Clinical presentations and surgical outcomes of hemifacial spasm involving the vertebral artery

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Research Article

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Abstract

Objectives

We aimed to determine whether vertebral artery (VA) affects the success rate of microvascular decompression (MVD) in hemifacial spasm (HFS) patients. We compared the clinical presentations and surgical outcomes between VA-involved and non-VA HFS patients.

Methods

The study comprised 313 HFS patients who underwent MVD between January 2015 and December 2018. There were 59 patients in the VA-involved group and 254 patients in the non-VA group. The clinical results mainly included the rate of HFS remission and the complications. Postoperative neurosurgery-related problems and neurological issues were among the complications.

Results

Among the 313 enrolled patients, 288 were spasem-free: 52 (88%) in VA-involved group and 236 (91.4%) in non-VA group. Delayed and partial remissions were frequent in VA-involved group. Furthermore, VA was significantly associated with partial remission \( (P=0.014) \). The total rate of complications was comparable between the two groups. However, motor or sensory impairments mainly occurred in the VA-involved group.

Conclusions

The rates of long-term remission and overall complication after MVD were not significantly different between the groups. VA-involved HFS may be at high risk for severe neurological complications and the partial spasem-free.

Introduction

Hemifacial spasm (HFS) is a benign functional disease with an average incidence of about one in 100,000 people, and the number of female patients is about twice that of males \([1, 4]\). The main manifestation of HFS is paroxysmal and involuntary twitching of the facial muscles innervated by the face nerve, which is not relieved by rest. Although Nerve Origin Hypothesis/ Peripheral Theory and Nuclear Origin Hypothesis/ Central Theory have been proposed, neurovascular compression remain the relatively recognized pathogenesis\([7, 8, 37]\). Anticonvulsants may be recommended as drug treatments in early stages of the disease, but they are often ineffective\([2]\). Botulinum toxin therapy is currently a recognized treatment method, although 20% of patients experience postoperative complications and symptom relief can last just a few months. Microvascular decompression (MVD) is thought to be the only treatment that can cure HFS. The overall success rate of MVD surgery has exceeded 90%, with complications occurring in less than 1%, due to the advancement of minimally invasive neurosurgery and nerve monitoring technology.
The main purpose of MVD surgery is to use bio-soluble materials to adequately separate the problematic blood vessels from the facial nerve and relieve nerve compression. The anterior inferior cerebellar artery and the posterior inferior cerebellar artery are the most commonly reported blood vessels that cause HFS during surgery. The vertebral artery (VA) is relatively rare. However, because the vertebral arteries are often thick and tortuous, and part of the atherosclerosis develops, the procedure is obviously more difficult. Furthermore, injury to the small perforating arteries that nourish vital surrounding brain tissues may cause serious complications\cite{13,23}. However, several studies have found no significant difference in clinical outcomes between VA-involved and non-VA HFS\cite{15,32,35}. Therefore, this study used single-center data to retrospectively analyze the long-term effects and postoperative complications of patients with VA-involved HFS.

**Methods**

**2.1 Study population and method**

This study included 313 patients, with well-diagnosed primary HFS, who attended the West China Hospital of Sichuan University from January 2015 to December 2018. The basic information and surgical findings of all patients were extracted from the inpatient database. The patients were divided into two groups based on whether the relevant vessels were linked to the vertebral artery (VA) during surgery: VA-involved and non-VA HFS. This research was approved by the Institutional Ethic Committee of West China Hospital of Sichuan University.

**2.2 Patient management and follow-up**

All patients were subjected to magnetic resonance imaging (MRI) before surgery, to ensure correct diagnosed. The MVD procedure of each patient was performed by the same surgeon under electrophysiological monitoring. The clinical results mainly included the remission degree of HFS after the operation: free spasm, partial remission, ineffective, delayed remission, and postoperative recurrence. Complications mainly included postoperative neurosurgery-related problems and neurological issues. Nerve complications included vertigo, facial palsy, motor or Sensory disturbances, whereas neurosurgical complications comprised cerebellar edema, CSF leak, intracranial infection, car infection, and fat liquefaction. The short-term clinical outcomes and complications were mainly obtained through clinical records, whereas the long-term outcomes and complications were mainly acquired through outpatient follow-up or telephone interviews. All 313 patients were followed-up for more than two year.

