#### **ORIGINAL ARTICLE**



# The outcome of microvascular decompression for hemifacial spasm: a systematic review and meta-analysis

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#### Abstract

Microvascular decompression (MVD) is the first choice of surgery for hemifacial spasm (HFS). MVD surgery for vertebral artery (VA)-associated HFS is more difficult than for non-VA-associated HFS. There is controversy about the cure rate and complication of MVD for HFS in previous studies. We searched PubMed, Web of Science, and Embase for relevant publications. Based on the search results, we compared the outcomes of MVD for VA-associated HFS and non-VA-associated HFS. At the same time, we analyzed spasm-free rates and the complications and assessed the relationship between VAassociated HFS and gender, left side, and age. For analysis, six studies that included 2952 patients in the VA-associated group and 604 in the non-VA-associated group were selected. The effective rate of MVD was not significantly different between both groups (OR = 1.16, 95% CI 0.81–1.67, P = 0.42). Compared to non-VA-associated group, the transient complications (OR = 0.64, 95% CI 0.46–0.89, P = 0.008) and permanent complications (OR = 0.28, 95% CI 0.15–0.54, P = 0.0001) occurred more frequently in VA-associated group. The rate of hearing loss was significantly higher in VA-associated HFS than non-VA-associated HFS (OR = 0.35, 95% CI 0.19-0.64, P=0.0007); the facial paralysis after operation was not significantly different between both groups (OR = 1.25, 95% CI 0.91-1.72, P=0.17). There were older patients (WMD = 3.67, 95% CI 3.29-4.05, P < 0.00001) and more left-sided HFS (OR = 0.23, 95% CI 0.19 - 0.29, P < 0.0002) in the VA-associated HFS group than non-VA-associated HFS group, while the non-VA-associated HFS group was female-dominated (OR = 1.58, 95% CI 1.32 – 1.89, P < 0.00001). Both groups achieved good results in MVD cure rates. In VA-associated HFS, the complication rate of decompression and the rate of hearing loss after operation were higher than in non-VA-associated HFS, but the facial paralysis after operation was similar in both groups, and most complications were transient and disappeared during followup. VA-associated HFS is more prevalent in older adults, less prevalent in women, and more predominantly left-sided. More clinical studies are needed to better compare the efficacy and complication of MVD between both groups.

Keywords Meta-analysis · MVD · HFS · Microvascular decompression · Hemifacial spasm

# Introduction

Facial spasm is a common neurovascular syndrome that manifests as involuntary twitching of the muscles innervated by the facial nerve [1]. The incidence of hemifacial spasm is 4/10000, which is more common in the fifth year of life and is more prevalent in women [2, 3]. The currently accepted etiology of hemifacial spasm is the long-term neurovascular compression (NVC) at the root exit zone (REZ) of the facial

nerve, which leads to abnormal excitation of the facial nerve nucleus or abnormal transmission of nerve fiber telecommunications signals [4–6]. The most common compressions are from the anterior inferior cerebellar artery and the superior cerebellar artery. The compression from VA is less common, and vertebral arteries often indirectly compress nerves together with small branch vessels. The treatment methods include drug therapy, botulinum toxin therapy, and MVD. However, the drug therapy is currently considered less feasible, while botulinum toxin treatment is the first-line therapy. Considering the short duration and high complications of botulinum toxin treatment, microvascular decompression (MVD) is currently the only treatment to cure HFS. The effectiveness of MVD is well known for VA-associated HFS or non-VA-associated HFS. But there are some associated

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risks, and it is not always successful. Compared to non-VAassociated HFS, MVD is more difficult for VA-associated HFS and has a relatively poor clinical outcome [7, 8]. A recent study revealed that there was no significant difference between VA-associated HFS and non-VA-associated HFS [9–11]. In this study, we conducted a meta-analysis to compare the treatment outcomes for VA-associated HFS and non-VA-associated HFS. Provide some useful advice for surgeons using MVD for HFS.

