



Physical performance decreases in the early stage of cervical myelopathy before the myelopathic signs appear: the Wakayama Spine Study

Keiji Nagata¹ · Noriko Yoshimura² · Hiroshi Hashizume¹ · Hiroshi Yamada¹ · Yuyu Ishimoto¹ · Shigeyuki Muraki² · Yukihiro Nakagawa³ · Akihito Minamide¹ · Hiroyuki Oka⁴ · Hiroshi Kawaguchi⁵ · Sakae Tanaka⁶ · Koza Nakamura⁷ · Munehito Yoshida^{1,8}

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Abstract

Purpose We previously revealed a prevalence rate of 24.4% for cervical cord compression (CCC) in a population-based magnetic resonance imaging study. This study aimed to investigate the occurrence of cervical myelopathy (CM) among CCC cases and to reveal the predictors for CM.

Methods This study is a part of “The Wakayama Spine Study,” a large-scale population-based MRI cohort study. At baseline, 238 patients were diagnosed with CCC. We followed 238 patients who had CCC for more than 4 years, of which 158 (mean age, 68.9 years) participated in the second survey (follow-up rate, 66.3%). In the second survey, de novo CM was defined clinically as the presence of myelopathic signs (e.g., Hoffmann reflex, hyperreflexia of the patellar tendon, and Babinski reflex). Physical performance on 10-s grip and release test (GRT), grip strength, 6-m walking time at a usual and a maximal pace, step length at a usual and a maximal pace, chair stand time (CST), and one-leg standing (OLS) time was measured.

Results Among the 158 participants, nine (mean age, 68.8 years; incidence rate, 6.3%) were newly diagnosed with CM in the second survey. CST, 6-m walking time at a usual and a maximal pace, and step length at a maximal pace had already decreased in the de novo CM (+) participants at baseline compared to baseline findings of de novo (−) CM participants, but not the grip strength, OLS, or GRT.

Conclusions We clarified the incidence rate of CM in CCC patients and the predictors of de novo CM.

Graphical abstract

These slides can be retrieved under Electronic Supplementary Material.

Key points

1. Physical performance
2. Presymptomatic cervical myelopathy
3. Myelopathic signs

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Table: Comparison of baseline physical performance between patients with and without de novo CM

	de novo cervical myelopathy (-)	de novo cervical myelopathy (+)	p value
Grip strength, kg	29.5 ± 9.1	26.2 ± 8.8	0.29
One leg standing time, sec	35.3 ± 23.9	27.4 ± 21.5	0.34
Grip and release test, N	23.2 ± 5.3	21.3 ± 6.8	0.41
Chair stand time, s	8.8 ± 3.2	14.1 ± 10.9	0.0004
Step length at a usual pace, cm	56.0 ± 11.8	48.9 ± 9.6	0.007
6-m walking time at a usual pace, s	5.5 ± 1.4	7.0 ± 2.9	0.0012
Step length at a maximal pace, cm	63.9 ± 11.7	55.7 ± 10.5	0.011
6-m walking time at a maximal pace, s	3.8 ± 1.2	5.2 ± 2.4	0.0019

Significantly different according to the Mann-Whitney U test (*p<0.05).
Values represent the mean ± standard deviation (SD).

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Take Home Messages

1. We clarified, for the first time, the incidence rate of cervical myelopathy in subjects with cervical cord compression and the natural course of cervical myelopathy.
2. The lower limb function decreased before signs of myelopathy becomes clear.
3. The lower limb function decreased before signs of myelopathy, indicating that cervical cord compression influences physical performance, especially of the lower limbs, chair stand time, 6-m walking time at a usual and a maximal pace, and step length at a maximal pace can be useful new diagnostic tools for the early stages of cervical myelopathy.