**2.3 Statistical analyses**

The continuous variables were reported as Mean±SD and analyzed using the Student’s t-test. Patients with favorable or adverse outcomes were compared using χ2 or fisher exact test for categorical variables and clinical data. All analyses were performed using the SPSS program (Version 25.0, IBM Corp., Armonk, New York, USA), which was also used to generate illustrations. Statistical significance was set at $P < 0.05$. 


Results

The 313 HFS patients underwent MVD between January 2017 and December 2018. Detailed information on demographic features and baseline characteristics are shown in Table 1. There were 59 (67.4%) patients with VA-involved and 254 (32.6%) patients non-VAHFS. The mean age and duration in the VA-involved group were 51 years and 63 months, respectively; 31 patients were female, and 41 cases were on the left side. In the non-VA group, 182 patients were female, and the mean age and duration were 50 years and 68 months, respectively, and 138 cases were on the left side. The female-male ratio was obviously higher in the VA-involved group ($P=0.005$). The difference in mean age and duration between the VA-involved group and non-VA group was not statistically significant ($P>0.05$). However, the VA-involved HFS was more severe on the left side ($P=0.034$). The most frequently offending vessels in the VA-involved group were the VA with anterior inferior cerebellar artery (58.7%) and the anterior inferior cerebellar artery alone (64.3%) in the non-VA HFS.

All patients were followed up for at least two years. In the VA-involved group, 52 (88%) patients were spasem-free, 44 patients experienced immediate postoperative remission, and 10 patients had delayed remission which lasted from half a month to a year. Two patients relapsed during the follow-up period. In the non-VA group, 288 (92.8%) patients were spasem-free, 208 experienced immediate postoperative remission, and 34 patients had delayed remission. Two patients relapsed during the follow-up period. The rate of partial remission (8.5%) in the VA-involved group was significantly higher than in the non-VA group ($P=0.014$).

There was no discernible difference between the two groups (all $P>0.05$) in terms of neurosurgery-related complications and neurological issues. Furthermore, vital complications and mortality were not recorded among the patients.

Discussion

It has been generally accepted that HFS is caused by a vascular compression of the facial nerve at the root exit zone (REZ)[2, 12]. Vertebral artery (VA) involvement has previously been reported in 4.4−18.4 % of HFS patients[18, 27, 31]. In our case series, patients with VA and non-VA compressed the facial nerve in 59 (18.8%) and 254 (81.2%) cases, respectively. In the VA-involved group, indirect compression by the VA along with the small branches occurred more frequently than direct compression by the VA alone. When compared to non-VA HFS, we found female predominance and left-sided predominance in VA-associated HFS, and the difference was statistically significant. A similar outcome has been proven in extensive research[35]. The left-sided predominance may result from several factors, including the origin of the left VA directly from the aortic arch, a higher percentage of left-dominant VA, and higher flow velocity and volume in the left VA[32]. Compared with the mean duration of patients in the previous studies, the duration in this study is relatively longer, and there was no significant difference between the VA and non-VA group. This phenomenon may be attributed to the fact that most patients decline surgical treatment until their lives are significantly affected by the symptoms.
Since Jenetta’s first vascularonever compression for hemifacial spasm (HFS) in 1966[12], Microvascular decompression has been widely used in the treatment of vascular nerve syndrome, Safety and efficacy of MVD in HFS have also been verified, with a success rate ranging from 90.9–94.3%[17, 33]. Patients with HFS are often in their 50s. Aging promotes atherosclerosis of vertebral arteries and makes their walls to become more rigid and brittle. Therefore, MVD is considered more difficult and is associated with a worse outcome when compared to MVD for HFS unrelated to the VA[34]. Several studies have investigated the effect of vertebral artery on HFS. The total spasem-free rate does not differ significantly between the VA involved and the non-VA groups which was in line with the results obtained in this study[10, 21, 22]. Meantime, we also found the delay and partial remissions were more frequent in the VA-associated group. The recurrence rate of VA involved groups was comparable to non-VA groups in our study. Some hypotheses have been proposed for the pathogeneses of delayed healing for HFS[5]. Demyelination of the nerve fibers and hyperexcitability of facial motor nucleus are widely acknowledged and edema of the facial nerve may be another risk factors. According to the findings in the operation, most of the vertebral arteries not only make facial nerve displacement but also cause obvious indentation. The facial nerve becomes demyelinated due to the long-term and continuous blood vessel compression. Even if the facial nerve is fully decompressed, it often takes a long time to repair the myelin sheath. It has been reported that delayed cure is associated with the slow reversal of the plastic changes in the facial nucleus [29]. According to the findings in the second surgery, the causes for persistent or recurrent NVC were often associated with Teflon adhesions and secondary granulomas[6]. Vasculature changes are also a frequent causative factor, especially elongated vertebral artery[3, 28]. Therefore, VA-linked HFS may be a risk factor for delay and partial remissions. However, there is no significant difference in recurrence rate between the two groups in our study, it may be related to the insufficient follow-up period.

