness in the questionnaire enhanced the validity of the NDI in the assessment of

patients with cervical disorders. In addition, the modified NDI had a higher correlation with the assessment by both physicians and patients and had a higher effect size and SRM than the original NDI. Accordingly, the modified NDI may be a better choice for studies of patients with cervical disorders. On the other hand, the original NDI is still useful for epidemiological studies of nonspecific neck pain.

In summary, we demonstrated the validity, reliability and responsiveness of both versions of the Japanese NDI, and the modified NDI more accurately reflected the numbness and mental health-related QOL, while the original NDI better reflected the neck pain.

**Conflict of interest** The authors declare that K. Takeshita received payment for lectures that had no direct relationship with the submitted work from Pfeizer Japan Inc., Tokyo, Japan.

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Spine

SRS Focus Issue

SPINE Volume 37, Number 5, pp E315–E317


# Is Surgery Indicated for Asymptomatic or Mildly Myelopathic Patients With Significant Ossification of the Posterior Longitudinal Ligament?

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**Study Design.** Review article.

**Objective.** To discuss indications and timing of surgery for patients with significant ossification of the posterior longitudinal ligament (OPLL) who show no or only mild myelopathic symptoms.

**Summary of Background Data.** Among patients with cervical spinal cord injury, the incidence of patients with OPLL is relatively high, and most had no obvious symptoms of cervical myelopathy.

**Methods.** These topics were discussed on the basis of clinical practice guidelines for ossification of the posterior longitudinal ligament as published in 2005 by the Japanese Orthopaedic Association and the Committee on Research into OPLL under the auspices of the Ministry of Health, Labor and Welfare.

**Results.** No evidence supports the usefulness of surgery for patients with significant OPLL without or with only mild cervical myelopathy.

**Conclusion.** "Prophylactic" surgery for patients with significant OPLL without or with only mild cervical myelopathy cannot be recommended on the basis of the existing evidence.

**Key words:** ossification, spinal ligament, laminoplasty, anterior surgery. **Spine 2012;37:E315–E317**

Surgical treatment of ossification of the posterior longitudinal ligament (OPLL) is clearly indicated when the patient shows severe and/or progressive cervical myelopathy, and surgery should be performed as soon as possible. However, for patients without myelopathic symptoms or with only mild myelopathy instead of evident OPLL on plain radiography of the cervical spine, the indications and timing of surgical treatment remain controversial. Some surgeons advocate decompressive surgery for patients on the basis of improvements in surgical techniques, and OPLL is reportedly frequent among patients with cervical spinal cord injury.[1,2] Conversely, some surgeons oppose "prophylactic" surgery because any type of surgery for OPLL carries a risk of surgical complications and adverse effects, and evidence regarding the natural course of OPLL is currently insufficient to warrant prophylactic surgery.[3]

The Japanese Orthopaedic Association published clinical practice guidelines for OPLL in 2005, on the basis of a systemic review of the literature on OPLL.[4] Based on these guidelines, the topic discussed here is whether surgery is indicated for asymptomatic or mildly myelopathic patients with significant OPLL.

When we consider the choice and timing of treatment of OPLL, what should be taken into consideration? The following items provide clues to answering this question: (1) the nature of OPLL and myelopathy; (2) the natural course of OPLL and myelopathy; (3) the effectiveness of conservative treatment; (4) the effectiveness of surgical treatment; and (5) the invasiveness and adverse effects of surgery.

## NATURE OF OPLL AND MYELOPATHY

Two processes of ossification are observed in OPLL: endochondral ossification and intramembranous ossification. Endochondral ossification is always observed, whereas intramembranous ossification is not always present. In any case, the ossified lesion represents histologically normal bone tissue, and spontaneous resorption of the ossified lesion is thus not to be expected. Furthermore, development of drug agents to dissolve ossified tissue consisting of normal bone cannot be anticipated in the near future. In OPLL, the pathology causing myelopathy is a thick, ossified ligament in front of the spinal cord, so removal of the ossified ligament is a rational but radical treatment when myelopathy appears.

## NATURAL COURSE OF OPLL AND MYELOPATHY

The natural course of OPLL has not yet been clarified. No evidence that a small ossified lesion that can be found only on computed tomography will become large enough to compress the spinal cord has been verified. OPLL large enough to be observed on plain x-ray films can become large under some

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conditions. In terms of the progression of OPLL, local and general factors such as age and positive family history have been studied, but no factors have been confirmed as predictors of OPLL progression. On the contrary, progression of OPLL after posterior decompression has been widely recognized, with approximately 60% of patients who underwent laminoplasty showing progression (≥2 mm in thickness or length).[5]

Various surveys on relationships between type and progression of OPLL have been performed. The mixed type is said to be progressive, but results of these studies have been variable.

Development of cervical myelopathy is reportedly related to the thickness of the ossified lesion (occupancy ratio: thickness of the ossified lesion divided by the anteroposterior diameter of the spinal canal), the space available for the spinal cord (SAC), and dynamic factors. The pathomechanisms underlying cervical myelopathy in OPLL have not been clarified yet, and a static factor, that is, OPLL is not a sole etiological factor for myelopathy. However, many reports have found that occupancy ratio is closely related to the development of myelopathy. The critical ratio for the development of myelopathy has been reported within a range of 30% to 60%.[6,7] Several authors have focused on the size of the SAC. This indicator of myelopathy varied from 6 to 9 mm.[8,9] Differences in the size of SAC may arise because so-called dynamic factors play a role in the development of myelopathy. In summary, occupancy ratio and SAC can be important factors when surgical treatment is considered for an OPLL patient without myelopathic symptoms or with only mild myelopathy.