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Extended author information available on the last page of the article

Keywords Myelopathic signs · Physical performance · Population-based cohort · Presymptomatic cervical myelopathy · Wakayama Spine Study

Introduction

Cervical myelopathy (CM) causes various disorders, including neck pain, upper and lower extremity paresthesia, muscle weakness, muscle spasticity, and gait disturbance [1, 2]. In the current aging society, the prevalence of patients with cervical cord compression (CCC) is expected to increase. In a population-based magnetic resonance imaging (MRI) study, the prevalence rate of CCC was 24.4%, and it was higher with increasing age in both men and women [3]. Therefore, the number of CM cases is expected to increase in the aging society. In terms of natural history of CM, several authors have described the clinical course of patients with CM. Clarke and Robinson retrospectively described 120 patients with cervical spondylotic myelopathy, 26 of whom were treated conservatively [4]. Almost 80% of these patients presented with weakness or sensory loss in one or more limbs, while 18% presented with pain. Clarke and Robinson showed that approximately 75% of patients showed episodic progression of symptoms with intervening stability, although approximately two-thirds of patients showed subtle clinical decline during periods of stability. In 20% of patients, slow and steady deterioration occurred. In 5%, onset of symptoms and signs was followed by a long period of stability without any additional deterioration. Several authors have suggested that CM has a rapidly progressive course [5, 6]. Matsumoto et al. described a case series in which one-third of patients had mild CM [7]. In clinically asymptomatic CCC, questions arise as to whether this compression causes any functional deterioration and whether CCC is predictive of an unfavorable clinical course, thus justifying meticulous clinical examination before any neurological deficit manifests clinically. The purpose of this study was to investigate the occurrence of CM among CCC cases and to reveal the predictive factors for CM.

Materials and methods

The present study is a part of “The Wakayama Spine Study: a population-based cohort,” which was a large-scale population-based magnetic resonance imaging (MRI) study. Because a detailed profile of the Wakayama Spine Study has already been described elsewhere, only a brief summary is provided here [3, 8]. The Wakayama Spine Study was conducted between 2008 and 2010 in a mountainous region in Hidakagawa, Wakayama, and a coastal region in Taiji, Wakayama. From the inhabitants of the Hidakagawa and

Taiji regions, 1063 potential study subjects were recruited for MRI examinations. Among them, 52 declined the examination; therefore, 1011 inhabitants were invited in the present study. Inclusion criteria were the ability to walk to the survey site, report data availability, and provision of informed consent. Among those 1011 participants, individuals with MRI-sensitive implanted devices (such as a pacemaker) and other disqualifiers, four participants who had undergone a previous cervical operation, and another four participants whose MRI interpretation was difficult because of poor image quality were excluded in this study. After these exclusions, 977 participants were enrolled in this study. The participants completed an interviewer-administered questionnaire of 400 items that included lifestyle information, and anthropometric and physical performance measurements were taken. For evaluation of physical performance, the following tests were conducted: a 10-s grip and release test (GRT), grip strength, 6-m walking time, step length, chair stand time (CST), and one-leg standing (OLS) time. Grip strength was measured for each hand using a TOEI LIGHT handgrip dynamometer (TOEI LIGHT CO., LTD, Saitama, Japan). To measure walking speed, the time taken to walk 6 m at a usual pace in a hallway was recorded. Similarly, the 6-m walking time at a maximal pace was measured. The time taken for five consecutive chair rises without the use of hands was also recorded. One-leg standing time with each leg was measured using a stopwatch (upper limit, 60 s), and the time adopted was the mean of the times for both legs. The participants were given a full explanation of each test but were not given any training.

All participants had completed questionnaires for the Medical Outcomes Study Short Form 8 (SF-8) and the Euro QOL (EQ-5D). All study participants provided informed consent, and the study design was approved by the appropriate ethics review boards. Demographic measurements included height (m), weight (kg), and body mass index (BMI) [weight (kg)/height² (m²)].

We intend to follow up the three population-based cohorts of the ROAD study for at least 10 years.

In October 2012 and 2013, after a follow-up period of 4 years, a second comprehensive clinical examination was completed. We will repeat the baseline measurements during the second examination. A third and fourth examination will be performed at 7 and 10 years, respectively, after the baseline examination.

