Factors Affecting the Surgical Outcomes of Hirayama Disease: A Retrospective Analysis of Preoperative Magnetic Resonance Imaging Features of the Cervical Spine

Fei Zou, Shuo Yang, Feizhou Lu, Xiaosheng Ma, Xinlei Xia, Jianyuan Jiang

■ OBJECTIVE: **We explored the factors affecting the surgical outcomes of Hirayama disease (HD).**

■ METHODS: **We enrolled 40 patients with a diagnosis of HD in the present study. Cervical spine magnetic resonance imaging (MRI) was performed before surgery with the neck in the cervical neutral and flexion positions. Fusion surgery was performed at the most severely compressed 2 levels according to the flexion sagittal MRI findings. The patients were divided into improvement and no-improvement groups according to Odom's scale 6 months after surgery. The axial MRI parameters in the neutral and flexion positions at the most severely compressed segment were measured. P values < 0.05 were considered statistically significant.**

■ RESULTS: **The average age was 18.4 ± 2.27 years, and the average disease duration was 1.8 ± 1.2 years. The main symptomatic side of HD statistically matched the atrophied side of the spinal cord ($P < 0.001$). Based on the pathophysiology of spinal cord flattening with flexion, the parameters indicating atrophy of the spinal cord and the ability of the spinal cord to recover from flattening were significantly larger in the improvement group ($P < 0.05$). Receiver operating characteristic curves showed good prognostic capacity for these parameters ($P < 0.05$).**

■ CONCLUSIONS: **The main side of the symptoms in patients with HD corresponded with ipsilateral spinal cord atrophy found on MRI. Also, atrophy of the spinal cord in the neutral position MRI study and the ability of the spinal cord to recover were significantly related to the surgical outcome. These factors might be used as potential indications for surgery of HD.**

INTRODUCTION

Hirayama disease (HD) is a juvenile muscular atrophy of the unilateral upper extremity. It was discovered and named by the Japanese scholar Hirayama in 1959.[1] At that time, HD was considered a self-limiting lower motor neuron disease, and most of the patients with HD were reported in Asian countries, such as Japan, China, and India, with very few cases reported in Europe and America. The male/female ratio of the disease has been ~20:1.[2] In recent years, with the development of electrophysiology technology and magnetic resonance imaging (MRI) technology, studies of HD have made great progress.

The pathophysiology of HD has been attributed to forward displacement of the posterior cervical dural sac on neck flexion. This results in spinal cord compression and venous congestion, which leads to damage of the anterior horn cells.[3,4] All the treatments for HD have been aimed at this pathophysiology. Neck collar therapy was used in patients with HD to avoid neck flexion and reduce spinal cord injury. However, the results were not satisfactory owing to poor patient compliance.[5] Cervical duraplasty was performed to decompress the spinal cord in flexion and has proved to be effective.[6,7] With the progress of spine surgery, anterior cervical discectomy and fusion (ACDF) became 1 of the surgical treatments for HD.[8,9] Because of the limitation of flexion

Key words
- Cervical spine
- Follow-up
- Hirayama disease
- Image study
- Retrospective study
- Surgical treatment

Abbreviations and Acronyms
ACDF: Anterior cervical discectomy and fusion
AUC: Area under receiver operating characteristic curve
CI: Confidence interval
HD: Hirayama disease
MRI: Magnetic resonance imaging
RI: Rebounce index
RI′: Rebounce index of atrophied side
ROC: Receiver operating characteristic

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Citation: World Neurosurg. (2019) 122:e296-e301.
https://doi.org/10.1016/j.wneu.2018.10.025

Journal homepage: www.journals.elsevier.com/world-neurosurgery

Available online: www.sciencedirect.com

in the surgical segments, spinal cord injuries in the neck flexion position were avoided, and the progression of the disease was limited. The results of a short-term follow-up protocol showed satisfactory effects.[8,9] Previous studies have also shown that not all patients will benefit from surgery.[8,9]

However, few studies have focused on the correlation between the preoperative images and patient prognosis. At present, flexion cervical MRI is the major imaging modality for the diagnosis of HD. Forward displacement and flattening of the spinal cord were observed on flexion MRI. In clinical practice, we found that the flattening of the spinal cord could partially recover when the cervical spine was returned to a neutral position; however, the extent of this recovery varied for different patients. In the present study, we hypothesized that the flattening of the spinal cord before surgery could have an effect on the prognosis. Thus, we sought to identify the correlation between the MRI findings and outcomes of ACDF surgery in patients with HD.