Although the incidence of permanent complications don’t have difference, postoperative transient nerve complications in HFS with VA were more common than HFS attributed to small vascular compression[10]. The MVD procedures were mainly comlleted through the narrow space between vessels and nerves. Due to the large VA maybe obscured surgical field, excessive retraction of the cerebellar flocculus and overstretching of the cranial nerves sometimes were need to achieve sufficient decompression, which increase the complications. Thus, MVD might has a higher surgical risk for VA-involved HFS. Adequate evaluation of preoperative imaging may identify neurovascular contacts and reveal more accurate details of the neighbouring structures, and then help surgeon choose the appropriate operative approach[25]. The appropriate craniotomy, full release of arachnoid membrane and effective use of the natural space of the brain sulcus are often important for providing us with more space[19, 30]. Meantime, endoscopic microvascular decompression provide an more clear field of vision for surgeron and is a better alternative for the treatment of hemifacial spasm[36]. Some new surgical techniques have also been reported to mobilize the VA safely[9, 11, 14, 16, 20, 24]. However, these techniques are not always effective in all cases, particularly in cases with a high number of perforator blood vessels. Minor damages to the small perforator blood vessels that supply brainstem can have catastrophic repercussions. In this situation, intraoperative electrophysiological monitoring may be an important and usefull auxiliary tool. Because intraoperative electrophysiological monitoring can provide
the real-time response and help the surgeon to judge whether decompression is adequate and when to finish surgery. This help surgeon avoid complications caused by unnecessary harassment for surrounding important structures[26]. Therefore, MVD may pose a higher surgical risk for VA-involved HFS. Adequate preoperative imaging evaluation Intraoperative electrophysiological monitoring are needed to assist in the development of better surgical strategies to minimize postoperative complications.

**Conclusion**

There was no significant difference in the rate of surgical outcomes and complications between the VA involved group and the non-VA group. VA-associated HFS has the tendency to delay remission. Preoperative imaging evaluation and intraoperative electrophysiological monitoring should be advocated to have favorable postoperative outcome.

**Declarations**

**Authors' contributions:** All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Jianguo Li, Cheng chen and Liang Lyu. Senlin Yin performed picture editing and revised the manuscript. Shu Jiang and Peizhi Zhou supervised the study concept and revised the manuscript for intellectual content. Jianguo Li has written the first draft of the manuscript and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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**Availability of data and material:** Not applicable.