On the contrary, we have encountered a patient with thick OPLL showing neither signs nor symptoms of myelopathy.[8,10] Unfortunately, the mechanisms by which a chronically compressed spinal cord avoids manifesting clinical symptoms have not been clarified.

So-called dynamic factors play important roles in the development of myelopathy.[7,11] Symptomatic patients reportedly show increased mobility at the level of the disc at which OPLL shows discontinuity.

## EFFECTIVENESS OF CONSERVATIVE TREATMENT

Conservative treatment techniques including skull traction, immobilization with a collar, steroids, and prostaglandin E1 have been adopted for patients with mild myelopathy, with varying degrees of effectiveness. However, most such reports have been in the form of case series, with a relatively low level of evidence, and the durability of treatment effects has not been made clear. No conservative modalities have thus been confirmed as suitable alternatives to surgery.

## EFFECTIVENESS OF SURGICAL TREATMENT

With modern advances in techniques for cervical spine surgery, surgery is increasingly rewarding for patients with moderate or severe myelopathy when performed properly and with the right timing.[12–16] Of course, decompressive surgery cannot restore spinal cord damage caused by chronic compression, and the results of surgery are influenced by history of trauma, severity of myelopathy before surgery, age at surgery, duration of symptoms prior to surgery, and other factors. Obviously, the lower the degree of spinal cord damage, the better the surgical results are likely to be in the short term. This may be the major reason for considering "prophylactic surgery." However, OPLL is a kind of systemic disease, and surgery cannot resolve the condition. That is, ossified lesions remain with posterior decompression and frequently progress, although such progression rarely results in a need for reoperation. Even with anterior removal or floating of ossified lesions, ossification of the longitudinal ligament may progress at unoperated levels. Given these issues, some surgeons oppose "prophylactic surgery."

## INVASIVENESS AND ADVERSE EFFECTS OF SURGERY

Surgery has become safer and less invasive with improvements in surgical techniques and accumulation of knowledge regarding OPLL.[12,15,17–21] However, each procedure has peculiar problems, and some are quite serious. Spinal cord injury after laminoplasty is occasionally reported. Swelling of the spinal cord due to reperfusion has been suggested as a contributing factor, although the etiology remains unclear. Nerve root palsy after anterior or posterior surgery is a relatively common and notorious complication. Reductions in range of motion of the neck after anterior or posterior surgery, bone graft–related complications after anterior surgery, and neck pain after posterior decompression are unavoidable and unpredictable.

## SUMMARY

Surgical decompression is the treatment of choice for patients with progressive or severe myelopathy secondary to OPLL because the duration of symptoms prior to surgery is known to be one of the factors most significantly associated with negative prognosis.

No evidence has been accumulated for surgical treatment of asymptomatic or mildly myelopathic patients showing high occupancy ratio (<50%) or narrow SAC (≤8 mm). Considering the risks of surgery and the variable natural course of OPLL, prophylactic surgery remains hard to recommend.

Whether a small ossified lesion found incidentally is likely to become large enough to compress the spinal cord is still unclear, and surgery is not immediately indicated in such cases.

### ➢ Key Points

- ❑ For patients without myelopathic symptoms or with only mild myelopathy instead of evident OPLL on plain radiography of the cervical spine, indications and timing of surgical treatment remain controversial.
- ❑ Surveys on the natural course of OPLL have not identified any predictors of OPLL progression.
- ❑ Not only static compression factors from OPLL but also dynamic and other factors play roles in the development or progression of cervical myelopathy secondary to OPLL. Indications for surgical treatment cannot be decided solely on the basis of the extent of OPLL.
- ❑ No evidence supporting prophylactic decompression surgery has been established to date.

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Spine

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CERVICAL SPINE

# 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

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**Study Design.** Case studies of patients with cervical spondylotic amyotrophy used compound muscle action potentials (CMAPs) of deltoid and biceps brachii muscles and central motor conduction time (CMCT).

**Objective.** To discuss surgical outcome for proximal-type cervical spondylotic amyotrophy in the context of results obtained with CMAPs and CMCT.

**Summary of Background Data.** There have been no reports that correlate surgical outcome with CMAPs of deltoid and biceps brachii muscles or with CMCT.

**Methods.** A retrospective study was performed for 24 patients with proximal-type cervical spondylotic amyotrophy who underwent surgical treatment of the cervical spine. Erb-point–stimulated CMAPs were recorded in the deltoid and biceps. The percent amplitude of CMAPs was calculated in comparison with the opposite side. Motor-evoked potentials were recorded from bilateral abductor digiti minimi. CMAPs and F waves were recorded after supramaximal electric stimulation of ulnar nerves. CMCT was calculated as follows: motor-evoked potentials latency – (CMAPs' latency + F latency – 1)/2 (ms). Muscle strength was evaluated using manual muscle testing. Improvements in strength were classified as excellent, good, or fair.

