ORIGINAL ARTICLE

Maximum voluntary ventilation as a sensitive measure to monitor the ventilatory function in cervical spondylotic myelopathy

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Study design: A prospective clinical cohort study.

Objectives: To test if maximum voluntary ventilation (MVV), which is currently underutilized in diseases, serves for assessing subclinical ventilatory impairment in cervical spondylotic myelopathy (CSM).

Setting: Kochi Medical School, Japan.

Methods: We studied ventilatory function in 49 CSM patients and 20 age- and sex-matched control patients with either lumbar stenosis or lower limb osteoarthritis. All patients underwent ventilatory function studies consisting of flow volume curves, vital capacity (VC) and the MVV in 12 s before and after surgery. Tetraparesis was assessed by the functional scale of the Japanese Orthopaedic Association (JOA).

Results: The CSM group had significantly smaller %forced VC, %peak expiratory flow rate (%PEFR) and %MVV than the control group preoperatively. In contrast to the control group, the CSM group showed a significant increase in %MVV from $74.9 \pm 18.7\%$ preoperatively to $80.3 \pm 19.0\%$ postoperatively ($P < 0.005$), but not in any other ventilatory measures. This postoperative increase in %MVV significantly correlated with the JOA score ($r = 0.493$; $P < 0.001$). As a possible effect of diaphragmatic recovery, the %PEFR significantly increased postoperatively only in patients with the primary site of involvement at or rostral to C3–4.

Conclusion: Of the various ventilatory measurements, MVV was most sensitive to changes in tetraparesis in CSM, presumably because MVV, unlike the other ventilatory measures, reflects the coordination in addition to the strength of respiratory muscles.

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Keywords: cervical spondylotic myelopathy; ventilatory function; maximum voluntary ventilation; ventilatory muscle coordination; spasticity

INTRODUCTION

Cervical spondylotic myelopathy (CSM) is the most common non-traumatic spinal cord disorder in Japan. The ventilatory function in CSM, however, has not been investigated as extensively as that in cervical spinal cord injury (SCI);^{1–3} only a few studies^{4,5} have attempted to demonstrate a difference in routine spirometric data and flow volume curves between chronic-onset cervical myelopathies with various etiologies and control groups with lumbar lesions. However, those studies did not use the maximum voluntary ventilation (MVV) test, which, in one study,⁶ has been shown to be more sensitive than vital capacity (VC) and forced expiratory volume in 1 s (FEV₁) to the improved respiratory endurance after a form of respiratory muscle training in athletes.

In general, a common feature in the majority of spastic patients is functional impairment of fast movements and rapid repetitive movements of the limbs.⁷ In fact, unlike SCI patients, slowness and clumsiness of voluntary movement, rather than weakness, tend to predominate in mild to moderate CSM patients. Viewed in this light, MVV in 12 s, in which the patients are requested to breathe as fast and as deeply as possible for 12 s, may improve

the diagnostic yield in assessing the ventilatory function in this type of SCI.

In a previous brief report⁸ in which we showed a postoperative increase of MVV in a relatively small cohort of CSM patients without using control groups, we postulated that the improvement in MVV might be a result of spinal cord decompression. To confirm this hypothesis, we have now analyzed a series of 49 CSM patients as compared with 20 age- and sex-matched control patients before and after surgery.

MATERIALS AND METHODS

Subjects

A total of 49 CSM patients (24 men; age 48–84 years, mean, 71 years) and age- and sex-matched 20 patients (9 men) with either lumbar spinal stenosis or osteoarthritis in the lower limb (control group; age 44–82 years, mean, 69 years) underwent MVV measurement in addition to routine spirometry before and after surgery. We excluded patients with compression myelopathy from other causes such as the ossified posterior longitudinal ligament, rheumatoid arthritis of the cervical spine, destructive spondyloarthropathy and trauma causing

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cord damage immediately after injury. None of the patients had cardiopulmonary diseases or any pulmonary symptoms at the time of the study.