METHODS

Subjects

From January 1, 2015, to December 31, 2016, 43 patients with a diagnosis of HD had undergone surgery at our hospital. The diagnosis criteria of HD were those proposed by Hirayama et al.[1]: 1) weakness and wasting, predominantly in the C7, C8, and T1 myotomes in 1 upper limb or asymmetrically in both upper limbs; 2) insidious onset in adolescents or adults in their early 20s; 3) initial fast progression for 1–3 years, followed by disease arrest or a relatively benign course; 4) irregular coarse tremors in the fingers of the affected hand or hands; 5) mild transient worsening of symptoms on exposure to the cold; 6) electromyographic evidence of chronic denervation in the clinically or subclinically affected muscles; and 7) an absence of objective sensory loss. The exclusion criteria were female sex, cervical spine trauma history,

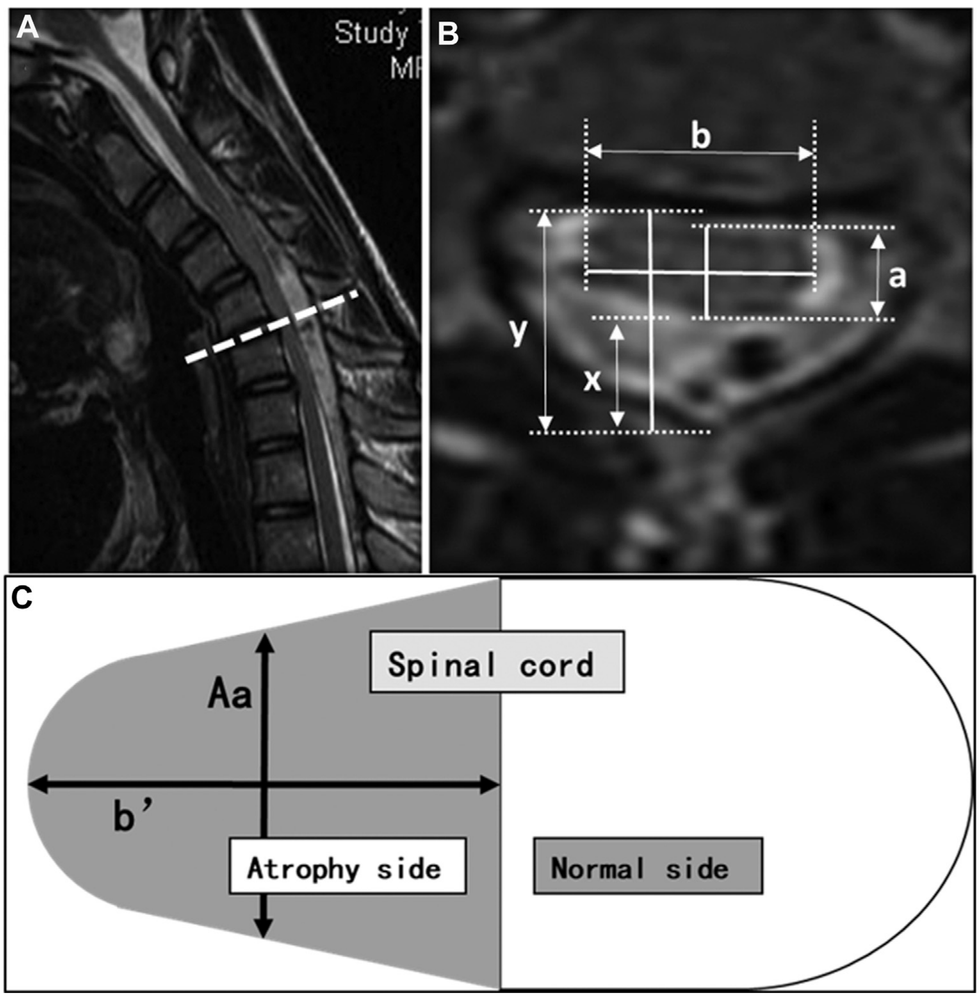

Figure 1. Illustration of the measurements of the parameters on the magnetic resonance imaging (MRI) scan. (**A**) The most severely compressed segment was determined from the flexion sagittal MRI findings before surgery. (**B**) MRI scan and (**C**) diagram showing the parameters to be measured on the transverse cervical spine MRI scan.

