

Keywords Cervical spondylotic amyotrophy · Surgical outcome · Surgical procedure · Duration of symptoms · Multicenter study

Introduction

Cervical spondylotic amyotrophy (CSA) is a rare form of cervical spondylosis, which causes muscle weakness of the upper extremities without apparent sensory disturbance. Surgical treatment is recommended for patients with CSA for whom conservative treatment has not been successful [1]. Distal-type CSA is more uncommon than proximal-type CSA. The surgical outcomes for distal-type CSA are considered inferior to the outcomes for proximal-type CSA [2, 3]; this is possibly because the distance between the cervical lesion and the atrophic muscles is large, and such a distance can cause poor neurological recovery.

The exact pathophysiology of CSA remains unknown. Previous studies suggested that distal-type CSA involves impingement against the anterior horn and/or ventral nerve roots [4]. However, it is still unclear whether the muscle weakness is attributed to the anterior horn (AH), the ventral nerve root (VNR) or both and whether the responsible lesion is located at a single level or at multiple levels. The appropriate surgical methods for CSA also remain controversial. Some authors have advocated that anterior decompression is reasonable to eliminate anterior and anterolateral lesions [5–7], while other authors reported posterior decompression methods, such as laminoplasty and/or selective foraminotomy, as effective treatments for most patients with CSA [4, 8, 9].

Because of the rarity of this disease, the surgical outcomes of distal-type CSA have been reported only in a few small case series with small sample sizes [7, 10]. In this multicenter retrospective study, we evaluated the clinical outcomes and radiographic findings, including compressive lesions on magnetic resonance imaging (MRI), in 43 surgically treated distal-type CSA patients. We also compared the surgical procedures (anterior vs. posterior) in terms of neurological improvement.

Materials and methods

The current retrospective study was approved by the institutional review boards in all 3 of the institutions that participated in this study. The authors executed a retrospective analysis of the outcomes of consecutive 43 spinal surgeries performed on 43 distal-type CSA patients from 2009 to 2017. There were 39 males and 4 females, with an average age of 60.1 years (17–82 years).

Distal-type CSA was defined as weakness and wasting of hands and forearms without gait impairment or any sensory symptoms or signs in the lower limbs on the basis of the definitions provided in previous studies [7, 10]. To distinguish CSA from other motor neuron diseases prior to surgery, the patients consulted with neurologists. In all these distal-type CSA patients, patients' age, duration of symptoms, perioperative manual muscle test (MMT) results, radiological findings, surgical procedures, and perioperative complications were reviewed (Table 1).

In radiographs of these patients, we retrospectively investigated the C2-7 angle, local lordosis at the surgical site, and C7 slope at the neutral position in lateral cervical radiographs before surgery and/or at the last follow-up. To diagnose CSA, the authors assessed the presence of a compressive lesion involving AH of the spinal cord, VNR, or both sites, as seen on MRI [10]. Patients with AH compression were characterized by a spinal cord lesion at the medial or paramedial site of the spinal canal with or without signal intensity change on sagittal MRI, while patients with VNR impingement had nerve root lesions only at the intervertebral foramen on T2-weighted axial view (Fig. 1). We also collected data on the levels of spinal stenosis and high-intensity areas (HIA) on T2-weighted MR images (both sagittal and axial views). Two independent spinal surgeons (S.U. and T.T.) evaluated compressive lesions, including HIA, in the cervical spine on a DICOM viewer and reached a consensus. Prior to the image review, these testers read images from the same 20 patients to determine interobserver agreement. The average kappa coefficient of interobserver agreement was 0.70, which was considered to indicate substantial agreement.