Of the 49 CSM group patients, 28 had anterior microsurgical decompression followed by fusion and the other 21 had spinous process splitting laminoplasty. The anterior procedure involved a single level fusion in 23 patients, two-level fusion in 3 patients and three-level fusion in 2 patients. The laminoplasty was from C3 to C7 in 12 patients, C3 to C6 in 4 patients, C2 to C7 in 2 patients, and C1 to C2, C2 to T1 and C3 to T2 in one patient each. The same surgical team performed all operative procedures. On the basis of the ASIA Impairment Scale,⁹ the degree of preoperative impairment fell into 'D' in all patients, that is, at least half of the key muscles below the neurological level had a muscle grade ≥ 3 . One patient walked normally despite signs of spinal cord compromise (Nurick's grade¹⁰ 1), 27 had some difficulty but were able to walk unaided (grade 2), 14 required walking aids (grades 3 and 4) and 7 were chairbound (grade 5). All patients had a loss of fine finger movement in doing up buttons and in opening and closing fists.¹¹ Stretch reflexes were generally hyperactive although responses were diminished for the biceps in 9 patients, for the triceps in 4, for the quadriceps in 4 and for the gastrocnemius in 5. Babinski extensor plantar responses¹² were elicited in 28 patients. During surgery, all patients underwent serial intervertebral recording of ascending spinal cord evoked potentials from either the intervertebral disk or the ligamentum flavum after epidural stimulation. The intraoperative electrophysiological studies, by identifying the waveform changes consistent with conduction block,^{13,14} localized the level responsible for the main functional change in all patients, one patient each at C1–2 and C2–3, 14 at C3–4, 21 at C4–5, 11 at C5–6, and one at C7–T1. According to the lesion site, we classified the CSM patients into two subgroups to investigate the possible effect of diaphragmatic involvement on ventilatory function; 16 patients having the primary site of involvement at or rostral to C3–4 (upper lesion subgroup); and 33 patients, at or caudal to C4–5 (lower lesion subgroup).

Of the 20 control group patients, 10 had lumbar spine surgery, 6 total hip arthroplasty and 4 total knee arthroplasty. Surgeries for lumbar spinal stenosis included decompression by laminectomy or fenestration procedure at one to three intervertebral levels in eight patients and decompression with additional posterolateral fusion at one to two levels in two patients. Preoperatively, one of the patients walked normally (Nurick's grade 1), eight had some difficulty but were able to walk unaided (grade 2), eight required walking aids (grades 3 and 4) and three were chairbound (grade 5). The operations improved the patients' ability to walk; the average Nurick's grade improving from 3.0 preoperatively to 2.4 at the time of postoperative ventilatory function studies.

All subjects agreed in writing to participate in the study after reading and signing an informed consent form.

Ventilatory function studies

All ventilatory function was measured by one of the authors (TN), who was blinded to the preoperative data at the time of postoperative measurement. All data were under control of another author (TT) for post-evaluation. A computer-interfaced automated testing and analysis system (MINATO system 7, Minato Medical Science Co., Osaka, Japan) allowed us to measure VC, the flow volume curve data including forced VC (FVC), FEV₁, peak expiratory flow rate (PEFR), forced expiratory flow rate at 50% of FVC (FEF50%) and 25% of FVC (FEF25%) and MVV in 12 s.¹⁵ After a few familiarization trials for the spirometric measurements, acceptable maneuvers were repeated at

least three times with subjects seated on an adjustable chair in a quiet room, and the reported data represent the best values.¹⁶ Although the repeatability criteria were based on those provided by Miller *et al.*,¹⁶ the difference between the largest and the next largest values of <0.21 , rather than <0.1501 , was also accepted for VC, FVC and FEV₁ according to the guidelines of the Japanese Respiratory Society.¹⁷ A brief interval of 5 min between measurements minimized respiratory muscle fatigue. Also to minimize the adverse effects of general anesthesia and surgical intervention on ventilatory function, post-operative measurements were not taken until at least 4 weeks had passed; 5.8 ± 2.9 weeks (mean $\pm$ s.d.) after operation for the CSM group and 4.4 ± 1.2 weeks for the control group. None of the patients reported any pain that might affect the data during the respiratory function studies.