Table 1. Correlation Between Major Affected Side of Hands and Spinal Cord Atrophy Side on Magnetic Resonance Imaging

	Spinal Cord Atrophied Side		
Major Affected Side	Left	Right	Total
Left	15 (37.5)	1 (2.5)	16 (40.0)
Right	3 (7.5)	21 (52.5)	24 (60.0)
Total	18 (45.0)	22 (55.0)	40 (100.0)

Data presented as *n* (%).

and hand surgery history.[10] Finally, 40 patients were enrolled in the present study.

MRI Protocol

Cervical spine MRI was performed before surgery with patients in the cervical neutral position and flexion position. To obtain full flexion of the neck in the MRI scanner, the trunk was tilted down using a pelvic wedge, as suggested by Hirayama and Tokumaru.[3] The degree of neck flexion in each subject was not uniform but depended on the patient's body size and tolerance. All the cervical MRI scans were performed using a 1.5 T Signa Excite MRI machine (GE Healthcare, Milwaukee, Wisconsin, USA). The center of the magnetic field was set at the C6 level. The routine spin-echo sequence was used for scanning to obtain sagittal T1-weighted and T2-weighted images and axial T2-weighted images. For the axial T2-weighted images, the scanning plane was parallel to the anteroposterior axis of the disc in the sagittal images. The scanning image was stored in the PACS system (Centricity 3.0; General Electric Medical System, Milwaukee, Wisconsin, USA), and the parameters were measured.

Table 2. Correlation Between Predictors and Surgical Outcomes

Factor	Improvement Group ($n = 26$)	No Improvement Group ($n = 14$)	*P* Value
Age (years)	17.90 ± 1.88	19.10 ± 2.69	0.134
Disease duration (years)	1.67 ± 0.76	2.06 ± 1.69	0.32
F-x/y	0.50 ± 0.09	0.51 ± 0.07	0.781
F-a/b	0.33 ± 0.06	0.34 ± 0.06	0.627
F-a/b′	0.54 ± 0.12	0.50 ± 0.13	0.328
N-a/b	0.47 ± 0.05	0.38 ± 0.08	<0.001
N-a/b′	0.70 ± 0.10	0.54 ± 0.12	<0.001
RI	1.45 ± 0.22	1.13 ± 0.18	<0.001
RI′	1.33 ± 0.29	1.12 ± 0.24	0.018

Data presented as mean ± standard deviation.
F, flexion; N, neutral; RI, rebounce index; RI′, rebounce index of atrophied side.

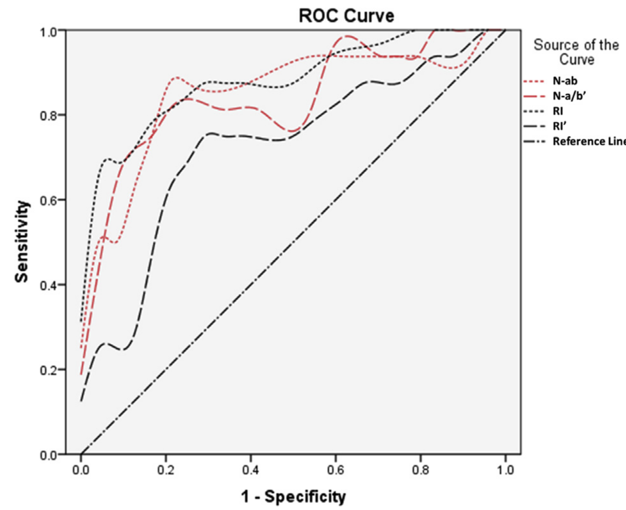

Figure 2. Receiver operating characteristic (ROC) curves of effective magnetic resonance imaging measurement predictors of the surgical outcome. N, neutral; RI, rebounce index; RI′, rebounce index of atrophied side.