**Results.** The improvement was graded as excellent in 12 cases, good in 2 cases, and fair in 10 cases. The average percentage for CMAPs' amplitude on the affected side compared with the normal side in deltoid and biceps brachii muscles was significantly different between the excellent and fair patient groups. The CMCT on the affected side was not significantly different between excellent and fair patient groups.

**Conclusion.** The average percentage range of deltoid and biceps brachii muscle CMAPs' amplitude determined at the onset of illness correlated significantly with postoperative recovery. Surgical intervention of the cervical spine should be performed in patients in whom the average percentage of CMAPs' amplitude in deltoid and biceps brachii muscles ranges from 30% to 50%.

**Key words:** cervical spondylotic amyotrophy, compound muscle action potentials, central motor conduction time, surgical outcome.

**Spine 2012;37:E1444–E1449**

Cervical spondylotic amyotrophy (CSA) is a rare type of cervical spondylotic disorder. The clinical characteristics of CSA are severe muscle atrophy and weakness in the upper extremities without significant sensory deficits or myelopathy. CSA can be classified into 2 types according to the affected muscles in the upper extremities: proximal type (unilateral scapular, deltoid, and biceps brachii muscles) and distal type (triceps, forearm, and hand muscles). In this study, we describe 24 patients with proximal-type CSA from the C5 to C6 myotome. We demonstrate that the pathology and prognosis of proximal-type CSA can be assessed using compound muscle action potentials (CMAPs) of deltoid and biceps brachii muscles, described in a previous study by our group.[1] Tani *et al*[2] have reported that side-to-side comparison of CMAP amplitudes served as the best measure for functional recovery. Central motor conduction time (CMCT) has been used to detect dysfunction in the corticospinal tract.[3] However, so far there have been no reports that correlate surgical outcome with CMAPs of deltoid and biceps brachii muscles or with CMCT in the upper extremity of the affected side. The surgical outcome for proximal-type CSA is discussed here in the context of results obtained with CMAPs and CMCT.

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## PATIENTS AND METHODS

### Diagnosis of Proximal-Type CSA

Yanagi *et al*[4] described the diagnosis of CSA as being characterized by severe muscular atrophy in the upper extremities with an absent or insignificant sensory deficit in patients with cervical spondylosis. CSA can be classified into 2 types according to the affected muscles in the upper extremities: proximal type (scapular, deltoid, and biceps brachii muscles) and distal type (triceps, forearm, and hand muscles). In this study, the diagnosis of proximal-type CSA was established on the basis of the presence of severe unilateral muscle atrophy and severe unilateral weakness of the shoulder girdle muscles, with an absent or insignificant sensory deficit in the C5 or C6 dermatome, or both, and magnetic resonance imaging–documented cervical spinal cord compression and/or foraminal stenosis with a varying degree of bulging disc and with a focal bony spur. But the shoulder girdle muscles on the opposite side (normal side) and the bilateral intrinsic muscle were intact. In this study, we excluded the patients with pain in the upper extremity and shoulder girdle and with bilateral weakness.

### Patients

A retrospective study was performed for 32 patients with proximal-type CSA who underwent surgical treatment of the cervical spine between April 1997 and December 2010 at the Department of Orthopaedic Surgery at Yamaguchi University. Informed consent was obtained from each patient. Excluded were patients with cervical flexion myelopathy, multifocal motor neuropathy, amyotrophic lateral sclerosis, neuralgic amyotrophy, torn rotator cuff lesions, subjective symptoms, or neurological findings associated with neuropathy. Thus, from the initial 32 patients, 24 (22 men and 2 women) were selected for analysis. Their mean age was 61.2 years (range, 45–83 yr) and the mean length of clinical history before admission was 18.8 months (range, 3 mo to 12 yr). The mean duration of postoperative follow-up was 50 months (range, 6 mo to 12 yr). All 24 patients had severe unilateral muscle atrophy of the shoulder girdle muscles but the intrinsic muscles were intact.

For light touch and pinprick sensation, impaired levels were recorded according to the dermatome proposed by Brain and Walton.[5] Sensory examination revealed no abnormalities, except for 12 patients who had a sensory disturbance for light touch and pinprick in the C5 or C6 dermatome, or both. The clinical symptoms and results of neurological examination are summarized in Table 1. Informed consent was obtained from each patient before enrollment in this study.

### Assessment of Muscle Strength

Muscle strength was evaluated using manual muscle testing (MMT).[6] Preoperative and postoperative strength of the most atrophic muscle was evaluated using MMT. Improvements in strength were classified as excellent (>2 grades of recovery by MMT), good (1 grade of recovery by MMT), or fair (no improvement by MMT).

### Electrophysiological Investigation

All electrophysiological examinations were performed using a Nicolet Viking instrument (Nicolet Biomedical, Madison, WI). Denervation potentials and decreased motor unit potentials were observed in the atrophic muscle (C5–C6 myotome) on standard needle electromyography, but no abnormal findings were observed in the thoracic paraspinal muscles or lower limb muscles (tibialis anterior muscles) for all patients. The results of sensory nerve conduction velocity tests for the bilateral median and ulnar nerves were normal in all patients.