**Code availability:** Not applicable.

**References**

1. Auger RG, Whisnant JP (1990) Hemifacial spasm in Rochester and Olmsted County, Minnesota, 1960 to 1984. Arch Neurol 47:1233–1234. https://doi.org/10.1001/archneur.1990.00530110095023

2. Baldauf J, Rosenstengel C, Schroeder HWS (2019) Nerve Compression Syndromes in the Posterior Cranial Fossa. Dtsch Arztebl Int 116:54–60. https://doi.org/10.3238/arztebl.2019.0054
3. Bigder MG, Kaufmann AM (2016) Failed microvascular decompression surgery for hemifacial spasm due to persistent neurovascular compression: an analysis of reoperations. Journal of neurosurgery 124:90–95. https://doi.org/10.3171/2015.1.Jns142714

4. Blitzer AL, Phelps PO (2020) Facial spasms. Dis Mon 66:101041. https://doi.org/10.1016/j.disamonth.2020.101041

5. Dai Y, Ni H, Xu W, Lu T, Liang W (2016) Clinical analysis of hemifacial spasm patients with delay symptom relief after microvascular decompression of distinct offending vessels. Acta Neurol Belgica 116:53–56. https://doi.org/10.1007/s13760-015-0471-7

6. Dou NN, Zhong J, Liu MX, Xia L, Sun H, Li B, Li ST (2016) Teflon Might Be a Factor Accounting for a Failed Microvascular Decompression in Hemifacial Spasm: A Technical Note. Stereotact Funct Neurosurg 94:154–158. https://doi.org/10.1159/000446192

7. Dou NN, Zhong J, Zhou QM, Zhu J, Wang YN, Xia L, Yang XS, Ying TT, Zheng XS, Li ST (2015) The mechanism of hemifacial spasm: a new understanding of the offending artery. Neurological research 37:184–188. https://doi.org/10.1179/1743132814Y.0000000424

8. Green KE, Rastall D, Eggenberger E (2017) Treatment of Blepharospasm/Hemifacial Spasm. Curr Treat Options Neurol 19:41. https://doi.org/10.1007/s11940-017-0475-0

9. Inoue T, Shitara S, Goto Y, Arham A, Prasetya M, Radcliffe L, Fukushima T (2021) Bridge technique for hemifacial spasm with vertebral artery involvement. Acta Neurochir. https://doi.org/10.1007/s00701-021-05006-8

10. Jiang C, Liang W, Wang J, Dai Y, Jin W, Sun X, Xu W (2020) Microvascular decompression for hemifacial spasm associated with distinct offending vessels: A retrospective clinical study. Clinical neurology neurosurgery 194:105876. https://doi.org/10.1016/j.clineuro.2020.105876

11. Jiang X, Wu M, Fu X, Niu C, He F, Sun K, Zhuang H (2018) Microvascular Decompression for Hemifacial Spasm Associated with Vertebral Artery: Biomedical Glue-Coated Teflon Sling Transposition Technique. World neurosurgery 120:e342–e348. https://doi.org/10.1016/j.wneu.2018.08.073

12. Kaufmann AM, Price AV (2019) A history of the Jannetta procedure. Journal of neurosurgery 132:639–646. https://doi.org/10.3171/2018.10.JNS181983

13. Kim JP, Park BJ, Choi SK, Rhee BA, Lim YJ (2008) Microvascular decompression for hemifacial spasm associated with vertebrobasilar artery. J Korean Neurosurg Soc 44:131–135. https://doi.org/10.3340/jkns.2008.44.3.131

14. Kim JY, Jung S, Song TW, Kim IY, Moon KS, Jung TY, Jang WY (2019) The Cornerstone Technique of Microvascular Decompression for Hemifacial Spasm with Vertebral Artery Offender. World neurosurgery 126:e94–e100. https://doi.org/10.1016/j.wneu.2019.01.199

15. Lee S, Han J, Park SK, Lee JA, Joo BE, Park K (2021) Involvement of the vertebral artery in hemifacial spasm: clinical features and surgical strategy. Scientific reports 11:4915. https://doi.org/10.1038/s41598-021-84347-x
16. Lee SH, Park JS, Ahn YH (2016) Bioglu-Coated Teflon Sling Technique in Microvascular Decompression for Hemifacial Spasm Involving the Vertebral Artery. J Korean Neurosurg Soc 59:505–511. https://doi.org/10.3340/jkns.2016.59.5.505

17. Li Z, Gao J, Wang T, Li Y (2018) Retrospective clinical analysis of 320 cases of microvascular decompression for hemifacial spasm. Medicine 97:https://doi.org/10.1097/MD.0000000000011825