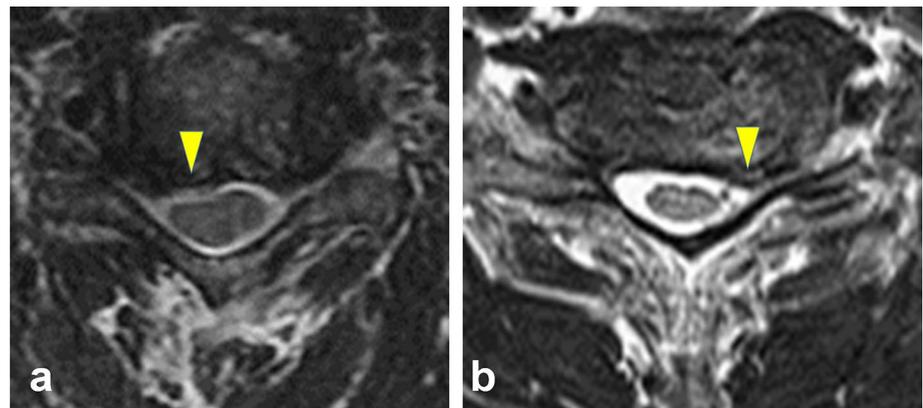
The surgical procedures were divided into 2 groups: the anterior approach included anterior cervical corpectomy and fusion (ACCF) and/or anterior cervical discectomy and fusion (ACDF); the posterior approach included laminoplasty, selective foraminotomy, and/or posterior spinal fusion (PSF) (Fig. 2). The surgical methods were determined by the surgeons based on multiple factors, such as general condition, comorbidities, imaging features of spinal cord compression, and the sagittal alignment of the cervical spine. Generally, the anterior approach was selected if patients had kyphotic alignment, if the pathology was clearly located in the anterior, and if patients did not have respiratory problems. The posterior approach was selected if patients had developmental spinal stenosis, preoperative comorbidities such as dysphagia, respiratory diseases or other severe comorbidities, and history of anterior

Table 1 Demographics and surgical results

Age, average, years			60.1 ± 14.0 (17–82)
Sex, female/male, No			4/39
Unilateral/bilateral			37/6
Duration of disease, months			18.5 ± 22.7 (2–86)
Follow-up period, months			36.1 ± 28.4 (6–102)
Surgical procedure	Anterior approach	ACCF/Hybrid/ACDF	13/5/11
	Posterior approach	Foraminotomy/laminectomy/PSF	8/2/4
Surgical outcomes	MMT grade	Preop/postop	2.4 ± 1.0 / 3.1 ± 1.2*
	Classification	Good/poor	26(60.5%)/17(39.5%)
Complications		Subsidence	5 (11.6%)
		Nonunion	2 (4.7%)
		Displacement of bone graft/cage	2 (4.7%)
		Proximal junctional kyphosis	1 (2.3%)
		C5 palsy	1 (2.3%)
Radiological parameters	Levels of stenosis	Preop	2.5 ± 0.9 (1–4)
	C2-7 angle	Preop/postop	1.4 ± 12.8/5.8 ± 9.9
	ΔC2-7		4.0 ± 7.0 (–12 to 19)
	Local lordosis	Preop/postop	– 0.5 ± 8.3/2.0 ± 7.3
	Δlocal lordosis		2.5 ± 6.5 (– 4 to 21)
	C7 slope	Preop	22.5 ± 9.0 (0–40)
	T2 HIA (+)		16 (37.2%)

Data were shown average ± SD; No. indicates number; MMT, manual muscle test; T2 HIA, high-intensity area on T2-weighted magnetic resonance images; ACCF, anterior cervical corpectomy and fusion; Hybrid, Hybrid of ACCF and ACDF; ACDF, anterior cervical discectomy and fusion; PSF, posterior spinal fusion; Preop, preoperative; Postop, postoperative

Fig. 1 Type of impingements in distal-type CSA. **a** Axial T2-weighted MRI in case with impingement against anterior horn (AH) at the C5/6 intervertebral level (arrow head). **b** Axial T2-weighted MRI in case with impingement against ventral nerve root (VNR) at the C6/7 intervertebral level (arrow head)