Definition of clinical CM at baseline

Medical information concerning neck pain, sensory disturbances, Hoffmann reflex, Babinski reflex, and deep tendon reflex of the patellar tendon was gathered by an experienced orthopedic surgeon. The Hoffmann reflex was elicited with the hand in a neutral position by flicking the distal phalanx of the middle finger and observing flexion of the distal phalanx of the thumb [9, 10]. The Babinski reflex was elicited by firmly sweeping from the lateral part of the sole to the base of the toes with the pointed end of a reflex hammer and observing the hallux extensor response [11, 12]. Hyperreflexia of the patellar tendon, a positive Hoffmann reflex, and a positive Babinski reflex were defined as aggravation on both sides. A myelopathic sign was defined as the presence of hyperreflexia of the patellar tendon, Hoffmann reflex, or Babinski reflex.

Myelopathy was defined clinically by the presence of myelopathic signs (e.g., Hoffmann reflex, hyperreflexia of the patellar tendon, and Babinski reflex), usually accompanied by bilateral sensory deficits, or sensory level and bowel/bladder symptoms. Among participants with myelopathic signs, cervical cord compression was the essential condition for diagnosing CM.

Definition of de novo CM at second survey

New-onset CM was called de novo CM. The diagnosis was made as having the following two conditions: (1) cervical cord compression at baseline and (2) absence of myelopathic signs at baseline and appearance of new myelopathic signs

(e.g., Hoffmann reflex, hyperreflexia of the patellar tendon, and Babinski reflex), usually accompanied by bilateral sensory deficits, or sensory level and bowel/bladder symptoms.

At the baseline survey, we diagnosed 238 subjects as having CCC. We followed the 238 subjects for more than 4 years. Among these subjects, 15 subjects (6.3%) had died by the time of the review 4 years later, 7 subjects (2.9%) did not participate in the follow-up study due to bad health, and 58 subjects (24.3%) did not participate for unknown reason. Therefore, 158 subjects (61 men and 81 women; mean age, 68.9 years) participated in the second survey (follow-up rate, 66.3%) (Fig. 1).

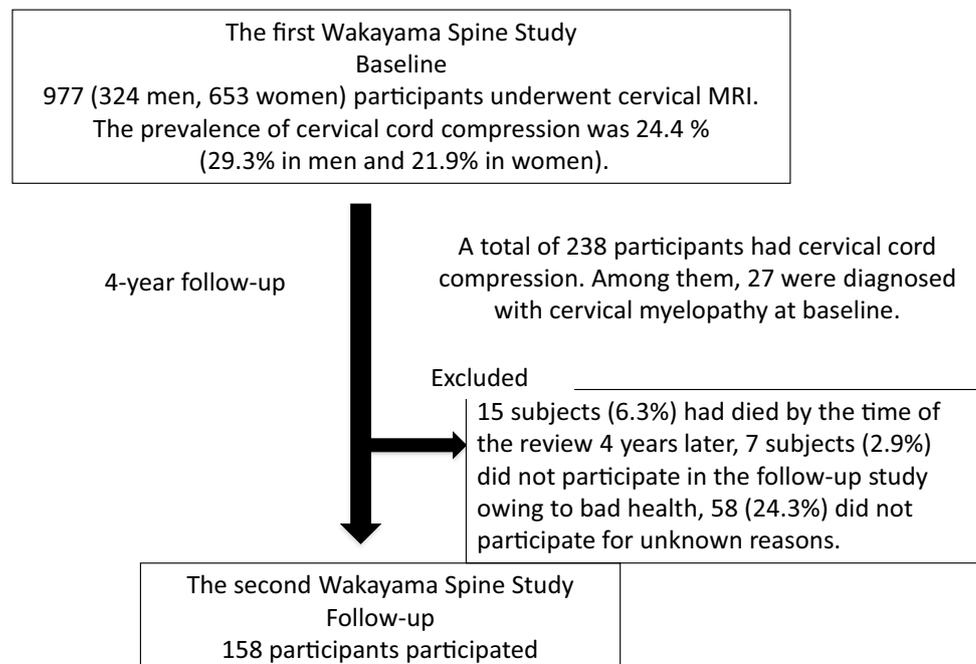
MRI measurements

Mid-sagittal T2-weighted images were assessed by an experienced orthopedic surgeon (K.N.), who was blinded to participants' clinical status.