# Method

We conducted a search in PubMed, Web of Science, and Embase for relevant publications. The searching time was from the inception of databases to September 2021. Potential studies were also selected by reviewing the citations. The keywords were "hemifacial spasm" and "vertebral artery." In addition, this systematic review was conducted in strict compliance with the principles of PRISMA [12], which was not registered before.

## Search strategy and selection criteria

We included studies reporting MVD for VA-associated HFS. The inclusion criteria were (I) reports of at least 20 patients; (II) patients first treated with MVD for HFS; (III) studies published in English; and (IV) studies provide the effective rate of MVD and post-operative complications of in patients with VA-associated HFS and non-VA-associated HFS. The exclusion criteria included (I) not published in English; (II) sample size  $\leq$  20 patients; (III) lack of comparison groups or lack of baseline data comparison; (IV) overlapping data sets or duplication of articles; and (V) expert opinions, comments, letters, and reviews.

## **Outcome and quality assessment**

The primary objective of this systematic review and metaanalysis were as follows: (i) to compare the success rate of MVD and complication rate in patients with VA-associated HFS and non-VA-associated HFS; (ii) to examine the preoperative clinical characteristics including age, gender, and side of HFS. The post-operative outcome was classified as "spasm-free" and "uncontrolled spasm." For review, spasmfree was defined as no HFS or good HFS > 90% resolved, while others were defined as uncontrolled spasm. The complication was defined as an early complication, including the onset of new defects and deterioration of pre-operative clinical conditions after the surgical treatment.

The quality assessment was performed using Newcastle–Ottawa Scale (NOS) [13–15]. An assessment checklist was prepared for 2 independent reviewers to determine the quality of studies, with a maximum of 9 stars per study. Studies that received  $\geq 6$  stars were considered moderate-tohigh quality. Afterward, 2 independent reviewers performed data extraction. Any disagreements were resolved by a third reviewer. Publication bias and a funnel plot analysis were performed to detect publication bias when more than 10 studies were included.

## Analysis

Data synthesis and analysis were performed using Review Manager (RevMan) version 5.3. Risk ratios (95% confidence intervals) were calculated to compare dichotomous outcomes, while standardized mean difference and the corresponding 95% confidence intervals (CI) were used to compare continuous data. When the mean and the standard deviation (SD) were not available, they were calculated based on the reported median and range [16]. The degree of heterogeneity has been reported to be low, medium, and high, with  $I^2$  values of 25%, 50%, and 75%, respectively [17]. Therefore, we used the  $I^2$  value to assess the degree of heterogeneity between studies.  $I^2 > 50\%$  suggested high heterogeneity and therefore required a random effects model for analysis, while the fixed effects model was employed when  $I^2 < 50\%$ . P < 0.05 indicates a statistically significant difference.

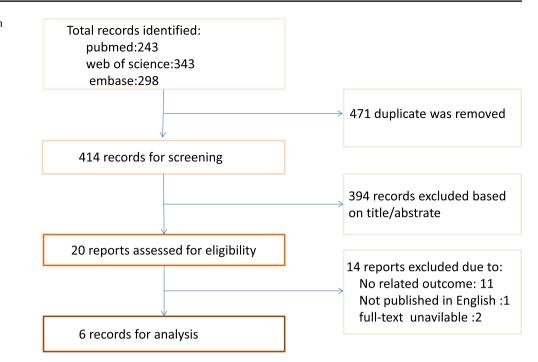
# Results

A total of 884 initial articles were retrieved from PubMed, Embase, and Web of Science. After screening and assessing according to the flow chart (Fig. 1), 6 articles [9–11, 18–20] were finally included. The quality of included studies was assessed by the NOS tool. According to the number of stars, all the studies were considered as moderate-to-high quality.