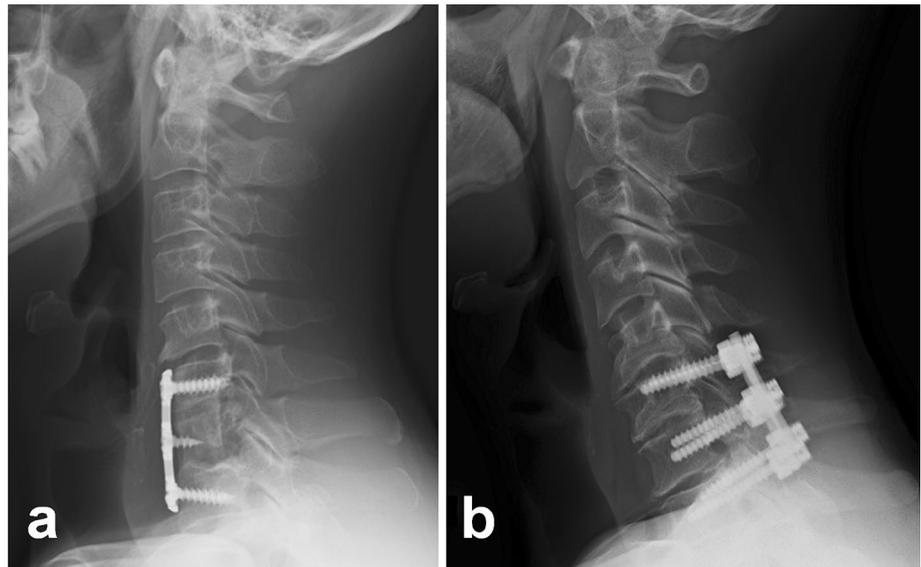
neck surgeries. In general, the patients got out of bed on postoperative day 2 and started rehabilitation therapies.

To evaluate the effect of surgical treatment, we used MMT. Perioperative muscle strength was generally evaluated by an independent surgeon using the 6-point Medical Research Council (MRC) scale (5, Full range of motion, full resistance; 4, Full range of motion, some resistance; 3, Full range of motion, no resistance; 2, Decreased range of motion; 1, Muscle flicker; 0, Complete paralysis) [11], and improvements in the muscle strength of the most atrophic and impaired muscles were classified into 2 groups: good outcomes included full recovery or recovery to an MMT

grade of at least 1; poor outcomes included no improvement and a worsening effect.

We retrospectively compared surgical outcomes between the anterior and posterior approaches in terms of multiple clinical parameters. We also examined the factors related to poor outcomes following CSA surgery by applying univariate analyses. Statistical analysis was performed using Mann–Whitney *U* tests for nonnormally distributed variables and Fisher’s exact tests for categorical variables. All data are expressed as the means ± standard deviation (SD). A *p* value less than 0.05 was considered to indicate a statistically significant difference.

Fig. 2 Postoperative lateral X-rays. **a** Anterior decompression with fusion. **b** Posterior decompression with fusion



Results

A total of 43 patients with distal-type CSA in this study tolerated the surgical procedure well and were followed up for an average of 36.1 months (range 6 to 102 months). The duration of symptoms averaged 18.5 months (range 2 to 86 months) (Table 1). The preoperative comorbidities recorded in this study included diabetes mellitus in 7 cases (16.3%), hypertension in 8 cases (18.6%), lung disease in 3 cases (7.0%), cancer in 2 cases (4.7%), heart failure in 1 case (2.3%), myasthenia gravis in 1 case (2.3%), and ossification of the posterior longitudinal ligament of the cervical spine in 1 case (2.3%).

Twenty-nine patients received the anterior procedure, and 14 patients received posterior decompression with or without PSF (Table 2). The mean preoperative MMT grade was 2.4. It significantly improved to 3.1 after cervical surgery ($p=0.0035$). The surgical results were good for 26 patients (60.5%) and poor for 17 patients (39.5%). Perioperative complications occurred in 11 patients (25.6%), including subsidence of cage ($n=5$), nonunion ($n=2$), displacement of bone graft/cage ($n=2$), and C5 palsy ($n=1$) in the anterior group. Proximal junctional kyphosis was found in 1 patient in the posterior group.