Evaluation of cervical cord compression

CCC was defined as compression with an anterior and/or posterior component of the spinal cord [3] as previously shown. CCC was evaluated at each intervertebral level from C2/3 to C7/Th1. Grading was defined as follows: grade 0 = no compression of the spinal cord but the subarachnoid space remains; grade 1 = no compression of the spinal cord without subarachnoid space; grade 2 = compression of less than one-third of the spinal cord; grade 3 = compression of more than one-third but less than two-thirds of the spinal cord; and grade 4 = compression of more than two-thirds

Fig. 1 Flowchart of the steps involved in the study



of the spinal cord. CCC was defined as grade 2 or more at the most severely affected intervertebral disk level. Severe CCC was defined as grade 3 or higher. Multilevel CCC was defined as having more than two levels of stenosis.

Evaluation of signal intensity of the spinal cord

Increased signal intensity was defined as a high-intensity area in contrast with the adjacent isointense portion of the spinal cord [13]. The increased signal intensity was evaluated in the area from C2 to T1.

Statistical analyses

A comparison of baseline characteristics between patients with and without de novo CM was performed using the Mann–Whitney *U* test. For categorical outcomes, comparisons were assessed using Fisher's exact test. Differences in the physical performance among patients with and without de novo CM at baseline were also determined using the Mann–Whitney *U* test. In addition to determine predictive factor for CM, logistic regression analysis was used after overall adjustment for age, sex, and BMI.

In order to measure the differences in the prevalence of myelopathic signs among the 238 subjects at baseline survey, they were divided into three groups according to age as follows: less than 60 years, between 60 and 75 years, and above 75 years. Fisher's exact test was used for comparisons among the three age groups.

All statistical tests were performed at a significance level of 0.05 (two-sided). Data analyses were performed using JMP version 8 (SAS Institute, Inc., Cary, NC, USA).

Results

Among the 158 participants, nine (mean age, 68.8 years; incidence rate, 6.3%) were newly diagnosed as having CM in the second survey (Table 1). Physical performance of 16 participants who were diagnosed with CM at baseline was not decreased for 4 years. There was no significant difference among patients with and without de novo CM in terms of BMI, age, height, or weight. No participants had brain disease such as brain infarction, cerebral hemorrhage, and brain tumor in these two groups. Table 2 shows the comparison of MRI findings among patients with and without de novo CM. There was no MRI finding which could predict de novo CM. The CST ($P=0.0002$), 6-m walking time at a usual ($P=0.0032$), at a maximal pace ($P=0.0019$), and step length at a maximal pace ($P=0.0063$) have already decreased in the de novo CM (+) participants at baseline compared to baseline findings of de novo CM (–) participants, but not grip strength ($P=0.29$), OLS ($P=0.34$), and

Table 1 Baseline characteristics among patients with and without de novo cervical myelopathy at baseline

	De novo cervical myelopathy (–)	De novo cervical myelopathy (+)
<i>N</i> (142)	133	9
Sex, male (%)	59 (44)	2 (22)
Age at baseline	68.9 ± 11.7	68.8 ± 14.1
Height (cm)	156.6 ± 9.6	154.6 ± 9.0
Weight (kg)	57.8 ± 10.2	62.2 ± 14.4
Body mass index (kg/m ²)	23.5 ± 3.0*	25.9 ± 4.6

For continuous outcomes, comparison was by the Mann–Whitney *U* test

For categorical outcomes, comparison was by the Fisher's exact test (* $P<0.05$)

Values are the mean ± standard deviation (SD). *N*=number

GRT ($P=0.41$) (Table 3). Logistic regression analysis was performed using de novo CM (yes, 1; no, 0) as an objective factor, after adjusting for age, sex, and BMI, and showed that CST, 6-m walking time at a usual, at a maximal pace, and step length at a maximal pace were the predictive factors for de novo CM (Table 4).

Figure 2 shows the prevalence of myelopathic signs by age strata in those with cervical cord compression at baseline. The prevalence of Hoffmann reflex and Babinski reflex at baseline survey was 5%, 3.9%, and 2.5% and 0%, 3.9%, and 5.8% in groups aged < 60, 60–75, and over 75 years, respectively. However, the prevalence of hyperreflexia of the patellar tendon was 10%, 13.2%, and 4.9% in groups aged < 60, 60–75, and over 75 years, respectively. Regarding myelopathic signs, there was no significant difference among the three age groups.