### Measurement of CMAPs

Erb-point–stimulated CMAPs were recorded in the deltoid and biceps in all patients. A disc electrode, 11 mm in diameter, was placed over the middle of the deltoid as an active electrode, on the acromion as a reference electrode in the deltoid, over the middle of the biceps brachii muscle, and on the lateral epicondyle of humerus in the biceps brachii muscle. The skin was treated with an abrasive solution to reduce impedance and a ground strap was wrapped around the elbow. The bipolar stimulator consisted of a pair of bare metal contact surfaces approximately 3 mm in diameter and with an adjustable interelectrode distance. The stimulus intensity was gradually increased until it no longer altered the size of the recorded response. Measurement of CMAPs included the negative peak amplitude from baseline to peak. The percent amplitude of CMAPs was calculated in comparison with the opposite side.

### Measurement of CMCT

Self-adhesive surface recording electrodes were placed on abductor digiti minimi (ADM). Motor-evoked potentials (MEPs) were recorded from bilateral ADM. Transcranial magnetic stimulation (TMS) was delivered by Magstim 200 (Magstim, Machida City, Tokyo) using a circular coil with an outer diameter of 140 mm. TMS was applied while the patient exerted isometric voluntary contraction of ADM. The coil was held with its center on the Cz position of 10–20 system for recording MEPs from ADM. TMS intensity was set at 20% above the MEP threshold. At least 4 consecutive trials were recorded and superimposed. The shortest onset latency of the MEPs was recorded. CMAPs and F waves were recorded after supramaximal electric stimulation of ulnar nerves at the wrist. Sixteen serial responses were obtained and the shortest latency of F waves was measured. CMCT was calculated as follows: MEP latency –(CMAPs latency + F latency – 1)/2 (ms). All muscle responses were amplified and filtered with a bandpass of 5 to 5000 Hz.

Statistical analysis was performed using the Mann-Whitney $U$ test, with $P < 0.05$ considered as statistically significant.

## RESULTS

### Electrophysiological Investigation

The improvement in MMT was graded as excellent in 12 cases, good in 2 cases, and fair in 10 cases. Surgical outcome and the average percentage of CMAPs' amplitude on the

**TABLE 1. Clinical and Neurological Findings**

| Cases | Age | Sex | MMT* | | BTR | TTR | Sensory Disturbance Area† | Duration of Symptom | Method of Operation |
|---|---|---|---|---|---|---|---|---|---|
| | | | Deltoid (Initial) | Biceps Brachii Muscle (Initial) | | | | | |
| 1 | 63 | M | P | F | Diminished | Exaggerated | ... | 4 | ASF |
| 2 | 45 | F | P | F | Diminished | Absent | ... | 12 | L + F |
| 3 | 73 | M | F | F | Absent | Diminished | ... | 9 | L + F |
| 4 | 72 | F | P | F | Absent | N | C5 | 3 | L + F |
| 5 | 70 | M | P | F | Diminished | Diminished | ... | 5 | L + F |
| 6 | 75 | M | P | F | Diminished | Exaggerated | ... | 5 | L + F |
| 7 | 46 | M | P | F | Diminished | N | C5 | 10 | ASF |
| 8 | 83 | M | P | F | Diminished | Diminished | C5 | 3 | L + F |
| 9 | 56 | M | F | F | Diminished | Diminished | ... | 3 | ASF |
| 10 | 59 | M | F | F | Absent | Diminished | C5 | 60 | ASF |
| 11 | 55 | M | P | F | Diminished | N | ... | 12 | ASF |
| 12 | 52 | M | F | F | Diminished | Diminished | | 12 | ASF |
| 13 | 56 | M | P | F | Diminished | Diminished | C5 | 6 | ASF |
| 14 | 61 | M | T | P | Diminished | Diminished | C5 | 9 | L + F |
| 15 | 53 | M | P | F | Diminished | Diminished | ... | 130 | L + F |
| 16 | 67 | F | T | F | Diminished | Diminished | ... | 4 | ASF |
| 17 | 60 | M | P | F | Absent | Absent | C6 | 36 | L + F |
| 18 | 55 | M | P | F | Absent | N | C6 | 48 | L + F |
| 19 | 64 | M | P | F | Absent | Exaggerated | C5 | 72 | L + F |
| 20 | 60 | M | P | F | N | Exaggerated | ... | 7 | ASF |
| 21 | 50 | M | P | F | Diminished | Diminished | C5 | 4 | ASF |
| 22 | 62 | M | T | F | Absent | Diminished | C5, C6 | 3 | ASF |
| 23 | 65 | M | P | P | Diminished | Diminished | | 144 | L |
| 24 | 66 | M | T | T | Absent | Absent | C5, C6 | 3 | L |

*Adapted from Daniels et al.[6]*

*†The impaired level was recorded to the dermatome proposed by Brain and Walton.[5]*

*MMT indicates manual muscle test; BTR, biceps tendon reflex; TTR, triceps tendon reflex; M, male; P, poor; F, female; ASF, anterior spinal fusion; F, fair; L, laminoplasty; F, foraminotomy; N, normal; T, trace.*

affected side compared with the normal side in deltoid and biceps brachii muscles are shown in Figure 1. Ten of the 12 patients graded as excellent showed more than 30% CMAPs' amplitude on the affected side that that on the normal side. For the 2 remaining patients, the CMAPs' amplitude ranged from 10% to 30%. One of the 2 patients graded as good showed a CMAPs' amplitude of more than 30% on the affected side than that on the normal side. For the other patient, the range for CMAPs' amplitude was 10% to 30%. All 10 patients graded as fair had less than 30% CMAPs' amplitude on the affected side than that on the normal side. The average percentage for CMAPs' amplitude on the affected side compared with the normal side in deltoid and biceps brachii muscles was significantly different between the excellent and fair patient groups ($P < 0.0004$).