18. Li ZM, Gao J, Wang TY, Li YN (2018) Retrospective clinical analysis of 320 cases of microvascular decompression for hemifacial spasm. Medicine 97:https://doi.org/ARTN e118251097/MD.0000000000011825

19. Liang QH, Shi XW, Wang Y, Sun Y, Wang RX, Li ST (2012) Microvascular decompression for hemifacial spasm: technical notes on pontomedullary sulcus decompression. Acta Neurochir 154:1621–1626. https://doi.org/10.1007/s00701-012-1387-0

20. Lin CF, Chen HH, Hernesniemi J, Lee CC, Liao CH, Chen SC, Chen MH, Shih YH, Hsu SP (2012) An easy adjustable method of ectatic vertebrobasilar artery transposition for microvascular decompression. Clinical neurology neurosurgery 114:951–956. https://doi.org/10.1016/j.clineuro.2012.02.021

21. Masuoka J, Matsushima T, Nakahara Y, Inoue K, Yoshioka F, Kawashima M, Abe T (2017) Outcome of microvascular decompression for hemifacial spasm associated with the vertebral artery. Neurosurgical review 40:267–273. https://doi.org/10.1007/s10143-016-0759-y

22. Mikami T, Minamida Y, Akiyama Y, Wanibuchi M, Sugino T, Houkin K, Mikuni N (2013) Microvascular decompression for hemifacial spasm associated with the vertebral artery. Neurosurgical review 36:303–308. https://doi.org/10.1007/s10143-012-0425-y discussion 308-309.

23. Nagahiro S, Takada A, Matsukado Y, Ushio Y (1991) Microvascular decompression for hemifacial spasm. Patterns of vascular compression in unsuccessfully operated patients. Journal of neurosurgery 75:388–392. https://doi.org/10.3171/jns.1991.75.3.0388

24. Nonaka Y, Hayashi N, Matsumae M, Fukushima T (2019) Wedge-technique for transposition of the vertebral artery in microvascular decompression for hemifacial spasm: technical nuances and surgical outcomes. Acta Neurochir 161:1435–1442. https://doi.org/10.1007/s00701-018-03793-1

25. Ocal R, Tunc T, Ayas ZO, Yilmaz O, Inan LE (2016) Comparison of brain MRI angiography and brain MRI cisternography in patients with hemifacial spasm. Acta Neurol Belgica 116:593–598. https://doi.org/10.1007/s13760-016-0619-0

26. Park SK, Joo BE, Park K (2019) Intraoperative Neurophysiological Monitoring during Microvascular Decompression Surgery for Hemifacial Spasm. J Korean Neurosurg Soc 62:367–375. https://doi.org/10.3340/jkns.2018.0218

27. Qi HW, Zhang WN, Zhang XD, Zhao CX (2016) Microvascular Decompression Surgery for Hemifacial Spasm. Journal of Craniofacial Surgery 27:124–127. https://doi.org/10.1097/Scs.0000000000002306

28. Shu W, Zhu HW, Li YJ, Liu RC (2019) Clinical analysis of repeat microvascular decompression for recurrent hemifacial spasm. Acta Neurol Belgica 119:453–459. https://doi.org/10.1007/s13760-019-
29. Sindou M, Keravel Y (2009) [Neurosurgical treatment of primary hemifacial spasm with microvascular decompression]. Neurochirurgie 55:236–247. https://doi.org/10.1016/j.neuchi.2009.02.012

30. Tsunoda S, Inoue T, Naemura K, Akabane A (2021) The efficacy of temporary clamping of V3 with a suboccipital far-lateral approach in microvascular decompression for Hemifacial spasm associated with the vertebral artery. Neurosurgical review 44:625–631. https://doi.org/10.1007/s10143-020-01262-x

31. Xu ZH, Tang YS, Yan YH (2018) Clinical analysis on hemifacial spasm treated by microvascular decompression. Chinese Journal of Contemporary Neurology Neurosurgery 18:754–757. https://doi.org/10.3969/j.issn.1672-6731.2018.10.012