Discussion

This study revealed the natural history and incidence rate of CM using a population-based MRI cohort. Given the 4-year follow-up, the rate of incident CM was 6.3%. To the best of our knowledge, this is the first study to show the natural course of CM in a population-based cohort. We showed that the lower limb function decreased before signs of myelopathy become clear.

Delayed diagnosis of CM is a clinical problem. There are two reasons for this delay; the first is due to patient delay. Cervical myelopathy does not typically cause symptoms until the spinal cord is compressed by at least 30% [14]. It is important to know that cervical stenosis is asymptomatic in many cases, indicating that the spinal cord is compressed, but the patient is not experiencing any common symptoms. Teresi et al. reported that in 100

Table 2 Comparison of MRI findings between the two groups in the present study

	De novo cervical myelopathy (–)	De novo cervical myelopathy (+)
<i>N</i> (142)	133	9
Presence of high signal intensity, <i>N</i> (%)	13 (8)	1 (11)
Severe cervical cord compression, <i>N</i> (%)	16 (12)	1 (11)
Multilevel cervical cord compression, <i>N</i> (%)	55 (41)	3 (33)
Presence of lumbar spinal stenosis, <i>N</i> (%)	54 (41)	5 (56)

Comparison was made by the Fisher's exact test (* $P < 0.05$)

Values are the mean \pm standard deviation (SD). *N* = number

Table 3 Comparison of physical performance with and without de novo cervical myelopathy at baseline survey

	De novo cervical myelopathy (–)	De novo cervical myelopathy (+)	<i>P</i> value
Grip strength (kg)	29.5 \pm 9.1	26.2 \pm 8.8	0.29
One-leg standing time (s)	35.3 \pm 23.9	27.4 \pm 21.5	0.34
Grip and release test (N)	23.2 \pm 5.3	21.3 \pm 6.8	0.41
Chair stand time (s)	8.8 \pm 3.2	14.1 \pm 10.9	0.0004
Step length at a usual pace (cm)	56.6 \pm 11.8	48.9 \pm 9.6	0.057
6-m walking time at a usual pace (s)	5.5 \pm 1.4	7.0 \pm 2.9	0.0032
Step length at a maximal pace (cm)	63.9 \pm 11.7	53.7 \pm 10.5	0.011
6-m walking time at a maximal pace (s)	3.8 \pm 1.2	5.2 \pm 2.4	0.0019

Significantly different from women by Student's *t* test

Values are the mean \pm standard deviation (SD). *N* = number

Table 4 Predictive factor for de novo cervical myelopathy among physical performance measures at baseline

	OR	95% CI	<i>P</i> value
Chair stand time, s (+1 s)	1.22	1.06–1.46	0.019
6-m walking time at a usual pace, s (+1 s)	1.56	1.09–2.30	0.016
6-m walking time at a maximal pace, s (+1 s)	1.75	1.13–2.81	0.012
Step length at a maximal pace, cm (+1 cm)	0.93	0.87–0.99	0.025