### **Clinical characteristics of patients**

Six studies provided data on gender with low heterogeneity [9–11, 18–20]. The meta-analysis showed that the women were more common in the non-VA-associated HFS group than in the VA-associated HFS group (OR = 1.58, 95% CI 1.32 – 1.89,  $P < 0.02 \ l^2 = 67\%$ ), as shown in Fig. 2. In addition, the left-side predominance was more prevalent in the VA-associated HFS group (OR = 0.23, 95% CI 0.19 – 0.29, P < 0.0002,  $l^2 = 79\%$ ), as shown in Fig. 3. Five studies reported data on the average age with low heterogeneity [9, 10, 18–20]. As shown in Fig. 4, the patients in the VA-associated HFS group were older than those in the non-VA-associated group (WMD = 3.67, 95% CI 3.29–4.05, P < 0.00001,  $l^2 = 81\%$ ).

process



	non-VA	HFS	VA-involve	d HFS		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	CI M-H, Fixed, 95% CI
Jiang 2020	519	954	95	198	37.9%	1.29 [0.95, 1.76]	ı] <b>†</b> ∎−
Lee 2021	1078	1500	150	271	37.8%	2.06 [1.58, 2.68]	j
Masuoka 2016	62	78	10	22	1.7%	4.65 [1.71, 12.68]	ı]
Mikami 2013	24	35	10	18	2.2%	1.75 [0.54, 5.64]	
Yang 2017	42	89	16	29	6.7%	0.73 [0.31, 1.69]	j <u> </u>
Zhao 2019	162	296	35	66	13.7%	1.07 [0.63, 1.83]	
Total (95% CI)		2952		604	100.0%	1.58 [1.32, 1.89]	」
Total events	1887		316				
Heterogeneity: Chi <sup>2</sup> =	15.29, df =	5 (P = 0	0.009); l <sup>2</sup> = 67	%			
Test for overall effect:	Z = 5.05 (F	<b>P</b> < 0.00	001)				0.01 0.1 1 10 100 Favours [VA-involved HFS] Favours [non-VA HFS]

**Fig. 2** The meta-analysis showing the women were more common in the non-VA-associated HFS group than in the VA-associated HFS group (OR = 1.58, 95% CI  $1.32 - 1.89, P < 0.02 I^2 = 67\%$ )

	non-VA	HFS	VA-involve	d HFS		Odds Ratio		Odds I	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C		M-H, Fixed	d, 95% Cl	
Jiang 2020	497	954	145	198	27.8%	0.40 [0.28, 0.56]				
Lee 2021	683	1500	234	271	52.1%	0.13 [0.09, 0.19]				
Masuoka 2016	39	78	18	22	3.4%	0.22 [0.07, 0.72]				
Mikami 2013	15	35	17	18	3.1%	0.04 [0.01, 0.37]	←			
Yang 2017	41	89	19	29	3.7%	0.45 [0.19, 1.08]				
Zhao 2019	153	296	52	66	9.9%	0.29 [0.15, 0.54]				
Total (95% CI)		2952		604	100.0%	0.23 [0.19, 0.29]		•		
Total events	1428		485							
Heterogeneity: Chi <sup>2</sup> =	23.93, df =	5 (P = 0	0.0002); I <sup>2</sup> = 7	79%						40
Test for overall effect:	Z = 13.40 (	(P < 0.0	0001)				0.01	0.1   1 Favours [non-VA HFS]	10 Favours [VA-involve	10 d HFS]

**Fig. 3** The left-side predominance was more prevalent in the VA-associated HFS group than in the non-VA-associated HFS group (OR = 0.23, 95% CI 0.19 – 0.29, P < 0.0002,  $I^2 = 79\%$ )