For the radiographic parameters, there were no significant changes between preoperative C2-7 angle and postoperative C2-7 angle or local lordosis. According to the MRI findings, compressive lesion of AH or VNR was found at an average of 2.5 intervertebral levels (range 1–4 levels). Compressive lesions relevant to distal-type CSA were located at the C6/7 and C7/Th1 preforaminal zones ($n=32$, and $n=18$, respectively), which could impinge against the C7 and C8 VNRs or the C5/6 level and the C6/7 level in the canal ($n=23$, and $n=14$, respectively), leading to impingement mainly

against AHs of the C7 and C8 spinal cord segments (Fig. 3). In our study of 43 patients, impingements against AH alone were found in 6 cases (14.0%), while impingements against VNR alone were found in 15 cases (34.9%). Among them, CSA cases due to only one compressive level of AH or VNR were observed in 4 and 7 cases, respectively, and the remaining 32 cases (74.4%) showed multiple lesions. Twenty-two cases (51.2%) had both AH and VNR. Overall, the pathophysiology of CSA could be attributed to multiple impingements against AH and/or VNR (an average of 1.0 levels of AH + 1.2 levels of VNR). HIA on T2-weighted MRI was confirmed in 16 of 43 patients (37.2%) (Table 1).

Nineteen of 29 patients (65.5%) who received anterior approach methods were included in the good group, whereas 7 of 14 patients (50.0%) in the posterior group were classified as good. Comparing the anterior group and the posterior group, there were no significant differences in terms of clinical outcomes and cervical alignment except for postoperative MMT grade (3.4 ± 1.1 vs 2.5 ± 1.2 , $p=0.0139$). In the anterior group, the mean MMT grade significantly improved from 2.6 to 3.4 ($p=0.0035$) regardless of the higher rate of perioperative complications (34.5% vs 7.1%), while it increased from 2.0 to 2.5 ($p=0.2403$) in the posterior group (Table 2).

According to univariate analyses of surgical outcomes, the duration of symptoms was substantially associated with a poor outcome after surgery (26.2 ± 27.9 months vs 13.5 ± 17.2 months, $p=0.0721$). There was a trend for patients with bilateral symptoms to have a better surgical outcome compared to patients with unilateral symptoms. The good group included a higher number of female patients. Cervical alignments, preoperative MMT grade, and type of surgical procedure were not statistically associated with poor outcomes (Table 3).

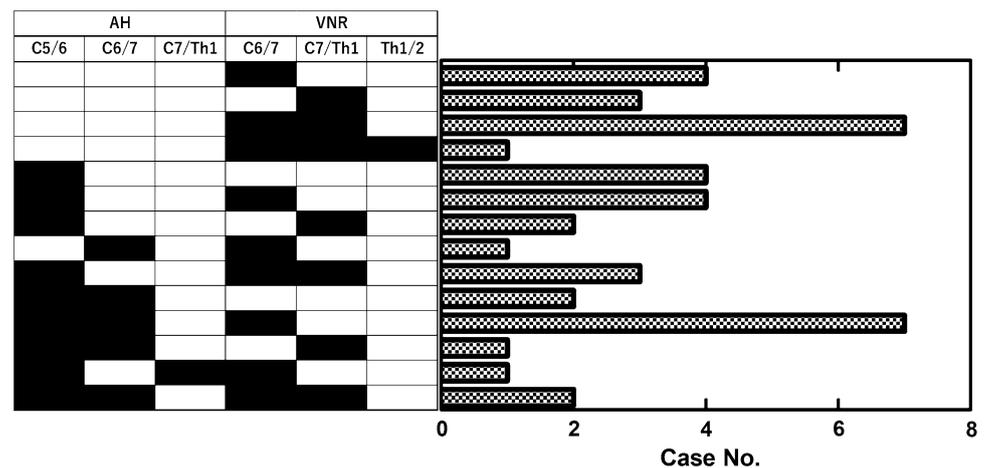
Table 2 Comparison between the cases treated by anterior procedures and the cases treated by the posterior procedures