Spirometric data were expressed as percentages of the normal predicted values given by the Japanese Respiratory Society¹⁸ for VC and those given by the Japan Society of Chest Diseases¹⁹ for FVC and PEFR, as follows:

VC (l) for men = $(0.045 \times \text{height (cm)}) + ((-0.023) \times \text{age (years)}) - 2.258$;

VC (l) for women = $(0.032 \times \text{height (cm)}) + ((-0.018) \times \text{age (years)}) - 1.178$;

FVC (ml) for men = $(3.01 - 0.013 \times \text{age (years)}) \times \text{height (cm)} \times 10$;

FVC (ml) for women = $(2.05 - 0.006 \times \text{age (years)}) \times \text{height (cm)} \times 10$;

PEFR (l s^{-1}) for men = $(7.18 - 0.024 \times \text{age (years)}) \times \text{height (m)}$ and

PEFR (l s^{-1}) for women = $(4.83 - 0.012 \times \text{age (years)}) \times \text{height (m)}$.

Percentage of MVV was computed by using the following formulae given by Grimby and Soderholm,²⁰

MVV (ml) for men = $28.6 + 34.5 \times \text{FEV}_1 \text{ (ml)}$ and

MVV (ml) for women = $23.7 + 30.3 \times \text{FEV}_1 \text{ (ml)}$.

Functional assessment of tetraparesis

To investigate the correlation between the effects of the operation on ventilatory function with that on tetraparesis, we used the functional scale of the Japanese Orthopaedic Association (JOA)²¹ to assess the patients' disability. Under this scoring system, the motor function of the upper and lower limbs ranges from 0 to 4, as follows for the upper limb: 0, unable to feed oneself; 1, can manage to feed oneself; 2, writing is possible but not practical; 3, writing is clumsy but practical and 4, normal; and for the lower limb: 0, chairbound; 1, requires walking aids; 2, needs support when going up and down stairs; 3, capable of fast walking but with some difficulty and 4, normal. The sphincter function ranges from 0 to 3 as follows: 0, retention and/or incontinence; 1, sense of retention and/or incomplete continence; 2, retardation and/or pollakiuria and 3, normal. Sensory function of the upper limbs, lower limbs and trunk ranges from 0 to 2, respectively, as follows: 0, severe sensory loss; 1, mild sensory loss and 2, normal. Thus, the total score ranges from 0 to 17.

Data analysis

All statistical analyses were performed using SPSS software, version 15 (SPSS, Inc., Chicago, IL, USA). For continuous variables, the normality of distributions was assessed using the Shapiro–Wilk test. When the data were normally distributed, 2-group comparisons were performed with the Student's *t*-test. For a non-normal distribution, Wilcoxon's signed-rank test was used in paired observations and the Mann–Whitney *U*-test in unpaired observations. Categorical variables were compared using the χ^2 test. Interrelation between parameters was studied with the Spearman rank correlation coefficients. Values are given as mean $\pm$ s.d. and were considered significant at $P < 0.05$.

RESULTS

There were no significant differences in gender, age, height and weight between the CSM and control groups, nor were there any differences between the upper and the lower lesion subgroups in CSM patients (Table 1).

Preoperative ventilatory function studies revealed that the CSM group had significantly smaller values than the control group in %MVV (74.9 ± 18.7 vs $89.2 \pm 13.4\%$; $P < 0.004$), %FVC (83.2 ± 18.1 vs $94.4 \pm 11.8\%$; $P < 0.02$) and %PEFR (64.0 ± 20.2 vs $80.8 \pm 20.3\%$; $P < 0.004$), while the trend observed in %VC was not significant (86.0 ± 17.5 vs $94.0 \pm 12.8\%$; $P < 0.07$; Table 2). In the control group, operations with general anesthesia did not affect any ventilatory measures including %MVV, which showed no significant change from $89.2 \pm 13.4\%$ preoperatively to $86.7 \pm 14.8\%$ postoperatively. In contrast, cervical decompression surgeries for the CSM group significantly increased %MVV from $74.9 \pm 18.7\%$ preoperatively to $80.3 \pm 19.0\%$ postoperatively ($P < 0.005$) and respiratory rate during MVV in 12 s from 15.6 ± 4.6 to 17.1 ± 4.4 breaths/12 s ($P < 0.01$), but not the other respiratory measures such as %VC, %FVC, FEV₁, FEV₁%, %PEFR, FEF50% and FEF25% (Figure 1 and Table 2). This postsurgical MVV increase accompanied an improvement of tetraparesis with a significant increase of the JOA score from 8.2 ± 3.0 to 11.2 ± 2.7 ($P < 0.0001$; Table 2). The ratio of postoperative to preoperative MVV averaging $108.8 \pm 17.3\%$ (range, 72.1–172.6%) showed a significant correlation with that for JOA score averaging $150.2 \pm 48.8\%$ (range, 100.0–340.0%; $r = 0.493$; $P < 0.001$; Figure 2).