#### Post-operative recovery outcomes complication

All six studies mentioned surgical outcomes with low heterogeneity. The difference was not statistically significant in comparison of the spasm-free between two groups (OR = 1.16, 95% CI 0.81–1.67, P = 0.42,  $I^2 = 0\%$ ), as shown in Fig. 5. Overall complications and permanent complications were reported in 6 [9–11, 18–20] and 4 studies [9, 10, 18, 19], respectively. Compared with the non-VA-associated HFS group, the following outcomes are more frequent in the VA-associated HFS group: the transient complications (OR = 0.64, 95% CI 0.46–0.89, P = 0.008,  $I^2 = 28\%$ , Fig. 6) and permanent complications (OR = 0.28, 95% CI 0.15–0.54, P = 0.0001,  $I^2 = 0\%$ , Fig. 7). Although facial paralysis after

operation was not significantly different between both groups (OR = 1.25, 95% CI 0.91–1.72, P = 0.17,  $I^2 = 12\%$ , Fig. 8), hearing loss was more frequent in VA-associated HFS than non-VA-associated group (OR = 0.35, 95% CI 0.19–0.64, P = 0.0007,  $I^2 = 0\%$ , Fig. 9).

## Discussion

This systematic review and meta-analysis summarized the outcome of MVD for VA-associated HFS and non-VAassociated HFS. Consistent with the previous studies, the results of this study show that MVD is an effective treatment for HFS. Besides, VA-associated HFS are predominantly

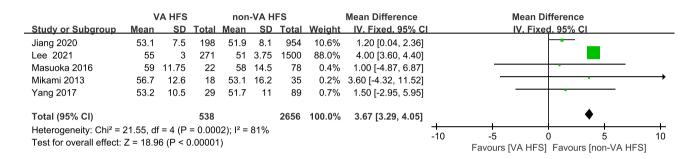
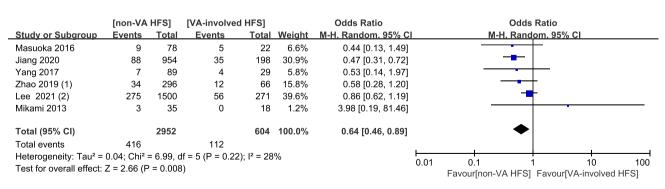


Fig. 4 The patients in the VA-associated HFS group were older than those in the non-VA-associated group (WMD=3.67, 95% CI 3.29–4.05, P < 0.00001,  $l^2 = 81\%$ )

Fig. 5 The difference was	Study or Subaroup	non-VA Events		VA-involve Events		Weight	Odds Ratio M-H, Random, 95% C	I		s Ratio dom. 95% Cl		
not statistically significant in	Lee 2021	1330	1500	241	271	76.9%	0.97 [0.65, 1.47]		-	-		
comparison of the spasm-free	Yang 2017	87	89	28	29	2.2%	1.55 [0.14, 17.79]		-	· ·		
between two groups ( $OR = 1.16$ ,	Zhao 2019	285	296	62	66	9.4%	1.67 [0.52, 5.42]			<u> </u>		
between two groups ( $OR = 1.10$ ,	Masuoka 2016	74	78	20	22	4.2%	1.85 [0.32, 10.84]					
95% CI 0.81–1.67, $P = 0.42$ ,	Mikami 2013	34	35	17	18	1.6%	2.00 [0.12, 33.97]			-		
$I^2 = 0\%$ )	Jiang 2020	950	954	195	198	5.8%	3.65 [0.81, 16.46]		-			
	Total (95% CI)		2952		604	100.0%	1.16 [0.81, 1.67]		•	♠		
	Total events	2760		563								
	Heterogeneity: Tau <sup>2</sup> = Test for overall effect:				58); l² =	0%			0.1 /A-involved HFS	1 ] Favours [no	10 m-VA HFS]	100

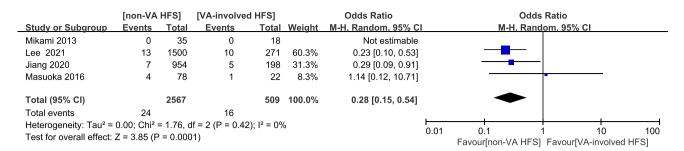


Footnotes

(1) 34 296 12 66

(2) 7 89 4 29

Fig. 6 Compared with the non-VA-associated HFS group, the transient complications are more frequent in the VA-associated HFS group (OR = 0.64, 95% CI 0.46–0.89, P=0.008,  $l^2$ =28%)