		Anterior (n = 29)	Posterior (n = 14)	p value	
Age, average, years		62.2 ± 10.6	55.6 ± 18.8	NS	
Sex, female/male, No		3/26	1/13	NS	
Duration of disease, months		15.7 ± 21.4	24.5 ± 24.9	NS	
Follow-up period, months		41.3 ± 31.6	25.4 ± 16.1	NS	
Unilateral/bilateral		26/3	11/3	NS	
Surgical outcomes	Preop MMT grade	2.6 ± 0.9	2.0 ± 1.0	NS	
	Postop MMT grade	3.4 ± 1.1*	2.5 ± 1.2	0.0139	
	p value	0.0035	NS		
	Good	19 (65.5%)	7 (50.0%)		
	Poor	10 (34.5%)	7 (50.0%)	NS	
Complications		10 (34.5%)	1 (7.1%)	NS	
Levels of stenosis		Preop	2.6 ± 0.9	2.4 ± 1.2	NS
C2-7 angle	Preop	- 0.6 ± 13.1	5.7 ± 11.5	NS	
	Postop	4.8 ± 10.0	7.7 ± 9.8	NS	
ΔC2-7		5.0 ± 6.4	2.0 ± 7.9	NS	
Local lordosis	Preop	- 1.9 ± 9.2	2.5 ± 4.8	NS	
	Postop	1.1 ± 7.6	3.9 ± 6.5	NS	
Δlocal lordosis		2.9 ± 7.2	1.4 ± 4.8	NS	
C7 slope		Preop	21.9 ± 8.0	23.9 ± 10.9	NS
T2 HIA (+)		11 (37.9%)	5 (35.7%)	NS	

Data were shown average ± SD; No. indicates number; T2 HIA, high-intensity area on T2-weighted magnetic resonance images; Preop, preoperative; Postop, postoperative; MMT, manual muscle test; NS, not significant

*p < 0.05 when compared to the preoperative status

Fig. 3 Compression lesions in distal-type CSA. The black cell in the chart represents the compression lesion. Compressive lesions in the cervical spine were mainly located at the C5/6, C6/7, and C7/Th1 intervertebral levels. The pathophysiology of distal-type CSA is mostly caused by a combination of lesions in AH and VNR. AH, anterior horn; VNR, ventral nerve root



Nine of 27 patients (33.3%) without HIA on T2 MRI were included in the poor outcome group, whereas 8 of 16 patients (50.0%) with HIA were classified as poor. In the non-HIA group, the mean MMT grade significantly improved from 2.3 to 3.3 (p = 0.0027), whereas it increased from 2.6 to 2.9 (p = 0.4241) in the HIA group (Table 4).

When the surgery was performed within 6 months of onset, there was no significant difference in surgical outcomes. However, the mean MMT grade significantly improved from 2.2 to 3.2 (p = 0.0118) in the < 6 months group, while there was no

significant difference between pre- and postoperative MMT on and after 6 months from onset (Table 5).

Discussion

CSA is a rare clinical syndrome caused by cervical spondylosis. Patients usually demonstrate severe muscle weakness and atrophy in the upper extremities without significant sensory disturbance. CSA is categorized depending

Table 3 Comparison between the cases with poor clinical outcomes and the cases with good outcomes

		Poor (n = 17)	Good (n = 26)	p value
Age, average, years		60.4 ± 15.5	59.9 ± 13.2	NS
Sex, female/male, No		0/17	4/22	0.1404
Duration of disease, months		26.2 ± 27.9	13.5 ± 17.2	0.0721
Follow-up period		36.7 ± 27.4	35.7 ± 29.5	NS
Unilateral/bilateral		17/0	20/6	0.0662
Surgical outcomes	Preop MMT grade	2.4 ± 1.0	2.5 ± 1.0	NS
	Postope MMT grade	2.2 ± 1.1	3.7 ± 0.9*	<0.0001
	p value	NS	<0.0001	
Surgical procedure	Anterior	10	19	
	Posterior	7	7	NS
Levels of stenosis	Preop	2.5 ± 1.1	2.5 ± 0.8	NS
C2-7 angle	Preop	0.4 ± 15.3	2.1 ± 11.2	NS
	Postop	4.8 ± 9.9	6.6 ± 10.0	NS
ΔC2-7		4.4 ± 8.1	3.7 ± 6.3	NS
Local lordosis	Preop	- 1.8 ± 10.3	0.5 ± 6.7	NS
	Postop	1.4 ± 8.4	2.4 ± 6.6	NS
Δlocal lordosis		3.2 ± 7.6	2.0 ± 5.8	NS
C7 slope	Preop	24.1 ± 10.3	21.5 ± 8.0	NS
T2 HIA (+)		8 (47.1%)	8 (30.8%)	NS