Surgery and Follow-Up Examinations

For surgery, ACDF was performed at 2 levels—those that the most severely compressed according to the flexion cervical MRI findings.[11] The posterior longitudinal ligament was preserved during the surgery. Decompression of the spinal cord was approached by improvement of the cervical spine alignment. Autologous iliac bone and an Atlantis plate (Medtronic Sofamor Danek, Memphis, Tennessee, USA) were used for intervertebral fusion. All ACDF procedures were performed as 1 procedure. The patients were followed up at 6 months after surgery, and Odom's scale was used to evaluate the surgical outcome.[12] The outcomes were classified as excellent, good, fair, or poor. The patients with good or excellent outcomes were assigned to the improvement group, and the patients with fair or poor outcomes were assigned to the no-improvement group.

MRI Measurement

The parameters of the axial MRI scan in the neutral and flexion positions at the most severely compressed segment, which was determined by the flexion sagittal MRI scan before surgery, were measured (Figure 1A). The distance between the posterior edge of the cervical spinal cord and posterior edge of the spinal canal was termed x, the distance between the anterior edge and posterior edge of the spinal canal was termed y, and the anteroposterior diameter and transverse diameter of the cross section of the spinal cord were termed a and b, respectively. The cervical flexion position x/y was used as the indicator of the forward shifting of the spinal cord. The flexion position a/b was used as the indicator of a flattening change in the spinal cord[13] (Figure 1B). The flattening changes of the spinal cord on the atrophied side were also measured. The half of the transverse diameter of the cross section of the spinal cord was termed b' ($b' = 0.5 \times b$). Vertical lines were made at the quartile of the atrophied side to measure

Table 3. Receiver Operating Characteristic Curve Analysis of Predictors of Surgical Outcomes

Factor	AUC	95% CI	Youden Index	Best Cutoff Point	*P* Value
N-a/b	0.862	0.732—0.992	0.667	0.435	<0.001
N-a/b′	0.841	0.706—0.977	0.667	0.605	<0.001
RI	0.885	0.773—0.998	0.645	1.2491	<0.001
RI′	0.729	0.562—0.896	0.5	1.2132	0.015

ROC, receiver operating characteristic; AUC, area under receiver operating characteristic curve; CI, confidence interval; N, neutral; RI, rebounce index; RI′, rebounce index of atrophied side.

the anteroposterior diameter of the atrophied spinal cord, which was termed *Aa* (Figure 1C). The flattening change in the atrophied half of the spinal cord was termed *Aa/b′*. The rebounce index (RI) was defined as the ratio of the neutral position *a/b* to the flexion position *a/b*. The RI indicates the ability of the spinal cord to recover from the flattening, with the position changing from flexion to neutral. The RI of the atrophied side (RI′) was defined as the ratio of the Aa/b′ in the neutral position to the Aa/b′ in the flexion position. The parameters were measured by 2 certified spine surgeons who were unaware of the surgical outcomes.

Statistical Analysis

Statistical analyses were performed using SPSS, version 21.0 (IBM Corp., Armonk, New York, USA). Fisher's exact test was used to analyze the correlation between the major affected side of the hands and the spinal cord atrophied side on the MRI scan. An independent sample *t* test was used for the comparison of the factors affecting the surgical outcome between the improvement and no-improvement groups. To confirm the predictors of the surgical outcome, receiver operating characteristic (ROC) curves were constructed, and the areas under the ROC curves (AUCs) were determined. Youden's index was used to calculate the best cutoff point. A P value of < 0.05 was considered to indicate statistical significance.

RESULTS

The average age of the 40 patients was 18.4 ± 2.27 years, and the average disease duration was 1.8 ± 1.2 years. Of the 16 patients whose major affected side was the left side, 15 had ipsilateral spinal cord atrophy. Of the 24 patients whose major affected side was the right side, 21 had ipsilateral spinal cord atrophy ($P < 0.001$; Table 1).