OR odds ratio, CI confidence interval

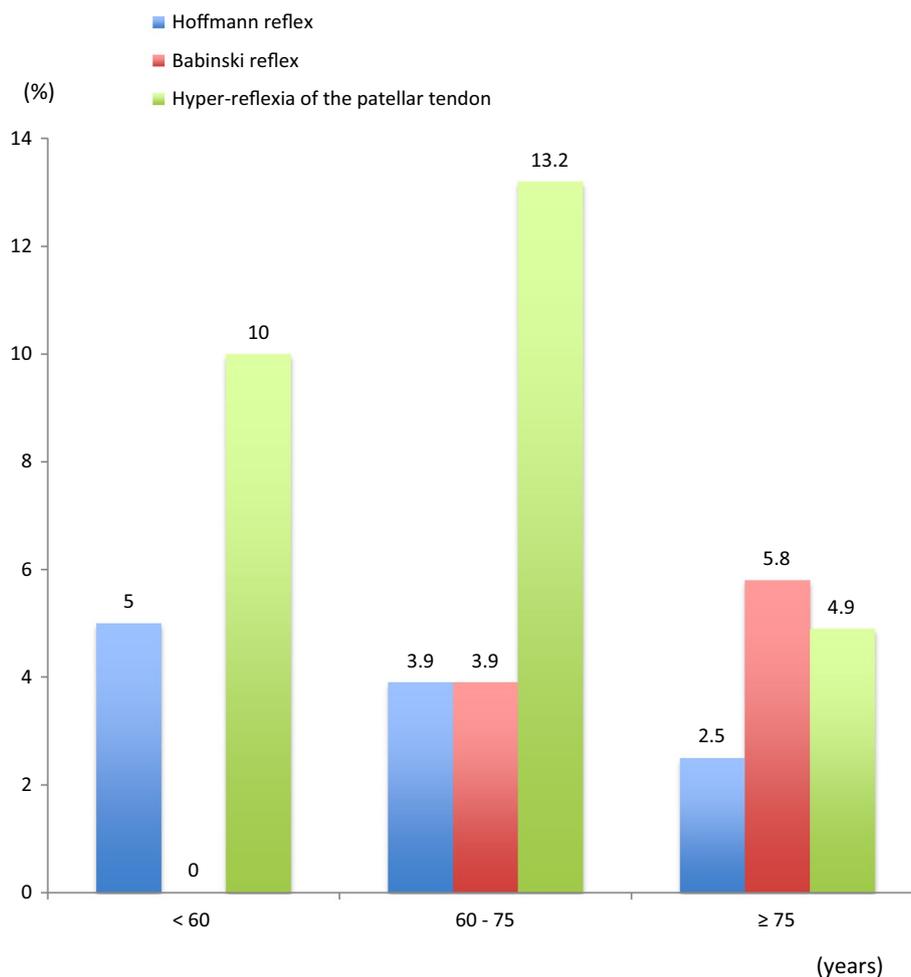
OR was calculated by multiple logistic regression analysis after adjustment for age, sex, and body mass index

asymptomatic patients who underwent MRI, cervical stenosis was found in 16% of patients under age 64 years and in 24% of patients above this age [15]. In these cases, the patient may be simply monitored to ensure that the spinal cord continues to function normally and that myelopathy (i.e., spinal cord dysfunction) does not develop as a result of the compression. In the present study, we used a 1.5 T MRI scanner [3]. Recently, 3.0 T MRI is spreading in clinical practice. In addition to the use of high precision MRI apparatus, a new analysis method such as diffusion

tensor imaging might improve early imaging diagnosis of CM in the future [16, 17].

The second reason is due to doctors' delay. When patients exhibit a gait disturbance, muscle weakness, or sensory loss in the clinic, with the lower extremity showing a negative exaggerated reflex, only the lumbar spine might be examined initially. Eyal et al. reported delayed diagnosis of cervical spondylotic myelopathy by primary care physicians [18]. One of the main obstacles in diagnosing CM is the lack of pathognomonic signs and symptoms, necessitating a high index of suspicion to entertain the diagnosis. Rhee et al. showed that although myelopathic signs are significantly more common in CM patients, they may be negative in approximately one-fifth of patients and cannot be relied on for diagnosis [11]. Moreover, among the elderly, exaggerated reflexes are not uncommon, whether it is caused by peripheral neuropathy or various other causes. We also showed the prevalence of myelopathic signs in those with CCC at baseline survey. The prevalence of hyperreflexia of the patellar tendon was only 4.9% in participants more than 75 years old, which may result in delayed diagnosis of CM in elderly patients. Furthermore, in this study, the diagnosis of CM was made based on myelopathic signs, which may also lead to underestimation of the incidence rate of CM. Eyal et al. pointed out that delayed diagnosis of patients with CM