Data were shown average ± SD; No. indicates number; T2 HIA, high-intensity area on T2-weighted magnetic resonance images; Preop, preoperative; Postop, postoperative; MMT, manual muscle test; NS, not significant

* $p < 0.05$ when compared to the preoperative status

Table 4 Relevance between clinical outcomes and signal intensity change on T2 weighted MRI

	T2 HIA		p value
	No [No. (%)]	Yes [No. (%)]	
Good	18/27 (66.7)	8/16 (50.0)	Fisher's test $p = 0.3427$
Poor	9/27 (33.3)	8/16 (50.0)	
Preoperative MMT	2.3 ± 1.0	2.6 ± 1.0	NS
Postoperative MMT	3.3 ± 1.2*	2.9 ± 1.2	NS
p value	0.0027	NS	

Data were shown average ± SD; MMT indicates manual muscle test; T2 HIA, high-intensity area on T2-weighted magnetic resonance images; No., number; NS, not significant

* $p < 0.05$ when compared to the preoperative status

on the most predominantly affected muscles as proximal-type or distal-type. The proximal-type patients have muscular atrophy in the C5 and C6 myotomes (mainly deltoid, and biceps) [12, 13], whereas patients with distal-type CSA have muscular atrophy in C7, C8, and Th1 (mainly the forearm and hand). Several studies have investigated different aspects of distal-type CSA, including clinical features, diagnostic methods, prognosis, etc., during the last two decades [10, 14–19]. However, the exact pathogenic

mechanism of distal-type CSA, optimal treatment method, and timing of surgery is still unclear. To address these issues, we investigated the surgical outcomes of distal-type CSA with a large number of subjects in this multicenter study.

At the clinical sites, there were elderly CSA patients with a tendency to have multiple stenotic lesions due to cervical spondylosis [10]. In the present study, 51.2% of cases had impingement against both AH and VNR relevant to distal-type CSA. Additionally, we found compressive lesions in an average of 1.0 levels of concomitant AH in addition to 1.2 levels of VNR in the MRI images. These results suggest that the pathophysiology of CSA was mostly caused by a combination of multiple lesions in AH and/or VNR, as previously reported [4, 12, 19, 20]. Some cases had multiple lesions at multiple spinal cord segments (e.g., C5/6AH + C6/7AH), and others had several compressive sites leading to impairment of the same segment (e.g., C5/6AH + C6/7VNR). The condition of CSA is considered to be caused not only by mechanical compression of the spinal cord but also by damage to the AH of the spinal cord secondary to circulatory disturbance [21]. In some patients, coexisting spinal cord compression was seen at the upper level (e.g., C3/4 and/or C4/5). Although radiological stenosis at the upper level itself does not directly affect the clinical features of distal-type CSA, this lesion can contribute to circulatory insufficiency

Table 5 Relevance between clinical outcomes and duration of disease

	Duration of disease		<i>p</i> value			<i>p</i> value
	< 6 months [No. (%)]	> 6 months [No. (%)]		< 9 months [No. (%)]	> 9 months [No. (%)]	
Good	10/14 (71.4)	16/29 (55.2)	Fisher's test <i>p</i> = 0.3434	17/22 (77.3)	9/21 (42.9)	Fisher's test <i>p</i> = 0.0305
Poor	4/14 (28.6)	13/29 (44.8)		5/22 (22.7)	12/21 (57.1)	
Preoperative MMT	2.2 ± 0.9	2.5 ± 1.1	NS	2.3 ± 0.9	2.5 ± 1.1	NS
Postoperative MMT	3.2 ± 1.3*	3.1 ± 1.2	NS	3.5 ± 1.1*	2.9 ± 1.2	NS
<i>p</i> value	0.0118	NS		0.0009	NS	

Data were shown average ± SD; MMT indicates manual muscle test; No., number; NS, not significant

**p* < 0.05 when compared to the preoperative status

in the spinal cord in addition to mechanical compression of the C7, 8 or Th1 segment. Zheng et al. analyzed central motor conduction time, suggesting that corticospinal tract damage caused by proximal spinal cord compression may induce or worsen distal motor unit loss in some cases with distal-type CSA [16].