Of the 40 patients, 26 were assigned to the improvement group and 14 to the no-improvement group. Patient age and disease duration were not significantly different between the 2 groups ($P = 0.134$ and $P = 0.32$, respectively). On the flexion position MRI, the x/y, a/b, and a/b′ positions were not significantly different between the improvement group and no-improvement group ($P = 0.781$, $P = 0.627$, and $P = 0.328$, respectively). On the neutral position MRI scan, the a/b and a/b′ positions were larger in the improvement group than in the no-improvement group, and these differences were statistically significant ($P < 0.001$ and $P < 0.001$, respectively). The comparison of the RI and RI′ between the 2 groups showed that the RI and RI′ were significantly larger in the improvement group than in the no-improvement group ($P < 0.001$ and $P = 0.018$, respectively; Table 2).

ROC curve analysis was performed to identify the effective MRI measurement predictor for the surgical outcome. We analyzed the ROC curves of the a/b and a/b′ positions on the neutral position MRI scan and those of the RI and RI′ (Figure 2). The AUC of the a/b and a/b′ positions on the neutral position MRI scan were 0.862 (95% confidence interval [CI], 0.732—0.992; $P < 0.001$) and 0.841 (95% CI, 0.706—0.977; $P < 0.001$), respectively. The AUC of the RI and RI′ were 0.885 (95% CI, 0.773—0.998; $P < 0.001$) and 0.729 (95% CI, 0.562—0.896; $P = 0.015$), respectively. The best cutoff points of the a/b and a/b′ positions on the neutral position MRI scan and the RI and RI′ calculated using the Youden index were 0.435, 0.605, 1.2491, and 1.2132, respectively (Table 3).

The operative data between the 2 groups, including operative time, blood loss, and length of stay after surgery, were not significantly different ($P = 0.896$, $P = 0.091$, and $P = 0.758$, respectively). No complications or unplanned reoperations occurred (Table 4).

DISCUSSION

The pathogenesis of HD mainly depends on the MRI findings of the cervical spine in the flexion position. The MRI findings will show forward shifting of the posterior dural sac, enhancing the posterior epidural mass from the engorged epidural venous plexus, and spinal cord compression with or without cord atrophy.[13] Xu et al.[14] showed that an increased flexion range of motion in the cervical spine contributes to the pathophysiological changes in HD. Therefore, preventing the spinal cord from shifting forward and becoming compressed has become one type of treatment. In a study of the indications for surgery, Guo et al.[9] demonstrated that multilevel ACDF was the favored treatment for patients with cervical kyphosis. In the study by Lu et al.,[8] the result of postoperative electromyography follow-up showed that the proportion of patients with neurophysiological improvement was 57.1% and 62.5% in the discectomy decompression and fusion group and the corpectomy decompression and fusion group,

Table 4. Correlation Between Operative Data and Surgical Outcomes

Factor	Improvement Group ($n = 26$)	No Improvement Group ($n = 14$)	*P* Value
Operative time (hours)	1.25 ± 0.41	1.27 ± 0.31	0.896
Blood loss (mL)	24.25 ± 17.24	15.56 ± 12.45	0.091
Postoperative length of stay (days)	4.83 ± 0.82	4.75 ± 0.86	0.758

No complications or unplanned reoperation occurred.