Surgical outcome and the percentage of CMAPs' amplitude on the affected side compared with the normal side in deltoid muscle are shown in Figure 2. All patients had a CMAPs' amplitude on the normal side that was greater than 5 mV. All patients graded excellent had more than 10% CMAPs' amplitude on the affected side than that on the normal side. All patients graded as fair had less than 30% CMAPs' amplitude on the affected side than that on the normal side. The CMAPs' amplitude on the affected side in deltoid was significantly different between the excellent and fair patient groups ($P < 0.01$). The percentage of CMAPs' amplitude on

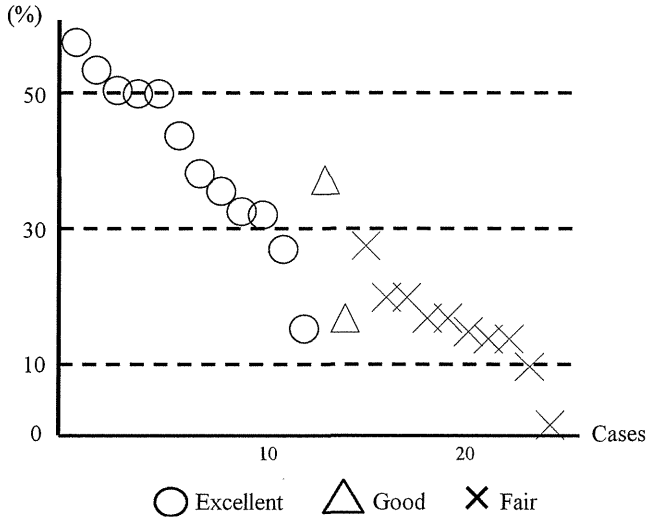


**Figure 1.** Surgical outcome and the average percentage of CMAPs' amplitude on the affected side compared with the normal side in deltoid and biceps brachii muscles. CMAPs indicates compound muscle action potentials.

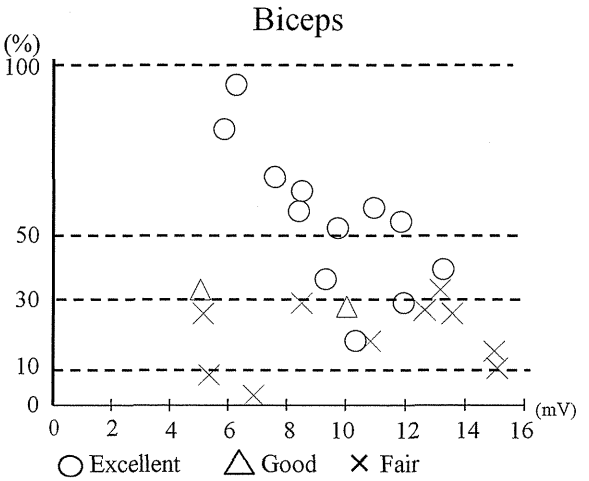


**Figure 3.** Surgical outcome and the percentage of CMAPs' amplitude on the affected side compared with the normal side in biceps brachii muscle. CMAPs indicates compound muscle action potentials.

the affected side compared with the normal side in deltoid was also significantly different between the excellent and fair patient groups ($P < 0.004$).

Surgical outcome and the percentage of CMAPs' amplitude on the affected side compared with the normal side in biceps brachii muscle are shown in Figure 3. All patients had a CMAPs' amplitude greater than 5 mV on the normal side. Eight of the 12 patients graded as excellent had more than 50% CMAPs' amplitude on the affected side than that on the normal side. Nine of the 10 patients graded as fair showed less than 30% CMAPs' amplitude on the affected side than that on the normal side. The CMAPs' amplitude on the affected side in biceps brachii muscle was significantly different between the excellent and fair patient groups ($P < 0.002$). Likewise, the percentage of CMAPs' amplitude on the affected side compared with the normal side in biceps brachii muscle was significantly different between the excellent and fair patient groups ($P < 0.007$).

Surgical outcome and CMCT are shown in Figure 4. Kaneko *et al*[3] reported that the normal value for CMCT was 5.2 ± 1.1 ms. Six of the excellent and 3 of the fair patients showed CMCT on the affected side that was less than 6.3 ms. The CMCT on the affected side was not significantly different between excellent and fair patient groups ($P > 0.05$).