**Fig.7** Compared with the non-VA-associated HFS group, permanent complications are more frequent in the VA-associated HFS group (OR = 0.28, 95% CI  $0.15-0.54, P=0.0001, l^2=0\%$ )

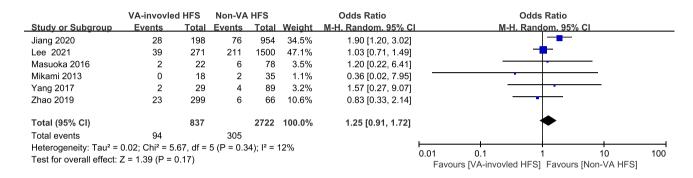


Fig. 8 Facial paralysis after operation was not significantly different between both groups (OR = 1.25, 95% CI 0.91–1.72, P = 0.17,  $I^2 = 12\%$ )

	Experim	ental	Contr	ol		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C	M-H, Random, 95% Cl
Jiang 2020	7	954	4	198	23.6%	0.36 [0.10, 1.24]	
Lee 2021	13	1500	10	271	51.9%	0.23 [0.10, 0.53]	
Masuoka 2016	1	78	0	22	3.5%	0.87 [0.03, 22.12]	
Mikami 2013	0	35	0	18		Not estimable	
Yang 2017	2	89	1	29	6.1%	0.64 [0.06, 7.37]	
Zhao 2019	9	296	2	66	14.9%	1.00 [0.21, 4.76]	
Total (95% CI)		2952		604	100.0%	0.35 [0.19, 0.64]	◆
Total events	32		17				
Heterogeneity: Tau <sup>2</sup> =	0.00; Chi <sup>2</sup>	= 3.38, d	df = 4 (P =	= 0.50);	l² = 0%		
Test for overall effect:	Z = 3.39 (F	P = 0.000	07)				0.01 0.1 1 10 100 Favours [non-VA HFS] VA-associated HFS]

Fig. 9 Hearing loss was more frequent in VA-associated HFS than non-VA-associated group (OR = 0.35, 95% CI 0.19–0.64, P = 0.0007,  $l^2 = 0\%$ )

left-sided with older patient age, while women are more prevalent in non-VA-associated HFS patients. However, MVD for VA-associated HFS may pose a higher surgical risk for post-operative complications, including transient complications and permanent complications.

#### Age

In previous studies, patients with HFS were more common in their fifth decade of life. The age of VA-associated HFS patients was similar to that of non-VA-associated HFS patients [9, 10]. However, patients with VA-associated HFS are older than those with non-VA-associated HFS in this analysis. The number of samples may be an important influencing factor. In addition, the incidence characteristics of populations in different regions may be a potential influencing factor. In this meta-analysis, the patient age in the VA-associated HFS group is significantly higher than the non-VA-associated HFS group in the Asian population. At the same time, there is no significant difference in age in the European and American populations. This phenomenon also may be associated with the mechanisms of HFS. Neurovascular compression is a relatively well-recognized etiology. After long-term compression of blood vessels, abnormal nerve conduction or high excitability of the facial nerve nucleus leads to involuntary twitching of facial muscles. Similarly, hypertension is a risk factor for HFS [21]. As age increases, the incidence of hypertension is higher, and blood vessels become less elastic due to atherosclerosis. Also, the vessel wall of the VA is thicker than that of the branch vessels. The VA is more tolerant to atherosclerosis and hypertension, which may be associated with higher age of onset in the VA-associated HFS group.