32. Yang DB, Wang ZM (2017) Microvascular decompression for hemifacial spasm associated with the vertebral artery. Acta Neurol Belgica 117:713–717. https://doi.org/10.1007/s13760-017-0766-y

33. Yeo M, Park BJ, PratapMalla H, Rhee BA, Lim YJ (2017) A clinical analysis on microvascular decompression surgery for treatment of hemifacial spasm: 2500 cases review in a single institute. Clin Neurosurg 64:259. https://doi.org/10.1093/neuros/nyx417

34. Zhang X, Xu L, Zhao H, Tang Y, Zhu J, Li S (2017) The Effect of Microvascular Decompression on Hemifacial Spasm With Atherosclerosis of Vertebral Artery. J Craniofac Surg 28:e579–e582. https://doi.org/10.1097/scs.000000000003900

35. Zhao H, Tang Y, Zhang X, Zhu J, Yuan Y, Zhou P, Li S (2019) Long-term Outcomes of Microvascular Decompression in the Treatment of Hemifacial Spasm Based on Different Offending Vessels. Journal of neurological surgery Part A. Central European neurosurgery 80:285–290. https://doi.org/10.1055/s-0039-1685199

36. Zhao Z, Chai SS, Xiao DD, Zhou YJ, Gan JL, Jiang XB, Zhao HY (2021) Microscopic versus endoscopic microvascular decompression for the treatment of hemifacial spasm in China: A meta-analysis and systematic review. Journal of Clinical Neuroscience 91:23–31. https://doi.org/10.1016/j.jocn.2021.06.034

37. Zhou QM, Zhong J, Jiao W, Zhu J, Yang XS, Ying TT, Zheng XS, Dou NN, Wang YN, Li ST (2012) The role of autonomic nervous system in the pathophysiology of hemifacial spasm. Neurological research 34:643–648. https://doi.org/10.1179/1743132812Y.0000000057

Tables

Table 1

Clinical characteristics of patients with VA-involved HFS and non-VA-involved HFS.
|                         | VA (N = 59) | Non-VA (N = 254) | p value |
|-------------------------|------------|------------------|---------|
| Median age (years)      | 51         | 50               |         |
| Sex (F:M)               | 31:28      | 182:72           | 0.005   |
| Affected side (right:left) | 18:41    | 116:138          | 0.034   |
| Duration (month)        | 63         | 68               |         |
| **Offending vessels**   |            |                  |         |
| VA + AICA               | 44         | AICA             | 180     |
| VA only                 | 9          | PICA             | 54      |
| VA + PICA               | 1          | AICA + PICA      | 13      |
| VA + AICA + PICA        | 1          | Others           | 5       |

VA vertebral artery, AICA anterior inferior cerebellar artery, PICA posterior inferior cerebellar artery, M male, F female.

**Table 2** Clinical outcomes and complications after MVD
| Parameter                        | VA (N = 59) | Non-VA (N = 254) | p value |
|---------------------------------|-------------|------------------|---------|
| **Median age (years)**          | 44 (74.5%)  | 208 (81.8%)      | P = 0.201 |
| **Delayed remission**           | 10 (16.9%)  | 34 (13.4%)       | P = 0.478 |
| **Partial remission**           | 5 (8.5%)    | 4 (1.6%)         | p = 0.014 |
| **No improvement**              | 0           | 6 (2.4%)         | P = 0.599 |
| **Spasem relapse**              | 2 (3.4%)    | 6 (2.4%)         | p = 0.648 |
| **Nerve complications**         | 7 (11.9%)   | 22 (8.7%)        | P = 0.420 |
| Vertigo                         | 2           | 7                |         |
| Never palsy                     | 2           | 15               |         |
| Partial hearing loss            | 1           | 0                |         |
| Motor or Sensory disturbances   | 2           | 0                |         |
| **Neurosurgical complications** | 3 (5.1%)    | 11 (4.3%)        | P = 0.733 |
| Cerebellar edema                | 1           | 1                |         |
| CSF leak                        | 1           | 2                |         |
| Intracranial infection          | 1           | 7                |         |
| Scar infection                  | 0           | 0                |         |
| Fat liquefaction                | 0           | 1                |         |