## DISCUSSION

CSA is a clinical syndrome characterized by severe muscular atrophy in the upper extremity and concurrent with the absence of, or insignificant, sensory deficit.[4] We previously reported that the pathophysiology of CSA involved a combination of lesions in the anterior horns (AHs) and the ventral

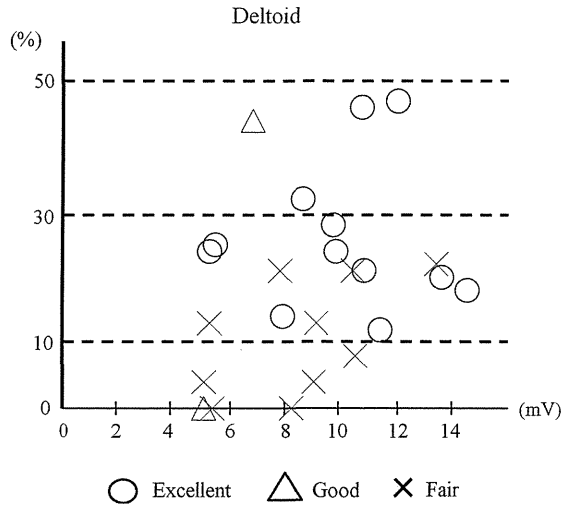


**Figure 2.** Surgical outcome and the percentage of CMAPs' amplitude on the affected side compared with the normal side in deltoid muscle. CMAPs indicates compound muscle action potentials.

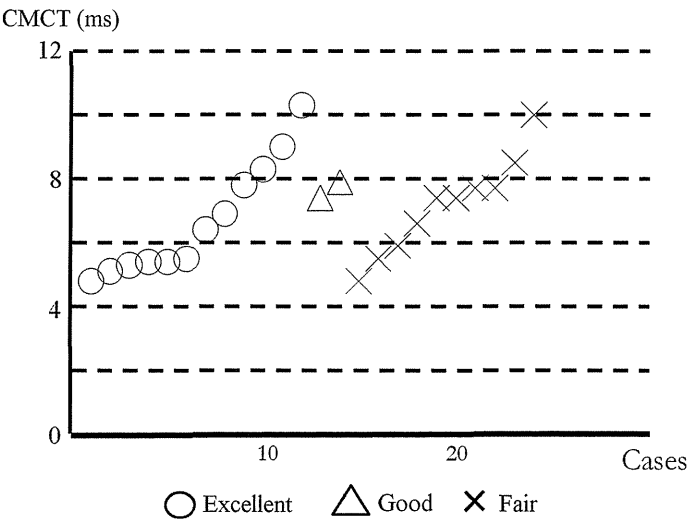


**Figure 4.** Surgical outcome and CMCT in the upper extremity of the affected side. CMCT indicates central motor conduction time.

nerve roots (VNR).[1] Several groups have reported that surgical treatment of proximal-type CSA was effective.[7–9] However, in this study the outcome for 10 of 24 cases (42%) was graded as fair only. Tani *et al*[2] reported that Erb-point–stimulated CMAPs in deltoid were useful for predicting the natural history of proximal-type CSA. In particular, patients with CMAPs exceeding 50% of the normal side showed a most complete return of function, despite severe weakness.[1,2,10,11] However, very few articles have reported on the relationship between surgical outcome and Erb-point–stimulated CMAPs. Fujiwara *et al*[7] found that patients in whom the percentage amplitude of CMAPs in the most severely atrophic muscle was more than 10% on the affected side than that on the normal side were able to recover muscle function. In this study, 12 of 12 (100%) of the patients graded as excellent, 2 of 2 (100%) as good, and 5 of 10 (50%) as fair showed more than 10% CMAPs' amplitude in deltoid on the affected side than that on the normal side (Figure 2). Two of the fair patients had less than 10% CMAPs' amplitude in biceps brachii on the affected side than that on the normal side (Figure 3). The percentage in biceps brachii was higher than in deltoid, and CMAPs' amplitudes were shorter in biceps brachii than in deltoid on the normal side, indicating the involvement of C6 AH.

Patients with proximal-type CSA had a characteristic distribution of unilateral motor loss that corresponded to C5 and C6 myotomes. It is generally accepted that upper limb muscles are innervated by several nerve roots.[12,13] In general, C5 and C6 nerve roots distribute to deltoid and biceps brachii muscles.[14,15] A small number of patients with proximal-type CSA had isolated C6 root compression, associated with deltoid weakness.[2] We therefore considered it necessary to assess CMAPs' amplitude in deltoid and biceps brachii muscles. We hypothesized that the surgical outcome for proximal-type CSA could be assessed using CMCT and the percentage amplitude of CMAPs in deltoid and biceps brachii muscles. All fair patients had an average CMAPs' amplitude of less than 30% for the affected side than that for the normal side (Figure 1). Patients in whom the average CMAPs' amplitude ranged from 30% to 50% were graded as excellent and good.

Two of the patients graded as excellent (cases 11 and 12) and one of the patients graded as good showed an average CMAPs' amplitude that ranged from 10% to 30%. We previously reported that patients with a CMAPs' amplitude on the normal side that exceeded 10 mV had no impingement of AH.[1] Two of the patients graded as excellent in this study with an average CMAPs' amplitude that ranged from 10% to 30% had a CMAPs' amplitude in both deltoid and biceps brachii on the normal side that was greater than 10 mV. Two patients (cases 11 and 12) had CMCT on the affected side that was less than 6.3 ms. These cases were confirmed to involve VNR.