Fig. 2 Prevalence of myelopathic signs by age strata in those with cervical cord compression at baseline survey



in the community is a frequent major concern; consequently, patients are referred for surgery at an advanced stage of the disease, at which point they are suffering from severe, often irreversible, neurological damage [18]. Previous studies have emphasized the importance of early diagnosis and treatment of cervical myelopathy. Indeed, Ebersold et al. showed that the only significant variable predictive of outcome is the duration of disease before surgical treatment [19]. Hence, early rather than late surgery is, therefore, desirable, with the best results obtained in those who underwent decompression within 6–12 months after symptom onset [20]. Because spinal cord damage tends to be irreversible, early surgery prevents neurological deterioration. Conversely, patients in advanced stages of the disease are less likely to regain neurological function following surgery [21–24]. Wiberg [25], who followed patients for 2–8 years after surgery, showed that decompression is successful in arresting the progression of CSM in 95% of patients [26]. Therefore, it is most important to diagnose CM at an early stage. Physical performance measured as CST and 6-m walking time should be evaluated while seeing patients with spinal disorders, especially in the older age group.

In the present study, we revealed that the CST and the walking speed decrease at the early stage of cervical myelopathy. Until now, quantitative assessment for lower limb function for CM has not been established. Yukawa et al. referred to the usefulness of the 10-s foot tapping test for evaluating CM [27]. The CST and walking speed could also be new simple quantitative tests for detecting early stage CM. These tests can be used promptly in clinic. On the contrary, the grip and release test, which has been conventionally used for upper limb evaluation for CM, did not show a decrease at baseline. Therefore, lower limb function tends to decrease before that of the upper limb. These physical performance tests for evaluating the lower limbs may be useful as supportive tools for detecting CM.

Study limitations

The present study had several limitations. First, there were a small number of newly diagnosed patients. Groups were not well balanced, and thus, the results may have been influenced due to bias. Second, the lower limb function test can be influenced by other medical conditions, such as

locomotor disorders. In this study, patients with rheumatoid arthritis, Parkinson's disease, stroke, thoracic myelopathy, lumbar spinal stenosis, and hip or knee osteoarthritis were also included. These confounding factors need to be taken into consideration. Third, the dynamic instability of the cervical spine was not assessed in this study. The development of CM sometimes may be affected by segmental motion.

Conclusions

In this study, we clarified, for the first time, the incidence rate of CM in subjects with CCC and the natural course of CM. The lower limb function decreased before signs of myelopathy, indicating that CCC influences physical performance, especially of the lower limbs. CST, 6-m walking time at a usual and a maximal pace, and step length at a maximal pace can be useful new diagnostic tools for the early stages of CM.

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Compliance with ethical standards

Conflicts of interest None.

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Affiliations

Keiji Nagata¹ · Noriko Yoshimura² · Hiroshi Hashizume¹  · Hiroshi Yamada¹ · Yuyu Ishimoto¹ · Shigeyuki Muraki² · Yukihiko Nakagawa³ · Akihito Minamide¹ · Hiroyuki Oka⁴ · Hiroshi Kawaguchi⁵ · Sakae Tanaka⁶ · Kozo Nakamura⁷ · Munehito Yoshida^{1,8}

✉ Hiroshi Hashizume
hashizum@wakayama-med.ac.jp

¹ Department of Orthopaedic Surgery, Wakayama Medical University, 811-1 Kimidera, Wakayama City, Wakayama 641-8509, Japan

² Department of Preventive Medicine for Locomotive Organ Disorders, 22nd Century Medical and Research Center, Faculty of Medicine, The University of Tokyo, Tokyo, Japan

³ Department of Orthopaedic Surgery, Wakayama Medical University Kihoku Hospital, Wakayama City, Wakayama, Japan

⁴ Department of Medical Research and Management for Musculoskeletal Pain, 22nd Century Medical

and Research Center, Faculty of Medicine, The University of Tokyo, Tokyo, Japan

⁵ Department of Orthopaedic Surgery, Tokyo Neurological Center, Tokyo, Japan

⁶ Department of Orthopaedic Surgery, Faculty of Medicine, The University of Tokyo, Tokyo, Japan

⁷ Rehabilitation Services Bureau, National Rehabilitation Center for Persons with Disabilities, Tokorozawa City, Saitama, Japan

⁸ Department of Orthopedic Surgery, Sumiya Orthopedic Hospital, Wakayama City, Wakayama, Japan