Comparison between the upper and the lower lesion subgroups in CSM patients revealed neither a significant difference in any of the ventilatory measures nor in JOA scores preoperatively (Table 3). Tetraparesis measured with the JOA score similarly improved in both subgroups postoperatively, but the concomitant increase in MVV was statistically significant only for the lower lesion subgroup (72.7 ± 17.5 vs $78.2 \pm 17.8\%$; $P < 0.03$), while the trend observed in the upper lesion subgroup was not significant (79.5 ± 20.7 vs $84.7 \pm 21.1\%$; $P < 0.08$). Of the other respiratory measures, only %PEFR showed a significant improvement postoperatively for the

Figure 1 Flow-volume tracings during MVV testing over 12 s before (dashed line) and after (solid line) laminoplasty from C3 to C7 in a 83-year-old woman with cervical spondylotic myelopathy. The abscissa shows time in sec. The ordinate on the left shows flow-volume in liters (l) for alternating inspiration and expiration, and the ordinate on the right for a cumulative flow-volume l. The cumulative flow-volume in liters (l) reached 10.7 l/12 s (%MVV=74%) preoperatively and 13.3 l/12 s (%MVV=92%) postoperatively. Respiratory rate during MVV in 12 s increased from 13 to 16 breaths.

Table 1 Demographic characteristics of the patients

Variables	CSM group, mean (s.d.)	Control group, mean (s.d.)	P-value ^a	CSM subgroup at or above C3/4, mean (s.d.)	CSM subgroup at or below C4/5, mean (s.d.)	P-value ^b
Sex (men/women)	24/25	9/11	NS	7/9	17/16	NS
Age (years)	70.8 (8.6)	68.9 (10.1)	NS	72.5 (8.4)	70.0 (8.7)	NS
Body height (cm)	153.8 (9.7)	154.2 (8.3)	NS	156.2 (11.2)	152.7 (8.8)	NS
Body weight (kg)	53.5 (11.5)	58.7 (9.4)	NS	52.6 (14.4)	54.0 (10.1)	NS

Abbreviations: CSM, cervical spondylotic myelopathy; NS, not significant.

^aP-value (for unpaired data), CSM group vs control group.

^bP-value (for unpaired data), CSM subgroup at or above C3/4 vs CSM subgroup at or below C4/5.

Table 2 Pre- and post-operative ventilatory function in CSM and control groups

Variables	Preoperative			Postoperative			
	CSM group, mean (s.d.)	Control group, mean (s.d.)	P-value ^a	CSM group, mean (s.d.)	P-value ^b	Control group, mean (s.d.)	P-value ^c
%MVV (%)	74.9 (18.7)	89.2 (13.4)	<0.004	80.3 (19.0)	<0.005	86.7 (14.8)	NS
%VC (%)	86.0 (17.5)	94.0 (12.8)	<0.07	87.4 (15.2)	NS	92.9 (12.2)	NS
%FVC (%)	83.2 (18.1)	94.4 (11.8)	<0.02	84.3 (15.8)	NS	92.1 (14.0)	NS
FEV ₁ (L)	1.8 (0.6)	1.9 (0.5)	NS	1.8 (0.5)	NS	1.9 (0.6)	NS
FEV ₁ % (%)	81.7 (10.1)	79.9 (8.8)	NS	81.2 (10.3)	NS	81.3 (5.4)	NS
%PEFR (%)	64.0 (20.2)	80.8 (20.3)	<0.004	65.6 (19.6)	NS	82.8 (18.3)	NS
FEF50% (L s ⁻¹)	2.3 (1.0)	2.8 (1.4)	NS	2.3 (1.0)	NS	2.7 (1.3)	NS
FEF25% (L s ⁻¹)	0.8 (0.4)	0.7 (0.4)	NS	0.8 (0.4)	NS	0.7 (0.4)	NS
JOA score	8.2 (3.0)	NA	NA	11.2 (2.7)	<0.0001	NA	NA