MEPs after TMS are useful in the evaluation of cervical spondylotic myelopathy (CSM). CMCT has been used to detect dysfunction in the corticospinal tract of patients with CSM. Previous studies showed that MEP abnormalities were present in 63% to 92% of patients with CSM.[2,16–20] Kaneko *et al*[3] reported that the normal value of CMCT was 5.2 ± 1.1 ms and the pathology in CSM with normal CMCT was at a relatively early stage. Ito *et al*[21] reported the progression pattern and histological findings of lesions in the spinal cord that were affected by CSM. Atrophy and neuronal loss in the AH and intermediate zone developed first, followed by degeneration of the lateral and posterior funiculi. We confirmed that CSA in patients with normal CMCT and a CMAPs' amplitude on the normal side that exceeded 10 mV had involvement of VNR.

The average percentage range of deltoid and biceps brachii muscle CMAPs' amplitude determined at the onset of illness correlated significantly with postoperative recovery of deltoid and biceps brachii muscle strength. Surgical intervention of the cervical spine should be performed in patients in whom the average percentage of CMAPs' amplitude in deltoid and biceps brachii muscles ranges from 30% to 50%. We established a diagnosis for the involvement of VNR based on CMAPs and CMCT. Surgical intervention was effective for patients with involvement of VNR and in whom the average CMAPs' amplitude ranged from 10% to 30%. These electrophysiological investigations play an important role in patient management, especially for the prediction of surgical outcome. The method of operation for proximal-type CSA is still controversial. Anterior spinal fusion or laminoplasty with or without foraminotomy has been reported.[22,23] We highlight the importance of assessing the pathology of proximal-type CSA by using CMAPs of deltoid and biceps brachii muscles and CMCT.

In this study, we excluded the patients with bilateral weakness. It was difficult to compare the affected side with the normal side for the patient with bilateral weakness. Sharrard[24] reported that muscle power was associated with residual motor cells in the AHs of poliomyelitic spinal cord. The position and number of residual motor nerve cells in the lumbosacral spinal cord were determined and compared with the corresponding cells in the normal number of cells. Motor cell destruction was always much more severe than would have been expected. One case in which there had never been any demonstrable weakness in any muscle in the lower limbs had losses of up to 40% of the normal number of cells in some cell columns. Tani *et al*[2] reported that the normal value for deltoid CMAPs in 20 men older than 60 years (range, 62–85 yr; mean, 72 yr) was 9.7 ± 1.6 mV (mean ± standard deviation). Trojaborg[25] reported that the normal value for biceps brachii muscle CMAPs in 4 patients older than 65 years (range, 65–74 yr) was 9 mV in amplitude. Therefore, we assumed that normal value for deltoid and biceps brachii muscle CMAPs was 10 mV. We reported that patients with CMAPs' amplitude on the normal side that exceeded 10 mV had no impingement of the AH.[1] On the contrary, patients in whom the CMAPs' amplitude range was from 5 to 10 mV on the normal side indicated the involvement of the AHs. The shoulder girdle muscles on the normal side were intact with patients in whom the CMAPs' amplitude range was from 5 to 10 mV on the normal side. Patients in whom the CMAPs' amplitude was lesser than 5 mV might be correlated with this conclusion.

## ➢ Key Points

- ❑ The average percentage range of deltoid and biceps brachii muscle CMAPs' amplitude determined at the onset of illness correlated significantly with postoperative recovery of deltoid and biceps brachii muscle strength.
- ❑ Surgical intervention of the cervical spine should be performed in patients in whom the average percentage of CMAPs' amplitude in deltoid and biceps brachii muscles ranges from 30% to 50%.
- ❑ Surgical intervention was effective for patients with involvement of VNR and in whom the average CMAPs' amplitude ranged from 10% to 30%.
- ❑ These electrophysiological investigations play an important role in patient management, especially for the prediction of surgical outcome.

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# Development of less invasive neuromuscular electrical stimulation model for motor therapy in rodents

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**Background:** Combination therapy is essential for functional repairs of the spinal cord. Rehabilitative therapy can be considered as the key for reorganizing the nervous system after spinal cord regeneration therapy. Functional electrical stimulation has been used as a neuroprosthesis in quadriplegia and can be used for providing rehabilitative therapy to tap the capability for central nervous system reorganization after spinal cord regeneration therapy.
**Objective:** To develop a less invasive muscular electrical stimulation model capable of being combined with spinal cord regeneration therapy especially for motor therapy in the acute stage after spinal cord injury.
**Methods:** The tibialis anterior and gastrocnemius motor points were identified in intact anesthetized adult female Fischer rats, and stimulation needle electrodes were percutaneously inserted into these points. Threshold currents for visual twitches were obtained upon stimulation using pulses of 75 or 8 kHz for 200 ms. Biphasic pulse widths of 20, 40, 80, 100, 300, and 500 μs per phase were used to determine strength–duration curves. Using these parameters and previously obtained locomotor electromyogram data, stimulations were performed on bilateral joint muscle pairs to produce reciprocal flexion/extension movements of the ankle for 15 minutes while three-dimensional joint kinematics were assessed.
**Results:** Rhythmic muscular electrical stimulation with needle electrodes was successfully done, but decreased range of motion (ROM) over time. High-frequency and high-amplitude stimulation was also shown to be effective in alleviating decreases in ROM due to muscle fatigue.
**Conclusions:** This model will be useful for investigating the ability of rhythmic muscular electrical stimulation therapy to promote motor recovery, in addition to the efficacy of combining treatments with spinal cord regeneration therapy after spinal cord injuries.