#### Left-sided predominance

As shown in Fig. 3, the left-sided HFS was more common in the VA-associated HFS group (RR = 0.60, 95% CI 0.57 – 0.64, P < 0.00001). This phenomenon was also reported in other studies, and the following reasons were proposed [22]. Left-sided VA originates directly from the aortic arch and is larger than right-sided [23, 24]. In addition, the hemodynamics of the left-sided VA is larger than that of the right-sided VA [25].

#### Female predominance

There are more female patients in the non-VA-associated HFS group, while the number of male and female patients is almost the same in the VA-associated HFS group. It is well known that neurovascular syndrome tends to develop more severely with insomnia, tired, and bad mood. Studies showed that women experience more sleep problems during sex hormones fluctuation, such as puberty and menopause [26]. Most patients also develop HFS around 50, which coincides with menopause. Therefore, fluctuations in female hormones can cause sleep or mood disorders and increase the incidence of HFS. However, the VA diameter is smaller in middle-aged women than in men, and the wide tortuous VA is a high-risk factor for VA-associated HFS [25, 27]. Considering the fluctuation of female hormones and the VA diameter, female patients are more common in the non-VAassociated HFS group. In the VA-associated HFS group, the number of men and women is similar. In order to clarify the relationship between gender and HFS, more prospective randomized studies should be conducted in the future.

#### The outcome of MVD and complication

Although MVD is effective in treating HFS, surgery is still difficult to provide adequate decompression of nerves and vessels, especially for VA-associated HFS. The key procedure of MVD is to accurately identify the relationship between the responsible vessels and the facial nerve and fully separate them. In most cases, the VA compresses the nerve indirectly combined with small branches [28]. In addition, the branches may supply the brainstem, blocking the surgical view and making separation more difficult. However, this meta-analysis showed no significant

difference in the success rate of MVD between the VAassociated HFS group and the non-VA-associated HFS group. This similar success rate maybe attributed to the surgical improvements, especially for VA-associated HFS. Although three of six included studies did not described the difference of surgical procedures in detail, the rest mentioned that the surgical techniques for VA-associated HFS were different and some special techniques were applied, for example, enlarged, building a bridge for VA, and sling retraction technique [10, 19, 29]. Some reports had reported that the new techniques had improved the outcome and complications, while a study has reported that the new techniques did not affect the outcome of MVD and complication [30-32]. This result may also benefit from many extraordinary technical, such as adequate preoperative imaging evaluation, neuroendoscopy, and preoperative electrophysiological monitoring [33, 34]. For example, neuroendoscopy significantly increases the surgical view, allowing surgeons to more directly observe the relationship between responsible vessels and peripheral nerves without extended craniotomy [35-37]. Furthermore, intraoperative electrophysiological monitoring can help the surgeon determine the responsible vessel and decide when to end the operation. Electrophysiological monitoring also contributes to understanding the nature of HFS [38–40]. Some new surgical techniques have also increased the success rate of surgery, such as the biomedical glue sling technique, the "bird-lime" technique, the wedge technique, and the cornerstone technique [30, 32], 41–43]. Unlike the previous results, transient post-operative complications remain higher in the VA-associated HFS group than the non-VA-associated HFS group in our meta-analysis [19, 20]. The following reasons can be considered: in most previous single-center studies, the number of cases was relatively small, the definitions of complications were different, and the specific surgical protocols and techniques in each study were different. Considering the vast majority of transient complications resolve completely within 1 year after surgery and the incidence of permanent complications is very low, MVD may still be an effective surgical method for VA-associated HFS. It is worth lighting that hearing loss is more frequent in VAassociated HFS than non-VA-associated HFS and has a statistical difference. The risk of surgery is still very high, especially for VA-associated HFS. The surgical procedures for VA-associated HFS should be pruned according to different conditions. Indeed, some studies have reported that new surgical techniques increased the success rate of surgery and reduced the complication of operation. The surgeon should also keep in mind that slight abnormal operations may turn transient complications into permanent complications, and decompression surgery for VAassociated HFS should be more cautious. It is a pity that