Abbreviations: CSM, cervical spondylotic myelopathy; FEV₁, forced expiratory volume in 1 s; FEF50%, forced expiratory flow rate at 50% of FVC; FEF25%, forced expiratory flow rate at 25% of FVC; FVC, forced vital capacity; JOA score, Japanese Orthopaedic Association score; MVV, maximum voluntary ventilation; NA, not applicable; NS, not significant; PEFR, peak expiratory flow rate; VC, vital capacity.

^aP-value (for unpaired data), CSM group vs control group.

^bP-value (for paired data), preoperative vs postoperative values in CSM group.

^cP-value (for paired data), preoperative vs postoperative values in control group.

upper lesion subgroup (59.3 ± 21.7 vs $70.1 \pm 16.5\%$; $P < 0.001$), but not for the lower lesion subgroup.

DISCUSSION

In contrast to the ventilatory function in SCI, only a few studies so far have dealt with this issue in cervical compression myelopathies (CCM) of various etiologies. Ishibe and Takahashi⁴ reported that CCM patients, if their myelopathies resulted from cord compression above the C4 level and/or multilevel compression, had significantly smaller %VC than the control group of lumbar spine disorders. In those particular CCM patients, they also found a significant improvement in

%VC responding to decompression surgery. In a small cohort of CSM patients, however, Yanaka *et al.*,²² who demonstrated a postoperative increase of tidal volume with a reduction of PCO_2 , failed to find such a favorable effect of surgery on %VC. Also as for %VC, Toyoda *et al.*⁵ reported that the CCM group showed significantly lower values than the control group with a further decrease for the CCM group with a higher lesion level of C3–4. All these studies, however, did not test MVV, which might be able to assess the subclinical impairment of ventilatory muscle coordination.

Spasticity is a motor disorder characterized by a velocity-dependent increase in tonic stretch reflex ('muscle tone') as one of the components of the upper motor neuron syndrome,²³ impairing rapid repetitive movements. Most CSM patients lose fine finger movement in using tableware, doing up buttons and writing, which can be assessed simply by testing how rapidly the patient can open and close fists in 10 s (grip-and-release test).¹¹ Difficulty with gait in those patients can be quantified by assessing how fast the patient can walk 30 m distance and counting the number of steps taken (a simple walking test).²⁴ Applying the same principle to ventilatory muscle examination, MVV documents how fast and deeply the patient can breathe.

First, this study confirms that CSM, as compared with other age-related conditions such as lumbar spinal stenosis or osteoarthritis in the lower limb, does affect ventilatory function subclinically, documenting significant reduction of some routine spirometric data as well as MVV. Second, our results indicate that MVV, out of various ventilatory function measurements, most consistently reflects the change of spinal cord function in CSM patients. In fact, MVV was the only measure to have increased significantly, responding to surgical decompression of the spinal cord. The rate of increase in MVV also significantly correlated with the rate of recovery from tetraparesis assessed by the JOA score. This effect of operation on ventilatory function delineated by the MVV test would be directly attributable to the improvement of spinal cord function rather than the increased physical activity after recovery from tetraparesis in CSM patients, because the MVV measure remained unchanged postsurgically in the control group despite a positive impact of the operations on lumbar spinal stenosis, or total hip or knee arthroplasty on achieving higher daily activities.

Figure 2 Relation between postoperative improvements of MVV and tetraparesis in 49 patients with cervical spondylotic myelopathy. The abscissa shows the ratio of postoperative to preoperative JOA score and the ordinate, the ratio of postoperative to preoperative MVV. There was a significant correlation ($r=0.493$, $P < 0.001$) between the two ratios.