**Keywords:** Spinal cord injuries, Neuromuscular electrical stimulation, Activity-based therapy, Rehabilitation, Rat, Kinematics, Motor therapy, Neuroregeneration, Neuroprotection

## Introduction

In contrast to incomplete spinal cord injuries, recovery of motor function in cases of complete spinal cord injuries is generally limited,[1] and cell transplantation as well as other types of regenerative therapies need to be investigated. At present, neuroprotection, axonal growth stimulation, lost tissue replacement, and axonal transmission enhancement are areas of research, but since each of these treatments has its limitations when used alone combining them may be beneficial.[2] Stimulation of the intrinsic plasticity of the nervous system via rehabilitation may improve functional recovery after incomplete spinal cord injuries, and it is hoped that rehabilitation can stimulate the reorganization of neural circuits after regenerative therapies.[2] In people with spinal cord injuries, repeated rhythmical exercise of the legs together with robot-assisted walking on a treadmill and functional electric stimulation therapy are believed to be clinically effective.[3–5] These improvements appear to be task specific and rely on sensory feedback mechanisms.[6,7]

Electrical stimulation has been reported to be effective in actual clinical cases when not only used as a

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method to restore function,[8–12] but also as a method to train motor functions.[4,13–15] Reorganization of the neural network of the central nervous system that results from rhythmical exercises has been cited as a mechanism that can improve motor function,[5,16,17] but the details of this mechanism remain unclear.[18] To understand the details of these mechanisms and investigate their effectiveness when combined with spinal cord regeneration therapies, basic research, including animal experiments, is necessary. However, since there are very few reports on the effectiveness of combined spinal cord regeneration therapies based on animal models, this area requires further study, including the development of experimental animal models.[2,19–21]

Jung *et al.*[22] have previously created neuromuscular electric stimulation (NMES) models using rats, stimulated the motor points of the major joints of the limbs using embedded electrodes[23], and reported significant short-term improvements in hindlimb synkinesia of rats with incomplete spinal cord injuries after NMES therapy of only hip joints.[24] Electrical stimulation of muscles for motor therapy would be able to start from acute stage after spinal cord injury or regeneration therapy of spinal cord injury, and it could become useful rehabilitative strategy in that stage. The use of intramuscular electrodes is highly invasive for rats after spinal cord injury because it requires long and invasive surgery and has many complications, such as electrode infection, chewing, etc. Thus, a less invasive method is very desirable to study the effectiveness of combination of spinal regeneration therapies. Surface electrodes are noninvasive and clinically may be better option for therapy application. In rats, it is difficult to stimulate continuously the motor points of muscles during motor therapy, because the skin of rats is very flexible. Thus, we used needle electrodes, which are comparatively less invasive than intramuscular electrodes in this study (Table 1). Our long-term goal is to create a less invasive electrical stimulation therapy model that can be used together with spinal cord regeneration therapies and to investigate its effectiveness for motor therapy especially in the acute stage after spinal cord injury.

This study tested the hypothesis that a muscular electrical stimulation therapy model that used needle electrodes instead of intramuscular electrodes can produce rhythmic movement of ankle joints in normal rats under the same stimulation parameters used in previous studies.[23,24] Jung *et al.*[24] reported the rapid range of motion (ROM) decreasing related to muscle fatigue. The maintenance of ROM may produce much more sensory feedback that could lead to be more functional recovery.[6,7] Ward and co-workers[25,26] reported the potential usefulness of kHz frequency alternating current for rapid muscle fatigue-associated functional electrical stimulation. In this study, we also tested the effect of kHz frequency for muscle fatigue associated with electrical stimulation.

## Materials and methods

### *Animals*

This study was approved by the Committee for the Care and Use of Animals at the Yamaguchi University. Ten mature female Fischer rats (160–175 g) were used. Needle electrodes were inserted in the tibialis anterior muscle (TA) (ankle flexor) and gastrocnemius muscle (Gc) (ankle extensor). An inhalation anesthestic (2–3% Sevoflurane) was used to anesthetize the rats.

### *Insertion of stimulation electrodes*

Stimulation electrodes (TECA Disposable Monopolar Needle Electrode 902-DMF25-TP, Carefusion Japan, Tokyo, Japan) with diameters of 0.30 mm and a recording area of 0.03 $mm^2$ were inserted while the rats were anesthetized. The rats were secured to a custom-made platform and electrodes were percutaneously inserted in TA and Gc on both hindlimbs of the animal. In order to insert the electrodes near the motor points of each muscle, anatomical motor points were referenced (Fig. 1) and electrodes were inserted at the point of greatest contraction after percutaneous stimulation of the target muscle using a low current (frequency, 75 Hz; pulse width, 40 μs; amplitude, 1 mA; and duration, 200 ms).

### *Strength–duration curve*

To assess whether the stimulation electrodes were positioned at the appropriate points near the motor points of the target muscles, after electrode positioning strength–duration (SD) tests were conducted for all

**Table 1 Invasiveness of needle electrodes and their potential application**

| | Noninvasive | Minimally invasive | NMES application | Therapy application |
|---|---|---|---|---|
| Surface electrodes | ○ | | ○ | ○ |
| Needle electrodes | | ○ | | ○ |
| Implanted electrodes | | | ○ | ○ |