Table 5. Summary of Surgery Treatment Studies for Hirayama Disease

Investigator	Population	Surgical Procedure	Outcome
Lu et al.[8]	48 Male patients (age range, 15—23 years)	Anterior cervical discectomy decompression (2-level) with autologous iliac crest bone grafting and internal plate f ixation (24 patients); anterior cervical corpectomy, posterior longitudinal ligament resection, autologous iliac crest bone grafting, internal plate fixation (24 patients)	64.6% (31/48) showed improvement after surgery on self-assessment; 60% (18/30) showed improvement on EMG; both procedures were shown to be equally effective
Ito et al.[7]	6 Consecutive male patients (age range, 17—23 years)	Cervical duraplasty with tenting sutures via laminoplasty	Grip strength of upper extremities had improved significantly (20 $\pm$ 14 to 26 $\pm$ 15 kg; $P = 0.001$); no significant changes were observed in muscular atrophy
Guo et al.[9]	4 Patients (3 males, 1 female; age range, 17—24 years)	Multilevel (C3—C7) ACDF with plate fixation	JOA score improved from average of 14 preoperatively to average of 16.3 at 6 months postoperatively
Sun et al.[15]	36 Patients (34 males, 2 females; average age, 19.41 $\pm$ 3.99 years)	Anterior cervical internal fixation and fusion (3-level) with cage and plate	36% (9/25) showed improvement in muscle weakness by self-assessment 1 year postoperatively; 85.7% (12/14) showed improved 2 years postoperatively
Goel et al.[16]	5 Male patients (age range, 16—28 years)	Multilevel cervical fixation (C3—C7 in 1 patient, C1—C6 in 1 patient, C1—C7 in 3 patients); posterior cervical facetal fixation using transarticular technique	Improvement in symptoms of weakness, wasting, and deformity of hands in all patients
Brandicourt et al.[17]	3 Male patients (age range, 16—20 years)	Cervical laminectomy and microresection of posterior venous plexus without duraplasty	Clinical and electrophysiological improvement noted in 2 patients, with stabilization in the third

EMG, electromyography; ACDF, anterior cervical discectomy and fusion; JOA, Japanese Orthopaedic Association.

respectively. Different surgery procedures have been demonstrated to be useful (Table 5). Among them, ACDF has been the most used procedure.[8,9,18] However, not all of the patients will benefit from this operation. Of the limited number of studies focusing on the prognosis of surgical treatment, Song et al.[19] reported that the age of the patient, disease duration, physiological reflex, and pathological reflex were the risk factors affecting the surgical results of HD. However, no imaging features of HD affecting the prognosis of surgery were reported.[19] In our study, we first determined that the main symptomatic side of HD statistically matched the atrophied side of the spinal cord in a relatively large sample. In the study by Hirabuki et al.,[20] which used the method of computed tomographic myelography, all 12 patients with the unilateral clinical form showed ipsilateral cord atrophy, and all 4 patients with the bilateral form showed bilateral cord atrophy. As such, Liao et al.[21] found that patients with HD with cord atrophy experienced a more severe denervation change in C5—C7 root-innervated muscles by comparing patients with HD with and without cord atrophy. These results were similar to ours. On the premise of our results, we divided our patients into a surgical improvement group and a no-improvement group and compared the preoperative imaging parameters between the 2 groups. We found significantly flattened changes in the spinal cord in the neutral position of the MRI scan in the no-improvement group. We also found that the ability of the spinal cord to recover from the flattening that occurs with the change of the neck position from flexion to neutral was significantly weak in the no-improvement group. ROC curve analysis of the related MRI parameters also showed good prognostic capacity for the surgical outcomes of HD. These parameters reflect whether the spinal cord atrophy had reached the status of irreversibility. Furthermore, the best cutoff points for these predictors were also calculated, and these might give us a good reference for determining the surgical indication.

The major limitation of our study was that it was a retrospective study, which could have induced a selection bias. Furthermore, we only used the Odom score to determine the grouping, because HD causes only muscle atrophy and weakness of the upper limbs. Therefore, the use of other functional scores might not be proper. However, further electromyography monitoring is necessary.

CONCLUSION

The main side of the symptoms in patients with HD correlated highly with ipsilateral spinal cord atrophy found on MRI, indicating that spinal cord flattening is closely related to the neurological function of the patients. In addition, atrophy of the spinal cord on the neutral position MRI scan and the ability of the spinal cord to recover are significantly related to the surgical outcomes. Thus, these factors might be used as potential indications for surgery for HD.

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Conflict of interest statement: This work was supported by the General Program of National Natural Science Foundation of China (grant 81601914).

Received 2 July 2018; accepted 3 October 2018

Citation: World Neurosurg. (2019) 122:e296-e301. https://doi.org/10.1016/j.wneu.2018.10.025

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