Table 3 Pre- and post-operative ventilatory function in upper and lower lesion CSM subgroups

	Preoperative			Postoperative			
	CSM at or above C3/4, mean (s.d.)	CSM at or below C4/5, mean (s.d.)	P-value ^a	CSM at or above C3/4, mean (s.d.)	P-value ^b	CSM at or below C4/5, mean (s.d.)	P-value ^c
%MVV (%)	79.5 (20.7)	72.7 (17.5)	NS	84.7 (21.1)	<0.08	78.2 (17.8)	<0.03
%VC (%)	81.1 (18.8)	88.8 (16.1)	NS	83.0 (14.2)	NS	89.5 (15.4)	NS
%FVC (%)	78.2 (21.4)	85.7 (16.1)	NS	82.3 (15.4)	NS	85.2 (16.1)	NS
FEV ₁ (L)	1.7 (0.7)	1.8 (0.5)	NS	1.8 (0.6)	NS	1.8 (0.5)	NS
FEV ₁ % (%)	85.1 (8.0)	80.1 (10.6)	NS	82.6 (9.7)	NS	80.6 (10.7)	NS
%PEFR (%)	59.3 (21.7)	66.3 (19.4)	NS	70.1 (16.5)	<0.001	63.4 (20.9)	NS
FEF50% (L s ⁻¹)	2.4 (1.0)	2.3 (0.9)	NS	2.3 (1.0)	NS	2.3 (1.0)	NS
FEF25% (L s ⁻¹)	0.9 (0.5)	0.7 (0.4)	NS	0.8 (0.4)	NS	0.8 (0.4)	NS
JOA score	8.0 (3.3)	8.2 (2.8)	NS	11.4 (2.5)	<0.0001	11.2 (2.8)	<0.0001

Abbreviations: CSM, cervical spondylotic myelopathy; FEV₁, forced expiratory volume in 1 s; FEF50%, forced expiratory flow rate at 50% of FVC; FEF25%, forced expiratory flow rate at 25% of FVC; FVC, forced vital capacity; JOA score, Japanese Orthopaedic Association score; MVV, maximum voluntary ventilation; NA, not applicable; NS, not significant; PEFR, peak expiratory flow rate; VC, vital capacity.

^aP-value (for unpaired data), CSM at or above C3/4 vs CSM at or below C4/5.

^bP-value (for paired data), preoperative vs postoperative values in CSM at or above C3/4.

^cP-value (for paired data), preoperative vs postoperative values in CSM at or below C4/5.

Finally, a comparison between the upper and lower lesion subgroups failed to show a possible effect of diaphragmatic involvement on preoperative ventilatory function, probably because the severity of the cord impairment varied widely among patients. The only evidence specific to the upper lesion subgroup was that the %PEFR in this subgroup significantly increased postoperatively, which might be consistent with the finding that there is a direct relationship between peak expiratory flow and the injury level in SCI patients.^{2,3} This relationship could predict a greater post-surgical recovery of reversible impairment of %PEFR in the upper than the lower lesion subgroup. Because %PEFR is known as a sensitive measure of cough effectiveness,^{2,3} a postoperative increase of the value may indicate an improvement of the ability to cough, which may be clinically important, particularly in elderly and fragile CSM patients.

There are some limitations to our study. First, although we measured ventilatory function from a series of at least three acceptable measurements that were free from artifact and without large variability among the trials, the repeatability criteria were not strictly based on those provided by Miller *et al.*¹⁶ Second, because the formulae for normal MVV in the Japanese population are not available, we are obliged to compute %MVV based on the formulae given by Grimby and Soderholm,²⁰ even though the equations are more appropriate for Caucasian groups than non-Caucasian groups. Nevertheless, this study contributes to a reassessment of the currently underutilized MVV in diseases as a useful technique for CSM patients.

CONCLUSIONS

Our study confirms that ventilatory function is subclinically compromised by CSM. Of the various ventilatory function measurements, MVV reflected the change in spinal cord function most consistently, presumably because MVV testing requires execution of rapid repetitive movements that tends to be impaired in CSM patients. This study contributes toward reassessing the currently underutilized MVV testing as a useful technique that complements routine spirometry for monitoring the ventilatory function in patients with spastic tetraparesis.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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