Zhao (2019) Retrospective J		Group	Patients number Gender (M/F) Age (years)	Gender (M/F)	Age (years)	HFS on left side	Cure sample Overall complic number	Overall complication number	Permanent complication number	Follow-up
Petrocnective	Retrospective January 2013 to January 2014	Not VA VA	296 66	134/162 31/35	AN AN	153 52	285 62	34 12	NA NA	36 months on average
ven ospeciive	February 2010 to February 2015	Not VA VA	29 29	47/42 13/16	$51.7 \pm 11.0$ $53.2 \pm 10.5$	41 19	87 28	4	NA NA	More than 1 year
Mikami (2013) Retrospective January 2003 to January 2011	January 2003 to January 2011	Not VA VA	35 18	11/24 8/10	$53.1 \pm 16.2$ $56.7 \pm 12.6$	15 17	34 17	ю Э	0	More than 1 year
Masuoka (2016) Retrospective April 2008 to April 2015	April 2008 to April 2015	Not VA VA	78 22	16/62 12/10	$58 \pm 14.5$ (21-79) $59 \pm 11.75$ (78-75)	39 18	74 20	9 5	4 1	More than 1 year
Lee (2021) Retrospective	Retrospective January 2008 to March 2015	Not VA VA	1500 271	422/1078 121/150	$51 \pm 3.75$ (43-58) $55 \pm 3 (48-60)$	683 234	1330 241	285 62	13 10	22.8 months (7.8–42.0)
Jiang (2020) Retrospective January 2014 to Decembe 2017	January 2014 to December 2017	Not VA VA	954 198	435/519 103/95	$51.9 \pm 8.1$ (21-75) $53.1 \pm 7.5$ (30-72)	497 145	950 195	88 55	5 7	mean 42.6 months(16 to 65 months)

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all the primary studies in this meta-analysis did not calculate the adjusted odds ratio to exclude the confounders. Therefore, a large of clinical studies are needed future.

# Conclusion

Non-VA-associated HFS occurs predominantly in women, while there is no difference in the number of male and female patients with VA-associated HFS. In addition, VAassociated HFS occurs primarily in the elderly and on the left side of VA. The results show that MVD is an effective treatment for HFS caused by small vascular compression and VA-associated HFS. Considering the high rate of complications in VA-associated HFS, MVD is more difficult and carries a higher risk. Surgeons should be more careful to achieve excellent surgical outcomes. In the future, more clinical studies are needed to better compare the efficacy and complication of MVD between VA-associated HFS and non-VA-associated HFS. Moreover, more clinical researches of MVD for hemifacial spasms should be analyzed by stratification future.

# Limitation

This meta-analysis has several limitations. First, the number of included studies was limited, and some outcomes of interest were not reported in each study. Second, there was a high degree of heterogeneity in the results of some studies between the two groups. Third, the surgical procedures for both groups are not unified. Fourth, we cannot perform an analysis of confounders because the primary studies all did not mention the adjusted odds ratio. Those heterogeneities were associated with the variability in defining or measurement standards. Despite these limitations, the present meta-analysis results provided a more comprehensive understanding of MVD for treating VA-associated HFS. MVD for VA-associated HFS and non-VA-associated HFS is a successful strategy, and the risk of complications is higher in the VA-associated HFS group (Table 1).

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Author contribution Shu Jiang and Jianguo Li conceptualized the study. Senlin Yin and Peizhi Zhou co-developed a designation. Jianguo Li, Liang Lyu, and Cheng Chen extracted the data; Senlin Yin checked the data. Jianguo Li analyzed the data and drafted the manuscript. All the authors interpreted the results and revised the manuscript.

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**Data availability** The original data used in the study are all included in the article; further inquiries can be directed to the corresponding author.

Code availability Not applicable.

#### Declarations

Ethics approval Not applicable.

Consent for publication Not applicable.

**Informed consent** Informed consents were required from all participants.

Competing interests The authors declare no competing interests.

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