Generally, neurological improvement after surgical treatment for distal-type CSA is considered inferior to the outcomes after treatment for proximal-type CSA. Zhang et al. reported that risk of poor outcome was significantly higher in distal-type compared with proximal-type CSA (odds ratio: 6.456) [19]. Fujiwara et al. reported that muscle power improved postoperatively in only 38% of patients with distal-type CSA [4]. One of the reasons for these poor outcomes may be the long distance from the cervical lesion to the affected muscles. Previous reports suggested that high signal intensity change in the spinal cord in T2-weighted images and cervical kyphosis was associated with a poor surgical outcome in cervical spondylotic myelopathy patients [2, 22]. In the current study, 37.2% of cases had HIA, consistent with previous reports (29.4%) [10]. The non-HIA cases showed a tendency toward better improvement of MMT levels in the hands compared to the cases with HIA (Table 4). The existence of an HIA region in the MRI generally indicated damage to the spinal cord, including AH. As previously reported [19, 20], the involvement of AH may influence the poor outcome after surgery for distal-type CSA. On the other hand, cervical kyphosis was not associated with poor outcomes in this study. Generally, appropriate decompression is sometimes difficult for kyphotic patients through a posterior approach. This study included more anteriorly operated patients compared with previous reports. This may be a reason for the absence of a correlation between radiological cervical alignment and a poor surgical outcome.

Overall, patients with poor outcomes had CSA symptoms for a longer duration. Inui et al. reported that patients with a duration of symptoms < 6 months improved by conservative treatment [1]. Conservative treatment, such as the administration of PGE1, should be initially tried in CSA patients

[23]. However, there was a close association between disease history and the recovery of muscle power in patients with CSA, and surgical treatment in some cases requires urgent action with regard to human neuroanatomy and neural innervation of the paralyzed muscles [2, 13]. Early surgery is especially recommended for distal-type CSA patients in whom conservative treatment has not been successful [3]. However, the timing of surgery is of crucial importance because CSA follows a self-limited course [13]. In the current study, when the surgery was performed on and after 6 months from onset, the mean MMT grade did not significantly improve, although the preoperative MMT grade did not significantly affect the surgical outcome. Zhang et al. also reported that symptom duration is a risk factor for poor outcome after surgery, especially in cases with a duration > 6 months [19]. Based on these results, we recommended surgery for distal-type CSA before irreversible change has been completed if conservative treatment has not been successful after 6 months.

The methods of operative treatment for CSA are still controversial. In this study, 26 of 43 patients showed improvement after surgical treatment, which is considered to be favorable in distal-type CSA [1, 3, 4]. When we compared the 2 approaches, patients treated by the anterior procedure showed better MMT grades in the hands. In previous reports, the number of patients who underwent anterior approaches was relatively small compared the number who underwent posterior approaches [3] because most of the patients showed multiple compressive lesions, which are more likely to be treated with a posterior approach [1]. The current study included a higher number of anterior surgeries, as described above, which may result in satisfactory surgical outcomes (good; 60.5%) compared to previous reports (38–44%). Because the pathogenesis of CSA is originally located at the anterior lesions, anterior decompression and fusion could produce more favorable results compared with the posterior approach [17].

This study has several limitations, including the following: 1. The patient's baseline was not controlled; 2. this was

a retrospective investigation; and 3. we did not compare the MRC scale, which was widely accepted and frequently used in evaluating forearm and hand muscles [19], to other tests. These limitations could be partially ascribed to the challenges of distal-type CSA surgery. Because this study lacks a powerful statistical analysis, prospective data collection is needed in the future to more precisely clarify clinical outcomes in distal-type CSA.

Conclusions

We demonstrated the clinical features of distal-type CSA and confirmed that surgical interventions for distal-type CSA patients can reliably produce improvements in neurological impairment if performed within 6 months. Any surgical procedure is acceptable as long as the mechanical compression and selective damage to AH or VNR are resolved. As the condition allows, the anterior approaches might be recommended because this procedure could significantly improve MMT levels in the hands beyond perioperative complications.

Compliance with ethical standards

Conflict of interest No benefits in any form have been or will be received from any commercial party related directly or indirectly to the subject of this article.

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